Sustainable synthesis of 5-hydroxymethylfurfural and levulinic acid

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Abstract

The conversion of biomass to chemicals on an industrial scale at a competitive cost requires the development of biorefineries analogous to petrochemical refineries. In a biorefinery, different biomass feedstocks are converted into platform chemicals which can, in turn, yield a large number of end-products. Hydroxymethylfurfural (HMF) and levulinic acid (LA) are two promising platform chemicals. They can be produced from carbohydrate or lignocellulosic feedstock via acid hydrolysis. Despite the potential importance of HMF and LA and extensive research on them at the laboratory level, few commercial production plants have been reported. For instance, only Switzerland-based AVA Biochem produces bio-based HMF at an industrial scale, synthesising 20 tons/year from fructose. This work aims to accelerate the deployment of HMF and LA as platform chemicals in a sustainable manner by optimising feedstock consumption and the use of catalysts, solvents and heating media.

The significant research interest that HMF and LA have elicited has resulted in a wide range of feedstocks, catalysts, solvents and heating mechanisms being investigated. These prior studies were examined in a comprehensive literature review (Chapter 2) to identify the strengths and shortcomings of existing reaction systems. Through this review, it was observed that the use of polysaccharides like starch and cellulose is preferable to commonly used substrates like glucose and fructose from both economic and environmental standpoints. However, the efficient use of these feedstocks requires an understanding of how the composition and the structure of the polysaccharides affect the product yields. The link between starch composition and LA yields was therefore studied in Chapter 3. Corn starch was fractionated into its constituents, amylose and amylopectin. These fractions, as well as the unfractionated starch, were converted to LA using aqueous HCl as the catalyst. It was demonstrated that amylopectin was converted more readily to LA due to its greater water solubility, and due to the formation of a resistant complex inhibiting amylose hydrolysis. This implied that starches containing a higher proportion of amylopectin would possibly be more suitable for LA synthesis than others.

This was confirmed by comparing the LA yields from starches with different amylose to amylopectin ratios (Chapter 4). A multi-reaction model was created using MATLAB to calculate the kinetic parameters of hydrolysis. The results obtained corroborated the earlier findings, with conversion of waxy (high amylopectin) corn starch to LA proving to be more facile than normal or high amylose corn starch. Alongside, the effect of the heating media was also studied. Microwave heating was found to give yields similar to those obtained using an oil bath, but at a lower equivalent temperature and a shorter reaction time.

After addressing starch composition, the next area of research focussed on was the development of a catalytic system that was environment-friendly, inexpensive and recyclable, while providing high HMF yields. Previous studies showed that the conversion of polyglucan feedstocks to HMF could be achieved at a high conversion and selectivity in the presence of metal salt Lewis acids and ionic liquids. The combination of boric acid and choline chloride is a cheaper, non-toxic and a more environment friendly alternative to the metal salt-ionic liquid systems, and hence its applicability as a catalyst for HMF synthesis from starch was investigated (Chapter 5). The effect of using a biphasic medium of either water-methyl isobutyl ketone (MIBK) or water-tetrahydrofuran (THF) as the solvent was also evaluated simultaneously. A Central Composite Design (CCD) based Response Surface Methodology was used to optimise the reaction parameters. A maximum yield of 35.9 mol% was obtained for water-MIBK, while for the water-THF system, the highest yield was 60.3 mol%. The advantage of using water-MIBK was the minimal decrease in HMF yields observed after ten rounds of catalyst reuse, indicating greater system recyclability.

Alongside starch, cellulose is an ideal feedstock for biorefineries owing to its wide availability. Therefore, the use of lignocellulosic biomass for HMF synthesis merits consideration. Ferric sulphate has been used to depolymerise cellulose in previous works, and being an inexpensive Lewis acid, was identified as a potential catalyst for converting hardwood and softwood pulp to HMF and furfural (Chapter 6). It was found that the use of ferric sulphate alone gave a yield of 31.6 mol% from hardwood pulp, and that the yield was not increased by the addition of the Brønsted acid HCl or the ionic liquid [BMIM]Cl. For softwood pulp, a combination of ferric sulphate and dilute HCl gave the maximum HMF yield (37.9 mol%).

In conclusion, this work has provided an insight into the roles played by four important factors: feedstocks, catalysts, solvents and heating media - on the synthesis of HMF and LA. It is clear that the wide diversity of options for each of these factors presents both challenges and opportunities in commercialising these promising chemicals. The work presented here, therefore, provides a foundation for further research in this field.

Résumé

La conversion de la biomasse en produits chimiques à l'échelle industrielle à coût compétitif exige le développement de bio-raffineries analogues aux raffineries pétrochimiques. Dans une bio-raffinerie, les productions agricoles végétales et la biomasse sont transformées en produits chimiques de valeur ajoutés qui peuvent à leur tour être utilisés afin produire un grand nombre de produits finis. L'hydroxyméthylfurfural et l'acide lévulinique sont deux produits chimiques prometteurs. Ils peuvent être synthétisés à partir de glucides ou de matières lignocellulosiques par hydrolyse acide. Malgré le potentiel de l'hydroxyméthylfurfural et de l'acide lévulinique, seulement une usine produit ces produits chimiques. AVA Biochem, basé en Suisse, produit du HMF à une capacité de 20 tonnes par année. La biomasse utilisée est le fructose. Ce travail vise à accélérer le déploiement de HMF et de LA en tant que produits chimiques de manière durable en optimisant la consommation de matières premières et l'utilisation de catalyseurs, de solvants et de modes de chauffage.

De nombreuses études portant sur l'hydroxyméthylfural et l'acide lévulinique furent effectuées. De ces recherches, plusieurs types de biomasses, catalyseurs, solvants ainsi que différents mode de chauffage ont été étudiés afin d'augmenter le rendement de ces produits chimiques. Ces études préalables furent l'objet d'une revue de la littérature (chapitre 2) afin d'identifier les forces et les lacunes des systèmes de réaction. De par cette revue de la littérature, il a été constaté que d'un point de vue environnemental et économique, l'utilisation de polysaccharides tels l'amidon et la cellulose est généralement préférable à d'autres substrats tels le glucose et le fructose. Toutefois, il est important de comprendre les rôles de la structure de la composition des polysaccharides sur le rendement des produits chimiques. Ainsi, le lien entre la composition de l'amidon et le rendement en acide lévulinique a été étudié au chapitre 3. Lors de cette étude, l'amidon de maïs a été fractionné en ses constituants, l'amylose et l'amylopectine. Ces fractions ainsi que l'amidon non fractionné ont été converti en acide lévulinique en utilisant de l'acide chlorhydrique en solution aqueuse comme catalyseur. Il a été démontré que l'amylopectine est transformée plus facilement en raison de sa plus grande solubilité dans l'eau. De plus, l'amylose forme un complexe résistant inhibant l'hydrolyse. Ceci implique que la fécule contenant une proportion plus élevée en amylopectine serait peut-être plus appropriée pour la synthèse de l'acide lévulinique.

Ceci fut confirmé en comparant les rendements en acide lévulinique en utilisant de l'amidon de maïs ayant différentes proportions en amylose et amylopectine (chapitre 4). Un modèle de réactions multiples a été créé à l'aide de MATLAB afin de calculer les paramètres cinétiques de l'hydrolyse. Les résultats obtenus ont corroborés les conclusions antérieures puisque la conversion de l'amidon de maïs cireux (forte concentration en amylopectine) en acide lévulinique s'est avérée plus facile qu'avec la fécule de maïs ayant une concentration en amylose normale ou élevée. Parallèlement, l'effet des méthodes de chauffage a également été étudié. Les rendements obtenus par chauffage micro-ondes furent similaires à ceux obtenus à l'aide d'un bain d'huile, mais à une température équivalente inférieure et un temps de réaction plus court.

Après cette étude, l'objectif de la recherche a porté sur la sélection d'un système catalytique favorable à l'environnement, peu coûteux et recyclable. Le système devait aussi offrir des rendements élevés en hydroxyméthylfurfural. Des études antérieures ont montré que la conversion de matières premières polyglucane en hydroxyméthylfurfural pouvait être atteinte à un taux de conversion élevé en présence de sels métalliques d'acides de Lewis et de liquides ioniques. L'acide borique et le chlorure de choline sont peu coûteux, et non toxique. De plus, ils sont moins dommageables pour l'environnement que les systèmes composés de liquides ioniques et de sel métalliques. C'est pourquoi le chapitre 5 porte sur l'utilisation de l'acide borique et du chlorure de choline comme système catalytique pour la synthèse d'hydroxyméthulfurfural. L'effet de l'utilisation d'un milieu biphasique (eau-MIBK ou eau-THF) comme solvant a également été évalué. Un plan composite centré a été utilisé comme plan de surface de réponse afin d'optimiser les paramètres de la réaction. Le rendement maximal obtenu fut de 35,9 % (mole) avec le système eau-MIBK, tandis que pour le système eau-THF, le rendement le plus élevé fut de 60,3 % (mole). Le système eau-MIBK a l'avantage de pouvoir être recyclé plusieurs fois. Il fut observé que le rendement ne diminuait pas de façon significative même après dix séries de réutilisation.

En plus de l'amidon, la cellulose est une excellente matière de base pour les bio-raffineries puisqu'elle est disponible en grande quantité. Par conséquent, l'utilisation de la biomasse lignocellulosique pour la synthèse de l'hydroxyméthylfurfural fut l'objet du chapitre 6. Des travaux antérieurs ont démontrés l'efficacité du sulfate ferrique afin de dépolymériser la cellulose. Étant un acide de Lewis peu coûteux, le sulfate ferrique a été identifié comme un catalyseur potentiel pour la conversion de pâte à papier provenant de feuillus et de résineux en hydroxyméhylfurfural et en furfural (chapitre 6). L'utilisation de sulfate ferrique seul a donné un rendement de 31,6 % (mole) pour le bois dur. Il a été constaté que le rendement n'a pas augmenté par l'ajout d'acide chlorhydrique ou de liquide ionique [BMIM]Cl. Un rendement maximal de 37,9 % (mole) a été obtenu pour la pâte de résineux lorsqu'un mélange de sulfate ferrique et d'acide chlorhydrique dilué fut utilisé.

En conclusion, cette thèse a donné un aperçu du rôle joué par quatre facteurs importants: les matières premières, les catalyseurs, les solvants ainsi que le mode de chauffage utilisé lors de la synthèse de l'hydroxyméthylfurfural et de l'acide lévulinique. Il est vrai que la grande diversité d'options pour chacun de ces facteurs présente à la fois des défis et des opportunités liés à la commercialisation de ces produits chimiques. Le travail présenté fournit une base afin de poursuivre des recherches dans ce domaine.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

Abbreviation	Details
[BMIM]Cl	1-Butyl-3-methylimidazolium chloride
2,5-DMF	Dimethylfuran
AMF	5-acetoxymethyl furfural
BA	Boric acid
BMF	5-bromomethyfurfural
CCD	Central Composite Design
ChCl	Choline chloride
CMF	5-chloromethyl furfural
DALA	δ-aminolevulinic acid
DCM	Dichloromethane
DFF	2,5-diformylfuran
DHMF	2,5-di(hydroxymethyl)furan
DHM-THF	2,5-di(hydroxymethyl)tetrahydrofuran
DM	Deutsche Mark
DMA	Dimethylacetamide
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
DSC	Differential Scanning Calorimetry
DTG	Differential thermogram
EMF	5-ethoxymethyl-2-furfural
FDC	2,5-furandicarboxyaldehyde
FDCA	2,5-furandicarboxylic acid
GC-MS	Gas Chromatography-Mass Spectrometry
GHL	γ-hexa-lactone
GVL	γ-valerolactone
HMF	Hydroxymethylfurfural
HPA	Heteropolyacid
HPLC	High Performance Liquid Chromatography
LA	Levulinic acid
MIBK	Methyl isobutyl ketone
MTHF	Methyltetrahydrofuran
NIST	National Institute of Standards and Technology
NMP	N-methylpyrrolidone
NMR	Nuclear Magnetic Resonance
PEG	Polyethylene glycol
PTSA	p-Toluenesulfonic acid
PVP	Poly(vinylpyrrolidone)
R&D	Research and development
RID	Refractive index detector
RSM	Response surface methodology
SAPO	Silicoaluminophosphate

SEM	Scanning Electron Microscope
TEAC	Tetraethylammonium chloride
TFA	Trifluoroacetic Acid
TGA	Thermogravimetric analysis
THF	Tetrahydrofuran
TsOH	Tosylic acid
VWD	Variable Wavelength Detector
XRD	X-Ray Diffraction
ZSM-5	Zeolite Socony Mobil–5

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Contribution of Authors

This thesis is submitted in the form of original papers published, accepted or to be submitted for publication to international and peer-reviewed scientific journals. The candidate, Agneev Mukherjee, was responsible for designing and conducting the experiments, handling the data analysis, as well as the preparation of the manuscript and the thesis. Dr Marie-Josée Dumont, supervisor of the candidate and Assistant Professor in the Department of Bioresource Engineering of McGill University, contributed to all aspects of this research work. She provided assistance, including planning and directing the research, editing and reviewing the thesis and the manuscript before submission for publication. Dr Vijaya Raghavan provided partial supervisory suggestions for the first paper and co-edited the manuscript. Guillermo Portillo Perez, a doctoral student under Dr Dumont, conducted a portion of the microwave experiments and was listed as a co-author on the fifth paper. The details of the papers that have been published, accepted for publication or submitted for publication are provided below:

1. Mukherjee, A., Dumont, M. J., & Raghavan, V. (2015), Review: Sustainable production of hydroxymethylfurfural and levulinic acid: Challenges and opportunities, *Biomass and Bioenergy*, **72**, 143-183.
2. Mukherjee, A., & Dumont, M. J. (2016), Influence of the starch structure in the synthesis and the yield of levulinic acid, *Starch/Stärke*, **68**, 943-952.
3. Mukherjee, A., & Dumont, M. J. (2016), Levulinic Acid Production from Starch Using Microwave and Oil Bath Heating: A Kinetic Modeling Approach, *Ind. Eng. Chem. Res.*, **55**, 8941-8949.
4. Mukherjee, A., & Dumont, M. J. (2017), Production of 5-hydroxymethylfurfural from starch through an environmentally-friendly synthesis pathway, to be submitted.
5. Mukherjee, A., Guillermo Portillo Perez & Dumont, M. J. (2017), Synthesis of Hydroxymethylfurfural from Hardwood and Softwood Pulp using Ferric Sulphate as Catalyst, to be submitted.

Chapter 1 : Introduction

1.1 General Introduction

Biomass has played a vital role throughout human civilisation, starting with the use of wood to make fire in the Palaeolithic era. Even today, biomass energy accounts for around 10% of the global energy supply, confirming its continued relevance as an energy source [1]. Alongside being an energy source, biomass has also been used to obtain chemicals since antiquity. Ethanol, acetic acid, lactic acid, methane, methanol, and terpenes are among the chemicals that have historically been synthesised from biomass [2]. Post-World War I, however, petrochemical sources displaced biomass as the primary source of chemicals, a situation that broadly persists till today. The 1980s saw a revival of interest in the concept of producing chemicals from biomass. Advocates realised that to be competitive from the standpoint of process economics, biomass needs to be processed in a manner and at a scale similar to petrochemical refineries [2]. This analogy with petroleum refineries led to the term ‘biorefining’ being coined in 1981 [3-5].

Despite this, research interest in biorefineries remained muted for decades, with only around 35 papers on the topic being published prior to 2000 [4]. Fears about fossil fuel depletion, and the attendant rise in petroleum prices, however, have led to a renewed research focus from the turn of the century [4]. Increasing concern about fossil fuel-induced climate change has only accelerated R&D on this subject. This can be gauged by the exponential increase in the number of publications on biorefineries and important biomass-derived chemicals like hydroxymethylfurfural (HMF) and levulinic acid (LA) in recent years (Figure 1-1).

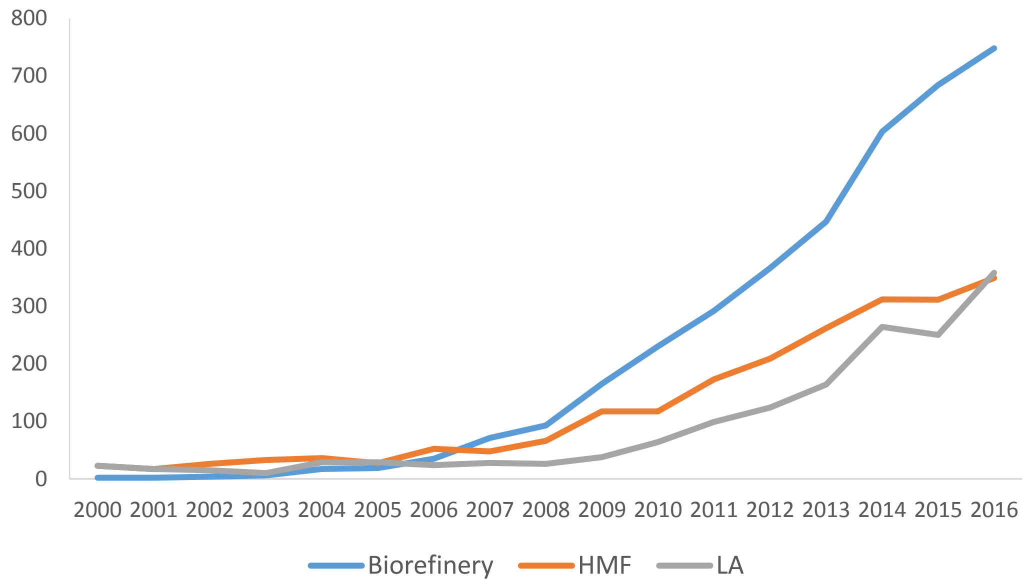


Figure 1-1: Number of publications on biorefineries, HMF and LA per year, as registered by Web of Science™

As stated, biorefineries have been proposed to be modelled after petrochemical refineries. The principle of operation of petrochemical refineries is the initial conversion of an array of feedstock into a small number of platform chemicals such as toluene, benzene, propylene, xylenes, butadiene, ethene and methanol [6, 7]. These chemicals are compounds with simple molecular structures and low molecular weights that can be reacted with each other to form a plethora of organic products. Biorefineries are expected to follow a similar scheme of operations. This raises the question as to whether it would be more appropriate for biorefineries to produce the same platform chemicals as petroleum refineries (direct substitution approach), or to develop new chemical intermediates as replacements (indirect substitution approach).

The direct substitution approach, also called the ‘drop-in’ strategy, has the advantage of being able to fit into the mature market, and therefore not requiring massive investments for developing new infrastructure. The primary drawback of this route is the fact that biomass, due to its high oxygen content, has a low H/C ratio, leading to an unfavourable stoichiometry for reactions converting biomass to petrochemicals such as olefins [7, 8]. This makes it difficult for a biomass-derived molecule to compete economically with the established, chemically identical petrochemical version.

The indirect substitution method, on the other hand, can permit the synthesis of chemicals with properties superior to petrochemical intermediates due to the functionality inherent in the parent biomass feedstock being utilisable to a much greater extent [7]. One example is the fact that biomass-derived starting materials may be optically active, unlike their petrochemical counterparts. This, combined with other properties such as hydrogen bonding and controlled crystallinity, enables the production of sophisticated materials with finetuned strength, elasticity, etc. [8].

It is clear that in the long run, the indirect substitution method, featuring novel intermediates, offers greater potential for optimally converting biomass to chemicals. For a chemical to be designated as a platform chemical, it must satisfy a number of criteria. One of these is the ease of its synthesis from diverse biomass feedstock. Another criterion would be the flexibility and breadth of options, in terms of derivative chemicals, that it provides to the biorefinery.

Two biobased chemicals that rank highly in terms of potential biorefinery applications are HMF and LA [2, 4, 9]. This is reflected in the research interest in them rising synchronously with that in biorefineries as a whole (Figure 1-1). Despite the extensive laboratory-scale research performed on HMF and LA, industrial-scale production of these chemicals remains limited. For example, in 2014 Ava Biochem inaugurated a 20 t/y commercial HMF production facility, billed as the 'world's first industrial plant for the production of renewable HMF' [10]. This is several orders of magnitude smaller than the 30,000-1,200,000 t/y plant sizes that have been postulated as being required to achieve the exponential drop in prices needed for HMF to make a significant dent in the bioplastics market [11]. Similarly, for LA, few commerical-scale units exist, with a newly inaugurated 10,000 t/y plant in Italy by GFBiochemicals, the largest facility at present [12].

The mismatch between the research interest and the commercial-scale production of HMF and LA is largely due to economic considerations. The synthesis of these chemicals is accomplished most readily via the use of monosaccharide feedstock, particularly fructose. However, monosaccharides are expensive, as they have to be produced from polysaccharides. This limits their suitability for commercial applications. Polysaccharides such as cellulose or starch would accordingly be more sustainable choices. However, since the process of converting polysaccharides to HMF and LA involves the in-situ production of monosaccharides as an intermediate step, the product yields obtained are generally considerably lower than those obtained from monosaccharides, particularly fructose. An understanding of the depolymerisation reaction is therefore necessary to increase the reaction yields. Starch, for instance, is a mixture of two polysaccharides, viz. amylose and amylopectin. Their proportion in different natural starches varies widely, as can be seen in Table 1-1. Additionally, numerous modified starches have been manufactured industrially with customised compositions.

Table 1-1: Composition of starches from different sources

Source	Amylose	Amylopectin	Reference
Acorn	19.5-34	66-80.5	[13]
Corn	26	74	[14]
Wheat	25	75	[14]
Rice	17	83	[14]
Potato	21	79	[14]
Sweet potato	13.8-19.5	80.5-86.2	[15]
Tapioca	17	83	[14]
Kudzu	22.5	77.5	[16]
Tapioca	20.5	79.5	[17]
Cassava	21.5	78.5	[17]
Green gram	38	62	[18]
Bengal gram	37	63	[18]
Pea	33.1-48.8	51.2-66.9	[19]

These two components differ in their molecular structure, and consequently in their physical and chemical properties. As the proportion of the components differs based on the origin of the starch, and can also be altered synthetically, it is important to find out exactly how the amylose:amylopectin ratio affects the yields of the dehydration products such as HMF and LA. This would enable selection, or development, of feedstocks which are optimal for high product yields.

Since the conversion of polysaccharides to HMF and LA involves acid hydrolysis, numerous acidic catalysts have been tested for this purpose. These include mineral acids like HCl and H_2SO_4 [20, 21]; metal halides and oxides such as $CrCl_3$ and TiO_2 [22, 23]; resins and zeolites [24, 25], etc. These catalysts have to be evaluated against parameters like cost, yields, corrosiveness, recyclability, toxicity, etc. It is probable that no catalyst will prove to be ideal for every criterion. Therefore, for environment-friendly production, it would be worthwhile to focus on catalysts that are inexpensive, non-toxic and environment friendly, while also providing reasonable yields.

Similar criteria can also be applied for selecting the appropriate solvent and heating media. This can include the use of a combination of inorganic and organic solvents like water and methyl isobutyl ketone (MIBK) or water and tetrahydrofuran (THF). Such biphasic media have been shown to improve HMF yields by extracting the HMF formed during hydrolysis into the organic phase and preventing its rehydration to byproducts [26, 27]. Likewise, the use of microwave heating has been labelled as being a ‘green’ alternative to conventional modes of heating, as it is held to allow high yields to be achieved in a short time period, reducing energy consumption [28, 29].

1.2 Hypotheses

The principal hypotheses that have been examined in this work are:

1. There is a correlation between the amylose:amylopectin ratio of a starch and the yields of LA obtained from that starch.
2. Microwave heating provides higher substrate conversion and HMF and LA yields than conventional heating for the same reaction temperature and reaction time.
3. Boric acid and choline chloride can be used as inexpensive and eco-friendly substitutes for metal salt Lewis acid- ionic liquid catalytic systems for HMF synthesis from polysaccharides.
4. Impregnation of wood pulp with ferric sulphate can lead to depolymerisation of holocellulose and catalysis of HMF synthesis.

1.3 Study Objectives

The objective of this work was to develop environment-friendly reaction systems that use inexpensive catalysts for producing HMF and LA from polysaccharide feedstock. Keeping this and the above hypotheses in mind, the specific study objectives were:

1. To review the state of the art in HMF and LA production systems in terms of feedstock, catalysts, solvents and heating media, and thereby decide on the research avenues meriting further investigation (Chapter 1)
2. To examine the influence of the starch structure on LA synthesis by fractionating starch into amylose and amylopectin, and analysing the result of acid hydrolysis of these fractions, along with unfractionated starch, into LA (Chapter 2)

3. To develop a kinetic model for LA synthesis from starch based on acid hydrolysis of three different starches using both oil bath and microwave heating, and thereby decide on optimal reaction parameters in terms of both feedstock composition and heating media (Chapter 3)
4. To develop a reaction system for HMF synthesis from starch using boric acid and choline chloride as co-catalysts, by evaluating the product yields and catalyst recyclability in both water-MIBK and water-THF solvent media (Chapter 4)
5. To synthesise HMF and furfural from hardwood and softwood pulp by impregnating them with ferric sulphate, and to examine the effect on wood depolymerisation by using the ionic liquid [BMIM]Cl and the mineral acid HCl as co-catalysts alongside ferric sulphate (Chapter 5)

Chapter 2 : Literature Review : Sustainable Production of Hydroxymethylfurfural and Levulinic Acid

2.1 Abstract

Hydroxymethylfurfural (HMF) and levulinic acid (LA) are two of the most promising chemicals derived from biomass owing to their convertibility into a large number of chemicals having applications in diverse industries. Their transition from niche products to mass-produced chemicals, however, requires their production from sustainable biomass feedstocks at low costs using environment-friendly techniques. In this review, the numerous reaction systems that have been developed to produce HMF and LA from various substrates have been looked at and their merits, demerits and requirements for commercialisation outlined. Special attention has been paid to microwave irradiation-heated systems due to their dual advantages of high product yields and low environmental footprint.

2.2 Introduction

The rapid depletion of fossil fuels has led to an increased international effort to augment the use of renewable energy. However, alongside being the predominant source of energy, fossil fuels are also the leading source of organic chemicals which are the backbone of modern life. The replacement for fossil fuels in this area can come from biomass, with biorefineries being presented as the future substitutes for the present-day petroleum refineries. In the same way that petroleum refineries use certain chemicals as the building blocks for more complex molecules such as polymers, a biorefinery will use simple molecules that can be readily obtained from a variety of feedstock as a base for the synthesis of biopolymers and other large molecules [6, 30]. Among the most promising building blocks are hydroxymethylfurfural (HMF) and levulinic acid (LA), which are the subject of this literature review.

HMF has been referred to as a ‘sleeping giant’ owing to the vast potential of this compound in the emerging bio-based economy due to the key position it holds in the production of biomass-derived intermediates [31]. It is said to be one of the few petroleum-derived chemicals that can also be readily synthesised from renewable resources, and is held to be a bridge between carbohydrate chemistry and industrial mineral oil-based organic chemistry [32]. While a vast number of chemicals can be produced from HMF, some of the most important ones are listed in Table 2-1 [33-38], along with their potential uses. Among the chemicals not listed in Table 2-1 is LA, the attributes of which are also of importance for discussion in this paper.

Table 2-1: Chemicals produced from HMF and their applications [33-38]

Chemicals	**Potential Markets/Applications**
Formic acid	- Commodity chemical - Textiles - Road salt - Catalysts - Fuel cells
Ethoxymethylfurfural	- Biofuels
5-hydroxymethylfuroic acid	-Polymers
2,5-furandicarboxylic acid (FDCA)	- Polymers - Pharmaceuticals
2,5-di(hydroxymethyl)furan (DHMF)	-Solvents -Polymers
Furfuryl alcohol	- Resins - Solvents
Dimethylfuran (2,5-DMF)	- Biofuels
2-methylfuran	- Biofuels
2,5-diformylfuran (DFF)	- Pharmaceuticals - Fungicides
2,5-di(hydroxymethyl) tetrahydrofuran (DHM-THF)	-Solvents
2,5-furandicarboxyaldehyde (FDC)	- Polymers - Resins

In addition to being an intermediate in the production of chemicals mentioned in Table 2-1, HMF also has some potential uses on its own, such as in fuel cells [39], the treatment of sickle cell disease [40], etc. Ultimately, however, the major potential of HMF is as a key platform chemical, and this depends on its availability and cost [41]. In 1993, it was estimated that the cost of producing HMF would be between Deutsche Mark (DM) 5000-10000 per ton based on a fructose price of DM 2000 per ton or inulin price of DM 1000 per ton [42], which at 2002 prices would be comparable to 2500-5000 €/ton [43]. These prices are fairly similar to those obtained for the pilot plant operated by Südzucker AG in the Federal Republic of Germany, with the manufacturing price of HMF being 6000 DM/ton for a fructose price of 500 DM/ton [41], and also the price of 2000 €/ton predicted by Bicker, et al. for a fructose price of 500 €/ton [44].

Some researchers have investigated whether HMF could be produced at reduced cost in order to be used as a substitute for certain target chemicals. Torres, et al. estimated the cost of production of HMF using a semi-batch biphasic reactor and compared it with the price of p-xylene, for which HMF can act as a substitute in the production of polyethylene terephthalate (PET) [26]. They obtained a minimum HMF cost of 0.248-0.273 \$/mol (1967-2165 \$/ton) for a fructose cost of 550 \$/ton, depending on the solvent used at the extraction stage. However, this was higher than the cost of p-xylene (0.109 \$/mol or 1027 \$/ton). Since the cost of fructose is the dominant factor in the HMF price, it was concluded that lower fructose costs are necessary alongside the development of more efficient processes for the HMF price to be competitive [26]. More recently, Kazi, et al. estimated that a plant co-producing dimethylfuran (2,5-DMF) and HMF from 300 metric ton/day of fructose would yield HMF with a minimum selling price of \$ 1.33/l, which translates into approximately \$ 1100/ton. However, this is still too expensive for HMF to be used as a feedstock for the production of FDCA as a replacement for terephthalic acid, which sells for around \$ 800/ton [45]. Recently, Liu, et al., stated that HMF produced at \$1210/ton would be cost competitive with the petroleum-derived paraxylene-terephthalic acid selling at \$1440/ton, and state that this HMF price is achievable for a fructose price of 460 \$/ton [46].

LA is a compound derived from HMF that is itself a promising chemical intermediate. It was listed among the top 12 most promising value added chemicals from biomass by the Biomass Program of the US Department of Energy in 2004 [30], and continues to rank highly in more recent reviews of most important biorefinery target products [9]. This recognition of the potential of LA is not a recent phenomenon. The compound was first identified in the 1870's, and in 1956 a detailed report outlining the many derivatives from LA and their potential applications was published [47]. Despite this, the commercial applications of LA have been slow to develop. Among the reasons cited for this are the expensive raw materials, low yields, high equipment cost, problematic recovery and handling, etc [47]. Nevertheless, it is currently used in several industries including personal care products, lubricants, adsorbents, electronics, photography, batteries and drug delivery systems [48]. The production of LA at lower costs, however, should greatly enhance its use as a chemical intermediate, given the range of chemicals having numerous market applications that can be produced from it. Table 2-2 summarises some of the important chemicals that can be synthesised from LA and the sectors they can be used in [36, 49-52].

Table 2-2: Potential applications for select chemicals produced from LA [36, 49-52]

Chemicals	**Potential Markets/Applications**
Diphenolic acid	- Epoxy resins - Lubricants - Adhesives - Paints - Polymers
Succinic acid	- Polymers - Solvents - Pesticides
δ-aminolevulinic acid (DALA)	- Herbicides - Insecticides - Cancer treatment
Methyltetrahydrofuran	- Fuel additive - Solvents
Ethyl levulinate	- Fuel additive - Food flavouring
γ-valerolactone (GVL)	- Solvents - Fuel additive - Biofuels - Polymers
Different esters of LA	- Plasticisers - Solvents
α-angelicalactone	- Fuel additive - Solvents
Sodium levulinate	- Antifreeze
Calcium levulinate	- Antifreeze - Pharmaceutical
1,4-butanediol	- Polymers - Solvents - Fine chemicals
Valeric (pentanoic) acid	- Fuel additive
5-nonanone	- Paints - Resins

The price for LA was about 8.8-13.2 \$/kg in 2000, which meant that it was mostly used as a speciality chemical [48]. The small market size of LA at this time, around 450,000 kilograms annually [53], meant that it was produced largely from maleic anhydride and other petrochemicals [54]. The price in 2010 was around 3.2 \$/kg, which was substantially lower than the earlier figures, but still too high for chemicals produced from LA to compete with those derived directly from petroleum [55]. Despite LA prices remaining in the range of 5-8 \$/kg in 2013, global LA consumption rose to around 2600 tons, and is expected to increase steadily in the near-future, reaching 3800 tons in 2020 [56].The Biofine process, which is dealt with in Section 2.10, has been projected to lower LA costs to as low as 0.09-0.22 $/kg [48], which should make a whole range of LA-derived chemicals economically attractive.

The above discussion has shown that while both HMF and LA have tremendous market potential, the realisation of this potential is dependent on the production of large quantities of these chemicals sustainably and at low prices. Hence, it is not surprising that these problems have attracted many researchers' interest. The large amount of research conducted on the synthesis of these two chemicals and the numerous reaction systems devised makes it necessary to analyse the merits and demerits of the different approaches, particularly with respect to the feedstocks used, the yields obtained, and the accompanying environmental impacts. The requirements for taking the laboratory schemes towards industrial production also need to be identified and addressed. This review, therefore, provides an overview of the production of HMF and LA from different carbohydrates and lignocellulosic biomass using various solvent and catalyst systems, and identifies the gaps that need to be filled for the two building blocks to attain the level of commercialisation they deserve. The use of 'green chemistry' techniques to synthesise HMF and LA is of particular interest to ensure that these chemicals are truly 'sustainable'. Microwave heating provides an energy-efficient method of increasing reaction rates and yields while using benign solvents and moderate temperatures. Therefore, a special focus of this review will be on systems that utilise microwave irradiation as the heating medium.

2.3 Chemistry of HMF synthesis

Hydroxymethylfurfural (HMF), also known as 5-(hydroxymethyl)-2-furancarboxaldehyde and 5-(hydroxymethyl)-2-furaldehyde [57], is a chemical that has been of interest to researchers for over a century [58]. The HMF molecule has various functionalities arising from the presence of hydroxyl and aldehyde groups as well as a furan ring [42]. HMF is a yellow solid with a melting point between 28 to 34 °C and a density of 1.206 to 1.243 g/cc [41, 57, 59, 60]. The boiling point of HMF is 114-116 °C at 1 mmHg [41], but at atmospheric pressure, it is 291 °C [61, 62]. It is soluble in a range of solvents, such as water, methanol, ethanol, benzene, acetone, chloroform, ethyl acetate and formaldehyde [57, 60].

Fundamentally, HMF is produced by the loss of three molecules of water from a hexose material in an acid-catalysed reaction [63]. Despite the apparent simplicity of the process, in reality, the occurrence of a number of side-reactions including the re-hydration of the HMF to LA and formic acid, and cross-polymerisation to soluble polymers and insoluble humins renders the HMF synthesis very complicated [58] [63]. A number of mechanisms have been proposed for the formation of HMF from fructose, and these can be broadly grouped into acyclic (Figure 2-1) and cyclic routes (Figure 2-2). Haworth [64] and Mednick [65] are among those whose work appears to favour the cyclic route involving a fructofuranosyl cationic intermediate, while Wolfrom [20] favoured the acyclic route featuring an enediol intermediate. Kuster [63] stated that the acyclic route was favoured by most researchers, but Antal [66] provided experimental evidence backing the existence of cyclic intermediates in the synthesis of HMF from fructose. It has also been noted that HMF synthesis is much more efficient and selective from fructose than from glucose, as the enolysation of glucose into an enediol is known to be an important step in the formation of HMF from glucose [58, 67].The reversible Lobry-de Bruyn-van Ekenstein transformation, via which glucose and fructose are converted into each other, therefore plays an important role in the synthesis of HMF from glucose [68]. When sucrose is used as the starting material, the acid-catalysed hydrolysis yields the fructofuranosyl ion and glucose, with the former acting as the key intermediate for the formation of HMF [66].

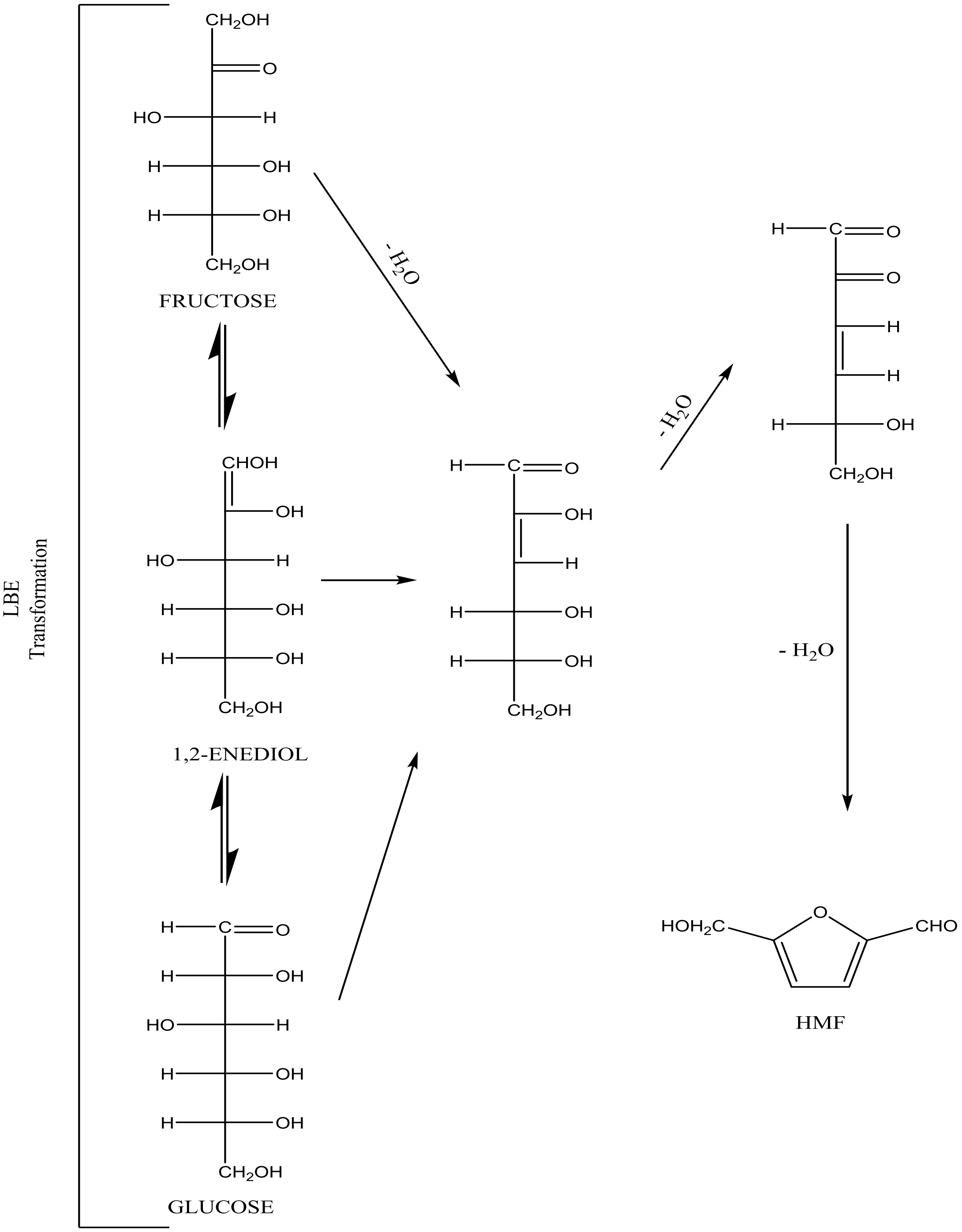


Figure 2-1: Acyclic route for HMF synthesis from fructose and glucose (based on [35] and [39]), along with the Lobry-de Bruyn-van Ekenstein transformation between glucose and fructose

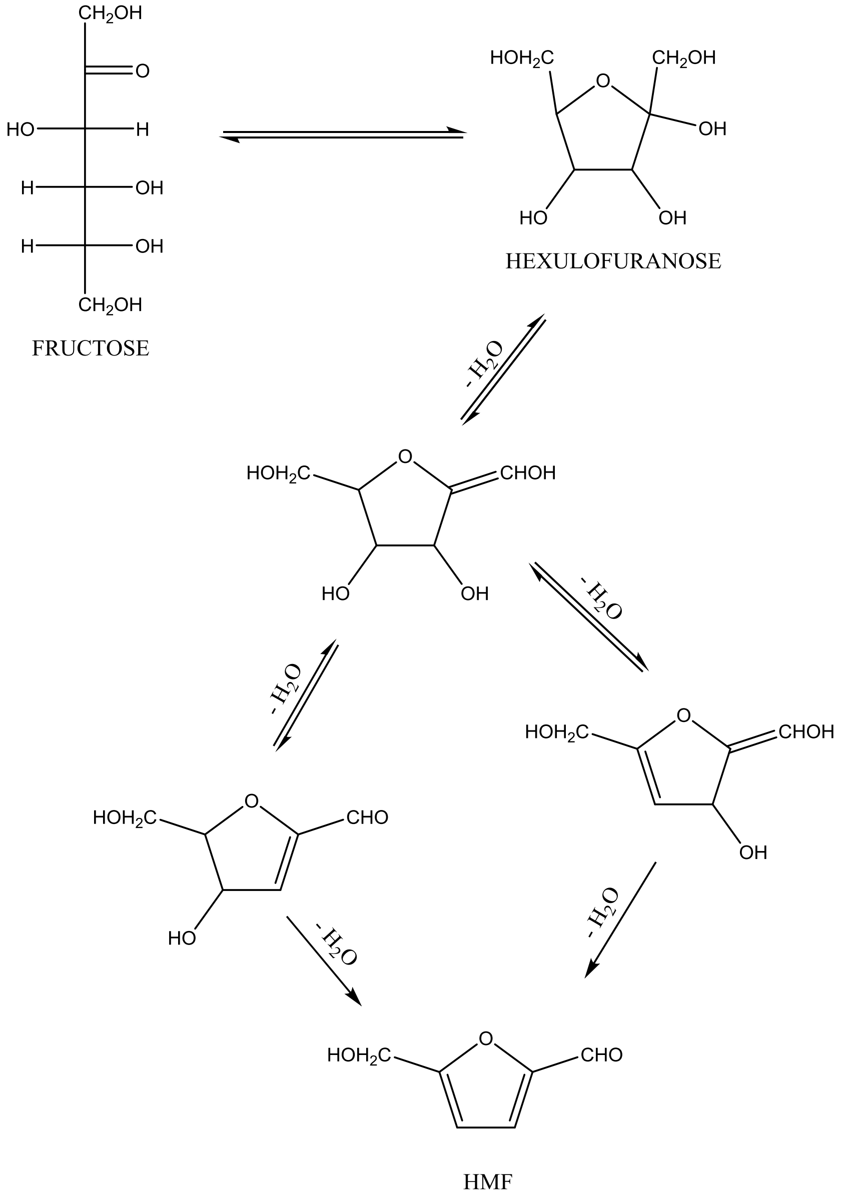


Figure 2-2: Cyclic route for HMF synthesis from fructose and glucose (based on [35] and [39])

2.4 Chemistry of LA synthesis

Levulinic acid (LA), also known as 4-oxopentanoic acid [57], is a colourless crystalline compound (commercial product being yellow) with a melting point ranging from 33 to 37°C, a boiling point between 245 to 246 °C and a density of around 1.14 g/cc [57, 60, 69]. LA is highly soluble in hot water, as well as in ethanol, diethyl ether, chloroform, acetone, dilute acids, etc. [57, 60, 69]. In water, LA has a pKa (25 °C) value of 4.59, which means that its acidity is comparable with most lower alkane carboxylic acids [69]. LA contains two highly reactive functional groups, a carbonyl and a carboxyl group, which renders this molecule suitable for a wide range of synthetic transformations [69].

Several routes for the production of LA from biomass have been described, such as [69, 70]:

- Enzymatic or acid-catalysed conversion of polymeric carbohydrates to hexoses. Of the hexoses, the glucose isomerises to fructose, which is then dehydrated using acid catalyst to HMF, which is in turn converted to LA
- Hydrolysis of furfuryl alcohol
- Acid treatment of pentoses followed by reduction
- Ring cleavage of furfural
- Ozonolysis of unsaturated hydrocarbons
- Oxidation of 5-methylfurfural with hydrogen peroxide in presence of formic acid
- Reduction of 4-(diphenylmethylsilyl)butyrolactone with the Grignard reagent methylmagnesium iodide
- Conjugate addition of nitroethane to acrolein to form 4-nitropentanal, which is subsequently oxidised to LA

Of these methods, the first route, in which HMF is converted to LA via the addition of a molecule of water to the double bond of the furan ring, is the most suitable for industrial scale production [69]. The pathways that have been proposed for the conversion of HMF to LA are shown in Figure 2-3 [69, 71, 72].

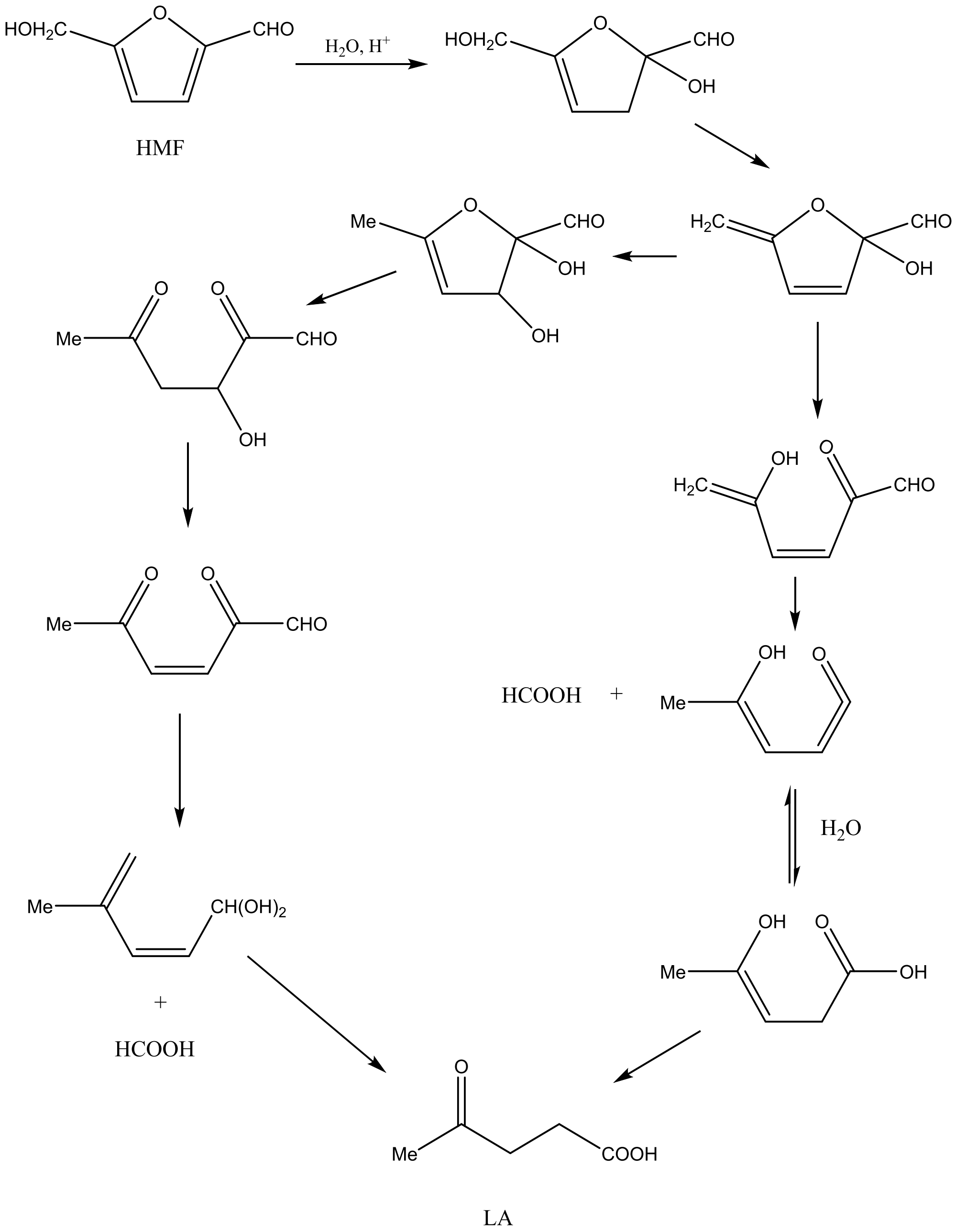


Figure 2-3: Conversion of HMF to LA (based on [42, 44, 45])

2.5 Feedstock for HMF and LA synthesis

2.5.1 Monosaccharides

Since HMF is basically a molecule formed by the dehydration of a hexose molecule, and HMF itself is used for LA production, the hexose sugars fructose and glucose have been the starting point for HMF and LA synthesis for many researchers. Of these, fructose is easier to convert into HMF, but the wider availability of glucose means that it might be a better candidate as HMF feedstock

[73]. One method of utilising glucose as feedstock is to use a catalyst that isomerises glucose to fructose. Solid catalysts (e.g. TiO_2 and ZrO_2) that can act as Lewis bases in addition to Lewis acids can be used for this purpose, with the basic sites on the catalyst isomerising the glucose, and the acidic sites converting the resultant fructose to HMF and LA [74]. An integration of an immobilised glucose isomerase enzyme, that converts glucose to fructose, with an acid catalyst that converts the fructose to HMF is another method that has been suggested [75].

2.5.2 Polysaccharides

The direct conversion of polysaccharides to HMF and LA has been the subject of increasing research interest in recent years. A number of polysaccharides have been identified as attractive candidates based on different parameters, such as starch being one of the cheapest and most abundant carbohydrates [76], cellulose being the major form of photosynthetically fixed carbon [77], chitin being the second-most abundant biopolymer on earth [78] and inulin being a carbohydrate that cannot be digested by humans [79]. However, the polysaccharides must be depolymerised via hydrolysis prior to dehydration of the monomer units to HMF. This introduces the possibility of side reactions which renders HMF production from polysaccharides a complex process [80].

2.5.3 Lignocellulosic biomass

Some biomass containing a high amount of soluble sugars, such as grapes, can be readily converted to HMF without pre-treatment [81]. However, sustainability concerns and commercial scale applicability dictate that efforts should focus on the production of HMF from untreated lignocellulosic biomass rather than edible crops-derived carbohydrates [82]. Lignocellulosics are a major type of biomass consisting primarily of cellulose (38-50%), hemicellulose (23-32%) and lignin (15-25%), with some amount of organic substances and inorganic ashes also present [83]. Agricultural residues, energy crops, forestry residues and municipal organic wastes all constitute different types of lignocellulosic biomass, but the exact composition varies depending on the source [84]. The cellulose and hemicellulose portions of the lignocellulosic biomass are of primary importance since these are composed of hexoses such as glucose, mannose and galactose whose dehydration produces HMF [80]. Typically, the differences in the chemical and physical properties of hemicellulose and cellulose necessitate separation of these two components before processing, but integrated conversion processes have also been reported [82, 85].

To conclude, although monosachharides are the easiest to convert to HMF and LA, and are hence the first substrates tried by researchers testing new catalysts, solvents or reaction schemes, polysaccharides and raw biomass are the feedstock that must eventually be used for any commercial unit to economically produce these products. The use of polysaccharides and raw biomass has therefore been given special attention and discussed separately from monosaccharides in Sections 2.7 and 2.9.

2.6 Reaction systems for HMF and LA synthesis

A large number of reaction systems have been investigated for the synthesis of both HMF and LA from a range of different feedstocks. One of the main differences between the various reaction systems is the catalyst, with some non-catalytic systems being used, while others employ either liquid or solid catalysts. These have been discussed in detail in Section 2.6.1. The other major difference is in the solvent used, with the use of various protic and aprotic solvents being discussed in Section 2.6.2. The use of microwave heating is another distinct feature in several recent studies, and must be dealt with separately. Accordingly, studies that employed microwave irradiation in either catalytic or non-catalytic systems are brought into focus in Section 2.12.

2.6.1 Catalysts

2.6.1.1 Non-catalytic systems

The vast majority of the work on HMF and LA production has been carried out using catalysts, since feedstock conversion and product selectivity are very poor for non-catalytic systems. However, at prolonged reaction times or high temperatures, autocatalysis can occur due to the formation of certain reaction products like formic acid or LA [86]. Conditions of high temperature and pressure can also lead to non-catalytic production. For instance, Jing and Lü reported the production of HMF in molar yields of up to 32% from glucose in liquid water at a temperature of 220 ^{o}C and a pressure of 10 MPa [87]. Also, in some cases, the solvent system itself acts as a catalyst. For example, Chheda et al. used dichloromethane (DCM) as the extracting solvent to form a biphasic system with the reaction solvent 3:7 (w/w) water:dimethyl sulfoxide (DMSO). These solvent conditions permitted the complete conversion of fructose and inulin with an HMF selectivity of 87% and 70% respectively. Moreover, under the same conditions, glucose, sucrose, starch and cellobiose also had high conversions with selectivity comparable to those obtained using hydrochloric acid (HCl) as catalyst [88]. In addition, ionic liquids, which are discussed in Section 2.6.2.4, can act as either solvents or catalysts.

2.6.1.2 Liquid catalysts

The dehydration of D-fructose to HMF can be catalysed by either a Brønsted acid or a Lewis acid. Accordingly, nearly one hundred inorganic and organic acidic compounds that can catalyse HMF synthesis have been identified, with mineral acids like sulphuric acid (H_2SO_4), phosphoric acid (H_3PO_4) and HCl being the most widely used due to their ready availability, low cost and the high HMF yields obtained. Some of the earliest work on HMF synthesis used these catalysts. For instance, Wolfrom, et al. used HCl as the catalyst to produce HMF from glucose in 1948 [20], while Haworth and Wiggin's patent for HMF manufacture in the same year mentions oxalic, phosphoric, maleic, fumaric and hydrochloric acids as possible catalysts [89].

The importance of strongly acidic conditions in HMF synthesis has, however, been disputed, with Mednick [65] obtaining the highest HMF yield from glucose (46 mol%) and starch (44 mol%) using pyridine and phosphoric acid as co-catalysts, and therefore concluding that a combination of weak acid and weak base as catalysts worked better than acid catalysts alone. Sinag, et al. also reported the formation of HMF from glucose in aqueous alkaline (K_2CO_3) solutions, albeit in small quantities [90]. Yin, et al. studied hydrothermal conversion of cellulose to HMF in acidic, neutral and alkaline conditions, and found that the HMF yields were highest in acidic and lowest in alkaline conditions, while in terms of purity, the order was neutral, acidic and alkaline conditions [91]. They concluded that under alkaline conditions, carboxylic acids like acetic, lactic and formic acids were the primary products formed, and the resultant reduction in pH led to the acidic route for conversion to HMF being followed. Under neutral conditions also the acid reaction pathway was followed owing to the self-dissociation of water [91]. However, in an earlier work, Antal, et al. had showed that only strong Brønsted acids like H_2SO_4 can catalyse the reaction, as formic acid showed very little catalytic activity [66]. This was corroborated by Girisuta, who showed that LA and formic acid cannot autocatalyse the production of HMF, LA or formic acid from glucose [92].

Since HMF is an intermediary in the formation of LA from biomass, it is unsurprising that liquid acid catalysts have also been used to produce LA for decades. Thomas and Schuette used HCl as the catalyst to produce LA from various carbohydrates in 1931 [93]. Carlson's 1962 patent states that

HCl is the most preferable catalyst for converting various carbohydrate-containing materials like wood tailings to LA owing to two factors: first, HCl can be recovered and recycled easily, and second, LA can be separated using simple vacuum distillation [94]. Generally, higher acid strengths and longer residence times are needed to produce LA as the final product than HMF.

2.6.1.3 Solid catalysts

The use of solid catalysts for HMF and LA synthesis is also fairly well-established. Redmon's 1956 patent, for instance, mentions the use of an acidic cation exchange resin for LA production with minimal formation of insoluble by-products [24]. For HMF manufacture, Garber and Jones recommended the use of aluminium sulphate and aluminium chloride as catalysts in their 1969 patent [95].

Nevertheless, the range of solid acid catalysts that have been studied for HMF and LA synthesis has been growing greatly in recent years. Solid acid catalysts are preferable to liquid acid catalysts since they can be separated easily from the product and recycled; can work at higher temperatures, reducing reaction time and HMF decomposition; and their surface acidity can be adjusted to improve selectivity [96]. Their easier recovery and recyclability makes solid catalysts preferable for industrial use [97]. Certain solid acid catalysts, however, dissolve in the solvent, such as the heteropolyacids employed by Chidambaram and Bell [98], which could negate the advantage of recyclability vis-a-vis liquid catalysts. Some of the solid acid catalysts that have been reported are zirconia and titania [23], stannous and stannic chloride [99], $SO_4^{2-}/ZrO_2-Al_2O_3$ (CSZA) [76], $AlCl_3.6H_2O$ [100], Sn-Mont [101], zirconium phosphate and ion-exchange resins [97], etc.

It has been observed that when solid catalysts are reused over a period of time, there is a drop in their catalytic activity. In general, such catalyst deactivation may either be due to a deposition of reaction by-products such as coke and humin on the surface of the catalyst, or due to a leaching of the active metal or acid groups from the catalyst [102-104]. One common method of regenerating used catalysts is by calcining them at high temperatures (400-500 ^{o}C) for three to four hours [104, 105]. While this does not recover any loss in catalytic action due to leaching of active species, it removes deposits such as humins from the surface, which often leads to the catalyst recovering activity levels close to that of the fresh catalyst [104, 105]. However, this method is unsuitable for catalysts which are unstable at high temperatures (>200 ^{o}C) [103]. In such cases, the catalyst may be washed with a reagent such as H_2O_2 [103, 106], HCl [107, 108], ethanol [108], methanol [109], NaOH [97], acetone [110], etc. Such treatment appears to be successful in recovering catalytic activity in a number of cases.

In order for a catalyst to be considered effective, it must provide both high conversion and high selectivity. Numerous solid catalysts that are highly selective in HMF production have been reported, but the substrate conversion is very low. Examples are the lanthanide catalysts ($LaCl_3$, $NdCl_3$, $EuCl_3$, $DyCl_3$ and $YbCl_3$), various zirconium, titanium and niobium-based catalysts, etc. [111-113]. The toxicity and cost of the catalysts is also important, and this goes against certain catalysts like $CrCl_2$ and $SnCl_4$, leading to other catalysts like $CrCl_3.6H_2O$, 12-tungstophosphoric acid, boric acid, Sn-MCM-41 and $GeCl_4$ possibly being preferable [114-118].

A different kind of solid catalyst was described by Alamillo, et al., who described the synthesis of an organic-inorganic nanocomposite catalyst by intercalating poly(vinylpyrrolidone) (PVP) into the pores of silica catalysts [119]. This catalyst achieved HMF selectivities above 80% at fructose conversions of around 85%. These yields are among the highest reported for solid catalysts, which typically offer lower yields than homogeneous catalysts. A microporous pillared-clay catalyst to provide shape-selective partial dehydration of glucose had also been described by Lourvanij and Rorrer, with the unpillared H-montmorillonite showing the highest selectivity to HMF [120].

2.6.2 Solvents

As will be detailed below, a large number of solvents have been utilised for the synthesis of HMF and LA. While the suitability of solvents in terms of substrate conversion, product selectivity and yields are detailed in Tables 2-3 to 2-11, another important factor is the environmental impact of these solvents. Ilgen, et al. carried out a preliminary ecological evaluation of a range of solvents, and found that only water was completely suitable in terms of the six parameters tested (mobility, acute toxicity for humans, chronic toxicity for humans, acute toxicity for aquatic organisms, persistency in environment and bioaccumulation) [121]. Most of the other common solvents, such as DMSO and ionic liquids, were found to be problematic on at least one front, and this is an issue that should be kept in mind when a solvent is selected for HMF and/or LA synthesis.

2.6.2.1 Protic solvents

Water is one of the most widely used solvents, owing to its ubiquity, physical and chemical characteristics, and environment-friendliness. In practical reaction systems, however, it has been seen that other solvents can provide higher product yields, particularly when HMF is the desired end-product, as HMF is easily rehydrated in aqueous media to LA, formic acid and humins [122]. This problem must be balanced against economic and ecological factors. Other protic solvents such as butanol have also been used, either by themselves, or in conjunction with water. While n-butanol (1-butanol) and iso-butanol can catalyse HMF production from fructose, it is the role of sec-butanol (2-butanol) that is the most important in this field. Not only is it one of the most effective solvents for fructose dehydration [123], it has also proved to be very effective as an organic co-solvent in bi-phasic mixtures (see Section 2.6.2.3) [124, 125].

2.6.2.2 Aprotic solvents

A number of polar aprotic solvents are widely used for HMF and LA synthesis, such as DMSO, dimethylformamide (DMF), dimethylacetamide (DMA), tetrahydrofuran (THF) and ethyl acetate. Among these, DMSO is one of the most important, particularly for HMF synthesis. A major reason for this is that DMSO suppresses the hydrolysis of HMF to LA and formic acid. Moreover, at high enough temperatures (> 150°C), the conversion of fructose to HMF in DMSO occurs without any added mineral or Lewis acid catalyst [126]. For instance, Musau and Munavu produced HMF in yields of up to 92 mol% using DMSO, with the reaction taking place at 150°C for 2 hours [127]. The optimum conversion was obtained at a fructose: DMSO molar ratio of 8. However, due to the high boiling point of DMSO (196°C), a large amount of energy is required to separate of the HMF from the solvent, which affects the economic feasibility of the process [128, 129]. Also, there is a possibility of toxic sulphur-containing by-products being formed when DMSO is used as the solvent [130].

Mushrif, et al. carried out a molecular dynamics investigation to find out the reason for the success of DMSO in protecting HMF from rehydration and humin formation and fructose from side reactions [129]. They concluded that the preferential arrangement of DMSO molecules around the hydrogen atoms of the hydroxyl groups of fructose leads to the water molecules directly contacting the oxygen atoms of the hydroxyl groups. This prevents the fructose molecule from forming reversion and polymerisation products and allows the water molecules to transfer protons to the hydroxyl oxygen, thereby initiating the dehydration to HMF. Also, DMSO preferentially solvates the carbonyl carbon atom of HMF, preventing further rehydration to LA and formic acid. Another study regarding the mechanism of dehydration of fructose to HMF in DMSO was conducted using Nuclear Magnetic Resonance (NMR) by Amarasekara, et al [126]. The authors proposed a mechanism for the reaction, and identified the formation of an intermediate established as (4R,5R)-4-hydroxy-5-hydroxymethyl-4,5-dihydrofuran-2-carbaldehyde, which could not, however, be isolated, due to its rapid conversion to HMF.

An important constraint in the use of DMSO in HMF production is the fact that distillation of HMF from DMSO leads to substantial carbonisation of the product, and so low-temperature separation processes such as vacuum evaporation and vacuum distillation are necessary [124]. These processes need to be optimised in terms of cost, energy expenditure and product recovery. Other commonly used polar aprotic solvents, such as THF, also have disadvantages of high cost and adverse environmental effects [131]. The use of novel aprotic solvents like N-methylpyrrolidone (NMP) has been proposed as an environment-friendly alternative to DMSO [88].

2.6.2.3 Extracting solvents

The rehydration of HMF in aqueous media can be reduced by removing HMF from the reaction mixture as it is being formed. For this purpose, an organic phase, which is immiscible with the aqueous phase and preferably has a higher partition coefficient for HMF with respect to water, can be used, with the HMF being then recovered from the organic phase [26]. Such a system is called a co-solvent system or a biphasic mixture. The partition coefficient between the phases is very important, since a low value will necessitate the use of large amounts of the organic solvent and the expenditure of large quantities of energy for HMF recovery [88]. Organic solvents like methyl isobutyl ketone (MIBK), dichloromethane (DCM) and sec-butanol have proved to be effective as extracting solvents.

2.6.2.4 Ionic liquids

In recent years, the focus on 'green chemistry' has led to a rise in the use of ionic liquids as solvents or catalysts. Ionic liquids are salts consisting of ions which are liquid at ambient temperatures [132] or below 100ºC [133]. The most important group of ionic liquids, both in terms of widespread industrial application [133] and use in research on HMF synthesis, is the imidazolium-based group, whose cations include 1-butyl-3-methylimidazolium ($[BMIM]^+$), 1-ethyl-3-methylimidazolium ($[EMIM]^+$), 1-octyl-3-methylimidazolium ($[OMIM]^+$),etc. It must be noted that occasionally different researchers may use the same abbreviation for different ionic liquids- for instance, [HMIM] has been used to denote both 1-hexyl-3-methylimidazolium [134] and 1-H-3-methyl imidazolium [135], and can also be used for 1-heptyl-3-methylimidazolium [136]. Several researchers accordingly prefer to use an alternative notation, with [C4-MIM] denoting 1-butyl-3-methylimidazolium, etc. [136].

The stability, low vapour pressure and recyclability of ionic liquids, coupled with the fact that their physical and chemical properties can be easily tuned by varying the ions, are some of the important reasons for the intense interest of researchers in these solvents [96, 133]. Another great advantage of ionic liquids over conventional solvents is that they can be used to convert raw biomass directly into the final products [137-139]. In addition, in numerous cases it has been seen that ionic liquids have the ability to act as catalysts alongside their solvation capability [139-141].

Nevertheless, ionic liquids also have certain drawbacks. Their status as ‘green solvents’ has been questioned, since the very fact that their properties can be tailor-made by changing the ions involved leads to an enormous diversity in both the number and properties of ionic liquids. Hence both the method of production of the ionic liquid and its properties (toxicity, explosivity, biodegradability, etc.) may not be environment-friendly [142, 143].

Another disadvantage of ionic liquids that can be alluded to is their poor transport properties [144]. Their high viscosity reduces mass transfer in the liquid and leads to only a small fraction of the liquid being in contact with the substrates and active [109]. Ionic liquids can also lead to severe corrosion in numerous metals, especially in the presence of water, which can lead to process equipment damage [145]. The need to purify them after recycling and their potential sensitivity to moisture and oxide impurities offer additional challenges [130].

The low vapour pressure of ionic liquids, which is held to be one of their ‘green’ characteristics, has a drawback in that it in many cases prevents recovery of used ionic liquids via distillation [146, 147]. This means that alternative methods for separating the reacting species and recovering the ionic liquid, such as solvent extraction (with solvents like diethyl ether [135, 140, 148], MIBK [149], ethyl acetate [73, 150], toluene [151], etc.) or adsorption through a zeolite column [46] may need to be used. Nevertheless, it has been demonstrated that certain ionic liquids can be distilled under appropriate conditions [152-155]. Given the thermal sensitivity of HMF, special distillation techniques like vacuum reactive distillation may be needed to efficiently separate HMF from the ionic liquid [156].

The effect of moisture in the feedstock on the performance of ionic liquids is also an area that needs to be considered, given that chemical properties such as anionic basicity can be adversely affected by the presence of water [157, 158], while physical properties such as viscosity can actually be improved by water addition [140]. A number of studies have been conducted to study the role of water in HMF synthesis using ionic liquids, and it seems that while small amounts of water may not affect the reaction significantly [140, 159], larger amounts adversely affect HMF yields [160]. This is a reflection not only on the effect of water on the properties of the ionic liquid but also the fact that water plays different roles in the process itself- essential for hydrolysis of carbohydrates, but disadvantageous for the dehydration reaction [38, 161]. In general, it appears that while suitable ionic liquids can be used for direct hydrolysis of raw biomass [137, 138], the removal from the ionic liquid of the by-product water that is produced during the conversion of carbohydrates to HMF may prevent a decrease in yields in subsequent runs [149, 162].

Finally, one of the greatest constraints of ionic liquids is their cost, which is estimated to typically be between two and one hundred times that of organic solvents [163]. The difference that this makes to the cost of the final product can be seen from the fact that it has been calculated that for a 10,000 ton/year HMF plant that uses fructose (700 €/ton) as feedstock and ionic liquid as solvent, the price of HMF produced will be 7000 €/ton [164], which is far higher than the prices mentioned in Section 2.2. This is especially concerning given that the cost of ionic liquid assumed for the calculations is only € 25/kg, which is one-tenth of the 2013 market price [164].

A number of efforts have been made to tackle the different problems associated with ionic liquids. The toxicity issue can be addressed by the use of benign ions, such as the cholinium cation ($[NMe_3(CH_2CH_2OH)]^+$) [142]. Choline chloride, for instance, has been used successfully for synthesising HMF from a number of carbohydrates [121]. Other researchers have experimented with ionic liquids that are cheaper than the conventionally used ones, such as tetraethyl ammonium chloride, to bring down costs [114, 165].

One method of reducing ionic liquid usage and increasing recyclability is the use of supported ionic liquid catalysts, which are prepared by immobilising the ionic liquid on a solid surface [109]. These catalysts, which combine the benefits of heterogeneous catalysts and ionic liquids, have been considered to be solid catalysts in Section 2.7 and discussed separately from the conventional ionic liquids.

2.6.3 Additives

It has been shown that NaCl increases rehydration of HMF to LA in a single phase aqueous medium due to a drop in the solution pH [100]. In a biphasic system of water/tetrahydrofuran (THF), however, HMF yield and selectivity both increase due to an increase in the partition coefficient and the suppression of the formation of lactic acid as by-product [100]. Wang, et al. also found that the addition of NaCl increases the partitioning coefficient between THF and water and prevents HMF from getting dehydrated to LA in the biphasic system [101]. Potvin, et al. reported that the molar LA yield obtained from cellulose in aqueous solution using a solid acid-supported catalyst increased from 14% without NaCl to 70% when a 20% NaCl solution was added, perhaps due to interactions between the NaCl ions and the hydrogen bonding of the cellulose structure [166]. The addition of brine was postulated as a simple alternative to the use of ionic liquids for cellulose hydrolysis.

NaCl may also have a role to play when microwave irradiation is used for heating, especially if water is used as the solvent, since the decrease in the dielectric constant of water at higher temperatures leads to decreased microwave absorbance, which in turn leads to the actual water temperature lagging behind the set temperature. This decreased microwave absorbance could be compensated by the addition of an ionic or polar species like NaCl, but the possibility of such an additive affecting the reaction pathways must also be considered and evaluated [68].

To summarise the discussion in this section, the difficulty in arriving at an optimum reaction scheme for HMF and LA synthesis can clearly be seen from the vast number of catalysts and solvents that have been tested. Homogeneous acid catalysts like HCl and H_2SO_4 generally give high product yields but may pose problems with respect to recycling and eco-friendliness. Solid catalysts offer easier recovery and their properties can be tailored to improve selectivity, but they generally offer lower yields and are prone to fouling and mechanical damage. When it comes to solvents, water is one of the most widely used and environment-friendly solvents, but often aqueous systems have to deal with excessive by-product formation. DMSO, which is another common solvent, greatly reduces the formation of reversion, rehydration and polymerisation by-products and increases product yields, but also opens up the possibility of the formation of sulphur-containing by-products and product carbonisation occurring during recovery. An ideal solvent should also provide a low energy and economic cost of product recovery. The shortcomings of the common solvents have led to a range of novel solvents being tested, with varied results. The use of an extracting co-solvent is promising from the point of view of increasing product yield, and hence research is underway to find a pair of co-solvents that can be used economically in larger scale operations. Ionic liquids, which can act as both solvents and catalysts, have attracted plenty of research attention due to their stability, low vapour pressure, good salvation capability and tunable physical and chemical properties.

However, their high cost, sensitivity to impurities, and challenges in product recovery has so far prevented their use in larger scale systems. The tables in Sections 2.7-2.10 enable a comparison of the different reaction schemes that have been discussed in this section, and the accompanying discussion will elaborate upon some of the points mentioned here.

2.7 Laboratory-scale production of HMF

A large number of researchers have studied a range of reaction conditions for the laboratory-scale production of HMF from a number of different feedstocks. Some of the major work done in this area has been summarised below. To enable a better understanding of the large number of factors at play, the experiments have been categorised based on the feedstock used, with runs based on fructose in Table 2-3 and on monosaccharides other than fructose in Table 2-4. The reason for studying fructose separately is the large amount of research that has been conducted on it owing to its high convertibility to HMF, which can help in discerning the broad trends that can be applied to other feedstocks. The conversion of polysaccharides to HMF presents more formidable challenges, and the work done on them is presented in Table 2-5. Where required, molar yields have been converted to mass yields based on the molar mass (162) of the anhydroglucose or anhydrofructose units, so as to facilitate comparison among the different polysaccharides. Ionic liquids are a unique category by themselves, and hence are summarised for all monosaccharide and polysaccharide feedstock in Table 2-6. Finally, the results of experimentation on direct biomass are given in Table 2-7. It must be noted that all yields mentioned are based on the reported values. In a majority of cases, these represent values obtained in solution by High Performance Liquid Chromatography (HPLC), Gas Chromatography-Mass Spectrometry (GC-MS), or other techniques. In other cases, the values are the isolated yields, which are typically lower than the in situ yields due to losses in product separation.

In Tables 2-3 to 2-7, conversion and yield are defined as

$$Conversion = 1 - \frac{Final\ mass\ of\ the\ substrate}{Initial\ mass\ of\ the\ substrate} \times 100\%$$

$$Yield = \frac{Mass\ of\ HMF\ produced}{Initial\ mass\ of\ the\ substrate} \times 100\%$$

Table 2-3: Laboratory-scale production of HMF from fructose (solvent systems marked with * are biphasic systems)

Fructose conc. (wt%)	Solvent	Catalyst	Catalyst conc.	Temp. (ºC)	Reaction/ residence time	Conversion (%)	Yield (wt%)	Ref
1	Subcritical acetone-water (90:10 v/v)	H_2SO_4	10 mM	180	2 min	90	48	[44]
1	Subcritical water	H_2SO_4	10 mM	180	10 min	80	20	[31]
30	Dioxane-water (86.5:13.5 w/w)	HCl	0.04 wt%	180	4 min	83.7	40	[167]
8	Water-PEG 4000 (50:50 v/v)	PTSA	1 M	88	5 h	97	32	[72]
8	Water-PEG 600 (60:40 v/v)	HCl	1 M	95	1 h	86	38	[122]
1	Subcritical water	HCl	pH=4	240	2 min	63	12	[168]
1	Subcritical water	H_2SO_4	pH=1.5	240	2 min	100	20	[168]
1	Subcritical water	H_3PO_4	pH=1.5	240	2 min	100	39	[168]
1	Subcritical water	Citric acid	pH=1.5	240	2 min	96	35	[168]
1	Subcritical water	Maleic acid	pH=1.5	240	2 min	96	28	[168]
1	Subcritical water	Oxalic acid	pH=1.5	240	2 min	94	13	[168]
0.5	Subcritical water	HCl	pH=2.3	240	1 min 40 s	99	12	[169]
25	Water	Oxalic acid	0.25 wt%	140	2 h 25 min	61	23	[170]
1	Subcritical water	H_2SO_4	2 mM	250	32 s	92	34	[66]
1	Subcritical water	Formic acid	2.4 mM	250	32 s	56	16	[66]
1	Water	HCl	pH=1	150	2 h	92	19	[171]
1	Water	Lactic acid	50 wt%	150	2 h	96	45	[171]
1	Water	Acetic acid	50 wt%	150	2 h	84	34	[171]
1	Water	Formic acid	20 wt%	150	2 h	100	38	[171]
7.5	Tetrahydrofurfuryl alcohol	H_2SO_4	0.25 M	178	5 s	N/A	56	[172]
1.5	Tetrahydrofurfuryl alcohol	HCl	0.08 M	178	5 s	N/A	56	[172]
8	Toluene-DMSO (8:1 v/v)	Borontrifluoride-etherate	0.07 M	N/A	30 min	N/A	42	[127]
24	Methyl Cellosolve	Borontrifluoride-etherate	0.025 M	100	1 h	N/A	55	[173]
30	DMF	Borontrifluoride-etherate	0.0125 M	100	1 h 30 min	N/A	38	[173]

17	DMSO	Borontrifluoride-etherate	0.05 M	100	45 min	N/A	69	[173]
10	Water-MIBK (1:3 v/v)*	HCl	0.25 M	140	15 min	~ 100	52	[174]
30	Water	HCl	0.25 M	180	3 min	50	18	[124]
50	Water-DMSO-MIBK-2-butanol (8:2:21:9 w/w)*	HCl	0.25 M	180	3 min	91	47	[124]
30	Water-DMSO-MIBK-2-butanol (8:2:21:9 w/w)*	H_2SO_4	0.25 M	180	3 min	85	42	[124]
30	Water-MIBK-2-butanol (10:21:9 w/w)*	H_3PO_4	0.25 M	180	3 min	65	30	[124]
10	Water-DMSO-MIBK-2-butanol (5:5:14:6 w/w)*	HCl	pH =1	170	4 min	95	64	[88]
2.5	DMSO	Acetic acid	0.007 M	80	5 h	74	20	[175]
8	Ethanol	NH_4Cl	1 wt%	100	12 h	97	25	[176]
8	Isopropanol	NH_4Cl	1 wt%	120	12 h	100	48	[176]
5	THF-DMSO (70:30 v/v)	Glucose-TsOH	2.5 wt%	160	1 h	99	69	[177]
7	DMF	Glucose-TsOH	5.6 wt%	130	1 h 30 min	98.3	42	[178]
7	DMA	Glucose-TsOH	5.6 wt%	130	1 h 30 min	97	42	[178]
7	NMP	Glucose-TsOH	5.6 wt%	130	1 h 30 min	97.9	60	[178]
7	DMSO	Glucose-TsOH	5.6 wt%	130	1 h 30 min	99.9	64	[178]
20	Water-MIBK (10:90 v/v)*	SPC 108	$0.61*10^{-3}$ (meq. H^+/mol fructose)	88	15 h	84	39	[179]
20	Water-MIBK (10:90 v/v)*	Spherosil S	$0.15*10^{-3}$ (meq. H^+/mol fructose)	88	15 h	100	34	[179]
25	Water	Aluminium sulphate octadecahydrate	0.8 wt%	271	11 s	N/A	35	[95]
4	Water	HCl; ROX 0.8 activated carbon	1 M HCl; 220 wt% ROX 0.8	90	7 h	79	29	[180]

4	Water	OC 1052 ion exchange resin; ROX 0.8 activated carbon	440 wt% OC 1052; 220 wt% ROX 0.8	90	48 h	83	34	[180]
10	Acetone-DMSO (70:30 w/w)	DOWEX 50WX8-100 cation exchange resin	4 wt%	150	20 min	99	58	[128]
20	Water-MIBK (10:90 v/v)*	Lewatitt SPC 118 ion exchange resin	$0.61*10^{-3}$ (meq. H^+/mol fructose)	88	15 h	85	39	[181]
20	Water-MIBK (10:90 v/v)*	Spherosil S ion exchange resin	$0.125*10^{-3}$ (meq. H^+/mol fructose)	88	15 h	100	34	[181]
10	Water-DMSO-PVP-MIBK-2-butanol (56:14:30:210:90 w/w)*	Ion-exchange resin	10 wt%	90	8-16 h	76	41	[124]
30	Water-DMSO-PVP-MIBK-2-butanol (56:14:30:210:90 w/w)*	Ion-exchange resin	30 wt%	90	8-16 h	83	38	[124]
30	Water-MIBK*	Niobium phosphate	30 wt%	180	8-16 h	62	32	[124]
1	Water	Niobic acid	5 wt%	180	2 h	92	13	[171]
1	THF	TiO_2 nanoparticles	0.5 wt%	150	3 h	>99	38	[182]
2	GVL-Water (9:1 w/w)	Amberlyst-70	3.3 wt%	130	9 min	89	50	[183]
2	GHL-Water (9:1 w/w)	Amberlyst-70	3.3 wt%	130	10 min	91	52	[183]
2	THF-Water (9:1 w/w)	Amberlyst-70	3.3 wt%	130	10 min	91	54	[183]
30	Water-MIBK (1: 4 v/v)*	$B(OH)_3$; $MgCl_2$	9 wt% ($B(OH)_3$); 39 wt% ($MgCl_2$)	150	45 min	81	52	[184]
3	DMF	Al/Mg hydrotalcite; Amberlyst-15	3 wt% (Al/Mg hydrotalcite); 3 wt% (Amberlyst-15)	100	3 h	>99	53	[185]

10	Water-MIBK (1: 5 v/v)*	Silicoaluminophosphate (SAPO)-44	2.9 wt%	175	1 h	89	55	[186]
2.5	DMSO	Nafion R50 ion exchange resin	1 wt%	80	5 h	95	55	[175]
2.5	DMSO	$CaCl_2$	0.08 wt%	80	5 h	95	39	[175]
9	Water-MIBK (1: 3 v/v)*	$Ag_3PW_{12}O_{40}$	0.3 wt%	120	1 h	83	54	[187]
9	Water-MIBK (1: 3 v/v)*	$H_3PW_{12}O_{40}$	0.27 wt%	120	1 h	86	31	[187]
5	DMSO	H-ZSM-5 zeolite	2.5 wt%	110	N/A	N/A	46	[188]
3.5	Water-MIBK (1: 1 v/v)*	SiO_2/H-MOR zeolites	0.7 wt%	165	5 h	75	33	[25]
0.5	Water-DMSO-THF (9:1:30 v/v)	Beta-Cal500	0.002 wt%	180	3 h	96	47	[189]
2.4	Water-Benzonitrile (1:9 v/v)*	Lewatit SPC 108 ion exchange resin	2 wt %	89	5 h	82	41.6	[190]
N/A	Water	Lewatit SPC 108 ion exchange resin	1.3 (meq. H^+/mol fructose)	78	7 h	N/A	52	[191]
3	DMSO	$GeCl_4$;LiCl	0.4 wt% $GeCl_4$;0.7 wt% LiCl	25	10 h	N/A	40	[118]
3	DMF	$GeCl_4$	0.4 wt%	25	12 h	N/A	25	[118]
0.5	DMSO	$H_3PW_{12}O_{40}$	50 wt%	120	2 h	97.9	68	[123]
0.5	sec-Butanol	$[MIMPS]_3PW_{12}O_{40}$	50 wt%	120	2 h	99.7	69	[123]
8	DMSO	Supported 1-(tri-ethoxy silyl-propyl)-3-methyl-imidazolium hydrogen sulphate nanoparticles	6 wt%	130	30 min	99.9	44	[109]
10	DMA	H_2SO_4; NaBr	6 mol% of substrate (H_2SO_4); 10 wt% (NaBr)	100	2 h	N/A	65	[192]
8	DMSO	Bi-functional polymeric ionic liquid	2.4 wt%	120	1 h	98.7	63	[193]

6	Water	γ-L-ZrP_2O_7	55 wt% of substrate	100	1 h	31.7	17	[112]
6	Water	C-ZrP_2O_7	55 wt% of substrate	100	1 h	52.2	31	[112]
6	Water	α-TiP	55 wt% of substrate	100	30 min	29.1	20	[112]
6	Water	γ –TiP	55 wt% of substrate	100	1 h	46.8	29	[112]
6	Water	C-TiP_2O_7	55 wt% of substrate	100	2 h	38.7	20	[112]
6	Water	Niobium Phosphate	4.3 wt%	100	3 h	48	23	[113]
30	Water	$[Fe(H_2O)]_{0.27}(VO)_{0.73}PO_4.2H_2O$	0.5 wt%	80	1 h	70.8	42	[194]
5	Water	$YbCl_3$	7 mol% of substrate	140	1 h	N/A	13	[111]
1.5	Water	H-Mordenite (Si:Al=11)	30 wt% of substrate	165	1 h	76	48	[195]
~75	1,4-dioxane	AC-SO_3H	12 mol% of substrate	120	4 h	N/A	46	[107]
6	Water	H_3PO_4-treated niobic acid	60% of substrate	110	30 min	31.2	20	[196]
8	Water	Niobium Phosphate	100% of substrate	130	30 min	57.6	31.5	[104]
5.6	Water	HSO_3-grafted polyethylene fibre	8.6 wt%	120	6 h	72	24	[108]
9	Water	α-$Sr(PO_3)_2$	10 wt% of substrate	200	5 min	88	55	[197]
1	Water	Zirconium phosphate	50 wt% of substrate	240	2 min	80.9	35	[198]
9	Water	α-$Cu_2P_2O_7$	10 wt% of substrate	200	5 min	82.2	25	[199]
9	Water	H_3PO_4	0.1 M	200	5 min	95	29	[200]
2	DMSO	$Sc(OTf)_3$	10 wt% of substrate	120	2 h	100	58	[201]

The following details are important and hence summarised from Table 2-3:

1. For liquid catalysts, the conversion of fructose to HMF occurs with higher HMF yields at low pH values. However, for the same pH value, different acids give different results, with HCl being the most successful catalyst in terms of both fructose conversion and HMF yield,

followed by H_2SO_4 and H_3PO_4. The numerous other acids tried, such as citric, maleic, oxalic and formic, give inferior results even at high concentrations.

2. The creation of a biphasic solvent system by the addition of an immiscible organic liquid like MIBK to water increases HMF yield. For instance, a water-MIBK or a water-DMSO-MIBK-butanol biphasic system shows much higher fructose conversion (>90%) and HMF yield (~50%) than a purely aqueous system under comparable conditions. This confirms the point raised in Section 2.6.2.3 about extracting solvents increasing HMF yields by reducing its rehydration.
3. Among solid catalysts, ion exchange resins enable the reaction to occur at relatively low temperatures (< 100 ^oC) with high yields (~50%). The downside is the long reaction times required, of the order of 5 hours or longer.
4. Solid acid catalysts such as niobium phosphate get deactivated fairly rapidly for continuous processes, possibly due to the deposition of insoluble humins or coke on the catalyst surface [202]. On the other hand, the deposition of secondary products on the catalyst surface may be responsible for an increase in HMF selectivity with increased fructose conversion under flow conditions [202]. A greater understanding of these contrasting factors is required to optimise catalyst life and HMF yields.
5. Given the respective molecular weights (180 for fructose and 126 for HMF), the maximum wt% yield that can be obtained is 70%. There are a few solvent-catalyst systems that arrive close to achieving this figure. These are DMSO: Borontrifluoride-etherate, THF-DMSO:glucose-TsOH, DMSO: $H_3PW_{12}O_{40}$ and sec-butanol:$[MIMPS]_3PW_{12}O_{40}$.
6. Most of the experiments were conducted at low fructose concentrations (<10%), which is unlikely to be economical at a commercial scale. At higher concentrations (30% or higher), HMF yields tend to be significantly lower. The most promising systems at high concentrations are water-MIBK:$B(OH)_3$-$MgCl_2$, and water-DMSO-MIBK-butanol:HCl.

Table 2-4: Laboratory-scale production of HMF from monosaccharides other than fructose (solvent systems marked with * are biphasic systems)

Substrate (conc. in wt%)	Solvent	Catalyst	Catalyst conc.	Temp. (°C)	Reaction/ residence time	Conversion (%)	Yield (wt%)	Ref
Sorbose (1.5)	Tetrahydrofurfuryl alcohol	H_2SO_4	N/A	178	5 s	N/A	49	[172]
Glucose (9)	Water-MIBK (1: 3 v/v)*	$Ag_3PW_{12}O_{40}$	1.2 wt%	130	4 h	89	53	[187]
Glucose (0.5)	Water-DMSO-THF (9:1:30 v/v)	Beta-Cal750/Beta-ST600	0.4 wt%	180	3 h	78	30	[189]
Glucose (25)	Water	Aluminium sulphate octadecahydrate	0.8 wt%	271	10 s	N/A	31	[95]
Sorbose (25)	Water	Aluminium sulphate octadecahydrate	0.8 wt%	271	11 s	N/A	25	[95]
Galactose (25)	Water	Aluminium sulphate octadecahydrate	0.8 wt%	271	12 s	N/A	26	[95]
Sorbose (30)	Glycol monomethyl ether-water (8:11 w/w)	H_2SO_4	0.3 wt%	180	3 min	78.4	36	[167]
Sorbose (30)	Dichloroethyl ether-water (9:12 w/w)	H_2SO_4	0.3 wt%	180	1 m 48 s	79.5	37	[167]
Sorbose (30)	MIBK-water (8:11 w/w)	H_2SO_4	0.3 wt%	180	3 min	81.5	37	[167]
Sorbose (30)	Mesityl oxide-water (19:8 w/w)	HCl	0.07 wt%	180	2 min	74.5	39	[167]
Sorbose (30)	Triethylene glycol-water (67:12 w/w)	HCl	0.04 wt%	180	3 min	83.6	47	[167]
Glucose (30)	Dioxane-water (104:17 w/w)	$AlCl_3.6H_2O$	0.06 wt%	210	3 min	79.2	29	[167]
Glucose (30)	Sym. dimethyl dioxane-water (159:82 w/w)	$AlCl_3.6H_2O$;HCl	0.06 wt%;0.03 wt%	210	2 min 30 s	78.9	29	[167]
Glucose (12)	Water	MCM-20	3 wt%	150	24 h	62	14	[203]
Glucose (5)	Water-2-sec-butylphenol (1:2 w/w)	HCl; $AlCl_3$	0.1 M HCl; 0.005 M AlCl3	170	35 min	91	43	[204]

Glucose (25)	Water	Oxalic acid	0.2 wt%	170-190	1 h	N/A	3.4	[89]
Sorbose (N/A)	Water	Lewatit SPC 108 ion exchange resin	1.3 (meq. H^+/mol sorbose)	78	12 h	N/A	33	[191]
Glucose (3)	DMSO	Borontrifluoride-etherate	0.0125 M	100	48 h	N/A	29	[173]
Glucose (20)	Water-p-dioxane (1:1 v/v)	Pyridine; H_3PO_4	0.9 wt% pyridine; 0.7 wt% H3PO4	200-228	53 min	N/A	32	[65]
Glucose (25)	Water	KOH; Oxalic acid	(1.25%+1.25%+0.5%+0.25%) KOH; 0.25% oxalic acid	50	(48+24+16+24) h	N/A	37	[64]
Glucose (1)	Water	NbOH	1 wt%	150	2 h	78	20	[171]
Glucose (2)	GVL-Water (9:1 w/w)	Amberlyst-70; Sn-β	3.3 wt% Amberlyst-70; 3.3 wt% Sn-β	130	20 min	92	41	[183]
Glucose (2)	GHL-Water (9:1 w/w)	Amberlyst-70; Sn-β	3.3 wt% Amberlyst-70; 3.3 wt% Sn-β	130	10 min	93	38	[183]
Glucose (2)	THF-Water (9:1 w/w)	Amberlyst-70; Sn-β	3.3 wt% Amberlyst-70; 3.3 wt% Sn-β	130	10 min	90	44	[183]
Glucose (10)	Water-DMSO-MIBK-2-butanol (5:5:14:6 w/w)*	HCl	pH =1	170	17 min	50	18	[88]
Glucose (30)	Water-MIBK (1:4 v/v)	Boric acid; NaCl	10 wt% Boric acid; 5 wt% NaCl	150	5 h	41	14	[184]
Glucose (4)	DMA	$CrCl_2$	0.3 wt%	120	3 h	100	40	[205]
Glucose (4)	DMSO	$CrCl_2$	0.3 wt%	120	3 h	100	27	[205]
Glucose (4)	DMF	$CrCl_2$	0.3 wt%	120	3 h	100	35	[205]
Glucose (10)	Water-MIBK (1: 5 v/v)*	Silicoaluminophosphate (SAPO)-44	2.9 wt%	175	4 h	83	47	[186]
Glucose (3)	DMF	Al/Mg hydrotalcite; Amberlyst-15	6 wt% (Al/Mg hydrotalcite); 3 wt% (Amberlyst-15)	80	9 h	73	30	[185]
Glucose (5)	DMSO	$AlCl_3$	10 mol% of substrate	130	4 h	N/A	37	[206]

Glucose (N/A)	Water-DMSO-MIBK-n-Butanol (2:8:3:7 v/v)*	Bi-functional polymeric ionic liquid	N/A	150	2 h	N/A	34	[193]
Glucose (5)	DMAC	AlI_3	10 mol% of substrate	120	15 min	>99	36	[207]
Mannose (10)	DMA	$CrCl_2$ + LiBr	6 mol% of substrate (CrCl2); 10 wt% (LiBr)	100	2 h	N/A	48	[208]
Galactose (10)	DMA	$CrBr_3$	6 mol% of substrate	120	3 h	N/A	23	[208]
Tagatose (10)	DMSO	H_2SO_4	6 mol% of substrate	120	2 h	N/A	43	[208]
Psicose (10)	DMSO	H_2SO_4	6 mol% of substrate	120	3 h	N/A	57	[208]
Sorbose (10)	DMSO	H_2SO_4	6 mol% of substrate	120	3 h	N/A	42	[208]
Glucose (10)	DMA	$CrBr_3$; LiBr	6 mol% of substrate ($CrBr_3$); 10 wt% (LiBr)	100	6 h	N/A	56	[192]
Glucose (3)	DMF	Amberlyst-15; Hydrotalcite	100 wt% of substrate (Amberlyst-15); 200 wt% of substrate (Hydrotalcite)	100	3 h	73	29	[209]
Glucose (7.6)	DMSO	CSZA-3	1.8 wt%	130	6 h	100	34	[210]
Glucose (5)	THF-DMSO (7:3 v/v)	Sn-Mont	3.3 wt%	160	3 h	98.4	37	[101]
Glucose (10)	Water-THF (1:3 v/v)*	Sn-Beta; HCl; NaCl	0.5 mol% of substrate (Sn-Beta); pH=1 (HCl); 3.5 wt% of substrate (NaCl)	180	1 h 10 min	79	57	[211]
Glucose (2)	Water	$ZnCl_2$	5 mol% of substrate	140	6 h	52	10	[212]
Glucose (9)	Water	α-$Sr(PO_3)_2$	10 wt% of substrate	220	5 min	61	15	[197]
Glucose (10)	Water-THF (1:2 v/v)*	HCl; $CrCl_3$; NaCl	0.1 M HCl; 18.6 mM $CrCl_3$	140	3 h	95	41	[22]

It can be seen from Table 2-4 that in general, HMF yields from monosaccharides other than fructose are considerably lower than those obtained from fructose. This illustrates the importance of a catalytic system that facilitates the isomerisation of other monosaccharides, particularly glucose, into fructose. The highest HMF yield from glucose is obtained using $CrBr_3$ and LiBr as catalysts in DMA solvent. This has been attributed to the ability of chromium to isomerise glucose to fructose and of the bromide ligand to facilitate the selective conversion of fructose [192]. High yields from glucose are also obtained in a biphasic solvent system (Water-MIBK) with $Ag_3PW_{12}O_{40}$ as the catalyst, whose high activity is attributed to the synergistic effect of Lewis acid sites and Brønsted acid sites [187]. Psicose, which is the C-3 epimer of fructose, has a high furanose propensity like fructose, and this is the reason for it being readily converted to HMF [208]. However, since psicose is a sugar that rarely exists in nature [213], its practical utility is very limited. At substrate concentrations of 30% or more, the most notable yield (47%) comes from the triethylene glycol-water: HCl system when used on sorbose, which is another rare sugar.

Table 2-5: Laboratory-scale production of HMF from oligosaccharides and polysaccharides (solvent systems marked with * are biphasic systems)

Substrate (conc. in wt%)	Solvent	Catalyst	Catalyst conc.	Temp. (°C)	Reaction/ residence time	Conversion (%)	Yield (wt%)	Ref
Kestose (1.5)	Tetrahydrofurfuryl alcohol	H_2SO_4	N/A	178	5 s	N/A	47	[172]
Inulin (1.5)	Tetrahydrofurfuryl alcohol	H_2SO_4	N/A	178	5 s	N/A	47	[172]
Sucrose (25)	Water	Aluminium sulphate octadecahydrate	0.4 wt%	271	8.2 s	N/A	38	[95]
Sucrose (30)	Dioxane-water (39:7 w/w)	$CrCl_3.6H_2O$;HCl	0.07 wt% ($CrCl_3.6H_2O$);0.04 wt% (HCl)	210	4 min	82.6	36	[167]
Sucrose (30)	Tetrahydro-2-methyl furan-water (41:20 w/w)	$AlCl_3.6H_2O$;HCl	0.06 wt% ($AlCl_3.6H_2O$);0.03 wt% (HCl)	210	2 min	81.5	34	[167]
Sucrose (30)	Dioxane-water (76:39 w/w)	$AlCl_3.6H_2O$;HCl	0.4 wt% ($AlCl_3.6H_2O$);0.05 wt% (HCl)	150	23 min	72.9	31	[167]
Sucrose (25)	Water	H_3PO_4	0.17 wt%	157-177	1 h	N/A	12.6	[89]
Sucrose (25)	Water	Maleic acid	0.2 wt%	160-180	1 h	N/A	13.2	[89]

Sucrose (25)	Water	Fumaric acid	0.2 wt%	175-195	1 h	N/A	11	[89]
Sucrose (25)	Water	HCl	0.02 wt%	160-180	1 h	N/A	14.1	[89]
Sucrose (25)	Water	Oxalic acid	0.17 wt%	150-160	3 h	N/A	18.5	[214]
Sucrose (25)	Water	Oxalic acid	0.17 wt%	125-145	2 h 30 min	N/A	20	[64]
Sucrose (2)	Water	H_2SO_4	1 mM	250	32 s	100	18	[66]
Starch (3)	Water	Boron trifluoride etherate	0.39 cc/g starch	100	48 h	N/A	29	[173]
Cellulose (4)	Water	Zirconium phosphate	4 wt%	220	15 min	36	10	[97]
Inulin (10)	Water-DMSO-MIBK-2-butanol (5:5:14:6 w/w)*	HCl	pH =1.5	170	5 min	98	63	[88]
Cellobiose (10)	Water-DMSO-MIBK-2-butanol (4:6:14:6 w/w)*	HCl	pH =1	170	10 min	52	22	[88]
Sucrose (10)	Water-DMSO-MIBK-2-butanol (4:6:14:6 w/w)*	HCl	pH =1	170	5 min	65	39	[88]
Starch (10)	Water-DMSO-MIBK-2-butanol (4:6:14:6 w/w)*	HCl	pH =1	170	11 min	61	22	[88]
Sucrose (3)	DMF	Al/Mg hydrotalcite; Amberlyst-15	100 wt% (Al/Mg hydrotalcite); 100 wt% (Amberlyst-15)	120	3 h	58	42	[185]
Cellobiose (3)	DMF	Al/Mg hydrotalcite; Amberlyst-15	100 wt% (Al/Mg hydrotalcite); 100 wt% (Amberlyst-15)	120	3 h	52	27	[185]
Maltose (10)	Water-MIBK (1: 5 v/v)*	Silicoaluminophosphate (SAPO)-44	2.9 wt%	175	4 h	100	44	[186]
Cellobiose (10)	Water-MIBK (1: 5 v/v)*	Silicoaluminophosphate (SAPO)-44	2.9 wt%	175	6 h	100	44	[186]
Starch (10)	Water-MIBK (1: 5 v/v)*	Silicoaluminophosphate (SAPO)-44	2.9 wt%	175	6 h	100	53	[186]

Sucrose (N/A)	Water	Lewatit SPC 108 ion exchange resin	1.35 (meq. H$^+$/mol sucrose)	78	12 h	N/A	64	[191]
Raffinose (N/A)	Water	Lewatit SPC 108 ion exchange resin	4.78 (meq. H$^+$/mol raffinose)	78	10 h	N/A	62	[191]
Inulin (N/A)	Water	Lewatit SPC 108 ion exchange resin	1.3 (meq. H$^+$/mol inulin)	78	12 h	N/A	52	[191]
Cellulose (2)	Water-THF (1:10 v/v)*	$NaHSO_4$ + $ZnSO_4$	1.8 mmol/g cellulose ($NaHSO_4$), 2.8 mmol/g cellulose ($ZnSO_4$)	160	1 h	96	41	[131]
Agarose (2)	Water	$MgCl_2$	1 wt% of substrate	200	35 min	82.9	32	[215]
Cellulose (2)	DMSO	$AlCl_3$, H_2SO_4	10 mol% of substrate (AlCl3); 40 mol% of substrate (H_2SO_4)	150	9 h	N/A	24	[206]
Lactose (10)	DMA	$CrBr_3$	6 mol% of substrate	120	3 h	N/A	32	[208]
Cellulose (5)	THF-Water (5:1 v/v)*	Sn-Mont; NaCl	3 wt% (Sn-Mont); 6 wt% (NaCl)	160	3 h	N/A	30	[101]
Starch (5)	THF-Water (5:1 v/v)*	Sn-Mont; NaCl	3 wt% (Sn-Mont); 6 wt% (NaCl)	160	3 h	N/A	35	[101]
Inulin (6)	Water	C-ZrP$_2$O7	55 wt% of substrate	100	2 h	50.2	28	[112]
Inulin (6)	Water	γ –TiP	55 wt% of substrate	100	2 h	91.9	51	[112]
Inulin (6)	Water	Niobium Phosphate	4.3 wt%	100	3 h	46.9	24	[113]
Inulin (6)	Water	$[Fe(H_2O)]_{0.27}(VO)_{0.73}PO_4.2H_2O$	4 wt%	80	1 h	50.2	31	[194]
Cellulose (9)	Water	α-$Sr(PO_3)_2$	10 wt% of substrate	230	5 min	N/A	12	[197]

The fact that the production of HMF from polysaccharides involves the hydrolysis of the polysaccharide molecules into simple sugars, either in situ or in an additional acid hydrolysis step, means that the HMF yields obtained from polysaccharides are, in general, lower than those obtained from monosaccharides, in particular fructose. Table 2-5 shows that the highest yields are obtained from the polyfructan inulin, while in case of polyglucans like starch and cellulose, biphasic solvent systems with solid catalysts like silicoaluminophosphate or sodium bisulphate and zinc sulphate appear to be the most suitable. Ion-exchange resins are also capable of giving high HMF yields from sucrose and raffinose, but only with reaction times of 10 hours or more.

Table 2-6: Use of ionic liquid systems to produce HMF from different feedstock

Substrate (conc. in wt%)	Ionic liquid	Co-solvent	Added catalyst	Temp. (ºC)	Reaction time	Conversion (%)	Yield (wt %)	Ref
Fructose (10)	[EMIM]Cl (93%)	-	-	84-87	1 h	90	60	[216]
Fructose (10)	[EMIM]Cl (93%)	-	H_2SO_4 (0.1 M)	84-87	5 min	100	58	[216]
Fructose (10)	[EMIM]Cl (93%)	-	$AlCl_3$ (0.1 M)	84-87	5 min	100	53	[216]
Fructose (10)	Cyphos 106	-	-	110	10 min	100	64	[216]
Fructose (2.5)	[BMIM]Cl	DMSO (1.8 mol/mol ionic liquid)	-	80	5 h	95	55	[175]
Fructose (35)	[DiEG(mim)2][OMs]2	-	-	120	40 min	100	49	[141]
Fructose (32)	[TriEG(mim)2][OMs]2	-	-	120	40 min	100	54	[141]
Fructose (30)	[TetraEG(mim)2][OMs]2	-	-	120	40 min	100	65	[141]
Fructose (21)	[TetraEG(mim)2][OMs]2	-	$NiCl_2.6H_2O$ (equimolar with fructose)	100	40 min	100	57	[141]
Fructose (24)	[TetraEG(mim)2][OMs]2	-	$FeCl_3$ (equimolar with fructose)	100	40 min	100	51	[141]
Fructose (21)	[TetraEG(mim)2][OMs]2	-	$CoCl_2.6H_2O$ (equimolar with fructose)	100	40 min	100	52	[141]
Fructose (21)	[TetraEG(mim)2][OMs]2	-	$CuCl_2.6H_2O$ (equimolar with fructose)	100	40 min	100	45	[141]

Fructose (5)	[HexylMIM]Cl	-	Sulphated zirconia (2 wt %)	100	30 min	100	62	[217]
Fructose (5)	[BMIM]Cl	-	Sulphated zirconia (2 wt %)	120	10 min	97.3	60	[217]
Fructose (10)	[OMIM]Cl	MIBK (EIVRD entrainer)	IrCl$_3$.(1-2)H$_2$O (0.3 wt%)	180	10 min	100	67	[156]
Fructose (10)	[OMIM]Cl	Hexane (EIVRD entrainer)	IrCl$_3$.(1-2)H$_2$O (0.3 wt%)	180	10 min	100	66	[156]
Fructose (5)	[BMIM]Cl	[bi-C$_3$SO$_3$HMIM] [HSO$_4$] (9 mol% of fructose)	MnCl$_2$ (3 mol% of fructose)	120	10 min	N/A	64	[218]
Fructose (9)	[EMIM]Cl	-	-	120	3 h	100	51	[219]
Fructose (8)	[EMIM][HSO4] (30% v/v)	MIBK (70% v/v)	-	100	30 min	100	62	[151]
Fructose (8)	[EMIM][HSO4] (30% v/v)	Toluene (70% v/v)	-	100	30 min	100	55	[151]
Fructose (3)	[BMIM]Cl (83% w/w)	DMSO (17% w/w)	GeCl$_4$ (10 mol% of fructose)	25	12 h	N/A	50	[118]
Fructose (10)	[BMIM]Cl	-	Dowex 50Wx8-200 ion exchange resin (10 wt%)	100	4 h	N/A	42	[110]
Fructose (<9)	[BMIM]Cl	-	1,3-bis(2,6-diisopropylphenyl) imidazolylidene /CrCl2 (9 mol% of fructose)	100	6 h	N/A	67	[220]
Fructose (8)	BMIM+BF4- (72% v/v)	DMSO (38% v/v)	Amberlyst-15 (200 wt% of fructose)	80	32 h	N/A	61	[221]
Fructose (8)	BMIM+PF6- (72% v/v)	DMSO (38% v/v)	Amberlyst-15 (200 wt% of fructose)	80	24 h	N/A	55	[221]
Fructose (5)	[BMIM]Cl	-	Amberlyst-15 (100 wt% of fructose)	80	10 min	99.6	58	[159]
Fructose (20)	[BMIM]Cl	-	SBA-15-SO$_3$H (5 wt% of fructose)	120	1 h	~100	57	[222]

Fructose (10)	[BMIM]Cl	-	H_2SO_4 (10 wt% of fructose)	120	1 h	100	58	[222]
Fructose (1.5)	[C2OHMIM]BF4	DMSO	-	160	2 h	N/A	67	[223]
Fructose (3)	[CMIM]Cl	DMSO	-	120	2 h	100	67	[224]
Fructose (9)	[BMIM]Cl	-	P_2O_5 (50 mol% of fructose)	50	1 h	N/A	57	[225]
Fructose (6)	[BMIM]Cl	-	D001-cc ion exchange resin (6 wt%)	75	20 min	~100	65	[226]
Fructose (9)	[BMIM]Cl	-	Cellulose-derived carbonaceous catalyst (40 wt% of substrate)	160	15 min	N/A	57	[227]
Fructose (5)	$[C_6(mpy)_2][NiCl_4]_2$- (15 wt%)	DMSO (85 wt%)	-	110	1 h	95.6	67	[228]
Fructose (33)	TEAC	-	-	120	1 h 10 min	100	57	[229]
Fructose (50)	TEAC	-	$NaHSO_4.H_2O$ (5 mol% of substrate)	120	1 h 10 min	100	55	[229]
Fructose (9)	[BMIM]Cl	-	HCl (9 mol% of fructose)	80	8 min	N/A	68	[230]
Fructose (33)	[BMIM]Cl	-	HCl (9 mol% of fructose)	80	35 min	90	57	[230]
Fructose (67)	[BMIM]Cl	-	HCl (9 mol% of fructose)	80	2 h	67	36	[230]
Fructose (9)	[BMIM]Cl	-	-	120	50 min	93.4	44	[231]
Fructose (9)	[EMIM]Br	-	$Sn[(O_3PCH_2)_2N CH_2CO_2H]$ (25% of substrate)	100	1 h 30 min	98	61	[232]
Fructose (9)	[EMIM]Br	-	$Zr[(O_3PCH_2)_2N CH_2CO_2H]$ (25% of substrate)	100	1 h 30 min	N/A	55	[232]
Fructose (25)	[HMIM]Cl	-	-	90	45 min	~ 100	64	[135]
Fructose (1)	Choline chloride citric acid monohydrate (17% w/w)	Ethyl acetate (83% w/w)	-	80	1 h	97.6	64	[162]

Fructose (38)	Choline chloride	-	pTsOH (4 wt %)	100	30 min	N/A	47	[121]
Glucose (38)	Choline chloride	-	$CrCl_2$ (10 mol%)	110	30 min	N/A	32	[121]
Glucose (5)	[BMIM]Cl	-	H-ZSM-5 (10 wt%)	110	8 h	N/A	32	[188]
Glucose (13)	TEAC (33% v/v)	DMA (67% v/v)	$CrCl_2$ (0.9 wt%)	110	4 h	N/A	39	[188]
Glucose (10)	[EMIM]Cl (93%)	-	$CrCl_2$ (0.1 M)	100	3 h	86	34	[216]
Glucose (30)	$[TetraEG(mim)_2][OMs]_2$	-	-	120	2 h 15 min	100	51	[141]
Glucose (10)	[AMIM]Cl/[EMIM]Cl/ [BMIM]Cl	-	$CrCl_3.6H_2O$ (6 mol% of glucose)	120	30 min	93	48	[233]
Glucose (9)	[EMIM]Cl	-	$CrCl_2$ (6 mol% of glucose)	100	3 h	94	48	[219]
Glucose (2.5)	[HexylMIM][Cl] (50% w/w)	Water (50% w/w)	ZrO_2 (1 wt%)	200	10 min	92	37	[73]
Glucose (16)	[EMIM]Cl	-	$AlEt_3$ (10 mol% of glucose)	120	6 h	100	36	[234]
Glucose (16)	[EMIM]Cl	-	$MeAl(BHT)_2$ (10 mol% of glucose)	120	6 h	100	35	[234]
Glucose (3)	[EMIM]Cl	DMA	$CrCl_2$ (10 mol% of glucose)	120	3 h	100	41	[205]
Glucose (3)	P[BVIM]Cl	DMF	$CrCl_2$ (10 mol% of glucose)	120	3 h	100	46	[205]
Glucose (3)	P[BVIM]Cl	DMF	Et_2 AlCl (10 mol% of glucose)	120	3 h	100	34	[205]
Glucose (9)	[EMIM]Cl	-	$CrCl_3(THF)_3$ (6 mol% of glucose)	100	3 h	N/A	50	[235]
Glucose (10)	[BMIM]Cl	-	Dowex 50Wx8-200 ion exchange resin (10 wt%)	100	4 h	N/A	49	[110]
Glucose (10)	[BMIM]Cl	-	Amberlyst 15 ion exchange resin	100	6 h	N/A	43	[110]
Glucose (8)	[BMIM]Cl	-	H_2SO_4 (0.01 mmol)	120	3 h	93	43	[98]
Glucose (8)	[BMIM]Cl	-	HNO_3 (0.01 mmol)	120	3 h	56	30	[98]

Glucose (8)	[BMIM]Cl	-	$H_3PW_{12}O_{40}$ (0.01 mmol)	120	3 h	82	46	[98]
Glucose (8)	[EMIM]Cl / [BMIM]Cl (72% w/w)	Acetonitrile (28% w/w)	$H_3PMo_{12}O_{40}$ (0.01 mmol)	120	3 h	99	68	[98]
Glucose (9)	[OMIM]Cl	MIBK (EIVRD entrainer)	$CrCl_3.6H_2O$ (0.2 wt%)	180	10 min	100	50	[156]
Glucose (9)	[OMIM]Cl	Hexane (EIVRD entrainer)	$CrCl_3.6H_2O$ (0.2 wt%)	180	10 min	100	49	[156]
Glucose (5)	[BMIM]Cl	[bi-C_3SO_3HMIM] [HSO_4] (9 mol% of sugar)	$MnCl_2$ (3 mol% of sugar)	120	2 h	N/A	41	[218]
Galactose (5)	[BMIM]Cl	[bi-C_3SO_3HMIM] [HSO_4] (9 mol% of sugar); Water	$MnCl_2$ (3 mol% of sugar)	120	1 h	N/A	11	[218]
Glucose (<9)	[BMIM]Cl	-	1,3-bis(2,6-diisopropylphenyl) imidazolylidene /$CrCl_2$ (9 mol% of glucose)	100	6 h	N/A	57	[220]
Glucose (1.5)	[C_2OHMIM]BF_4	DMSO	-	180	1 h	N/A	47	[223]
Glucose (3)	[CMIM]Cl	DMSO	$ZrOCl_2.8H_2O$ (100 mol% of glucose)	120	7 h	N/A	35	[224]
Glucose (10)	[BMIM]Cl	-	12-tungstophosphoric acid (20 wt% of glucose) + boric acid (10 wt% of glucose)	140	40 min	N/A	36	[115]
Glucose (9)	[BMIM]Cl	-	$CrCl_3.6H_2O$ (10 mol% of glucose) + $B(OH)_3$ (20 mol% of glucose)	120	30 min	N/A	55	[236]
Glucose (9)	[BMIM]Cl	-	Cellulose-derived carbonaceous catalyst (40	160	15 min	77.8	33	[227]

			wt% of substrate)					
Glucose (9)	TEAC	-	$CrCl_3.6H_2O$ (10 mol% of glucose) + $B(OH)_3$ (20 mol% of glucose)	120	30 min	N/A	52	[236]
Glucose (9)	[EMIM]Cl	-	$CrCl_3.6H_2O$ (6 mol% of glucose)	100	3 h	97	50	[237]
Glucose (16)	TEAC	-	$CrCl_2$ (0.03 M)	120	1 h	N/A	36	[165]
Glucose (9)	[EMIM]Cl	-	Boric acid (2.5 wt%)	120	1 h	95	29	[116]
Glucose (9)	[BMIM]Cl/[BEMIM]Cl	-	$CrCl_3.6H_2O$ (25 mol% of substrate)	120	1 h	N/A	47	[231]
Glucose (23)	[EMIM]BF_4	-	$SnCl_4$ (10 mol% of substrate)	100	3 h	99	43	[150]
Glucose (9)	[OMIM]Cl	-	$YbCl_3$ (10 mol% of glucose)	160	1 h	100	15	[134]
Glucose (9)	[BMIM]Cl	-	$Yb(OTf)_3$ (10 mol% of glucose)	140	6 h	65	17	[134]
Glucose (8)	[EMIM]Br	-	Sn-MCM-41 (8 wt%)	110	4 h	99	49	[117]
Glucose (9)	TEAC	-	$CrCl_3.6H_2O$	130	10 min	N/A	50	[114]
Glucose (9)	[EMIM]Cl	-	3,5-bis(trifluoromethyl)phenylboronic acid	120	3 h	96	35	[238]
Sucrose (48)	Choline chloride	$CrCl_2$	10 mol%	100	1 h	N/A	48	[121]
Inulin (48)	Choline chloride	pTsOH	10 mol%	90	1 h	N/A	44	[121]
Lactose (10)	[BMIM]Cl	-	Dowex 50Wx8-200 ion exchange resin (10 wt%)	100	3 h	N/A	30	[110]
Trehalose (10)	[BMIM]Cl	-	Dowex 50Wx8-200 ion exchange resin (10 wt%)	100	3 h	N/A	40	[110]

Maltose (10)	[BMIM]Cl	-	Dowex 50Wx8-200 ion exchange resin (10 wt%)	100	3 h	N/A	38	[110]
Sucrose (10)	[BMIM]Cl	-	Dowex 50Wx8-200 ion exchange resin (10 wt%)	100	3 h	N/A	55	[110]
Raffinose (10)	[BMIM]Cl	-	Dowex 50Wx8-200 ion exchange resin (10 wt%)	100	3 h	N/A	37	[110]
Inulin (10)	[BMIM]Cl	-	Dowex 50Wx8-200 ion exchange resin (10 wt%)	100	3 h	N/A	52	[110]
Sucrose (22)	[TetraEG(mim)$_2$][OMs]$_2$	-	-	120	2 h 30 min	100	52	[141]
Cellulose (10)	[EMIM]Cl	-	$CuCl_2/CrCl_2$ (χCuCl2= 0.17) (37 μmol/g ionic liquid)	120	8 h	100	44	[149]
Cellulose (5)	1-(4-sulfonic acid) butyl-3-methylimidazolium hydrogen sulphate (24 wt%)	MIBK (76 wt%)	$CoCl_2$ (0.4 mol/kg cellulose)	150	5 h	81	27	[239]
Cellulose (5)	1-(4-sulfonic acid) butyl-3-methylimidazolium hydrogen sulphate (24 wt%)	MIBK (76 wt%)	$MnCl_2$ (0.4 mol/kg cellulose)	150	5 h	88.62	37.48	[240]
Cellulose (5)	[BMIM]Cl	-	Cr([PSMIM]HSO$_4$)$_3$ (50 wt% of cellulose)	120	5 h	95	41	[241]
Inulin (4)	[BMIM]Cl (95 wt%)	Water (5 wt%)	Amberlyst-15 resin	100	30 min	~100	48	[79]
Sucrose (9)	[BMIM]Cl	[bi-C$_3$SO$_3$HMIM] [HSO$_4$] (9 mol% of sugar); Water	$MnCl_2$ (3 mol% of sugar)	120	1 h	N/A	69	[218]
Maltose (9)	[BMIM]Cl	[bi-C$_3$SO$_3$HMIM] [HSO$_4$] (9 mol% of sugar); Water	$MnCl_2$ (3 mol% of sugar)	120	30 min	N/A	60	[218]
Lactose (9)	[BMIM]Cl	[bi-C$_3$SO$_3$HMI	$MnCl_2$ (3 mol% of sugar)	120	30 min	N/A	30	[218]

		M] [HSO_4] (9 mol% of sugar); Water						
Cellulose (5)	[BMIM]Cl	[bi-C_3SO_3HMIM] [HSO_4] (9 mol% of cellulose); Water	$MnCl_2$ (3 mol% of cellulose)	120	1 h	84.15	49	[218]
Cellulose (5)	[BMIM]Cl	[bi-C_3SO_3HMIM] [CH_3SO_3] (9 mol% of cellulose); Water	$MnCl_2$ (3 mol% of cellulose)	120	1 h	N/A	52	[218]
Cellulose (3)	[EMIM][Cl]	Water	[C_4SO_3MIM]CH_3SO_3; $CuCl_2$ (0.1 mol/l)	160	3 h 30 min	N/A	69.7	[242]
Inulin (3)	[CMIM]Cl	DMSO	-	120	3 h	N/A	69	[224]
Sucrose (3)	[CMIM]Cl	DMSO	$ZrOCl_2.8H_2O$ (100 mol% of substrate)	120	7 h	N/A	57	[224]
Cellobiose (3)	[CMIM]Cl	DMSO	$ZrOCl_2.8H_2O$ (100 mol% of substrate)	120	7 h	N/A	36	[224]
Cellulose (2)	[BMIM]Cl (10 wt%)	DMSO (90 wt%)	$AlCl_3$ (10 mol% of substrate)	150	9 h	N/A	43	[206]
Cellulose (2)	[BMIM]Cl (25 wt%)	DMSO (75 wt%)	Bi-functional polymeric ionic liquid (0.5 wt%)	160	5 h	N/A	24	[193]
Sucrose (9)	[BMIM]Cl	-	Cellulose-derived carbonaceous catalyst (40 wt% of substrate)	160	15 min	N/A	49	[227]
Maltose (9)	[BMIM]Cl	-	Cellulose-derived carbonaceous catalyst (40 wt% of substrate)	160	15 min	N/A	36	[227]
Cellobiose (9)	[BMIM]Cl	-	Cellulose-derived carbonaceous catalyst (40	160	15 min	N/A	35	[227]

			wt% of substrate)					
Starch (9)	[BMIM]Cl	-	Cellulose-derived carbonaceous catalyst (40 wt% of substrate)	160	15 min	N/A	33	[227]
Cellulose (9)	[BMIM]Cl	-	Cellulose-derived carbonaceous catalyst (40 wt% of substrate)	160	15 min	N/A	32	[227]
Cellulose (4)	[EMIM]Cl	-	$CrCl_2$ (25 mol%);HCl (6 mol%)	140	1 h	N/A	37	[192]
Cellulose (6)	[BMIM]Cl	-	Zeolite (100 wt% of substrate); $CrCl_2$ (3 wt% of substrate)	120	6 h	N/A	37	[243]
Sucrose (9)	[EMIM]Cl	-	Boric acid (50 mol% of substrate)	120	8 h	N/A	51	[116]
Maltose (9)	[EMIM]Cl	-	Boric acid (50 mol% of substrate)	120	8 h	N/A	26	[116]
Starch (9)	[EMIM]Cl	-	Boric acid (50 mol% of substrate)	120	24 h	N/A	26	[116]
Cellulose (9)	[EMIM]Cl	-	Boric acid (50 mol% of substrate)	120	8 h	N/A	26	[116]
Sucrose (17)	[EMIM]BF_4	-	$SnCl_4$ (10 mol% of substrate)	100	3 h	100	51	[150]
Inulin (9)	[EMIM]Br	-	$Sn[(O_3PCH_2)_2NCH_2CO_2H]$ (25% of substrate)	100	3 h	97	38	[232]
Sucrose (9)	[EMIM]Br	-	$Sn[(O_3PCH_2)_2NCH_2CO_2H]$ (25% of substrate)	100	3 h	99	35	[232]
Cellulose (1)	$[C_3SO_3Hmim][HSO_4]$	DMSO	InCl3 (1 wt%)	160	5 h	84.6	45.3	[244]

Cellulose (8)	[EMIM]Cl	-	3,5-bis(trifluoromethyl)phenylboronic acid	120	3 h	95	26	[238]
Cellulose (9)	[EMIM]Cl	-	$CrCl_3$ (3 wt% of substrate); $CuCl_2$ (3 wt% of substrate)	140	5 min	80	31	[245]
Sucrose (9)	Proline chlorate	Water	-	90	3 h	N/A	31	[140]
Cellulose (9)	[EMIM]Cl	-	$CuCl_2/CrCl_2$ (6 mol% of substrate)	120	4 h	N/A	33	[149]
Cellulose (16)	[EMIM]Cl	-	$CrCl_2$ (10 mol% of substrate)	120	6 h	N/A	69	[160]

Table 2-6 shows why ionic liquids are considered to be so promising, as high HMF yields are obtained from most feedstock at relatively low temperatures and short reaction times. In case of fructose, it is seen that high (44-67 wt%) yields can be obtained using ionic liquids even without any added catalyst. More importantly, however, high yields of HMF from glucose have also been reported by a number of researchers. One of the pioneering works in this respect was carried out by Zhao, et al., who used $CrCl_2$ as catalyst in [EMIM]Cl to obtain yields of nearly 70% from glucose [219].

Subsequently, even higher yields have been obtained by other researchers using either $CrCl_2$ or $CrCl_3.6H_2O$. A nearly quantitative yield has been achieved using the heteropolyacid $H_3PMo_{12}O_{40}$ [98]. It is important to note that the mechanism proposed by the researchers for the dehydration of glucose to HMF using $H_3PMo_{12}O_{40}$ has the ring opening of the pyranose form of glucose as the first step and does not involve the isomerisation of glucose to fructose.

Ionic liquids are also effective at converting polysaccharides to HMF. Cellulose is generally difficult to convert into HMF with high yields, but an [EMIM]Cl-based system attaining nearly 70% HMF yield from cellulose, albeit at low concentrations, has been reported. Inulin has also been converted nearly quantitatively to HMF in a [CMIM]Cl-DMSO system without an added catalyst.

The only substrate that appears to have been tested at high concentrations is fructose. Tetraethyl ammonium chloride (TEAC) and [BMIM]Cl-based systems have been used to convert fructose at concentrations of 50% or more to HMF with reasonable yields. For other feedstock, however, it remains to be seen how higher concentrations affect the output in ionic liquids. Choline chloride deserves special mention, as, in combination with catalysts like $CrCl_2$ and pTsOH, it can be used to obtain relatively high HMF yields from high concentrations of glucose, sucrose and inulin. One point to be noted is that [BMIM]Cl and [EMIM]Cl give higher HMF yields when chromium-based catalysts are used than ionic liquids containing more bulky cations such as [BEMIM]Cl , [HEMIM]Cl and [OMIM]Cl, which can be attributed to steric effects and the hydrophilicity of the imidazolium cations [134, 231]. However, when ytterbium-based catalysts are used, the reverse pattern is seen, which may be due to the weaker ion pairing in larger ionic liquid molecules leading to increased reactivity of the ions [134]. Also, when liquid acids are used as catalysts, it is important to remember that the dissociation constants of these acids in ionic liquids is usually unknown, and it is thus difficult to predict their activity in carbohydrate dehydration in ionic liquids [98]. HMF has also been reported to react with [BMIM]Cl forming 1-butyl-2-(5'-methyl-2'-furoyl)imidazole at temperatures over 200 °C, which shows that ionic liquids cannot be considered to be inert solvents for HMF production [246]. More research is therefore needed to precisely identify the factors affecting the HMF yields in different ionic liquid media.

Table 2-7: Laboratory-scale production of HMF from raw biomass

Biomass (wt%)	Sugar type (wt% in biomass)	Solvent	Catalyst	Temp. (°C)	Reaction/ residence time	Yield (wt%)	Ref
Jerusalem artichoke tubers (N/A)	Inulin (50)	Water-2-butanol (1:1 v/v)	$FeCl_2$ (1.3 mM); H_2O_2 (0.47 M)	180	1 h 30 min	45.7	[125]
Cane juice (N/A)	N/A	N/A	Aluminium sulphate octadecahydrate (3 wt% of solids); H_2SO_4 (4.6%)	270	8 s	31	[95]
Crude cane juice (48)	Hexoses and disaccharides (62)	Water	Oxalic acid (0.2 wt%)	140-160	1 h	11	[89]
Crude cane juice (48)	Hexoses and disaccharides (62)	Water	Phosphoric acid (0.15 wt%)	149-169	1 h	9	[89]
Cassava waste (2)	Starch and cellulose (60 & 16)	Water-acetone-DMSO (90:7:3 w/w)	Sulphonated carbon-based catalyst (5 wt% of cassava waste)	250	1 min	12.1	[247]
Chicory roots (48)	Inulin (17.8)	Water	H_2SO_4 (pH=1.8)	140	2 h	9	[170]
Jerusalem artichoke (N/A)	Inulin (N/A)	Water	Lewatit SPC 108 ion exchange resin (1.3 meq. H^+/mol inulin)	78	15 h	57	[191]

Straw (5)	N/A	[BMIM]Cl ; [bi-C_3SO_3HMIM] [HSO_4]; Water	$MnCl_2$ (3 mol% of substrate)	120	1 h	24	[218]
Reed (5)	N/A	[BMIM]Cl ; [bi-C_3SO_3HMIM] [HSO_4]; Water	$MnCl_2$ (3 mol% of substrate)	120	1 h	25	[218]
Tapioca roots (N/A)	Starch (70-75)	[OMIM]Cl; Ethyl acetate (4:1 w/w)	CrF_3 (1 wt%)	120	1 h 30 min	52.6	[139]
Tapioca roots (N/A)	Starch (70-75)	[OMIM]Cl; Ethyl acetate (4:1 w/w)	CrF_3 (1 wt%); $CrBr_3$ (1 wt%)	120	1 h 30 min	68	[139]
Chicory roots (20)	Inulin (70-75)	[OMIM]Cl; Ethyl acetate (4:1 w/v)	HCl (0.3 M)	120	1 h	~70	[138]
Corn stover (10)	Cellulose (34.4)	DMA; EMIM[Cl] (8:5 w/w)	LiCl (5 wt%); $CrCl_3$ (10 mol% of substrate); HCl (10 mol% of substrate)	140	2 h	37	[192]
Maple wood (5)	Glucan (40.9)	THF; Water (4:1)	$FeCl_3$ (1 wt%)	170	1 h	40	[248]

Table 2-7 outlines some of the work that has been done on the conversion of raw biomass directly to HMF. Jerusalem artichoke and chicory roots, which are rich in inulin, give high HMF yields, while the use of the ionic liquid [OMIM]Cl and CrF_3 catalyst gives surprisingly high HMF yields from the starch-rich tapioca roots. In general, though, it is more common for researchers to pre-treat the biomass to make it more suitable for hydrolysis by increasing cellulose accessibility via removal of the lignin and hemicellulose [249], and therefore, the use of untreated raw biomass for HMF synthesis has been limited.

To summarise, a variety of feedstock and a range of reaction systems have been investigated at a lab-scale level. Fructose is the most convenient feedstock from the point of view of high yields and has hence been the substrate of choice for researchers investigating new reaction systems. Other monosaccharides generally give considerably lower yields, with catalysts that can isomerise these monosaccharides to fructose, like $CrBr_3$/LiBr and $Ag_3PW_{12}O_{40}$, giving higher yields, albeit at relatively low concentrations. Among polysaccharides, inulin, being a polyfructan, gives fairly high yields, while reasonable yields can be obtained from other polysaccharides using biphasic solvent systems and/or specific solid catalysts. For all feedstock, including raw biomass, ionic liquids give much higher yields than other reaction media, especially in conjugation with catalysts like $CrCl_3$.

2.8 Pilot and commercial-scale production of HMF

Despite the potential importance of HMF and the number of laboratory schemes devised, till date no full-scale commercial plants for HMF manufacture have been set up, and only a few pilot processes, which are generally of the kilogram scale, have been reported. One of the earliest was mentioned in a patent by Cope in 1959, which involved a batch non-catalytic conversion of sucrose or glucose to HMF using MIBK as solvent. A distilled HMF yield of up to 63% was reported from a 50 wt% sucrose solution after a total operation time of over 9 hours [250]. Another process was patented in 1988 by Süddeutsche Zucker-Aktiengesellschaft (Südzucker AG) for producing HMF from fructose and inulin with oxalic acid as catalyst [251]. The Südzucker AG unit was a batch process utilising fructose and inulin from chicory roots as feedstock. When fructose was used, a fructose conversion of 55% and HMF yield of 33% was obtained, while pre-treated chicory roots yielded 13% HMF and 30% fructose. Column chromatography was used for HMF purification [41, 170]. A process patented in 1982 by Roquette Frères, used cationic resins in a water-methyl isobutyl ketone (MIBK) system to synthesise HMF by fructose dehydration [251]. This process yields 38% HMF at a fructose conversion of 51% [41, 190]. A similar scale process, which also used fructose as the feedstock, was patented by Furchim, France, in 1990 [252]. This was a non-catalytic process where DMSO was used as the solvent and yielded 85% HMF, which was extracted in a counter-current column using DCM. The HMF was purified further to 98% purity using evaporation followed by crystallisation, with the overall molar yield from the process being over 75% [41].

For pilot scale production to develop into commercial scale manufacturing, one area of improvement that needs to be made is an improvement in the techno-economics, as was mentioned in Section 2.2. One possible avenue for this is by increasing solvent and catalyst recycling, which will also reduce the ecological footprint of the process. Heterogeneous catalysts have an advantage over homogeneous catalysts in this respect, but their cost, durability and lifespan needs to be improved. The HMF obtained must be of sufficient purity for use as a chemical intermediate, which necessitates the complete separation and proper disposal of the by-products.

2.9 Laboratory-scale production of LA

As LA is most commonly produced by a reaction route where HMF is an intermediate, it is understandable that the reaction systems used for LA synthesis are similar to those employed for HMF production. In general, it can be stated that higher temperatures, shorter reaction times, lower water concentration and higher pH maximise HMF production, while the opposite is true for LA [97, 122, 253, 254].

From Table 2-8, it can be seen that the LA yields obtained are lower than the HMF yields that had been obtained from the same substrates, which is to be expected given that HMF is an intermediate in LA production. The mineral acids HCl and H_2SO_4 generally give the highest yields, although which of the two is the better catalyst is debatable, with researchers variously claiming that HCl gives higher LA yields than H_2SO_4 [254], HCl shows higher kinetic rates but similar LA yields to H_2SO_4 [255] and H_2SO_4 gives higher yields than HCl [256]. A zeolite catalyst gave high LA yield at high fructose loading, but this run was conducted using only 1 gram each of fructose and catalyst, and so it remains to be seen if the results can be replicated at larger scales. For converting glucose to LA, it has been suggested that a combination of a Lewis acid like $CrCl_3$ and a Brønsted acid like HCl might be a better option than either option alone, as the Lewis acid catalyses the isomerisation of glucose to fructose, while the Brønsted acid catalyses the reaction of fructose to LA, enabling relatively high LA yields at moderate reaction temperatures [22].

In Tables 2-8 to 2-10, conversion and yield are defined as

$$Conversion = 1 - \frac{Final\ mass\ of\ the\ substrate}{Initial\ mass\ of\ the\ substrate} \times 100\%$$

$$Yield = \frac{Mass\ of\ LA\ produced}{Initial\ mass\ of\ the\ substrate} \times 100\%$$

Table 2-8: Laboratory-scale production of LA from monosaccharides

Substrate (conc. in wt%)	Solvent	Catalyst	Catalyst conc.	Temp. (°C)	Reaction/ residence time	Conversion (%)	Yield (wt%)	Ref
Fructose (30)	Water	PTSA	1 M	88	8 h 20 min	85	16	[72]
Fructose (8)	Water	PTSA	0.5 M	88	8 h 20 min	80	23	[72]

Fructose (8)	Water	Methane sulphonic acid	0.5 M	88	8 h 20 min m	75	24	[72]
Fructose (8)	Water	Perchloric acid	0.5 M	88	8 h 20 min	78	24	[72]
Fructose (8)	Water	HBr	0.5 M	88	8 h 20 min	85	29	[72]
Fructose (8)	Water-ethylene glycol (50:50 v/v)	PTSA	1 M	88	5 h	95	13	[72]
Fructose (4)	Water	HCl	2 M	95	1 h 36 min	96	39	[257]
Fructose (17)	Water	HCl	1 M	95	3 h	89	27	[257]
Fructose (1)	Subcritical water	HCl	pH=1.5	240	2 min	100	30	[168]
Fructose (1)	Subcritical water	PTSA	pH=1.5	240	2 min	100	22	[168]
Fructose (10)	Water-methanol	HCl	2 M	140	1 h 20 min	~ 100	46	[174]
Fructose (2)	Water	TFA	0.5 M	180	1 h	N/A	45	[258]
Fructose (30)	Water	HCl	5 wt%	162	1 h	N/A	25.1	[93]
Fructose (27)	Water	Amberlite IR-120	70 wt%	>85	27 h	N/A	23.5	[24]
Fructose (9)	Water	Amberlyst XN-1010	140 wt%	100	9 h	N/A	16	[259]
Fructose (8)	Water	HCl; NaCl	1 M HCl; 65 wt % NaCl	88	8 h 20 min	97	34	[72]
Fructose (8)	Water	HCl; $AlCl_3$	1 M HCl; 25 wt % $AlCl_3$	88	8 h 20 min	92	30	[72]
Fructose (8)	Water	HCl; $CrCl_3$	1 M HCl; 29 wt % $CrCl_3$	88	8 h 20 min	94	31	[72]
Fructose (8)	Water	HCl; $LaCl_3$	1 M HCl; 8 wt % $LaCl_3$	88	8 h 20 min	93	32	[72]
Fructose (50)	None	LZY-Zeolite	100 wt%	140	15 h	96	43.2	[260]
Fructose (8)	Water	TFA; Ru/C	0.5 M TFA; 10 wt% Ru/C	180	8 h	100	34	[258]
Glucose (30)	Water	HCl; NaCl	6 wt% HCl; 9 wt% NaCl	N/A	22 h	N/A	31	[261]
Glucose (2)	Water	H_2SO_4	1 M	140	2 h	96	38	[21]
Glucose (5)	Water	H_2SO_4	5 wt%	170	2 h	100	34	[262]
Glucose (27)	Water	Amberlite IR-120	19 wt%	N/A	124 h	N/A	6	[24]
Glucose (30)	Water	HCl	5 wt%	162	1 h	N/A	24.4	[93]
Glucose (13)	Water	Sulphonated graphene oxide	0.2 wt%	200	2 h	89	50	[263]

Glucose (1.8)	Water	HCl	1 M	141	1 h	67	29	[92]
Glucose (1.8)	Water	H_2SO_4	1 M	141	1 h	69	29	[92]
Glucose (2)	Water	TFA	1 M	180	1 h	100	37	[258]
Glucose (10)	Water	HCl	0.1 M	160	4 h	95	41	[97]
Glucose (10)	Water	Zirconium phosphate	0.1 M	160	3 h	73	14	[97]
Glucose (30)	Water	HCl; NaCl	6 wt% HCl; 9 wt% NaCl	N/A	22 h	N/A	31	[261]
Glucose (9)	Water	HCl	6 wt%	160	15 min	N/A	41.4	[94]
Glucose (33)	Water	HCl	-	125	10 min + 24 h	N/A	15	[264]
Glucose (1)	Water	$CrCl_3$+HY zeolite hybrid catalyst	12 wt% of substrate	145.2	146.7 min	~100	47	[265]
Glucose (2)	Water	H_2SO_4	0.5 M	180	15 min	N/A	42	[266]
Glucose (2)	Water	Methanesulfonic acid	0.5 M	180	15 min	N/A	41	[266]
Glucose (10)	Water	HCl; $CrCl_3$	0.1 M HCl; 18.6 mM $CrCl_3$	140	6 h	97	30	[22]
Glucose (12)	Water	H_2SO_4	30 wt%	100	24 h	~100	30	[267]
Glucose (7)	Water	$MgCl_2$; HCl	7 mol% of substrate $MgCl_2$; 7 mol% of substrate HCl	N/A	3 h	N/A	39	[268]

From Table 2-9, it can be seen that polysaccharides give LA yields that are roughly similar to those obtained from monosaccharides. Mineral acids are again the most commonly used catalysts, but their use for hydrolysis of polysaccharides generally follows two different approaches: high acid concentrations at low or moderate temperatures (<100 ^{o}C); and dilute solutions at higher temperatures (>160 ^{o}C). The major drawbacks of the former approach are the high operating cost of the acid recovery and the more expensive materials of construction required [269], while the latter approach has the drawback of LA yields being reduced due to the higher temperatures [255] and higher pH values. A mixture of gamma-valerolactone (GVL) and water is a promising solvent for LA production from cellulose, due to the ability of GVL to hydrolyse cellulose and inhibit humin formation [103].

Table 2-9: Laboratory-scale production of LA from oligosaccharides and polysaccharides

Substrate & conc. (wt%)	Solvent	Catalyst	Catalyst conc.	Temp. (ºC)	Reaction/ residence time	Conversion (%)	Yield (wt%)	Ref
Cellulose (1.6)	Water	HCl	0.927 M	180	20 min	~100	44	[270]
Cellulose (1.7)	Water	H_2SO_4	1 M	150	2 h	100	43	[269]
Sucrose (27)	Water	Amberlite IR-120	19 wt%	>85	41 h	N/A	15.6	[24]
Sucrose (15)	Water	Dowex MSC-1H ion exchange resin	9 wt%	100	24 h	29	17	[259]
Cellulose (10)	Water	HCl	3 wt%	250	2 h	79.2	28.8	[271]
Cellulose (10)	Water	HBr	3 wt%	250	2 h	79.4	26.9	[271]
Cellulose (10)	Water	H_2SO_4	3 wt%	250	2 h	67.3	25.2	[271]
Sucrose (30)	Water	HCl	5 wt%	162	2 h	N/A	29	[93]
Cellulose (2)	Water-GVL (10:90 w/w)	Amberlyst 70	6 wt%	160	16 h	N/A	49	[103]
Starch (31)	Water	HCl	1.7 wt%	200	25 min	99	34.6	[272]
Starch (30)	Water	HCl	5 wt%	162	1 h	N/A	23.5	[93]
Cellulose (1.98)	Water-GVL (1:1 w/w)*	HCl; NaCl	1.25 M HCl; 17 wt% NaCl	155	1 h 30 min	N/A	52	[273]
Cellulose (4)	Water	ZrP	4 wt%	220	2 h	51	12	[97]
Cellulose (2)	Water	$CrCl_3$	0.02 M	200	3 h	N/A	48	[274]
Cellulose (2)	Water-MIBK (1:10 v/v)*	[MIMPSH]H_2PW	0.7 mmol/g cellulose	140	12 h	N/A	45	[275]
Cellulose (9-17)	Water	H_2SO_4	3 wt% of cellulose	230	4 h	N/A	35.1	[276]
Inulin (2)	Water	Sulfonated hyperbranched poly(arylene oxindole)s	100 wt% of inulin	165	5 h	68.9	45	[277]
Cellulose (2)	Water	ZrO_2	2 wt%	180	3 h	100	39	[105]

Cellulose (4)	Water	Sulfonated chloromethyl polystyrene resin	500 wt% of substrate	170	10 h	100	24	[106]
Cellulose (4)	Water-GVL (10:90 w/w)	Sulfonated chloromethyl polystyrene resin	300 wt% of substrate	170	10 h	100	47	[106]
Cellulose (5)	Water	Al-$NbOPO_4$	80 wt% of substrate	180	24 h	95	38	[278]

Table 2-10 shows that the LA yields obtained from raw biomass are generally higher than the HMF yields from raw biomass. This may be because the higher acid concentrations and reaction times required for LA synthesis also facilitate the hydrolysis of the raw biomass into the simple sugar units that actually undergo the reactions to HMF and LA. Solid acid catalysts, especially ones that use transition metals like Cr and Zr, give LA yields comparable to those obtained using mineral acid catalysts, and have the advantages of easier recovery and recyclability, and so need to be tested at higher substrate concentrations to determine their suitability for industrial applications.

Table 2-10: Laboratory-scale production of LA from raw biomass

Biomass (wt%)	Sugar type (wt% in biomass)	Solvent	Catalyst	Temp. (°C)	Reaction/ residence time	Yield (wt%)	Ref
Water hyacinth (1)	Glucose,galactose (26.3)	Water	H_2SO_4 (1 M)	175	30 min	35	[279]
Water oak (without bark) (9)	Cellulose and hemicellulose (<60)	Water	HCl (6%)	160	30 min	~30	[94]
Fir sawdust (20)	Hexoses (50)	Water	HCl (12 wt% of hexose content)	190	30 min	36	[280]
Sugarcane bagasse (22)	Hexoses (40)	Water	H_2SO_4 (26 wt% of hexose content)	200	5 min	30	[280]
Beech (9)	Cellulose (48.5)	Water	H_2SO_4 (5 wt% of raw material)	240	2 h	17.8	[276]
Aspen (9)	Cellulose (45.7)	Water	H_2SO_4 (5 wt% of raw material)	200	4 h	15.5	[271]
Whole kernel grain sorghum (10)	Starch (73.8)	Water	H_2SO_4 (8%)	200	40 min	32.6	[256]
Wheat straw (6)	Cellulose (40.4)	Water	H_2SO_4 (3.5%)	209.3	37.6 min	49	[281]

Hardwood flour (10)	Cellulose (42)	Water	H_2SO_4 (5 wt%)	220+210	15.7 s +20 min	~42	[282]
Sugarcane bagasse (10.5)	Cellulose (42)	Water	HCl (4.45 wt%)	220	45 min	54	[283]
Paddy straw (10.5)	Cellulose (40)	Water	HCl (4.45 wt%)	220	45 min	59	[283]
Wheat straw (7)	Cellulose (39.2)	Water	HCl (11.5 meq)	200	1 h	49.3	[284]
Olive tree pruning (7)	Cellulose (39.4)	Water	HCl (11.5 meq)	200	1 h	47.2	[284]
Poplar sawdust (7)	Cellulose (57.6)	Water	HCl (11.5 meq)	200	1 h	37	[284]
Corn stover (6)	Cellulose (33)	Water-GVL (10:90 w/w)	Amberlyst 70 (6 wt%)	160	16 h	54	[103]
Corn stover (6.6)	Cellulose (N/A)	Water-GVL (20:80 w/w)	H_2SO_4 (0.2 M)	160	19 h	66	[85]
Bamboo shoot shell (2)	Hexoses (37.8)	Water;[BMIM] HSO_4 (0.9 mol/l)	-	145	1 h 44 min	46	[285]
Empty fruit bunch (1)	Cellulose (41.1)	Water	$CrCl_3$+HY zeolite hybrid catalyst (12 wt% of substrate)	145.2	146.7 min	38	[265]
Kenaf (1)	Cellulose (32)	Water	$CrCl_3$+HY zeolite hybrid catalyst (12 wt% of substrate)	145.2	146.7 min	38	[265]
Steam Exploded Rice Straw (6)	Cellulose (46.1)	Water	$S_2O_8^{2-}/ZrO_2$-SiO_2-Sm_2O_3 (13.3 wt%)	200	10 min	49	[286]

A point that must be noted is that while high LA yields can be achieved by a mineral acid, at a pilot or commercial scale, these processes face the problem of separation of the LA from the acid, which is necessary both for LA purity and acid recycle. Generally, the concentration of LA in the acid stream is relatively low, which makes its recovery difficult and expensive [287]. The high boiling point of LA also makes its recovery by distillation difficult, since the solvent, which is usually present in much larger quantities, needs to be evaporated, making the process energy intensive.

It was seen in Section 2.7 that numerous studies have been conducted on HMF production using ionic liquids. It is rather surprising that the same attention has not been paid to LA production, to the extent that no work in this direction had been conducted till 2011 [84]. Recently, though, Ya'aini and Amin have reported the use of the ionic liquid [EMIM]Cl for LA production [288]. A hybrid

$CrCl_3$-HY zeolite catalyst was used, and a yield of 46 wt% was obtained from cellulose, and 20 and 17 wt% from empty fruit bunch and kenaf. This study demonstrates that ionic liquids are a suitable media for LA production as well, and more work in this area can be expected to happen in the future.

While the numerous laboratory-scale reaction systems that have been discussed so far differ in a number of characteristics, they are similar in that most of them basically use a stirred heating chamber as the reactor. A different method, using a twin-screw extruder as the reactor, has been proposed as an alternative for production of LA [289]. This method, which has been used to produce LA from corn starch, has been claimed to have the advantages of being continuous and requiring lesser steps and reduced reaction times as compared to traditional batch reactors [290].

Overall, this section shows that LA yields broadly follow similar patterns to those found for HMF with respect to substrates and reaction systems. To prioritise LA formation, lower temperatures, longer reaction times, higher water concentration and lower pH levels need to be applied as compared to optimum conditions for HMF synthesis.

2.10 Pilot and commercial-scale production of LA

One major process for the conversion of lignocellulosic biomass to LA is the Biofine process. This process, which can process a range of heterogeneous lignocellulosic feedstocks, is a two-stage high temperature acid hydrolysis process using sulphuric acid that differs from most acid hydrolysis processes in that the final products are not monomeric sugars but LA and furfural [36, 291]. The first stage of the process is a plug flow reactor that hydrolyses the cellulose and other carbohydrate polysaccharides to soluble intermediates like HMF, which are converted in the mixed flow reactor of the second stage to furfural, LA, formic acid, and other products. The plug flow reactor used is small due to a residence time of only 12-25 seconds being required in the first stage, while the mixed flow reactor is much larger due to a required residence time of 15-30 minutes [36, 282]. The second reactor can also be operated as a stripping column to remove furfural continuously from the degrading mixture [292]. LA with purity of up to 98% is produced, while the H_2SO_4 catalyst is recovered and recycled. Around 50% of the mass of the 6-carbon sugars are converted to LA, with 20% forming formic acid and 30% tars, while in case of the 5-carbon sugars, 50% is converted to furfural, while the rest is converted to char. A 1 ton per day (tpd) pilot plant was initially set up in New York, USA, in 1996, with a 3000 tpd commercial plant commencing operation in 2006 [36].The commercial plant was constructed by Le Calorie, and used local tobacco bagasse and paper mill sludge as feedstock [293], although there were reportedly operational problems owing to the clogging of the first stage reactor due to deposition of salt and humins [284].

Another pilot plant for LA production, also based on acid hydrolysis, was commissioned in 2013 by Segestis, Inc. in Minnesota, USA [294]. The technology behind this plant was developed using high fructose corn syrup (HFCS)[295], but it has been stated that the process can be modified to use cellulosic sugars as feedstock [296]. This plant has a nameplate capacity of 80 metric tonnes per year and is expected to act as a source for the downstream production of LA-derivatives such as levulinic ketals [297]. A commercial-scale facility with an annual LA capacity of 10 million kilograms is expected to be constructed in the near future [296].

2.11 Microwave heating systems

Traditionally, heating apparatus like oil bath and muffle furnace have been used to carry out chemical synthesis. The pioneering work carried out by Gedye, et al [298], and Giguere et al [299] in 1986, however, demonstrated the feasibility of using microwave ovens for chemical synthesis. Subsequently, microwave heating has steadily gained in importance as a heating method for synthetic transformations. The most important advantage of microwave heating is the dramatic increase in reaction rates and yields [86]. Microwave heating also provides a more homogeneous heat distribution and fewer side-wall effects than conventional heating [68]. Additionally, the use of microwave heating allows for better control of reaction parameters and for the choice of reaction solvent to be decided based on properties other than the boiling point, although the dielectric properties, which can be changed by the addition of polar materials, do need to be considered [300]. In addition, microwave irradiation is more selective than conventional heating, as polar substances are heated rapidly, while non-polar substances are not heated, and this can be used to modify the selectivity of a reaction or avoid decomposition of thermally unstable species [301]. However, non-polar solvents can still be used for microwave-based syntheses if a small amount of inert polar solvent is added, since the presence of even low amounts of polar substances greatly increase the heating efficiency of the mixture [302]. Microwave heating may also be more energy efficient than conventional methods of heating [303, 304].

Microwave heating systems can broadly be divided into mono-mode (or single-mode) and multi-mode systems. The basic difference between the two is that in mono-mode systems, a stationary wave mode which penetrates the sample from one side is generated, while in multi-mode systems, the presence of a ‘field diffuser’ enables sample irradiation from all sides by different wave modes, which results in a more homogeneous heat distribution and uniform sample heating [300, 302]. Generally, small-scale systems (~50 ml) are mono-mode, while larger units are multi-mode [28].

In some experiments, microwave irradiation has been found to lead to product distributions different from those obtained using conventional modes of heating, in addition to the dramatically enhanced reaction rates, and this has been attributed to ‘specific’ or ‘non-thermal’ microwave effects [300]. While in a number of cases, the differences can be attributed to thermal kinetic effects leading to discrepancies between the actual temperature profiles in conventional and microwave heating, in other cases, factors other than thermal heating may play a part. For instance, it has been demonstrated that microwave irradiation can be used to successfully carry out reactions in a reaction vial placed in a block of ice without melting the ice [305, 306]. A number of factors have been envisaged to explain non-thermal effects, such as changes in the pre-exponential factor or activation energy in the Arrhenius equation, stabilisation of polar transition states and intermediates, microscopic hot spots, molecular agitation, etc. [301, 305, 307]. However, recent studies suggest that the discrepancies in the reaction rates using microwave and conventional heating can instead be attributed to the fact that microwave heating generally permits much more rapid heating and cooling than resistance-heated systems, which allows the reactions to follow optimal pathways [29]. Another explanation that has been given is that the infrared temperature sensors used in conventional microwave systems are often inaccurate, with the actual reaction temperature being substantially higher than the recorded temperature [308].

The point about microwave heating being more energy efficient than conventional heating methods deserves further elaboration. One reason that microwave heating is held to consume less energy than comparable conventional heating is simply the far lesser duration that microwave-heated reactions generally take. For single-mode batch microwave reactors, it has been established that any energy savings accrue only from the reduced heating time, rather than due to an efficiency of the process itself, which has efficiencies of 2-20% only [28]. Multi-mode reactors, however, have been found to be more energy-efficient in general than comparable heated-jacket reaction vessels, both for large lab-scale reactors (1-3 l) [309] and for pilot-scale reactors (20-40 l) [310]. It has been observed that microwave systems become more energy efficient as system size is increased for systems in the ~50 ml size range, due to reduced energy wastage via dissipation to the surroundings [311]. In larger microwave systems, however, the duplication of the rapid heating and cooling profiles becomes problematic, leading to longer processing times, higher energy consumption, and a dilution of the main advantages of microwave heating [28]. The use of frequencies lower than the standard 2450 MHz may be one way of increasing both energy efficiency and penetration depth of the microwaves, making larger reactors a realistic possibility [28].

2.12 Microwave heating systems for HMF and LA synthesis

All the advantages of microwave heating outlined in Section 2.11 have led researchers to investigate the possibility of using microwave heating for producing HMF, LA and other chemicals from cellulose and lignocellulosic biomass. Table 2-11 summarises some of the work on HMF and LA synthesis using microwave irradiation that has been carried out in recent years. Some of the items in the table have been explained in greater detail in the following paragraphs.

Table 2-11: HMF and LA synthesis using microwave irradiation

Substrate & conc.(wt%)	Solvent	Catalyst	MW power (W)	Primary final products	Temp. (^oC)	Reaction/ residence time	Conversion (%)	Yield (wt%)	Ref
Cellulose (8)	$[C_3SO_3Hmim]HSO_4$-Water (1:2 w/w)	-	800	LA	160	30 min	N/A	32	[312]
Fructose (10)	Acetone-DMSO (7:3 w/w)	DOWEX 50WX8-100 strong acidic ion-exchange resin (4 wt%)	700	HMF	150	20 min	99	58	[128]
Fructose (2)	Water	TiO_2 (0.4 wt%)	700	HMF	200	10 min	90.4	29	[74]
Fructose (2)	Water	H_2SO_4 (1 wt%)	700	HMF	200	5 min	97.3	33	[74]
Glucose (2)	Water	TiO_2 (0.4 wt%)	700	HMF	200	5 min	63.8	13	[74]
Cellulose (5)	[BMIM]Cl	$CrCl_3.6H_2O$ (0.5 wt%)	400	HMF	-	2 min 30 s	N/A	48	[313]
Corn stalk-hexose	[BMIM]Cl	$CrCl_3.6H_2O$ (0.5 wt%)	400	HMF	-	3 min	N/A	32	[313]

content 36.1%- (5)									
Rice straw-hexose content 37.5%- (5)	[BMIM]Cl	$CrCl_3.6H_2O$ (0.5 wt%)	400	HMF	-	3 min	N/A	33	[313]
Pine wood-hexose content 54%- (5)	[BMIM]Cl	$CrCl_3.6H_2O$ (0.5 wt%)	400	HMF	-	3 min	N/A	36	[313]
Cellulose (2)	[BMIM]Cl	$CrCl_3$/LiCl (1:1 molar ratio to glucose units)	N/A	HMF	160	10 min	N/A	49	[137]
Wheat straw-cellulose 38.5% (2)	[BMIM]Cl	$CrCl_3$/LiCl (1:1 molar ratio to glucose units)	N/A	HMF	160	15 min	N/A	48	[137]
Fructose (10)	Water	Phosphate buffer system (pH=2.1)	N/A	HMF	150	30 min	94	45	[314]
Glucose (10)	Water	Phosphate buffer system (pH=2.1)	N/A	HMF	150	1 h 30 min	33	13	[314]
Glucose (10)	Water	Phosphate buffer system (pH=2.1); Sodium borate (0.875 mol/mol glucose)	N/A	HMF	150	1 h 30 min	70.4	29	[314]
Fructose (10)	Water-MIBK-2-butanol (10:7:3 v/v)	Phosphate buffer system (pH=2.1)	N/A	HMF	150	30 min	95	62	[314]
Inulin (10)	Water-MIBK-2-butanol (10:7:3 v/v)	Phosphate buffer system (pH=2.1)	N/A	HMF	150	30 min	100	50	[314]
Glucose (10)	Water-MIBK-2-butanol (10:7:3 v/v)	Phosphate buffer system (pH=2.1); Sodium borate (0.875 mol/mol glucose)	N/A	HMF	150	2 h	83	44	[314]
Sucrose (10)	Water-MIBK-2-butanol (10:7:3 v/v)	Phosphate buffer system (pH=2.1); Sodium borate	N/A	HMF	150	2 h	100	46	[314]

		(0.875 mol/mol glucose)							
Fructose (4)	[BMIM]Cl	$ZrCl_4$ (10 mol%)	400	HMF	N/A	2 min	98.9	65	[315]
Glucose (4)	[BMIM]Cl	$ZrCl_4$ (10 mol%)	400	HMF	N/A	3 min 30 s	72.3	33	[315]
Cellulose (4)	[BMIM]Cl	$ZrCl_4$ (10 mol%)	400	HMF	N/A	3 min 30 s	N/A	40	[315]
Glucose (9)	[BMIM]Cl	$CrCl_3$ (3.6 wt%)	400	HMF	N/A	1 min	N/A	64	[316]
Glucose (9)	[BMIM]Cl	H_2SO_4 (10 wt%)	400	HMF	N/A	1 min	N/A	34	[316]
Cellulose (5)	[BMIM]Cl	$CrCl_3.6H_2O$ (10 wt% of cellulose)	400	HMF	N/A	2 min	N/A	48	[316]
Linter cotton cellulose fibre (4)	[BMIM]Cl (44 wt%);DMA-LiCl	$Zr(O)Cl_2$+$CrCl_3$ (20 mol% of cellulose)	300	HMF	120	20 min	N/A	48	[82]
Sugarcane bagasse (4)	[BMIM]Cl	$Zr(O)Cl_2$+$CrCl_3$ (20 mol% of cellulose)	300	HMF	120	5 min	N/A	33	[82]
Fructose (5)	DMSO	$AlCl_3$ (50 mol%)	300	HMF	140	5 min	N/A	49	[317]
Glucose (5)	DMSO	$AlCl_3$ (50 mol%)	300	HMF	140	5 min	N/A	37	[317]
Sucrose (5)	DMSO	$AlCl_3$ (50 mol%)	300	HMF	140	5 min	N/A	33	[317]
Starch (5)	DMSO	$AlCl_3$ (50 mol%)	300	HMF	140	5 min	N/A	24	[317]
Inulin (5)	DMSO	$AlCl_3$ (50 mol%)	300	HMF	140	5 min	N/A	30	[317]
Fructose (2)	Acetone-Water (70:30 w/w)	Dowex 50wx8-100 ion-exchange resin (2 wt%)	N/A	HMF	150	15 min	95.1	51	[318]
Fructose (10)	Water	-	1400	HMF	200	30 min	96	33	[68]
Glucose (10)	Water	-	1400	HMF	240	10 min	87	21	[68]
Fructose (5)	Water	HCl (2M)	250	LA	170	30 min	N/A	31.8	[319]
Glucose (5)	Water	HCl (2M)	250	LA	170	30 min	N/A	31.4	[319]
Cellobiose	Water	HCl (2M)	250	LA	170	30 min	N/A	29.9	[319]
Cellulose	Water	HCl (2M)	250	LA	170	50 min	N/A	31	[319]
MMw Chitosan	Water	HCl (2M)	250	LA	170	20 min	N/A	26.3	[319]
Fructose (5)	Water	H_2SO_4 (2M)	250	LA	170	30 min	N/A	27.5	[319]

Glucose (5)	Water	H_2SO_4 (2M)	250	LA	170	30 min	N/A	26.1	[319]
Cellobiose	Water	H_2SO_4 (2M)	250	LA	170	30 min	N/A	28	[319]
Cellulose	Water	H_2SO_4 (2M)	250	LA	170	50 min	N/A	23	[319]
MMw Chitosan	Water	H_2SO_4 (2M)	250	LA	170	20 min	N/A	22.8	[319]
Fructose (27)	Water	-	300	HMF	190	5 min	68	25	[86]
Fructose (27)	Water	HCl (0.01 M)	300	HMF	200	1 min	95	37	[86]
HMw chitosan (9.8)	Water	$SnCl_4.5H_2O$ (1.2 mmol/g substrate)	N/A	LA,HMF	200	30 min	N/A	25.1(LA),10.3 (HMF)	[78]
Fructose (3)	DMSO	ILIS-SO_3H	200	HMF	100	4 min	100	49	[320]
Fructose (3)	DMSO	ILIS-SO_2Cl	200	HMF	100	4 min	100	47	[320]
Fructose (3)	DMSO	SiO_2-SO_3H	200	HMF	100	4 min	95	44	[320]
Fructose (3)	DMSO	SiO_2-SO_2Cl	200	HMF	100	4 min	92.1	42	[320]
Fructose (8)	Ethanol	NH_4Cl (1 wt%)	600	HMF	120	10 min	99	39	[176]
Fructose (8)	Isopropanol	NH_4Cl (1 wt%)	600	HMF	120	10 min	92	26	[176]
Foxtail straw (5)	DMA-LiCl	$[DMA]^+[CH_3SO_3]^-$ (0.5 wt%)	300	HMF	120	2 min	N/A	58	[321]
Foxtail straw (5)	DMA-LiCl	$[NMP]^+[CH_3SO_3]^-$ (0.5 wt%)	300	HMF	120	2 min	N/A	52	[321]
Sweet sorghum juice (25)	N/A	H_2SO_4 (2 M)	135	LA	160	30 min	N/A	31.4	[322]
Fructose (48)	[BMIM]Cl	Lignin-derived carbonaceous catalyst (10 wt% of substrate)	100	HMF	110	10 min	N/A	50	[323]
Fructose (2.5)	[BMIM]Cl	Lignin-derived carbonaceous catalyst (10 wt% of substrate)	100	HMF	110	10 min	100	59	[323]
Glucose (2.5)	[BMIM]Cl-DMSO (6:4 w/w)	Lignin-derived carbonaceous catalyst (10 wt% of substrate)	100	HMF	160	50 min	99	48	[323]

Cellulose (0.5)	DMAc-LiCl	[TMG]BF$_4$ (40 wt% of substrate)	400	HMF	140	1 h	N/A	20	[324]
Fructose (5)	[BMIM]Cl-MIBK (1:1 v/v)	Zr(O)Cl$_2$ (10 mol%)	300	HMF	120	5 min	N/A	59	[325]
Starch (5)	[BMIM]Cl-MIBK (1:1 v/v)	Zr(O)Cl$_2$ (10 mol%)	300	HMF	120	5 min	N/A	34	[325]
Fructose (2)	Acetone-DMSO (7:3 w/w)	Sulphated zirconia (20 wt% of substrate)	700	HMF	180	5 min	91.3	46	[326]
Glucose (1)	Water-THF (1:3 v/v)*	AlCl$_3$.6H$_2$O (40 mol% of substrate); HCl (40 mol% of substrate)	N/A	HMF	160	15 min	100	43	[327]

Hansen, et al., used fructose as the raw material for HMF production in aqueous media, concentrating on maximising the initial fructose concentration and minimising use of the HCl catalyst [86]. Their work revealed that while some fructose conversion can take place without the use of a catalyst, higher conversion and selectivity require promotion by a catalyst. It was also seen that the use of highly acidic conditions led to enhanced by-product formation. The authors compared microwave heating with conventional oil bath heating and found that the product distribution was similar for the different heating modes, but microwave heating leads to much higher reaction rates and more precise control of reaction temperature than conventional heating. They also found that increasing microwave power beyond 90 W merely increases energy consumption without increasing conversion, yield or selectivity.

Möller, et al., investigated the hydrothermal conversion of glucose and fructose under microwave irradiation [68]. It was seen that the decomposition of glucose requires higher temperatures than fructose, with the decomposition rate constant at 220^{o}C being eight times higher for fructose than for glucose. Both fructose and glucose were detected as a by-product of the other's conversion owing to the reversible Lobry-de Bruyn-van Ekenstein transformation. The maximum HMF yield from fructose was 47%, while it was only 29.5% in case of glucose. The lower HMF yield from glucose decomposition was attributed to the preferential formation of HMF from ketoses as compared to aldoses. HMF yields showed a bell-shaped temperature curve, which meant that HMF was actually a reaction intermediary under these conditions, with LA and trihydroxy benzene being formed from HMF.

Zhang, Zhao and co-workers have reported a number of studies on the use of microwave irradiation for HMF production. In one case, they used microwave irradiation to produce HMF from cellulose and glucose in the ionic liquid [BMIM]Cl using $CrCl_3$ catalyst [316]. HMF yields of around 60% from cellulose and 90% from glucose were obtained, which was much higher than the corresponding yields obtained by conventional oil-bath heating, even when a much longer time was used for the latter. In another work, they studied the effectiveness of different metal salts in catalysing conversion of glucose to HMF in the ionic liquid [BMIM]Cl and found that $ZrCl_4$ was the most effective catalyst [315]. Furthermore, they used the $ZnCl_4$-[BMIM]Cl system to directly convert cellulose to HMF, obtaining maximum yields of around 50%, and showing that the microwave irradiation power had an optimal value, beyond which there was a decrease in yields caused by degradation of the HMF. The $ZnCl_4$-[BMIM]Cl system could be reused multiple times without any significant decrease in HMF yield. The same team also studied the [BMIM]Cl-$CrCl_3$ system for converting lignocellulosic biomass like corn stalk, rice straw and pine wood directly to HMF and furfural, obtaining yields of up to 52% and 31% respectively [313]. Like the two previous works, the yields obtained under microwave irradiation were much higher than those obtained using oil-bath heating.

De, Dutta, Saha and co-workers have also investigated the use of microwave irradiation for HMF production from various feedstocks. Noting that $AlCl_3$ has been shown to be an effective Lewis acid catalyst in ionic liquids, they investigated the efficacy of $AlCl_3$ in aqueous or aqueous biphasic solvents, which are less expensive than ionic liquids [317]. Fructose, glucose, sucrose, starch and inulin were used as the substrates and water, water/MIBK or DMSO was used as the solvent. The HMF yields obtained by microwave heating was as high as 71%, while for conventional heating, the maximum value was only about 36%. DMSO gave a higher HMF yield than aqueous media under microwave irradiation, which was attributed to the higher microwave absorbing ability of DMSO, the occurrence of less side reactions than in aqueous media, and the catalytic ability of DMSO. In case of glucose and sucrose, the maximum HMF yields obtained were 52.4% and 42.5% respectively, while for biopolymers like starch and inulin, the yields were lower, at around 30% and 39% respectively. In a separate work, these researchers used a dimethyl acetamide (DMA)-lithium chloride (LiCl) system to obtain HMF from cellulose and sugarcane bagasse under microwave irradiation [82]. A number of metal chloride catalysts were tried and it was discovered that $Zr(O)Cl_2$ was the most active. The effect of addition of the ionic liquid [BMIM]Cl was tested and it was found that the HMF yield from cellulose increased from around 30% to around 75%. [BMIM]Cl is believed to accelerate cellulose hydrolysis by increasing the concentration of Cl- ions in the reaction medium. For sugarcane bagasse, a $Zr(O)Cl_2/CrCl_3$-[BMIM]Cl system produced an HMF yield of up to 42%.

The research team involved in the previous study also carried out the direct conversion of a number of weeds (like red nut sedge, Indian doab, marijuana, water spinach, water hyacinth, datura, yellow dock, dodder, pigweed, gajar ghas, spiny pigweed, foxtail, wild elephant foot yam and cycus) to HMF and 5-ethoxymethyl-2-furfural (EMF) using microwave heating, Brønsted acidic ionic liquid and silica supported immobilized heteropolyacid (HPA) catalysts [321]. The ionic liquids used were $[DMA]^+[CH_3SO_3]^-$ and $[NMP]^+[CH_3SO_3]^-$, while the HPA used was phosphotungstic acid. A number of the species tested were found to have an HMF yield of more than 20% after treatment at 120°C for 2 minutes with the ionic liquid catalysts, which showed much superior catalytic activity as compared to methanesulfonic acid or the SiO_2-HPA catalyst, although the humin by-product formation was also shown to be higher for $[DMA]^+[CH_3SO_3]^-$ than for the SiO_2-HPA. Between the ionic liquids tested, $[DMA]^+[CH_3SO_3]^-$ had a higher effectiveness than $[NMP]^+[CH_3SO_3]^-$, which was attributed to the better proton donating ability of $[DMA]^+[CH_3SO_3]^-$. $[DMA]^+[CH_3SO_3]^-$ also showed good recyclability, and was hence said to have good potential for industrial application. Both the ionic liquids also showed good activity in converting either HMF or the weeds directly to EMF, with the ratio of EMF to the by-product ethyl levulinate being 7:1.

Qi, Watanabe, Aida and Smith have presented a considerable body of work relating to the production of HMF from a number of different carbohydrates using microwave irradiation. In one work, they stated that most of the processes used for HMF production have drawbacks [318]. Homogeneous acid catalysts achieve medium HMF yields and high fructose conversion but have drawbacks in separation, recycle and corrosion. Solid acid catalysts like H-form zeolites and metal phosphates have the ability to be recycled and high selectivity but offer low fructose conversion. Ion exchange resins are green catalysts but are apparently only suitable below 100°C, which limits reaction rates and therefore their usefulness. Aqueous processes are environment-friendly but inefficient because of the rehydration of HMF to LA and formic acid. Ionic liquids allow for controllability of properties but are often too expensive to be practical. All these issues led them to use an acidic cation exchange resin (Dowex 50wx8-100) in a mixed organic-aqueous system to convert fructose to HMF under microwave irradiation [318]. Since dehydration of fructose to form

HMF is thought to be most selective if fructose is in its furanoid form, acetone-water mixture was used as the solvent, being preferred to DMSO due to the lower boiling point of acetone. Pure acetone offers the highest HMF stability but low fructose solubility, and hence a 70:30 acetone-water mixture was used in this work. The fructose dehydration reaction was found to be of first order, with the obtained activation energy (103.4 kJ/mol) being comparable to literature values. The authors found that HMF yield decreases with increasing initial fructose concentration due to increasing humin formation, with a 2% concentration being the optimal. However, in practice, economic considerations will necessitate the use of higher fructose concentrations. At 20% fructose concentration, an HMF yield of 54.3% with fructose conversion of 89.3% was obtained. Both fructose conversion and HMF yield were much higher for microwave heating than for sand bath heating, which was attributed to 'specific' microwave effects [318].

The same reaction set-up as above, with the exception of acetone/DMSO mixture being the solvent, produced HMF yields of over 88% and fructose conversion of over 97% [128]. The activation energy of the reaction was reported to be only 60.4 kJ/mol, which is considerably lesser than that obtained for the acetone/water mixture in the previous study. Also, the acetone/DMSO mixture had better separation efficiency than pure DMSO, owing to acetone having a lower boiling point than DMSO [128]. In both of these studies, the Dowex resin used worked well at 150°C and showed no decrease in catalytic activity after being reused five times. Qi, et al. also investigated HMF synthesis from both fructose and glucose using TiO_2 and ZrO_2 as catalysts with water as the solvent [74]. In case of fructose, TiO_2 was the better catalyst than ZrO_2 in terms of both fructose conversion and HMF yield, while neither catalyst gave very good yields for glucose.

Wang, et al. prepared HMF from cellulose and wheat straw using microwave irradiation and [BMIM]Cl [137]. A number of solid acid and metal catalysts were tried, and $CrCl_3$/LiCl was found to give the highest HMF yields from cellulose. This catalyst was then used to hydrolyse wheat straw directly, and gave a maximum HMF yield of 61.4% (based on cellulose content) and maximum furfural yield of 43.8% (based on xylan content). The ionic liquid and catalyst showed no decrease in activity after being recycled three times. Lu, et al. used an acidic phosphate buffer system to convert concentrated solutions of fructose and glucose (up to 50 wt%) to HMF, with a conversion of over 85% and HMF yield of more than 62% being obtained in case of fructose [314]. Conversions and yields for glucose were much lower, but when borate was added as a promoter to increase isomerisation of glucose to fructose, a conversion of 87% and yield of 43% was obtained for a 30 wt% solution.

Szabolcs, et al. converted a number of carbohydrates to LA using microwave irradiation [319]. HCl and H_2SO_4 were used as the catalysts, and initially, compounds with small molecules, like fructose, glucose and cellobiose were hydrolysed to arrive at the optimum reaction conditions, before these conditions were used for cellulose. A maximum LA yield of 46% with HCl and 34.2% with H_2SO_4 was obtained, although the authors preferred the use of H_2SO_4, citing environmental concerns associated with the use of chlorine-containing catalysts. In case of chitin, the LA yield obtained using H_2SO_4 (37.8%) was higher than that obtained using HCl (32.7%).

Galletti, et al. investigated the hydrothermal conversion of different raw materials to LA using both autoclave heating and microwave irradiation [284]. HCl (37%) and H_2SO_4 (98%) were used as catalysts, with HCl proving to be better than H_2SO_4 with higher LA yields and lower salt precipitation and humins deposition. Microwave irradiation gave higher yields for runs conducted for 15 minutes than for autoclave runs for 1 hour for the biomass tested (olive tree pruning, poplar sawdust, paper sludge, wheat straw). However, the authors stated that when the traditional heating was carried out in two steps, with a pre-hydrolysis run being carried out at lower temperature before the actual conversion, yields even higher than those obtained using microwave irradiation were obtained, as the accessibility of cellulose was improved via solubilisation of a part of the hemicellulose fraction. The authors also investigated the suitability of niobium phosphate as a catalyst for producing HMF from inulin and wheat straw and obtained LA yields of up to 28% from inulin and 10% from wheat straw, although recovery of the niobium phosphate from the solid lignin residue was problematic.

This section clearly shows the research interest in using microwave heating for synthesising HMF and LA, which is justified by the high yields obtained from a variety of feedstock at moderate temperatures and short reaction times. Future work should be directed towards developing pilot scale reactors using microwave heating.

2.13 Conclusions

HMF and LA are promising biorefinery platform chemicals, but for these to be commercialised successfully, they will need to be synthesised economically in large yields from a range of different biomass feedstocks with a minimal environmental footprint. While monosaccharides like fructose may offer the highest product yields, the use of polysaccharides, and in particular lignocellulosic materials, is required for commercial-scale production to be viable from both the sustainability and economical viewpoints. While one-pot reaction systems which avoid extensive feedstock pre-treatment and product purification steps are preferable in this regard, in reality, the use of a range of biomass will necessitate pre-treatment to ensure homogeneity of the substrate fed to the reactors. The development of pre-treatment options that can economically handle a range of feedstock is therefore a pre-requisite.

For this to be achieved, improvements are needed in the catalyst and solvent systems. Liquid acid catalysts are used widely in laboratory scale syntheses, but in larger scale processes, there are challenges in separating the products with high purity and without degradation, recovering and recycling the catalyst, and tackling ecological and safety hurdles. Solid catalysts are easier to recover and recycle, but tend to give lower product yields than homogeneous catalysts, and need to be regenerated between runs. A vast number of catalysts have been tested to address these issues, with several promising candidates being identified on a lab-scale, but greater pilot-scale testing needs to be carried out to see if these results can be replicated economically at larger scales. The development of non-toxic, cheap, and easily recyclable solvents is another area where pilot studies have to complement the existing lab based efforts. Biphasic solvents, in particular, show great promise at smaller scales, and hence need to be used in pilot plants. Ionic liquid- and microwave irradiation-based reaction systems are the two most promising routes from the standpoint of high product yields from a range of feedstocks. Indeed, it may be said that ionic liquid-based methods have received more research attention in HMF production than almost any other reaction system. To an extent, this is justified by the product yields that have been achieved even at moderate temperatures and short reaction times from various substrates. Despite this, a number of barriers must be overcome, the most significant among them being their high cost. The influence of moisture and other impurities on the properties of ionic liquids is also an area of concern. In addition, despite the tag of ‘green solvents’ that ionic liquids have traditionally had, the synthesis of more environmentally-benign ionic liquids using sustainable process techniques is also under research. Therefore, it is likely to be a while before ionic liquids can be considered seriously for industrial-scale HMF production. In case of LA, even lab-scale data on the use of ionic liquids is scanty, and this may be of interest to future researchers.

Microwave irradiation, on the other hand, is more eco-friendly, offers rapid and uniform heating profiles, and has the added benefit of enabling the use of water or other environmentally benign solvents. It is an area where further research needs to be directed, particularly with the aim of reducing capital and operational costs, and to ensure larger scale operation than the present laboratory-scale systems. Continuous flow microwave heating systems also need to be developed as the semi-continuous stop-flow microwave systems that are often used in lab-scale studies offer low productivity even at high product yields. This is because a majority of the time in these systems is spent in heating and cooling, reducing the actual run-time in the overall process [328]. The energy-efficiency of microwave heating vis-a-vis conventional heating is mainly due to the reduced heating time, and this aspect needs to be preserved in larger scale systems, along with the other major advantage of uniform heating. Multi-mode heating, continuous operation, the use of lower frequencies, the incorporation of stirring, and other suggestions that have been put forward in this regard need to be validated at pilot scales.

One point that is often overlooked in HMF and LA production is the need for efficient isolation of the prepared compound from the solution. In literature, the yields stated have often been determined using HPLC or GC, but in industrial applications, the actual isolated yields obtained may be considerably lower [80]. The purity of the isolated compound will also differ for different isolation techniques. Therefore, alongside work on optimising HMF and LA yields, isolation techniques that can yield high purity products economically at industrial scales also need to be developed. This would solve what is currently one of the most pressing problems affecting industrial-scale production of these compounds [329, 330].

Connecting Statement 1

It was seen in Chapter 2 that polysaccharides are considered to be more sustainable feedstocks than monosaccharides like glucose and fructose. However, their depolymerisation to the constituent monosaccharides is the first step in their conversion to products like HMF and LA. Facilitating HMF and LA production therefore requires an understanding of the factors that affect polysaccharide depolymerisation. In case of starch, the most important difference between varieties is the composition, in terms of the amylose:amylopectin ratio. This can lead to differences in physical and chemical properties such as solubility and susceptibility to acid hydrolysis.

Chapter 3 examines the role played by the starch composition on LA yields by comparing the results obtained for unfractionated starch with those for the amylose and amylopectin fractions. This chapter is based on an article published in Starch/Stärke. This manuscript was co-authored by Dr Marie-Josée Dumont.

Chapter 3 : Influence of the starch structure in the synthesis and the yield of levulinic acid

3.1 Abstract

Starch is a promising feedstock for the synthesis of chemical intermediates like levulinic acid (LA), but the role played by the amylose-amylopectin ratio of starch in LA yields has not been investigated so far. In this work, corn starch was fractionated using the aqueous leaching-alcohol precipitation method and the morphological and thermal degradation characteristics of the amylose and amylopectin obtained were studied. A comparison of the results of acid-catalysed hydrolysis of the original starch and the fractions showed that differences in granule size, solubility, and susceptibility to acid hydrolysis are the main factors affecting LA yields. Amylopectin yielded LA at faster rates at 150 °C and 165 °C than amylose, which is a factor that may influence the selection of starches for the production of LA at industrial scale.

3.2 Introduction

The twin problems of global warming and fossil fuel depletion can be said to be among the most serious issues confronting humankind today. Accordingly, the replacement of fossil fuel-based energy systems with renewable alternatives has been on the agenda of researchers and policy makers in recent years [331]. Among the possible options for renewable resources, biomass stands out owing to the fact that it is the only renewable form of organic carbon. Therefore, unlike other renewable energy options, biomass is a potential substitute for petrochemicals, whose production accounts for a significant percentage of the world crude oil consumption. The replacement of petroleum refineries with biorefineries will necessitate the identification of platform chemicals that can be used to create thousands of products in a manner similar to the seven chemicals (toluene; benzene; xylene; 1,3- butadiene; propylene; ethene; methane) that are the backbone of the petrochemical industry [6]. Levulinic acid (LA) is one of the most promising potential biorefinery building blocks due to the numerous chemicals that can be derived from it and the ease with which it can be produced from a range of feedstock [9]. γ-valerolactone (GVL), ethyl levulinate, 2-

methyltetrahydrofuran, 1,4-pentanediol, diphenolic acid, β-acetylacrylic acid, and δ-aminolevulinic acid are some of the potential chemicals that can be derived from LA [332, 333].

Starch is one of the cheapest and most abundant carbohydrates. It can be produced from a variety of natural sources such as maize, wheat, potato, tapioca, rice, sorghum, etc. [334]. Additionally, numerous modified starches have been produced via chemical and physical modifications for applications requiring specific starch properties. Compared to cellulose and lignocellulosic biomass, starch can be depolymerised more easily to simple sugars [335]. This means that starch is amenable to relatively facile conversion to LA, and is hence a possible feedstock for LA manufacture. However, in order to avoid competition with food resources, it is imperative for the starch selected as feedstock to be capable of providing high LA yields. It is known that the properties of different starches vary based on their origin and are dependent on granular organisation and the structure of the constituent polymers. To find out which starch is best suited to LA manufacture, it is necessary to determine the role that starch structure plays in the reaction to form LA.

The conversion of a polysaccharide like starch to LA is an acid catalysed reaction involving the hydrolysis of the polysaccharide molecule into its constituent hexose monosaccharides, which is glucose in case of starch. The monosaccharides are converted via the loss of three water molecules to 5-hydroxymethylfurfural (HMF), which is then rehydrated to LA (Figure 3-1) [332].

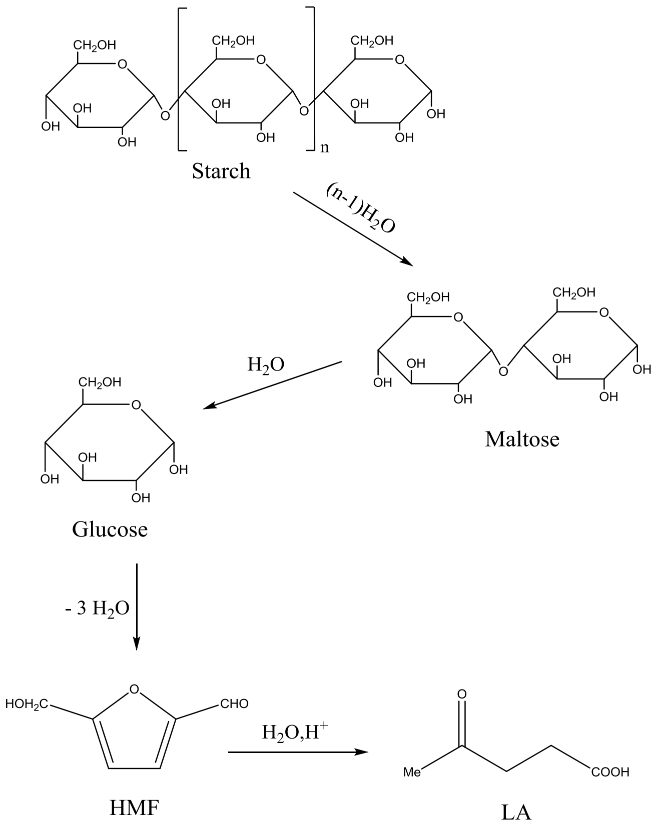


Figure 3-1: Reaction scheme showing the conversion of starch to LA

Starch is predominantly composed of amylose and amylopectin, with amylose mainly straight-chained, while amylopectin is branched. This difference arises because while amylose has mainly α-1,4-glycosidic bonds in a linear pattern, in amylopectin, the α-1,4-glycosidic chains are connected at branch points by α-1,6-glycosidic bonds. Due to the branching, the number- and weight-average molecular weights of amylopectin are generally of the order of 10,000,000 while the corresponding values for amylose are of the order of 100,000 [336, 337]. Amylose is almost insoluble in water, while amylopectin is relatively more soluble [338-340]. This can be attributed to their molecular structure, wherein amylopectin is less coiled than amylose due to its branching structure, leaving its –OH groups more exposed and accessible to H-bond formation [339]. Since the hydrolysis of starch is the first step in its conversion to LA, these differences in molecular structure and solubility can affect the product yield. For instance, Chun et al. found that both the yields of the LA precursor HMF and the relationship between the yields and HCl concentration used vary based on the starch source. They stated that this may be due to differences in starch hydrolysis and dehydration caused by different amylose to amylopectin ratios [341].

To verify this hypothesis, corn starch was separated into amylose and amylopectin, and the LA yields obtained from the fractions were compared to the yields obtained from unfractionated starch.

3.3 Materials and Methods

3.3.1 Chemicals

Corn starch containing 73% amylopectin and 27% amylose was purchased from Sigma Aldrich Co. LLC, USA. The 2M HCl catalyst used was prepared from 12.1N HCl purchased from Thermo Fisher Scientific, USA. The High Performance Liquid Chromatography (HPLC) mobile phase was prepared using 90% HPLC grade water and 10% HPLC grade acetonitrile, both purchased from Sigma Aldrich. For the HPLC and gas chromatography mass spectroscopy (GC-MS) analysis, 99% food grade levulinic acid and ≥ 99% butyric acid (both from Sigma Aldrich) were used for calibration and as internal standard respectively. For the starch fractionation, anhydrous (99.8%) 1-butanol and anhydrous (99.8%) methanol (both from Sigma Aldrich) were used.

3.3.2 Experimental Procedure

3.3.2.1 Starch fractionation

Numerous methods for fractionation have been reported in the literature. These typically involve either aqueous dispersion or aqueous leaching of the starch granules followed by selective retrogradation or alcohol precipitation of the components. Studies comparing the different methods showed that the best results in terms of purity and quantity of the separated fractions appeared to be obtained via a combination of hot water treatment and precipitation of the components with methanol and butanol [342, 343]. Accordingly, a 4% w/v slurry of corn starch in water was prepared and heated with constant stirring at 75 ^{o}C for 45 minutes. This led to penetration of water into the starch granules, causing them to swell. The amylose leached out of the granules into the water, and was separated from the residual amylopectin via centrifugation at 3000 g for 8 minutes. The precipitate obtained was leached again at 75 ^{o}C for 45 minutes and centrifuged. This step was repeated twice, after which methanol was added in equal volume to the final precipitate to obtain amylopectin. 100% butanol was added in 1/3rd volume to the pooled supernatant from all the runs, and amylose was obtained as the precipitate after two hours. Both the amylose and amylopectin fractions were then freeze-dried to obtain the final samples. The characterisation of the amylose and amylopectin fractions was done using the iodine binding procedure [344], with a comparison of the spectrophotometric curves (ThermoSpectronic (USA) UV 1 spectrophotometer) between 400 and 800 nm of the respective iodine complexes. This method relies on the ability of amylose to form helical inclusion complexes with iodine that display a blue colour characterised by a maximum absorption wavelength (λmax) above 620 nm [345]. The far greater iodine binding capacity of amylose (~ 20 mg/mg) compared to amylopectin (~0.2 mg/mg) [345] enables spectrophotometric differentiation of the two components.

3.3.2.2 Synthesis of LA

Acid hydrolysis is the preferred method of biomass depolymerisation, owing to the shorter reaction times involved as compared to enzymatic hydrolysis [266]. The acid catalysed hydrolysis of polysaccharides can either be carried out using concentrated mineral acids and low operating temperatures or dilute acids and high operating temperatures [332]. The latter approach is generally considered favourable due to reduced cost of acid recovery and reactor construction during industrial scale operation [269]. HCl has been shown to be more effective at catalysing LA synthesis than other mineral acids [254]. A trial experiment with different HCl concentrations showed 0.01M and 0.3M concentrations were too dilute to give high LA yields for reaction times of less than one hour, while a concentration of 2M gave high LA yields without being so concentrated as to negate the advantages of dilute acids mentioned above. Hence, in this work, 2M HCl was used as the catalyst. A temperature range of 135-165 ^{o}C was used, since in preliminary runs, very low LA yields were obtained at temperatures below 135 ^{o}C, while the use of temperatures above 165 ^{o}C led to charring even at short reaction times. The reaction times studied were 5, 15, 30, 45 and 60 minutes.

An oil bath was preheated to the desired reaction temperature and then Pyrex glass tubes containing 25 mg of the substrate and 2.5 ml of 2M HCl were inserted in the bath. The small quantity of sample in the tubes ensured a more even heat distribution and better turbulent mixing. The low concentration of the substrate (1% w/v) also helped ensure against mass transfer limitations. Once the appropriate reaction time was reached, the tubes were removed and put in an ice bath to stop the reaction. The contents of the tube were filtered using a syringe filter (0.2 μm) into 2 ml autosampler vials for further analysis. All the runs were carried out in triplicate.

3.3.3 *Analysis of substrates and products*

The morphology of the unfractionated starch and the freeze dried amylose and amylopectin fractions was studied using a Scanning Electron Microscope (SEM) (TM3000, Hitachi High-Technologies Co., Tokyo, Japan) at an accelerating voltage of 5000 V.

The crystallinity of the fractionated amylopectin and amylose, as well as the unfractionated starch, was studied using X-Ray Diffraction (XRD) (D8 Discovery X-Ray Diffractometer, Bruker Corporation, MA, USA), equipped with a VANTEC detector and a Cu-source. The crystallinity of the samples was studied in a diffraction angle range of 4-30°, and the results analyzed using the software Diffrac Eva 4.0 (Bruker Corporation, MA, USA).

The thermal behaviour of starch and its fractions was studied using a thermogravimetric analyser (TGA) (Q500, TA Instruments, New Castle, DE, USA). The thermogravimetric analyses were carried out under a stream of nitrogen at a flow rate of 60 ml/min. The weight of each sample taken was between 3 and 4 mg and was heated from room temperature to 600 °C at a constant rate of 20 °C/ min. All the samples were tested in duplicate.

Differential Scanning Calorimetry (DSC) runs were conducted using a Q100 DSC (TA Instruments, New Castle, DE, USA). The samples tested were in the weight range of 5-6 mg. All samples were prepared in duplicate in hermetically sealed aluminium pans and heated from 35 °C to 350 °C at a heating rate of 10 °C/min under a stream of nitrogen (50 ml/min).

The LA yields were determined using an Agilent 1260 HPLC system fitted with a Zorbax Eclipse Plus C18 (4.6 X 100 mm, 3.5 μm) column and a Variable Wavelength Detector (VWD) set at 250 nm. The column temperature was set at 60 °C and the mobile phase was an isocratic 90:10 mixture of water and acetonitrile with an eluent flow rate of 0.2 ml/min. The LA yields were expressed in terms of the wt% yields calculated from a calibration curve plotting concentrations of pure LA against areas obtained under the HPLC curve. The following formula was used for calculating the LA yields:

$$LA\ yield\ (wt\%) = \frac{Weight\ of\ LA\ produced\ (mg)}{Weight\ of\ substrate\ fed\ (mg)} \times 100\% \qquad (1)$$

A similar procedure was used for detecting the concentrations of the intermediates glucose and HMF.

To determine the intermediates, the vials were also subjected to GC-MS analysis (Agilent 6890N GC/Agilent 5973 Network MS with HP-5MS column). Butyric acid was used as the internal standard. The GC-MS oven temperature was programmed from 40 to 300 °C at a ramping rate of 10

°C/min. Both the initial and final temperatures were held for 5 minutes. The flow rate of the carrier gas (helium) was 1.3 ml/min. The mass spectra of the GC-MS results were analysed using NIST MS Search 2.0 library to identify the intermediates.

3.4 Results and Discussion

3.4.1 Starch fractionation

The separation of amylopectin and amylose obtained via starch fractionation are shown from their respective spectrophotometric curves in Figure 3-2.

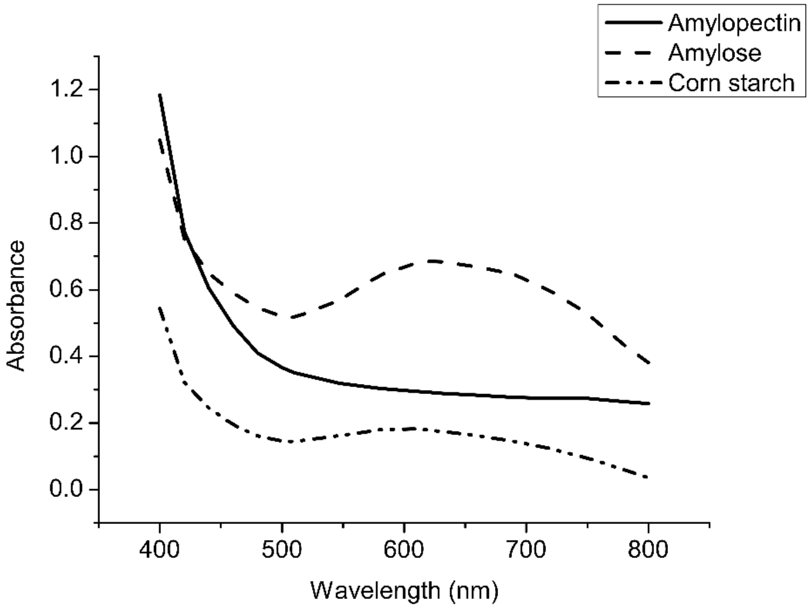


Figure 3-2: Spectrophotometric curves for amylopectin, amylose and corn starch

A clear difference in the iodine-binding characteristics is seen, reflecting the fact that amylose forms a strong complex with iodine, giving a deep blue colour, while the amylopectin-iodine complex is much weaker and has a pale purple-red coloration. These results are broadly consistent with literature [344, 346], and reflect the successful separation of the two components. The spectrophotometric curve of the unfractionated corn starch is also provided for comparison. The absorbance of the unfractionated starch is less than of the components, but the trend is as expected, with the curve parallel to that of amylopectin for most of the spectrum, with a rise in absorbance occurring in the region around 600 nm owing to the increase absorbance of the amylose component.

3.4.2 Scanning Electron Microscope (SEM)

The amylopectin was obtained in the form of a hard solid, while the amylose was in the form of a thin film. The SEM images of the amylopectin and amylose (Figure 3-3 (a) and (b) respectively) reflected the difference in morphology of the two fractions. The amylopectin can be observed to be densely packed, with very few spaces or pores apparent. The amylose, on the other hand, appears to be ribbon-like and porous. The structures of both amylopectin and amylose are markedly different from the unfractionated starch (Figure 3-3 (c)), which is in the form of discrete granules. At higher magnification (Figure 3-3 (d)), it is clear that the granules of corn starch are much smaller than 100 μm in size, which tallies with the 15μm size mentioned in literature [347]. The role played by this size difference between the corn starch granules and the fractions in determining LA yields is explained in the discussion of Section 3.4.6.

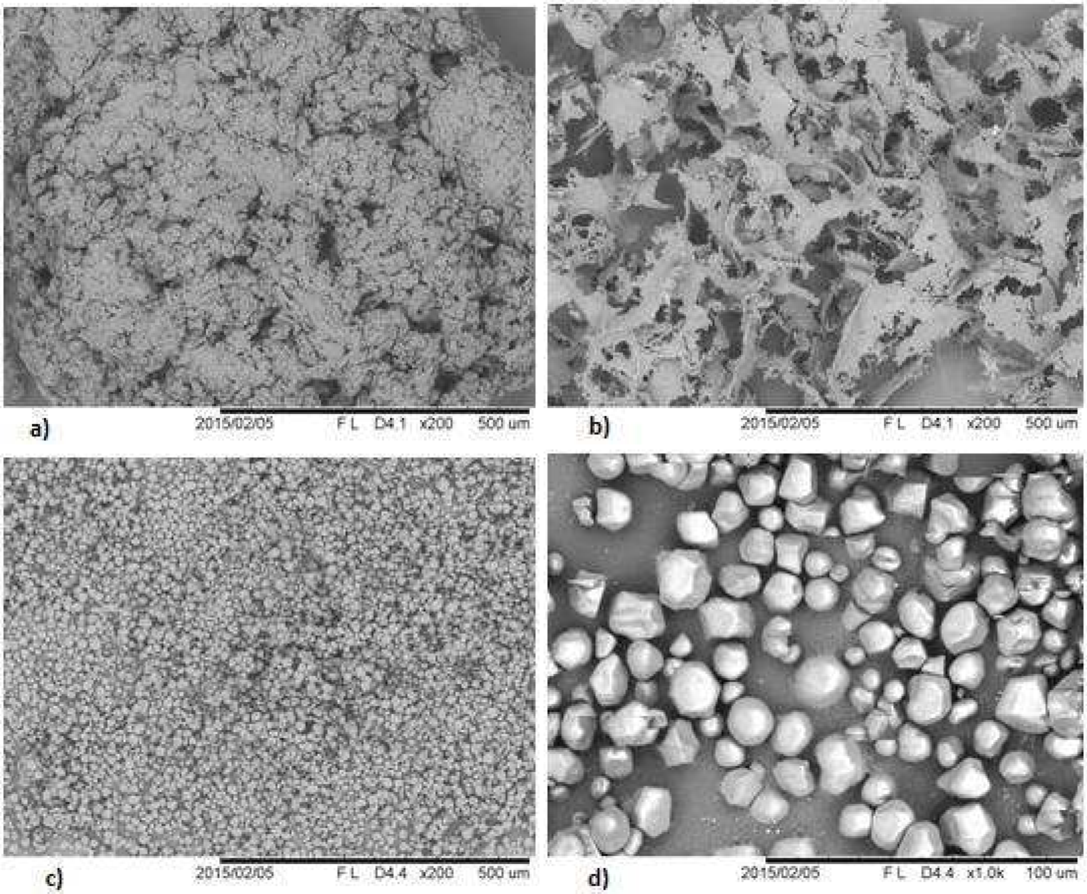
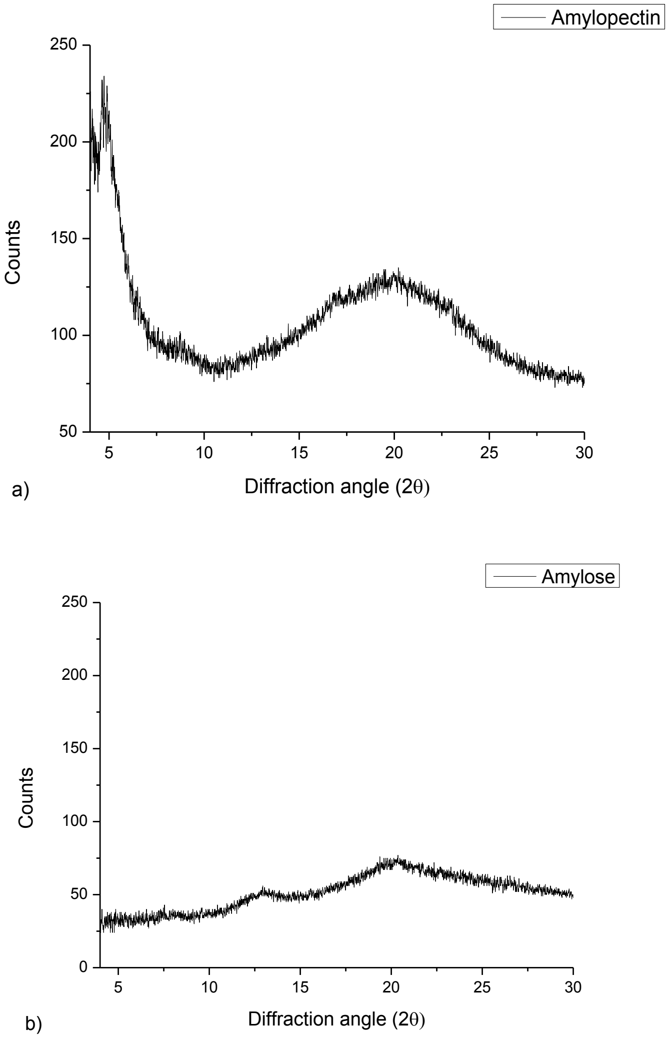


Figure 3-3: Scanning Electron Microscope scans of (a) amylopectin (x200 magnification) (b) amylose (x200 magnification) (c) corn starch (x200 magnification) (d) corn starch (x1000 magnification)

3.4.3 X-Ray Diffraction (XRD)

To compare the crystallinity of the fractionated amylopectin and amylose with each other and with the unfractionated starch, an X-Ray Diffraction (XRD) analysis was conducted, and the results are shown in Figure 3-4.



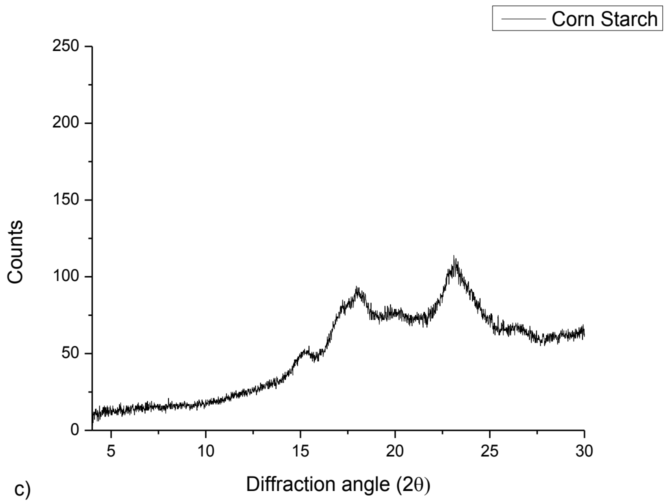


Figure 3-4: X-Ray Diffraction scans of a) amylopectin; b) amylose and c) corn starch

A diffraction angle 2θ range of 4-30^{o} was scanned, since this region covers all the significant diffraction peaks of starch crystallites [348]. In this range, it was calculated, using the software Diffrac Eva 4.0 (Bruker Corporation, MA, USA), that the crystallinity of the amylopectin is 14.5%, while those of the amylose and unfractionated starch are 1.3% and 6.5% respectively. The higher crystallinity of the amylopectin plays an important part in the LA yields obtained, as is explained in Section 3.4.6.

3.4.4 Thermogravimetric Analysis (TGA)

Since high temperature acid hydrolysis of starch and its fractions involves the breakage of glycosidic bonds via a combination of hydrolysis and thermal degradation, it was important to examine if there were any significant differences in the thermal degradation characteristics of the substrates. This was done by TGA, with the curves for amylopectin, amylose and corn starch shown in Figure 3-5. The differential thermogram (DTG) curve, denoting the weight loss of the sample per unit time, is also present in the figure. The temperatures at which the major thermal events of the samples occurred are outlined below.

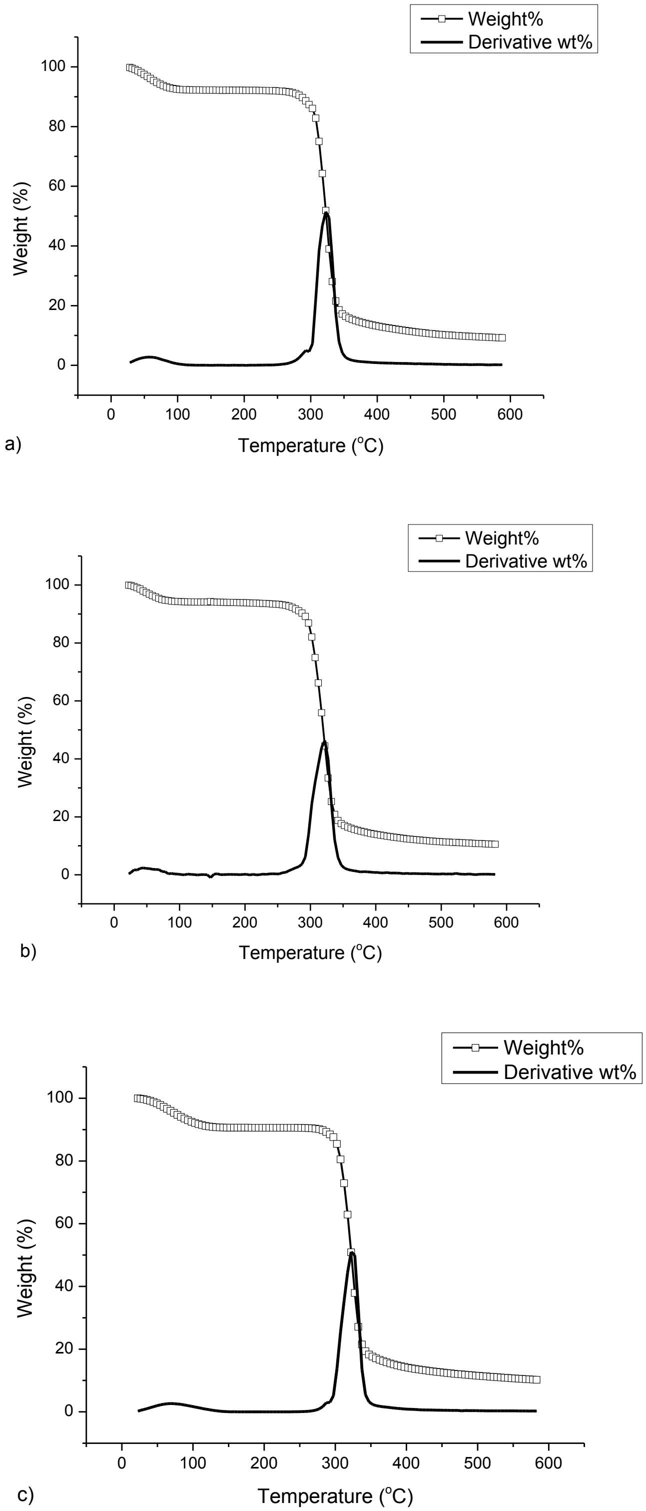


Figure 3-5: Thermogravimetric Analysis and Differential Thermogram curves of a) amylopectin; b) amylose and c) corn starch

The initial weight loss, occurring up to around 100 °C, denotes the loss of the moisture content of the sample, which can be estimated to be 7% for the amylopectin sample, with the corresponding values for starch and amylose being 8% and 5% respectively. The major weight loss for each sample occurs in the region of 270-360 °C and corresponds to thermal decomposition of the samples via breakage of the molecular chains. The thermal behaviours of the unfractionated starch and the fractions in this region are fairly similar, but slight differences, particularly in the respective temperatures of incipient devolatilisation can be observed. The incipient devolatilisation temperatures for corn starch, amylopectin and amylose, measured as the temperature at which the rate of weight loss exceeds 1 wt%/min, are 278 °C, 271 °C and 264 °C respectively, while the peak devolatilisation occurs at 324 °C, 322 °C and 322 °C respectively. The slightly higher incipient devolatilisation temperature for amylopectin as compared to amylose is due to its larger molecular weight and the presence of more α-1,6 linkages [349].

3.4.5 Differential Scanning Calorimetry (DSC)

A qualitative picture of the differences in the energy required for thermal degradation of the fractions was obtained by conducting DSC analysis of starch, amylopectin and amylose, the results of which are shown in Figure 3-6.

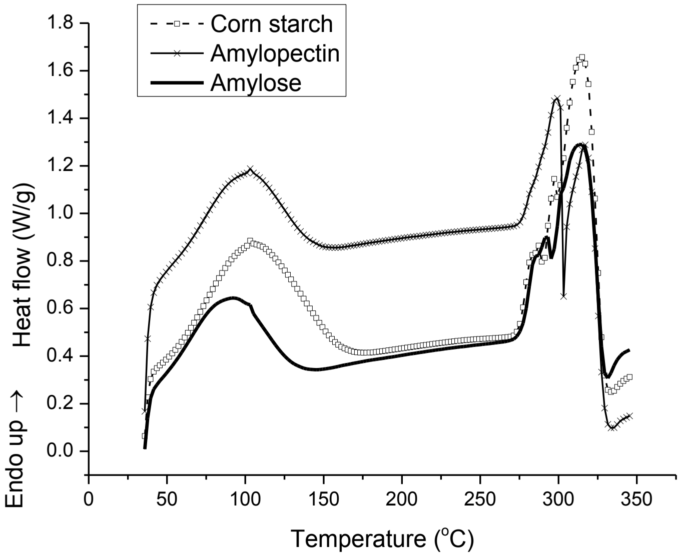


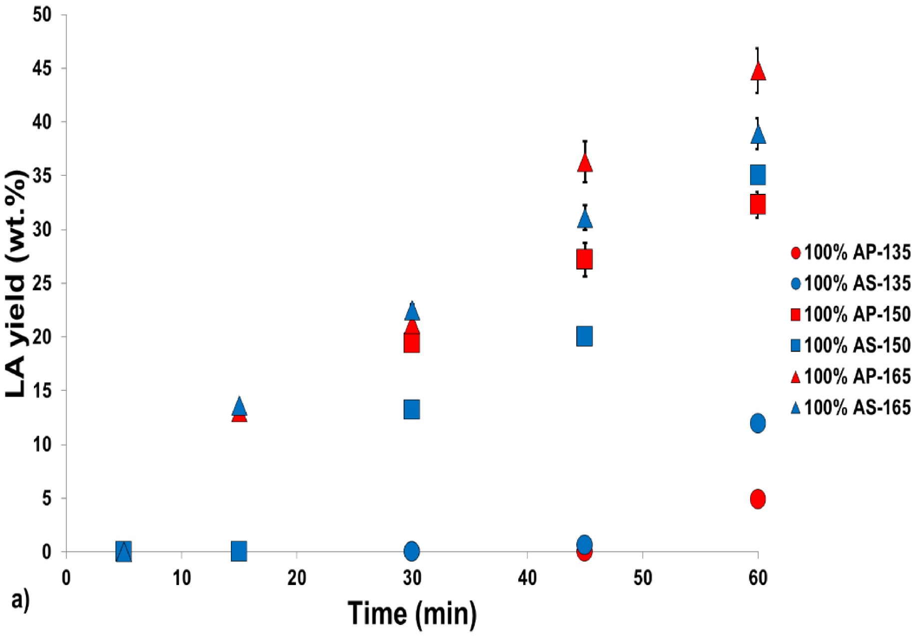
Figure 3-6: Differential Scanning Calorimetry curves for corn starch, amylopectin, and amylose

It may be noted that the general pattern of the heat flow corresponds to the thermal degradation patterns observed in the TGA. Overall, each curve shows two regions of endothermic heat flow. The first is an increase from around 60 ºC, with a peak at around 100 ºC. This represents heat absorption due to moisture evaporation. The next increase in endothermic heat flow occurs starting from about 280 ºC, peaking in the range 300-320 ºC. This heat flow is due to the thermal degradation of the samples and was also observed by TGA.

From a qualitative standpoint, it can be seen that the endothermic heat flow in the gelatinisation region was the greatest for amylopectin and the least for amylose, with the unfractionated starch being intermediate. The higher heat flow required for amylopectin to reach gelatinisation was probably due to its crystalline nature. This was in line with literature, where it has been observed that high amylopectin starches have a higher heat of gelatinisation than high amylose starches [350, 351], possibly due to the energy required to break down the crystalline regions of amylopectin [351].

3.4.6 Synthesis of LA

The LA yields were calculated based on HPLC results. The LA yields obtained from the different substrates are shown in Figure 3-7, along with the standard deviations for the triplicate runs. In all cases, the standard deviation between the triplicates was less than 12%.



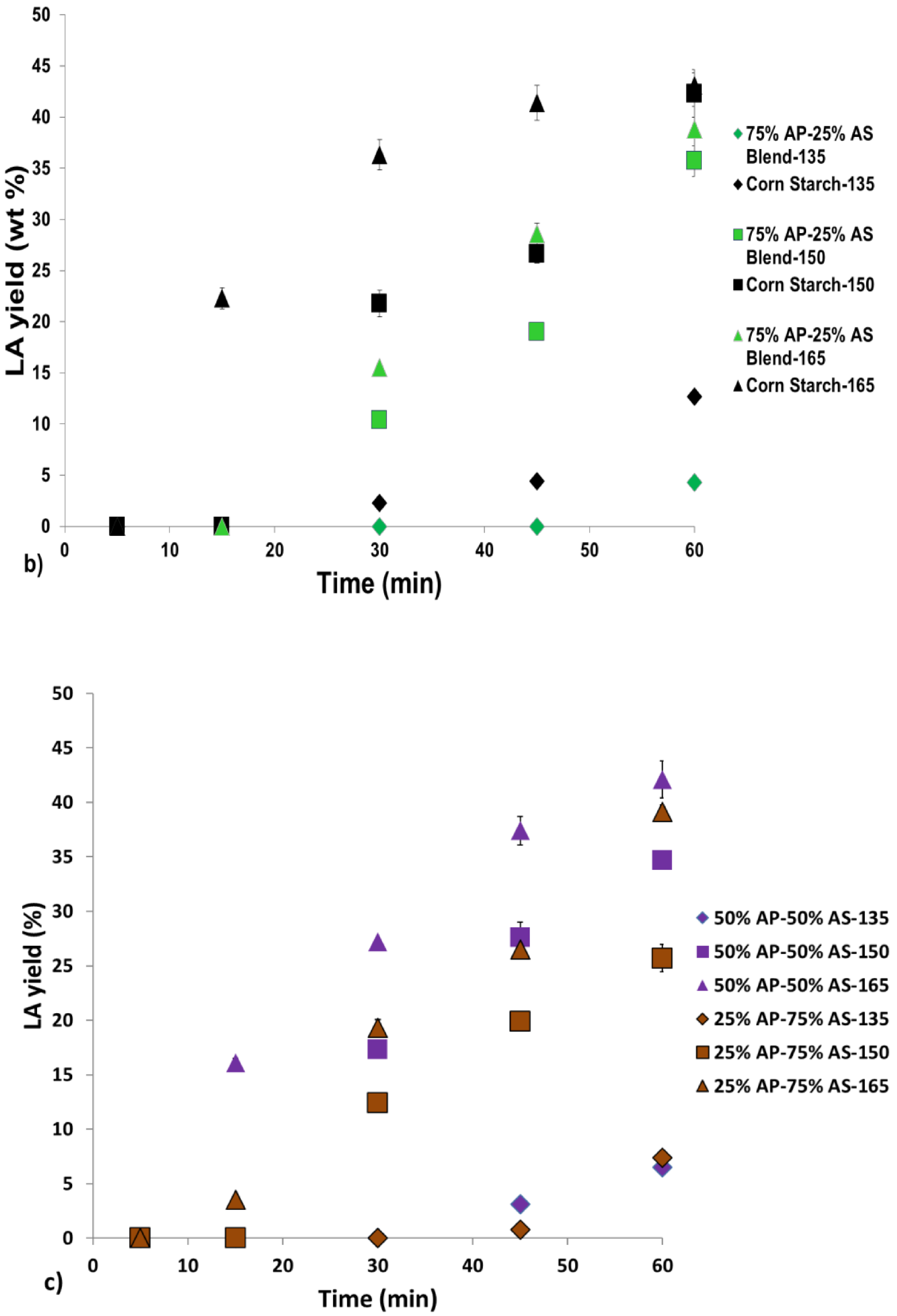


Figure 3-7: LA yields at different reaction temperatures from a) amylopectin (AP) and amylose (AM); b) 75% amylopectin–25% amylose blend and corn starch; c) 50% amylopectin–50% amylose blend and 25% amylopectin–75% amylose blend

The results for pure amylopectin (Figure 3-7 (a)) show that at 135 ºC, yields of LA are negligible until the reaction time reaches 60 minutes. Even at such a long reaction time, the LA yields are only around 5 %. An increase in reaction temperature to 150 °C leads to a jump in the yields obtained, with a 19 % yield after 30 minutes and 32 % after 60 minutes. This trend continues with a further increase in reaction temperature to 165 °C.

In case of pure amylose (Figure 3-7 (a)), while the broad trends are similar to those seen for amylopectin, there are some important differences in the behaviour exhibited. At 135 °C, the LA yield obtained is nearly 12 % for a reaction time of 60 minutes, which is much more than what had been obtained from amylopectin. At higher temperatures, however, the behaviour is reversed, and LA yields from amylose are either lower or comparable to those obtained from amylopectin. In particular, the maximum LA yields obtained, which are achieved at longer reaction times (45 and 60 minutes) at 165 °C, are significantly higher for amylopectin than for amylose.

Since the conversion of both amylose and amylopectin to LA involves the hydrolysis of the polysaccharide molecules to glucose as a preliminary step, the reason for this difference in the behaviour at low and high temperatures can be understood by comparing the physical properties and molecular structures of the isolated amylopectin and isolated amylose. As can be seen in Figure 3-3, and as was confirmed by XRD, isolated amylopectin has a densely packed crystalline structure, while the isolated amylose is in the form of a porous thin film. It is therefore suggested that at lower temperatures, the accessibility of the acid to the amylose molecules is higher than to the amylopectin. This leads to higher rates of hydrolysis for the amylose molecules, and consequently higher LA yields.

At increased temperatures (150 °C or above), however, the amylopectin particles disintegrate and offer more molecular access to the acid. At this stage, the branched structure of amylopectin offers greater accessibility for solubilisation, and hence the LA yields increase accordingly.

The corn starch used has an amylopectin to amylose ratio of 73:27. To examine the effect of the amylose-amylopectin linkages in the starch molecule on LA yields, the yields from 75:25 blend of amylopectin and amylose were compared with those from pure corn starch. The results are shown in Figure 3-7 (b). For all temperatures and reaction times, the corn starch gives a higher yield than the amylose-amylopectin blend. This largely boils down to the difference in the granule size and crystallinity. As was seen in Figure 3-3 (d), corn starch is present as discrete granules 15-100 μm in size, while the amylopectin granules (Figure 3-3 (a)) are of considerably larger size. The corn starch, therefore, offers much higher accessibility to acid due to its small granule size, compared to the relatively large pieces of isolated amylopectin that make up the major portion of the blend. The difference in the obtained yields is relatively smaller at longer reaction times and higher temperatures, which may be due to the amylopectin crystals slowly breaking down into smaller particles.

The curves of LA yields from corn starch showed a different trend at 150 °C and 165 °C than the other substrates. For pure amylose, pure amylopectin and amylose-amylopectin blends, it may be observed that the 150 °C and 165 °C curves are roughly parallel. For corn starch, however, in case of the 150 °C curve, it is seen that the LA yield rises fairly slowly initially, before moving up rapidly at 60 minutes reaction time. The 165 °C curve, on the other hand, shows an opposing trend, with relatively high yields achieved at 30 minutes reaction time, followed by the yields plateauing from reaction times 30 to 60 minutes. This behaviour appears to indicate that there exists an initial barrier to starch breakdown which requires either long reaction times or sufficiently high temperatures to overcome.

When starch is exposed to acid, the initial effect of the acid is to form a stable and resistant complex by the creation of additional hydrogen bonding between the amylose and segments of amylopectin [352]. This leads to the amylose fraction being protected initially, while the amylopectin molecules are attacked in their vulnerable parts. These are the portions of the amylopectin that lie in the intervening amorphous regions as the molecule stretches from one crystallite region to another [352]. After this, there is preferential hydrolysis of the rest of the amorphous region, where the amylose predominantly exists [14], and the crystallite region is hydrolysed at the end [353]. This sequence explains why LA yields are relatively low initially at 150 °C, followed by a rapid increase once the resistant complex is broken. At 165 °C, the higher temperature allows the activation energy barrier of the resistant complex to be overcome more easily, allowing for higher yields at shorter times.

The results of the runs on 50% amylopectin-50% amylose and 25% amylopectin-75% amylose blends are also given in Figure 3-7. In general, the patterns described for the other substrates are replicated for these blends. For instance, the 25% amylopectin-75% amylose blend shows greater yields at lower temperature (135 °C) and shorter reaction time than the 75% amylopectin-25% amylose blend, while the latter had higher or comparable yields at higher temperatures and longer reaction time. The 50% amylopectin-50% amylose blend, however, gave higher LA yields under almost all conditions than the other blends.

The substrates were completely hydrolysed except in case of the reactions carried out for 5 minutes at 135 ^{o}C. At the end of the 135 ^{o}C-5 minute runs, a white gelatinous residue remained at the bottom at the tube in all cases. In case of the 135 ^{o}C-15 min runs, however, a clear liquid was obtained as the end product, indicating complete hydrolysis of the substrates into soluble saccharides. For long reaction times (30 minutes and longer) and high temperatures (150 and 165 ^{o}C), a dark insoluble residue was obtained at the end. This was humin, the solid polymeric by-product obtained via cross-polymerisation during acid hydrolysis of carbohydrates[96], and whose rate of formation largely depends on the reaction temperature [354]. Humins are also known as pseudo-lignin [355], and they have been stated to be acid-insoluble material consisting of carbonyl, carboxyl, aromatic and aliphatic structures [356]. Humins are difficult to analyse, and their composition and formation pathways are poorly understood [41, 186, 354], and hence most researchers merely note their formation as dark brown solids without conducting further analysis [21, 99, 186, 357]. In this work also, only the liquid products were analysed further.

As shown in Figure 3-1, glucose and HMF are intermediates in the formation of LA from starch. The concentration of glucose can be expected to increase in the early stages of a run owing to starch hydrolysis, before reducing owing to the conversion of glucose to HMF and LA. This is the pattern that was observed during HPLC analysis of the samples. For instance, for the reaction temperature of 135 ^{o}C, the peak glucose yield of around 65 wt% occurred at a reaction time of 15 minutes for the starch sample. A kinetic analysis of the conversion of starch to glucose and the subsequent formation of HMF and LA will be the subject of a forthcoming work.

The production of HMF during the runs was also monitored using HPLC analysis. It was found that the HMF yield detected never crossed 2% for any of the runs. The reason for this is that the conversion of HMF to LA is kinetically much faster than the conversion of glucose to HMF [21, 270]. Therefore, once formed, the HMF is rapidly converted to LA, leading to the detection of only small quantities of this intermediate.

A GC-MS analysis was conducted to identify the intermediates and byproducts, other than humins, formed during the starch to LA reaction. A sample GC-MS chromatogram is shown in Figure 3-8.

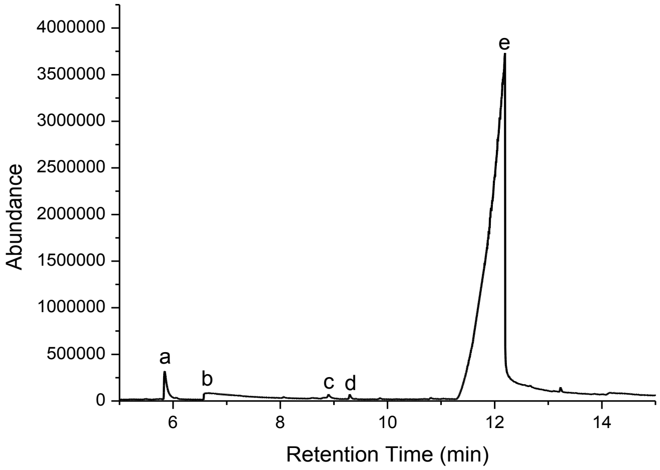


Figure 3-8: GC-MS chromatogram of products obtained from corn starch

The main peaks obtained in this run were (a) furfural; (b) butyric acid (internal standard); (c) 5-methyl-2(5H)-furanone; (d) HMF; (e) LA. In addition, in other runs, other compounds like levoglucosenone, 5-methyl 2-furaldehyde, formic acid, D-allose, α-angelica lactone, lactose, levoglucosan and maltose were detected. These byproducts are mostly either reversion products of glucose decomposition or formed from HMF, and are numerous but present in low concentrations.

3.5 Conclusion

The work in this paper shows that the amylose-amylopectin ratio of starch affects LA production via acid hydrolysis in two ways. Firstly, the difference in water solubility of the two fractions means that starches having higher amylopectin content will be more readily hydrolysed. Secondly, since the first action of the acid is to form a resistant complex between amylopectin and amylose, amylopectin is hydrolysed before amylose. Both factors mean that starches containing a greater proportion of amylopectin should be more readily converted to LA. While the final yields for the different substrates are relatively similar, the disparity in the reaction rates will make a substantial difference in industrial scale production. Hence, amylopectin-rich starches may be more suitable feedstock for LA synthesis. This hypothesis will be tested in a future work comparing LA yields from high amylopectin and high amylose starches.

Connecting Statement 2

Chapter 3 showed that fractionated amylopectin is converted more readily to LA than fractionated amylose. The next logical step is to extend this to starches having different amylose:amylopectin ratios and determine if amylopectin-rich starches are more amenable to acid hydrolysis than amylose-rich starches. This can be done most objectively by creating a kinetic model that accounts for the entire reaction chain from starch to LA, including the formation of intermediates such as glucose and HMF.

In Chapter 4, a MATLAB model was created to compare the results of acid hydrolysis of amylopectin-rich (waxy), normal and amylose-rich corn starches. Additionally, this model accounted for the differences in yields caused by conventional and oil microwave heating. This chapter is based on an article published in Industrial & Engineering Chemistry Research. Dr Marie-Josée Dumont co-authored this manuscript.

Chapter 4 : Levulinic acid production from starch using microwave and oil bath heating: A kinetic modelling approach

4.1 Abstract

This work examines the role played by starch composition and heating media in the synthesis of the promising biorefinery chemical levulinic acid (LA). Three corn starches with different amylose:amylopectin ratios were converted to LA using both microwave and conventional oil bath heating. The results obtained for the different reaction temperatures and times were used to calculate kinetic parameters using a multi-reaction model. It was observed that the long pre-heating and cooling times employed in microwave heating led to equivalent reaction temperatures below the set temperatures, and this in turn affected the product distributions via changes in the reaction kinetics. At low reaction temperatures, high amylopectin waxy corn starch gave higher LA yields than normal or high amylose corn starch. Similarly, LA yields were higher at lower temperatures for oil bath heating than for microwave heating. The maximum LA yield obtained was around 53-55% for all substrates and for both heating media, but was obtained for a shorter reaction time and at a lower equivalent temperature in case of microwave heating.

4.2 Introduction

The potential of levulinic acid (LA) as a biorefinery platform chemical has long been known. In the year 2000, the US Department of Energy identified LA as one of the top 12 value added chemicals from biomass, primarily because of the range of possible LA derivatives which could be utilised in numerous large volume chemical markets [30]. δ-aminolevulinic acid (DALA), γ-valerolactone (GVL), methyltetrahydrofuran (MTHF), α-angelicalactone, succinic acid, diphenolic acid and ethyl levulinate are some of the promising LA derivatives which can find applications in the manufacture of a range of products such as paints, polymers, lubricants, solvents, food flavouring and herbicides [48, 332]. Finding the appropriate feedstock is however a necessity for commercial scale LA production.

The most widely used route for LA synthesis is via the acid catalysed dehydration of hexose sugars. This explains the extensive use of the monosaccharides fructose and glucose in laboratory-scale LA synthesis [332]. However, given that high feedstock cost is one of the major reasons preventing commercial LA production [84], the use of less expensive polysaccharide feedstock is likely to be a better option at industrial scales. Being one of the most plentiful sources of hexose sugars, starch is a promising feedstock for LA synthesis, given that it is easier to depolymerise than cellulose or lignocellulosic feedstock [335]. Maximisation of LA yields from starch, however, entails an understanding of the role played by starch composition in LA synthesis. Our previous work showed that amylopectin is more readily hydrolysed to LA than amylose[358]. Accordingly, in this work, three corn starches having different amylose:amylopectin ratios have been utilised for LA production to verify if high amylopectin starches enable more facile LA production than high amylose and normal starches.

Apart from feedstock, another important factor that can affect the sustainability of a process is the heating mode used. While conventional heating media, in the form of apparatus such as oil baths, muffle furnaces, fired heaters and jacketed vessels, have traditionally been used at both the laboratory and industrial scales, in recent decades the use of microwave heating has become increasingly popular. Microwave heating is held to dramatically increase reaction rates and yields, and provide a more homogeneous heat distribution [68, 86]. However, the use of microwave energy to produce LA from starch has largely been neglected so far. In this work, both microwave and oil bath heating have been used to evaluate the effects of the heating media on the LA yield obtained.

The contrasts between LA yields obtained via hydrolysis of different starches under distinct heating regimes can be understood better if a kinetic model is coupled to a qualitative comparison of the experimental results. Therefore, in this study, a kinetic model has also been developed to identify the differences occurring during LA synthesis for the different feedstock and heating media, so as to identify promising strategies for LA production.

4.3 Materials and Methods

4.3.1 Chemicals

Unmodified (normal) corn starch (S4126, 27% amylose and 73% amylopectin), waxy corn starch (S9679, 100% amylopectin), and native high amylose corn starch (S4180, 70% amylose and 30% amylopectin) were purchased from Sigma Aldrich Co. LLC, USA. The 2M HCl catalyst used was prepared from 12.1N HCl purchased from Thermo Fisher Scientific, USA. The high performance liquid chromatography (HPLC) mobile phase used was prepared using HPLC grade water and HPLC grade acetonitrile, both purchased from Sigma Aldrich. For the HPLC analysis, 99% food grade LA, 99.5% glucose, 99% 5-hydroxymethylfurfural (HMF) (all from Sigma Aldrich) and 99% D-fructose (Alfa Aesar, USA) were used for the calibration runs.

4.3.2 Experimental procedure for microwave experiments

In this work, acid hydrolysis using HCl was used for synthesising LA from starch. Acid hydrolysis was preferred to enzymatic hydrolysis due to the shorter reaction times involved [266]. HCl was selected as the catalyst because it has been shown to be more effective for the synthesis of LA than other mineral acid catalysts [254]. It was decided use dilute acid and high reaction temperature, since this approach leads to lower acid recovery and reactor construction costs during industrial scale operation [269]. Based on preliminary experiments, 2M was chosen as the acid concentration. The set temperatures for the experiments were 135, 150, 165 or 180 ^{o}C. The starch concentration was kept at a low value (1% w/v) to minimise heat and mass transfer limitations.

The experiments in the microwave reactor involved a heating and cooling time of 10 minutes each for all the runs. In addition, a hold time of 0, 5, 10 or 15 minutes was applied to the runs, giving total reaction times of 20, 25, 30 or 35 minutes. The microwave experiments were conducted in a reactor operating at 2.45 GHz (MiniWAVE digestion module, SCP Science, Canada). In this reactor, the sample temperatures were monitored via infrared sensors located on the sidewalls, and the heating rate was automatically adjusted to ensure that the set temperature profile was accurately followed. For every run, 1% (w/v) solution of the substrate in 2M HCl was prepared and 10 mL was inserted into each of six quartz reaction tubes (maximum tube volume 50 mL). The tubes were then sealed using Teflon caps and mounted in the reactor. The desired reaction temperature and time were programmed, and the reaction was allowed to proceed for the appropriate duration. After the reaction, the contents of the tubes were filtered using a syringe filter (0.2 μm) into 2 mL autosampler vials for HPLC analysis. All the runs were carried out in duplicate, thereby giving a total of 12 readings for each data point.

4.3.3 Experimental procedure for oil bath experiments

The oil bath experiments were carried out in a Fisher Scientific High Temp Bath 160-A. The heating media was silicone oil purchased from Acros Organics, NJ, USA. In each run, Pyrex tubes with high temperature seals were filled with 5 mL of 1% (w/v) solution of the substrate in 2M HCl.

The tubes were inserted into the oil bath and heated for the desired reaction time of 15, 30, 45 or 60 minutes. The reaction temperatures employed were 135, 150, 165 and 180 °C. The oil bath temperature was monitored using a K-type thermocouple, with deviations maintained within ±1 °C. At the end of the reaction time, the tubes were removed and immediately placed in an ice bath in order to stop the reaction. The contents of the tubes were then filtered using 0.2µm syringe filter into 2 mL autosampler vials for HPLC analysis. All the oil bath runs were carried out in triplicate.

4.3.4 Product analysis

The LA, HMF, glucose and fructose yields were determined using an Agilent 1260 HPLC system. For determining the LA and HMF yields, a Zorbax Eclipse Plus C18 (4.6 X 100 mm, 3.5 µm) column was selected, and a variable wavelength detector (VWD) was used (λ_{LA} =250 nm, λ_{HMF} = 284 nm). In case of LA, the column temperature was set at 60 °C and the mobile phase was an isocratic 90:10 (v/v) mixture of water and acetonitrile with an eluent flow rate of 0.2 mL/min. To determine HMF, a 20:80 (v/v) mix of methanol and water was used as the mobile phase at a flow rate of 0.6 mL/min, with the column temperature maintained at 30 °C.

For determining the glucose and fructose yields, a Waters Carbohydrate Analysis (125 Å, 10 µm, 3.9 mm X 100 mm) column was used, with a refractive index detector (RID) being employed to obtain the glucose concentrations by measuring changes in the eluent refractive index. The column temperature was 30 °C and the mobile phase was an isocratic 20:80 (v/v) mixture of water and acetonitrile with an eluent flow rate of 0.6 mL/min.

The LA yields were expressed in terms of the wt% yields calculated from a calibration curve plotting concentrations of pure LA against areas obtained under the HPLC curve. The following formula was used for calculating the LA yields:

$$LA\ yield\ (wt\%) = \frac{Weight\ of\ LA\ produced\ (mg)}{Weight\ of\ substrate\ fed\ (mg)} \times 100\%$$

A similar procedure was used for calculating the HMF, glucose and fructose yields.

4.3.5 Kinetic model development

A kinetic model was developed to understand the effects of starch composition, reaction time and reaction temperature on LA yields. The kinetic scheme used is shown in Figure 4-1. This scheme, which has previously been applied to cellulose hydrolysis [269, 270], can likewise be applied to starch, as both are polyglucans, and hence glucose formation is the first step in both cases, with the further steps being similar.

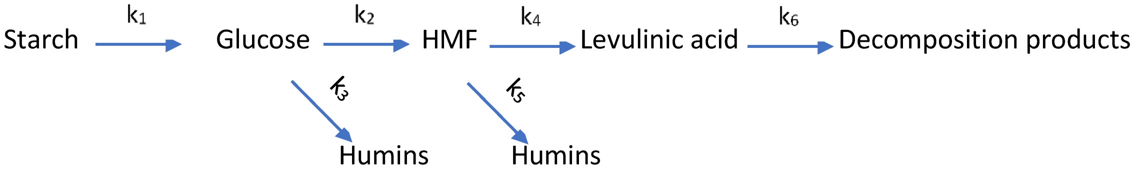


Figure 4-1: Reaction scheme used for kinetic modelling

In this scheme, the formation of LA begins with the hydrolysis of starch to glucose. LA production from hexoses like glucose is known to proceed via HMF as an intermediate [84], and accordingly, this has been incorporated in this model. The formation of dark insoluble by-products called humins invariably occurs via cross-polymerisation during acid hydrolysis of carbohydrates [96]. While the composition and formation pathways of humins are poorly understood [41, 354], previous studies have shown that they are likeliest to be formed via degradation of both glucose and HMF [21, 359]. Therefore, two side reactions for humin formation have been included. The humin terms also account for the numerous other by-products of glucose and HMF decomposition, such as levoglucosan, levoglucosenone, 5-methyl-2-furaldehyde, gentiobiose, etc., which are all formed in minute concentrations during the reaction [21, 358].

In this model, it has been assumed that starch is hydrolysed solely to glucose. Being a polyglucan, this is a reasonable assumption. While glucose may isomerise to fructose or other reducing sugars, an HPLC analysis showed that the concentration of fructose in the samples was negligible (less than 1% yield). This also indicates that the conversion of glucose to HMF does not involve fructose as an intermediate. This is in line with expectations, as it has been established that fructose is only formed as an intermediate when Lewis acid catalysts like $AlCl_3.6H_2O$ are used in this reaction [360]. When a strong Brønsted acid catalyst like HCl is used, glucose dehydration follows a route with 3-deoxy-glucosone as intermediate [237, 361]. 3-deoxyglucosone is difficult to characterise since it is converted very rapidly to HMF [361], and hence has been neglected in this model. Likewise, the conversion of HMF to LA involves the formation of numerous short-lived intermediates [71], whose formation has also not been considered separately here. All the reactions here have been deemed to be irreversible, in line with the literature [71, 270, 362].

Since HCl is a strong acid, it can be considered to be completely dissociated in water. Accordingly, the proton concentration in water is 2 M. A 1 wt% starch concentration equates to around 0.06 M, which implies that the proton concentration is greater than the starch concentration by a factor of 30. Therefore, in these conditions, the specific catalytic reaction of acid hydrolysis of starch has been considered to be a pseudo-first order reaction. In different studies, glucose dehydration to HMF and HMF rehydration to LA have been shown to largely follow first order kinetics under acidic conditions [269, 359], and hence these have been considered to be first order in this model. The reactions involving the decomposition of glucose, HMF and LA lead to the formation of a range of by-products with small but unknown concentrations, and hence for simplicity, first order kinetics has been considered for these reactions as well.

Formic acid is largely produced as a coproduct of HMF dehydration to LA. In this reaction, formic acid is produced in equimolar amounts with LA and is not in competition with LA yields, and hence it has not been included in the model. A small quantity of formic acid can however be produced by other reaction pathways [363]. This can be considered to be a part of the by-product formation from glucose and HMF.

Accordingly, let the starch, glucose, HMF and LA concentrations be S, G, H and L respectively. The change in these concentrations with time ‘t’ can be expressed as:

$$\frac{dS}{dt} = -k_1.S \tag{1}$$

$$\frac{dG}{dt} = k_1.S - (k_2 + k_3).G \tag{2}$$

$$\frac{dH}{dt} = k_2.G - (k_4 + k_5).H \tag{3}$$

$$\frac{dL}{dt} = k_4.H - k_6.L \tag{4}$$

As noted in Section 4.4.1 below, the HMF yields detected at the end of the runs were below 2% for every case, and hence have not been modelled. The HMF yield term has only been included here to derive the analytical expressions for LA concentration.

Equations 1, 2, 3 and 4 can be integrated under the initial conditions

$at\ t = 0, \quad S = S_o;$

$G = H = L = 0$

to yield the corresponding analytical expressions relating the concentration and time [364]:

$$\mathrm{S} = S_o.\exp(-k_1 t) \tag{5}$$

$$\mathrm{G} = \frac{k_1 S_o}{k_2 + k_3 - k_1}.[\exp(-k_1 t) - \exp(-(k_2 + k_3)t)] \tag{6}$$

$$\mathrm{L} = \frac{k_1k_2k_4S_o}{k_2+k_3-k_1}.\left[\frac{\exp(-k_1t)-\exp(-k_6t)}{(k_4+k_5-k_1)(k_6-k_1)} - \frac{\exp(-(k_2+k_3)t)-\exp(-k_6t)}{(k_4+k_5-k_2-k_3)(k_6-k_2-k_3)}\right] + \frac{k_1k_2k_4S_o(\exp(-(k_4+k_5)t)-\exp(-k_6t))}{(k_4+k_5-k_1)(k_4+k_5-k_2-k_3)(k_6-k_4-k_5)} \tag{7}$$

The kinetic parameters k_1-k_6 for every run were determined by fitting the analytical expressions (6) and (7) to the experimental data using the function fmincon in the programming software MATLAB. The fitting was done for the temperatures 135, 150 and 165 ^{o}C. No modelling was done for 180 ^{o}C since at this temperature the LA concentration was largely stable at all reaction times, and no glucose was detected (see Section 4.4.1 below).

4.3.6 Calculation of equivalent temperature

A common feature of microwave heating is that an initial pre-heat or ‘ramp’ time of the order of a few minutes is generally needed for the reaction system to reach the set temperature. A comparably long cooling phase, where the system is allowed to approach room temperature via heat dissipation, is also normally necessary [68]. In this work, the pre-heating and cooling phases both lasted 10 minutes for every run. This means that these periods together took up a majority of the run time for all the microwave runs, and hence it is necessary to account for them while calculating the reaction activation energies. This can be done by calculating an equivalent temperature for each run. This equivalent temperature is the temperature which under isothermal conditions would give the same product yields for the same reaction time as the non-isothermal temperature profile in question [365]. The method used for calculating the equivalent temperature value is given below.

Let the reaction temperature (K) measured at any time ‘t_i’ be denoted by ‘T_i’. The kinetic rate constant at that time (k_i) can then be written as:

$$k_i = A_o \exp\left(\frac{-E}{RT_i}\right) \tag{8}$$

where A_o = frequency factor; E = activation energy; R = universal gas constant

The average kinetic rate constant ($\bar{k}$) can be obtained by:

$$\bar{k} = \frac{\Sigma[A_o \exp\left(\frac{-E}{RT_i}\right).\Delta t_i]}{t} \tag{9}$$

where 'Δt_i' is the time interval between measurements, and 't' is the total run time. 't' can be written as:

$$t = N.\Delta t_i \tag{10}$$

where N is the total number of observations.

By definition, the equivalent temperature ($\bar{T}$) can also be used to arrive at $\bar{k}$:

$$\bar{k} = A_o \exp\left(\frac{-E}{R\bar{T}}\right) \tag{11}$$

From Equations (9), (10) and (11), the following can be arrived at:

$$A_o \exp\left(\frac{-E}{R\bar{T}}\right).N.\Delta t_i = \sum[A_o \ \exp\left(\frac{-E}{RT_i}\right).\Delta t_i] \tag{12}$$

Equation 12 can be rearranged to give

$$\bar{T} = \frac{-E/R}{\ln[\frac{1}{N}\sum \exp(\frac{-E}{RT_i})]} \tag{13}$$

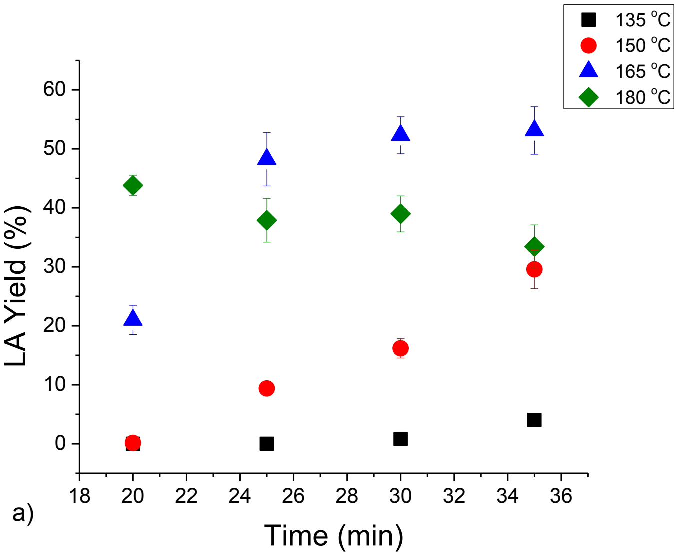
The calculation of $\bar{T}$ using Equation (13) requires the insertion of a previously calculated value of activation energy. For this purpose, the activation energies were first calculated considering the temperatures to be 135, 150 and 165 °C. These values were inserted into Equation 13 to obtain the equivalent temperature values. The activation energies were then recalculated, and this process was repeated iteratively till the difference between the latest equivalent temperature value and the previous iteration value was less than 1 °C.

For oil bath heating, the period of initial heating is far shorter, and the desired reaction temperature is obtained quickly. Likewise, at the end of the reaction, the immersion of the tubes in an ice bath leads to the temperature cooling to room temperature in less than 2 minutes. Therefore, as the heating and cooling periods account for only a small portion of the total reaction time, the calculation of an equivalent temperature is unnecessary in case of the oil bath runs. Hence, the set reaction temperatures can be considered to be the actual temperatures of the run.

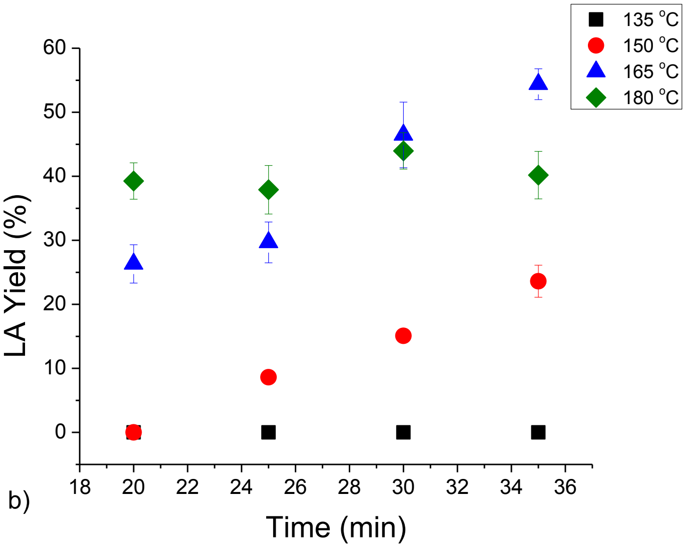
4.4 Results and Discussion

4.4.1 Synthesis of LA using microwave heating

The LA yields, as per HPLC results, obtained from the different substrates using microwave heating are shown in Figure 4-2, along with the standard deviations for each run. In all cases, the standard deviation within a data set was less than 12%.


135 °C
150 °C
165 °C
180 °C
LA Yield (%)
0
10
20
30
40
50
60
18
20
22
24
26
28
30
32
34
36
Time (min)

a)


135 °C
150 °C
165 °C
180 °C
LA Yield (%)
0
10
20
30
40
50
60
18
20
22
24
26
28
30
32
34
36
Time (min)

b)

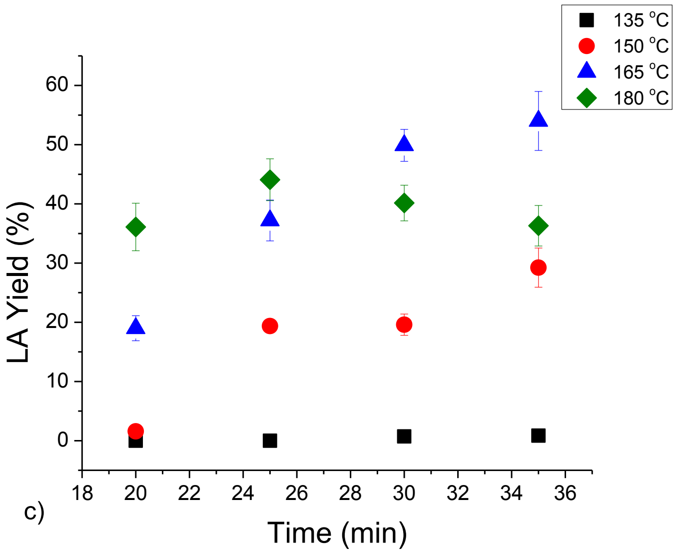
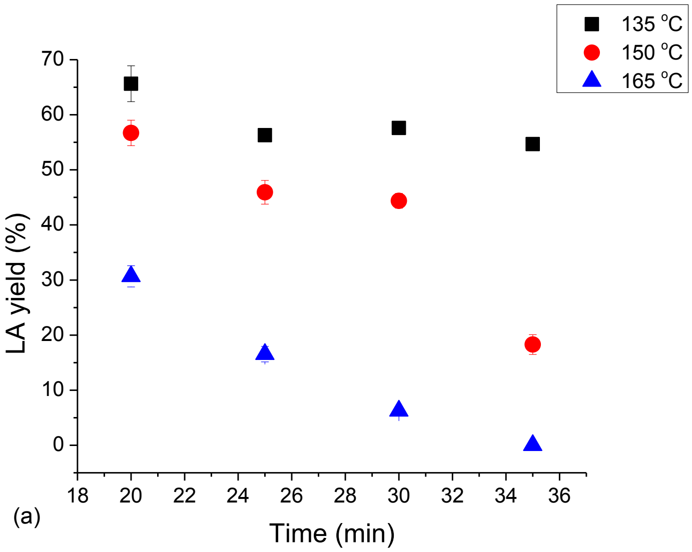


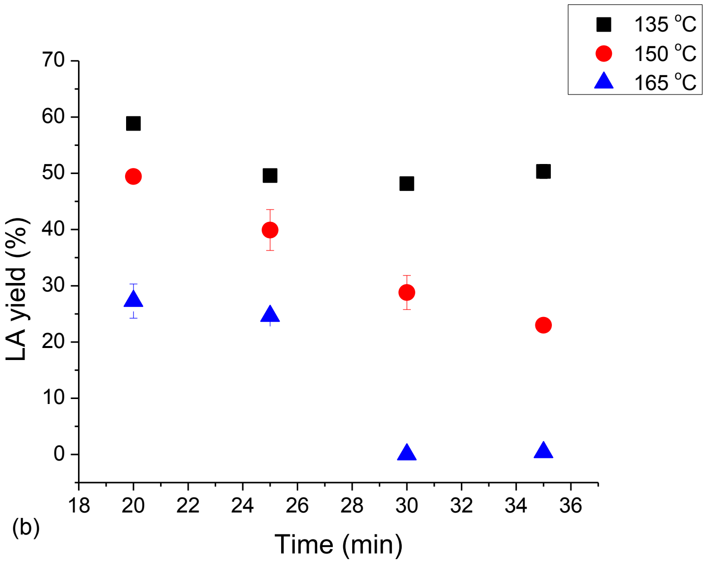
Figure 4-2: LA yields obtained during the microwave experiments for the different substrates: a) Normal corn starch; b) High amylose corn starch; c) Waxy corn starch

It can be observed from Figure 4-2 that at 135 °C, very little LA was produced at all reaction times. At 150 °C, however, differences were observed in the LA yields obtained for the different feedstock. The LA yields for waxy corn starch for the shorter runs (20 and 25 minutes) were considerably higher than those obtained for either normal corn starch or high amylose corn starch. At higher reaction times and temperatures, however, the differences were much less significant, and for all cases, the maximum yields were obtained for a total heating time of 35 minutes at 165 °C. When the reaction temperature was further increased to 180 °C, it was seen that the reaction yields plateaued at around 40%, which means that 165 °C is the optimal temperature under these reaction conditions. The divergence in the behaviours of the different starches can be better understood from the viewpoint of activation energies, and hence has been explained in Section 4.4.5 below.

The glucose yields for the different runs were also noted for use in the kinetic model, and these are shown in Figure 4-3. As glucose is an intermediate in the formation of LA from starch, it is understandable that the maximum glucose yields were obtained for low reaction temperatures and short reaction times. For instance, in case of waxy corn starch, a maximum glucose yield of 63.7% was obtained at 135 °C and 20 minutes reaction time in the microwave. The glucose yields became negligible at 165 °C and 30 or 35 minutes reaction time for all starches, and no glucose was detected for any of the runs conducted at 180 ºC. Therefore, the 180 ºC runs have not been shown in Figure 4-3.



(a)



(b)

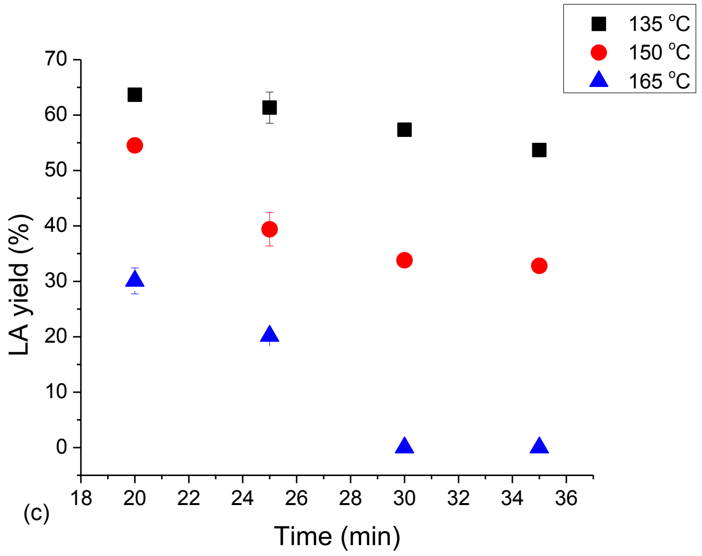


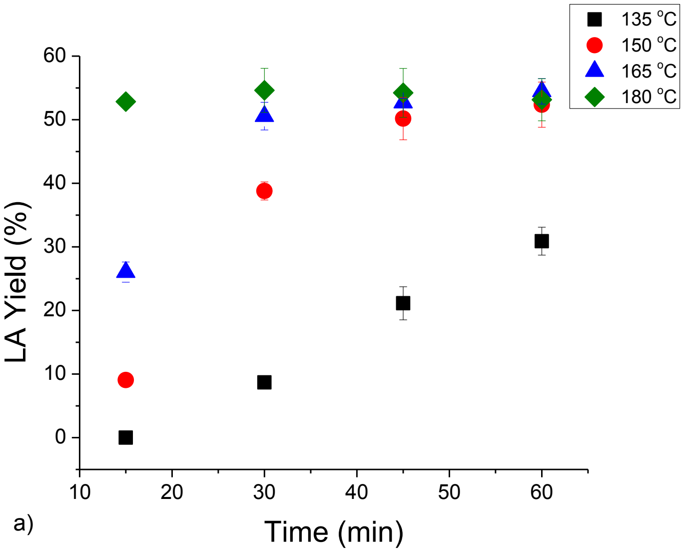
Figure 4-3: Glucose yields obtained during the microwave experiments for the different substrates: a) Normal corn starch; b) High amylose corn starch; c) Waxy corn starch

It was found that the HMF yields never went above 2% for any of the runs. This is because the conversion of glucose to HMF is generally a much slower reaction step than the subsequent conversion of HMF to LA, as will be explained in Section 4.4.3. This means that when HMF is formed, it is quickly converted to LA, leading to only small quantities of HMF remaining at the end of a run.

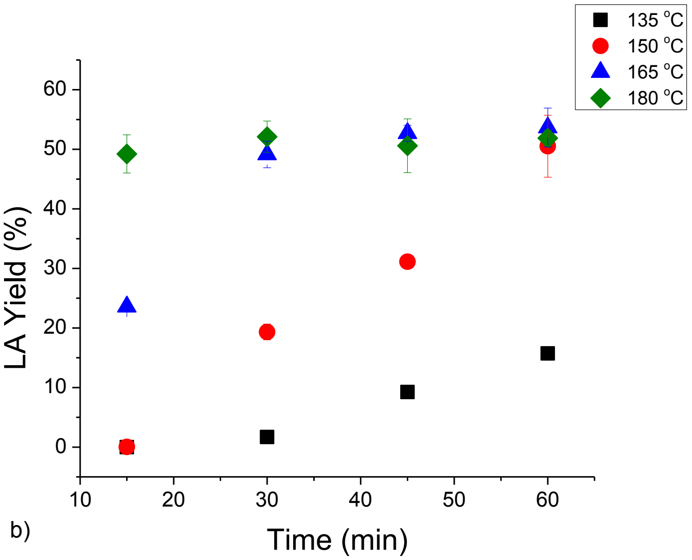
4.4.2 Synthesis of LA using oil bath heating

The LA yields obtained for the oil bath experiments are shown in Figure 4-4. It is seen that the maximum LA yield is around 54% for all starches, and is obtained at 165 °C in all cases. The drop in yield at 180 °C is however less pronounced than for the microwave runs. Significant LA yields are obtained at 135 °C for reaction times greater than 30 minutes, unlike in the case of microwave heating. The maximum LA yields obtained at 165 °C are however quite similar, despite the lower equivalent temperatures (see Section 4.4.3) and shorter reaction times prevalent for microwave heating.

Following a similar trend as observed in microwave heating, the LA yield for waxy corn starch is higher than for high amylose corn starch at lower temperatures. For instance, at 135 °C and 60 minutes, waxy corn starch gives an LA yield of 21.4% as compared to 15.7% for high amylose corn starch. However, at higher temperatures and reaction times, there is no significant difference between the yields obtained.



a)



b)

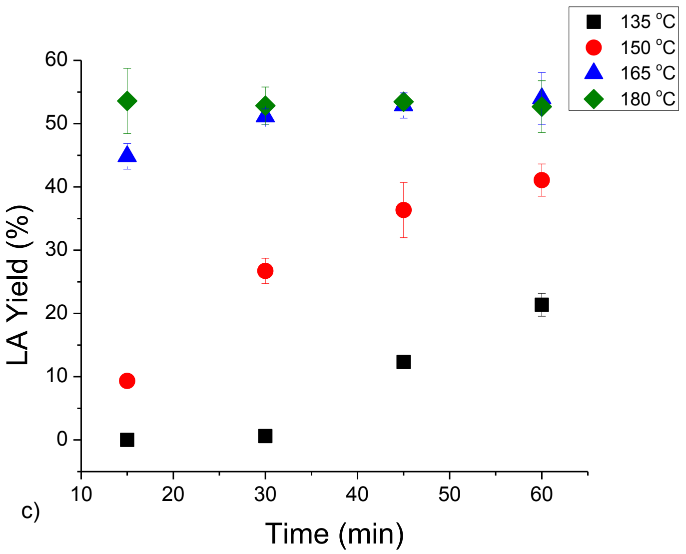
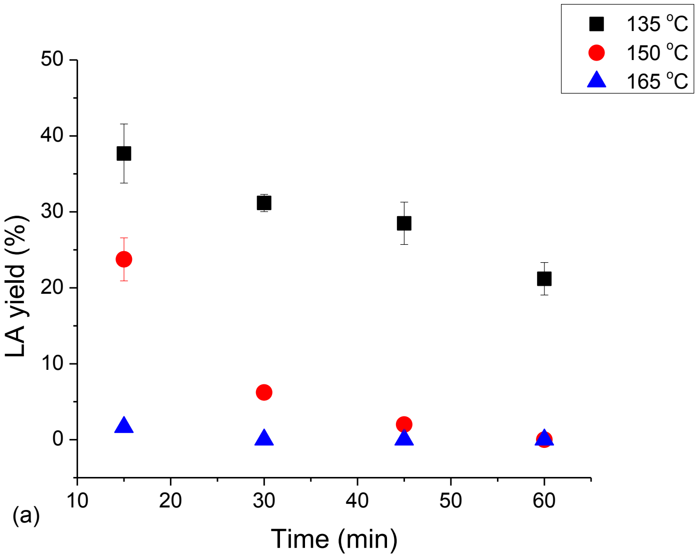


Figure 4-4: LA yields obtained during the oil bath experiments for the different substrates: a) Normal corn starch; b) High amylose corn starch; c) Waxy corn starch



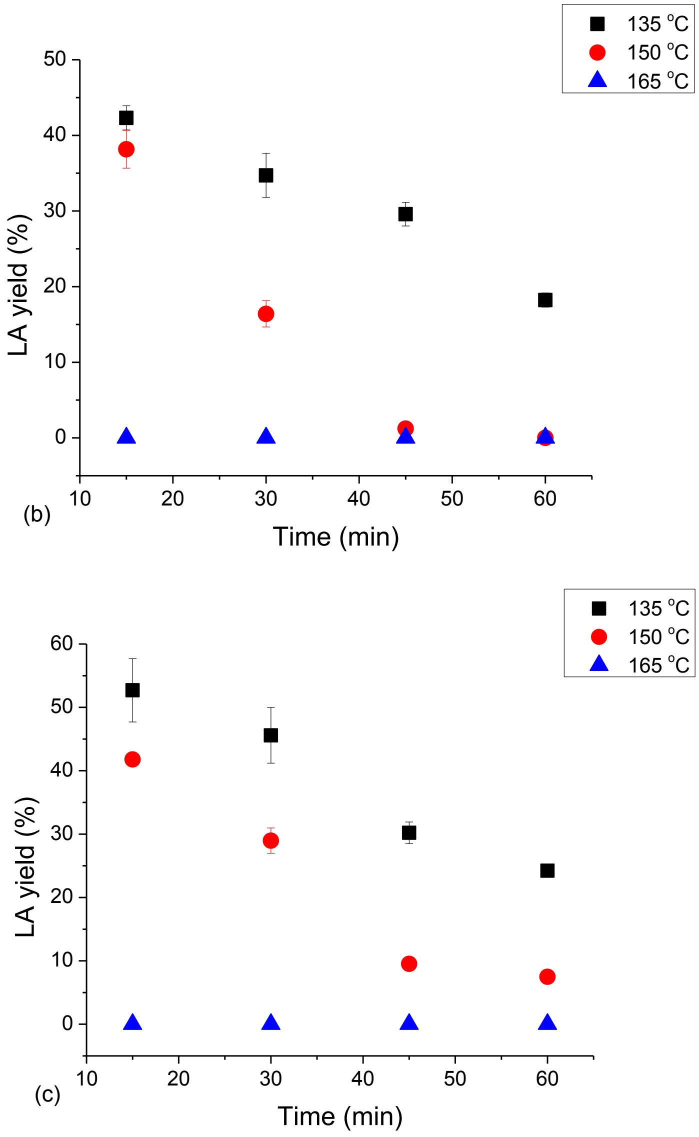


Figure 4-5: Glucose yields obtained during the oil bath experiments for the different substrates: a) Normal corn starch; b) High amylose corn starch; c) Waxy corn starch

The glucose yields detected at the end of the oil bath runs are shown in Figure 4-5. The maximum glucose yield was obtained for waxy corn starch after 15 minutes reaction time (52.7%). No glucose was detected for the 165 °C and 180 °C runs, except for the 15 minute run of normal corn starch at 165 °C. Similar to microwave heating, HMF yields detected were always below 2% due to its rapid conversion to LA.

4.4.1 Kinetic modelling of microwave heating data

A sample plot of the modelled curves against the experimental values obtained for microwave heating is given in Figure 4-6, while the values of the reaction constants calculated are given in Table 4-1.

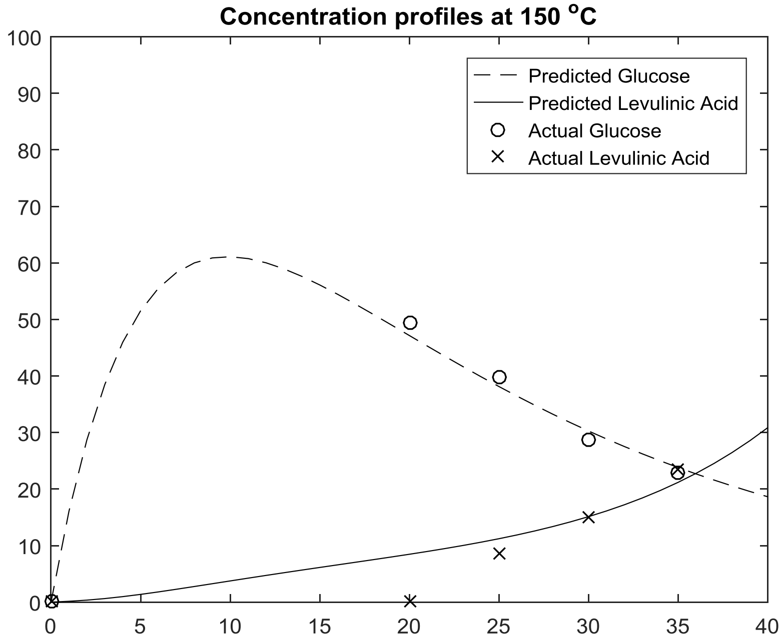


Figure 4-6: Experimental and modelled concentration profiles for the high amylose corn starch runs at 150 °C using microwave heating

Table 4-1: Kinetic rate constants (min^{-1}) for microwave heating runs

Type of corn starch	Nominal temperature (°C)	k_1 (x10^{-3})	k_2 (x10^{-3})	k_3 (x10^{-3})	k_4 (x10^{-3})	k_5 (x10^{-3})	k_6 (x10^{-3})
Normal corn starch	135	97.3	10.0	12.3	0.600	12.3	5.00
	150	120	15.0	29.0	150	145	16.5
	165	215	74.5	35.0	182	172	17.0
High amylose corn starch	135	79.0	12.3	13.6	0.600	12.3	2.00
	150	180	14.0	35.0	150	155	30.0
	165	215	74.5	40.0	250	232	38.8
Waxy corn starch	135	107	11.2	13.2	0.600	12.3	2.00
	150	180	15.0	25.0	150	135	35.0
	165	210	70.0	41.0	180	234	37.0

The kinetic scheme in Figure 4-1 shows that for optimal production of LA, the values of k_1, k_2 and k_4 should be maximised. It can be seen that for most cases, k_2 is much smaller than k_1 or k_4, and therefore, the conversion of glucose to HMF is the rate-determining step in the reaction scheme. The exception is for the runs at 135 ^oC, where k_4 is almost negligibly small, and hence virtually no LA is produced at this temperature. However, despite the value of k_2 being relatively greater than k_4 at 135 ^oC, it is still too small to permit the accumulation of significant amounts of HMF. At higher temperatures, HMF is converted almost instantaneously after its formation to LA, which explains the lack of HMF detected in the samples.

In spite of not being the rate determining step, an increase in the value of k_1 will lead to an increase in the overall reaction rate, or an increase in the LA yields obtained for a specific reaction time. It can be seen that the k_1 value for waxy corn starch is higher than for high amylose corn starch at 135 ^oC, although this advantage disappears at higher temperatures. This clearly implies a higher activation energy barrier for high amylose corn starch hydrolysis, as will be discussed in Section 4.4.5.

The side reactions yielding humin and other by-products have rate constants (k_3 and k_5) comparable to the main reactions (k_2 and k_4), a trend which unfortunately remains constant for the different temperatures and feedstock. This means that humin formation is largely unavoidable under the conditions used in these experiments.

The equivalent temperatures calculated for normal corn starch for the different nominal temperatures and temperature hold times are given in Table 4-2. The values for the other starch varieties are slightly different owing to the differences in the activation energy values, but are nevertheless within 1.5 ^oC of the values for normal corn starch.

Table 4-2: Equivalent temperature values for reactions of normal corn starch in microwave reactor

Nominal temperature (^oC)	Temperature hold time (min)	Equivalent temperature (^oC)
135	0	105.4
	5	116.4
	10	121.0
	15	123.7
	Average	116.6

150	0	117.4
	5	129.6
	10	134.7
	15	137.7
	Average	129.9
165	0	129.5
	5	142.9
	10	148.5
	15	151.7
	Average	143.1

It was observed that the equivalent temperatures depend not only on the nominal temperature, but also on the heating time. The average equivalent temperatures are considerably below the nominal temperature values, and this factor must be kept in mind when comparing the results for microwave and oil bath heating.

4.4.3 Kinetic modelling of oil bath heating data

A sample plot of the modelled curves against the experimental values for oil bath heating is given in Figure 4-7, while the values of the reaction constants calculated are given in Table 4-3.

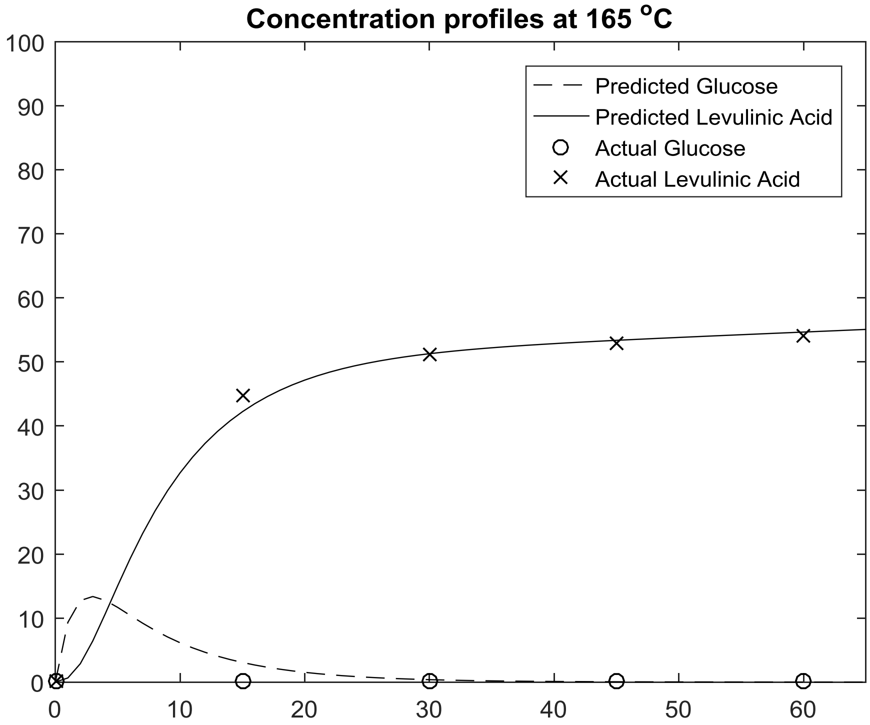


Figure 4-7: Experimental and modelled concentration profiles for the waxy corn starch runs at 165 ºC using oil bath heating

Table 4-3: Kinetic rate constants (min^{-1}) for oil bath heating runs

Type of corn starch	Nominal temperature (ºC)	k_1 (x10^{-3})	k_2 (x10^{-3})	k_3 (x10^{-3})	k_4 (x10^{-3})	k_5 (x10^{-3})	k_6 (x10^{-3})
Normal corn starch	135	49.0	6.00	40.0	60.0	3.00	1.50
	150	100	75.5	64.5	300	10.0	2.00
	165	140	600	100	480	380	2.50
High amylose corn starch	135	60.0	5.90	33.5	22.0	1.00	1.50
	150	108	15.0	64.5	111	16.0	1.80
	165	140	600	100	480	385	2.50
Waxy corn starch	135	90.0	4.50	32.0	25.0	4.20	1.50
	150	104	9.50	50.0	105	13.0	2.20
	165	140	600	100	500	370	2.30

A comparison of the rate constants obtained for oil bath heating and microwave heating makes it clear that the pathways followed differed. For instance, the values for k_1 are lower for oil bath than for microwave heating for the same nominal temperatures. This is despite the fact that the equivalent temperatures for microwave heating are considerably lower than the nominal temperature (as described in Section 4.4.3). As in case of microwave heating, the use of waxy corn starch leads to higher k_1 values at 135 °C, but at higher temperatures, the advantage disappears.

Also noteworthy is the case of k_2, which represented the rate determining step for microwave heating. However, for the oil bath heating at 165 °C, the value of k_2 is slightly higher than that of k_4, and considerably more than k_1, which then becomes the rate determining step. This shows that the conversion of glucose to HMF is highly temperature sensitive in this temperature range, as will be borne out by the activation temperature values in Section 4.4.6. The rapid conversion of glucose to HMF at 165 °C also explains the lack of glucose detected at this temperature for the oil bath runs. This is in contrast to microwave heating, where glucose yields of around 30% were noted for the 165 °C, 20 minute runs. Another difference is that the rate of LA decomposition (k_6) appears to be considerably less for oil bath heating than for microwave heating at higher temperatures. The humin forming steps, represented by k_3 and k_5, appear prominently for all the runs, as was the case for microwave heating.

4.4.4 Activation energy values for microwave heating

The calculated activation energy values for microwave heating using the procedure described in Section 4.3.6 are given in Table 4-4.

Table 4-4: Activation energy values (kJ/mol) for the different starches under microwave heating

Starch type	k_1	k_2	k_3	k_4	k_5	k_6
Normal corn starch	39.9	101	52.7	288	133	61.7
High amylose corn starch	50.7	90.9	54.7	306	149	150
Waxy corn starch	33.8	92.1	57.1	288	149	147

The rate constant k_1 reflects the ease of starch hydrolysis. It can be observed that the activation energy for k_1 is the least for waxy corn starch and the highest for high amylose corn starch. This is because during acid hydrolysis of starch, the acid initially leads to the formation of a stable and resistant complex between amylose and sections of amylopectin [352]. The amylose fraction is therefore protected initially, while the portion of the amylopectin lying in the amorphous regions of the starch granule is hydrolysed. The lower amount of amylopectin in high amylose corn starch as compared to normal corn starch contributes to the higher activation energy of k_1. In case of waxy corn starch, amylose is practically absent, and hence the starch is hydrolysed much more readily even at lower temperatures, as shown by the higher k_1 value at 135 °C (Table 4-1), as well as by the lower activation energy. This tallies with the findings of our previous research work, where it was observed that isolated amylopectin was converted more readily to LA than isolated amylose [358].

The conversion of HMF to LA is the most temperature sensitive reaction in this heating regime, with an activation energy of around 300 kJ/mol. The high activation energy value for k_4 provides an indication of why high temperatures are more favourable for high LA yields.

4.4.5 *Activation energy values for oil bath heating*

The activation energy values calculated for the different substrates for oil bath heating are given in Table 4-5. The activation energy for k_1 is lower for waxy corn starch than for high amylose corn starch, although normal corn starch has an even higher value for the oil bath heating. When compared to microwave heating, the activation energy values for the oil bath are higher for k_2, and lower for k_4 and k_6. The high activation energy of k_2 is a result of the large increase in k_2 at 165 °C, leading to the conclusion that temperatures above 150 °C are suitable for this reaction.

Table 4-5: Activation energy values (kJ/mol) for the different starches under oil bath heating

Starch type	k_1	k_2	k_3	k_4	k_5	k_6
Normal corn starch	51.6	228	45.4	102	243	25.2
High amylose corn starch	41.6	232	54.0	153	296	25.5
Waxy corn starch	22.1	246	56.8	149	225	20.8

The lower activation energy for k_4 clearly shows the effect of the higher actual temperature in oil bath heating as opposed to microwave heating, where the equivalent temperatures were in the 116-143 °C range. The reduction in activation energies at higher temperatures implies that the optimal temperature is greater than 143 °C. Comparing k_4 and k_5, the higher activation energy value for k_4 in microwave heating implies greater temperature sensitivity for LA synthesis as compared to humin formation under those conditions, while the reverse is true for oil bath heating. This means that an increase in temperature beyond 165 ^{o}C may increase humin formation without correspondingly increasing LA formation. The low activation energy for k_6 shows that the formation of decomposition products from LA is not greatly affected by the increase in the reaction temperature from 135 to 165 ^{o}C for oil bath heating.

The relatively high activation energy values of HMF and LA formation observed in Tables 4-4 and 4-5 show that a catalyst system that reduces these values will provide higher selectivity of LA formation as opposed to humin formation, and thus provide higher LA yields.

4.4.6 Comparison with previous kinetic models

The lack of previous kinetic models on microwave assisted conversion of starch to LA prevents a direct comparison of the model parameters obtained here for microwave heating with other works. However, similar kinetic models have been utilised for glucose/ cellulose feedstock in conventional heating media. The activation energy values obtained by these authors are given in Table 4-6.

Table 4-6: Activation energies obtained for LA synthesis via acid hydrolysis of cellulose or glucose

Feedstock	Temp. Range (^{o}C)	k_1	k_2	k_3	k_4	k_5	k_6	Ref.
Cellulose	160-200	95.6	137	N/A	144	147	59	[270]
Glucose	140-180	N/A	160	51	95	142	N/A	[359]
Cellulose	150-200	151.5	152.2	164.7	110.5	111.3	N/A	[269]
Glucose	120-200	N/A	64	76	61	70	N/A	[366]

It can be seen that a broad range of activation energies have been reported in the literature, which can be attributed at least in part to the fact that the catalyst and solvent systems that have been used in the studies vary. A comparison of Tables 4-4, 4-5 and 4-6 shows that the activation energy values obtained for oil bath heating in this work are largely in line with the literature values, while the microwave heating values are rather different. This reiterates the fact that the difference in the heating profile for the two heating modes affects the product formation by changing the activation energy values of the different reactions.

4.5 Conclusion

The results of this work show that waxy starches are more amenable to acid hydrolysis and therefore to LA synthesis at lower reaction temperatures and shorter reaction times than normal and high amylose starches. It has also been seen that the relatively long pre-heating and cooling times in microwave synthesis leads to an equivalent reaction temperature below that obtained for oil bath heating. This affects product distribution, owing to changes in the relative magnitudes of the activation energies of the competing reactions, and hence needs to be considered in a comparison between different heating media.

The temperature sensitivity of the conversion of HMF to LA below 140 ^{o}C and of the conversion of glucose to HMF in the range 150-165 ^{o}C, coupled with the relatively consistent rate of humin formation, leads to the conclusion that under the reaction conditions tested, an oil bath temperature of 165 ^{o}C is optimal for LA synthesis. This is corroborated by the reaction yields obtained. For microwave heating, a similar nominal temperature value leads to maximum LA production, although the equivalent reaction temperature and overall reaction times are markedly different.

Connecting Statement 3

The work in Chapter 4 showed that waxy corn starch is hydrolysed more readily than normal and high amylose starch, and hence is a more suitable feedstock for HMF or LA synthesis. Attention was then turned to developing a catalytic system that could convert waxy corn starch to HMF. This entailed selecting a catalyst that, ideally, is inexpensive, non-toxic and environment-friendly, while also being capable of giving high HMF yields. An option that can tick these boxes is the boric acid-choline chloride co-catalytic system. Therefore, Chapter 5 focusses on the use of these catalysts in a biphasic solvent medium of either water-MIBK or water-THF, with a Central Composite Design used to determine the optimum reaction parameters.

Based on initial runs, it was decided to use conventional oil bath heating instead of microwave heating in this work. This is because the long initial heating period during microwave heating led to starch settling and mass transfer limitations occurring with respect to the catalyst. In contrast, in oil bath heating, high temperatures were reached almost instantaneously, resulting in vigorous mixing due to convection.

This Chapter is based on a manuscript prepared for publication with Dr Marie-Josée Dumont as co-author.

Chapter 5 : Production of 5-hydroxymethylfurfural from starch through an environmentally-friendly synthesis pathway

5.1 Abstract

The commercial production of the promising biorefinery chemical 5-hydroxymethylfurfural (HMF) requires the development of a reaction system that can give high yields while being environment-friendly, inexpensive and recyclable. In this work, a system fulfilling these criteria was developed, with boric acid and choline chloride acting as co-catalysts for converting waxy corn starch to HMF. To prevent reduction in HMF yields occurring due to its rehydration to by-products, a biphasic medium of either water-MIBK or water-THF was used as the solvent. A Central Composite Design (CCD) based Response Surface Methodology was used to optimise the reaction parameters. The highest HMF yield obtained for water-MIBK was 35.9 mol%, while for water-THF, a maximum yield of 60.3 mol% was attained. However, the water-MIBK system was more recyclable, with minimal decrease in HMF yields observed even after ten rounds of reuse. Therefore, this system merits further investigation with other feedstock and on a larger scale.

5.2 Introduction

The twin concerns of global warming and fossil fuel depletion mean that replacement of petrochemical refineries by biorefineries seems increasingly probable in the near future. Although biorefineries will differ from petrochemical refineries since biomass will be used as feedstock instead of fossil fuels, their schemes of operation are expected to be similar. As is the case with petrochemical refineries, a biorefinery will convert the substrate into a few simple molecules, called building blocks, which can then be used as feedstock for the synthesis of a large number of different chemicals [367]. Among the candidates that have been proposed as potential biorefinery chemicals, 5-hydroxymethylfurfural (HMF) is one of the most promising. This can be attributed to the large number of chemicals, such as ethoxymethylfurfural, 2,5-furandicarboxylic acid (FDCA), 2,5-di(hydroxymethyl)furan (DHMF), 2,5-dimethylfuran, furfuryl alcohol, 2,5-diformylfuran, 5-hydroxymethylfuroic acid, etc. that can be produced from it [332]. These compounds have numerous applications in fields such as polymers, biofuels, solvents, pharmaceuticals, etc., and hence, HMF is definitely a potential replacement for petrochemical-based building blocks.

HMF can be produced readily from fructose in high yields. However, fructose is an expensive feedstock, and hence glucose is a more practical option. The use of a polysaccharide like starch, which is a natural polymer comprised of interlinked glucose units, can help make the process even more economically sustainable. However, the conversion of glucose to HMF produces low yields if Brønsted acid catalysts are used. If a combination of ionic liquids and Lewis acid catalysts is used, then glucose is isomerised to fructose, which is much more readily converted to HMF than glucose [368]. Unfortunately, ionic liquids are expensive and susceptible to deactivation in the presence of water. In contrast, choline chloride is inexpensive, biodegradable, and can form a deep eutectic solvent when added to aqueous solutions of hexoses. This enables it to be used in place of ionic liquids in the conversion of glucose to HMF [369].

The Lewis acid catalysts that have been studied have primarily been metal salts such as $AlCl_3$, CrCl3, $GeCl_4$, $ZrCl_4$, etc. [114, 317, 360, 370]. In recent years, boric acid has been proposed as a metal-free Lewis acid catalyst, being cheap, non-toxic and more environment friendly [116, 371]. A combination of choline chloride and boric acid is therefore an alternative to ionic liquid-metal salt systems, and a promising reaction system for HMF synthesis from the cost and environmental standpoints.

This combination, however, still leaves open the problem of by-product formation due to HMF rehydration by the aqueous phase, leading to lower final yields. Since water is necessary to hydrolyse starch into its constituent glucose units, elimination of the aqueous phase is not possible. Instead, it has been shown that if a biphasic medium comprised of an aqueous and an immiscible organic phase is used as the solvent, much higher HMF yields can be obtained [372]. This is because the transfer of the produced HMF from the aqueous to the organic phase shortly after formation reduces the possibility of its rehydration. Methyl-isobutyl ketone (MIBK) has been used by several researchers as the organic solvent in a biphasic system [23, 184, 373]. This is because its low boiling point makes it easier to separate out the HMF, and it is also relatively cheap and non-toxic. However, tetrahydrofuran (THF) has also been recommended as a possible option, owing to its high HMF partition coefficient in a biphasic system [372].

In this study, the conversion of starch to HMF in a biphasic system using choline chloride (ChCl) and boric acid (BA) as the catalysts has been investigated. The starch used was waxy corn starch, as this has been shown to be more susceptible to acid hydrolysis in our previous work [358, 374]. MIBK-water has been used as the biphasic medium in most of the runs, but the use of a THF-water system has also been tested for comparison.

5.3 Materials and Methods

5.3.1 Chemicals

Waxy corn starch (100% amylopectin) and choline chloride (≥ 98%) were purchased from Sigma-Aldrich Co. LLC, USA. The High Performance Liquid Chromatography (HPLC) mobile phase was prepared using HPLC-grade methanol (99.8%) and HPLC-grade water, both purchased from Sigma-Aldrich. Boric acid was purchased from Thermo Fisher Scientific, USA. The organic solvents used were methyl isobutyl ketone (MIBK) (≥ 99%) and tetrahydrofuran (THF) (≥ 99.9%), from Sigma-Aldrich. 5-hydroxymethylfurfural (≥ 99%) from Sigma-Aldrich was used to prepare samples for the calibration runs.

5.3.2 Experimental Procedure

All the experiments were carried out in a Fisher Scientific High Temp Bath 160-A. The heating medium was silicone oil purchased from Acros Organics, Morris Plains, NJ, USA. To ensure sufficient contact between the starch and the catalytic phase, the starch concentration was restricted to 2% w/v with respect to the total solvent concentration. 80 mg of starch was added to the appropriate amount of choline chloride in a Pyrex tube fitted with a high temperature seal. For runs involving THF as the organic solvent, 100 mg of sodium chloride (NaCl) was added to induce phase separation between the aqueous and organic phases. 670 µL of water, the appropriate amount of boric acid, and 3.33 mL of the organic solvent were added to the tube, following which the tubes were shaken vigorously on a vortex mixer for 15 seconds each. After this, the tubes were inserted into the oil bath and heated at the set temperature for the desired reaction time. The oil bath temperature was monitored using a K-type thermocouple, with deviations maintained within ±1 °C. At the end of the reaction time, the tubes were removed and immediately placed in an ice bath to stop the reaction. Subsequently, the organic phase of each tube was first removed and then the aqueous phase was extracted six times with the organic solvent. The pooled organic solvent was filtered using a 0.2 µm syringe filter into 2 mL autosampler vials for HPLC analysis. All runs were conducted in triplicate.

To test the reusability of the catalytic system, the aqueous phase containing the used boric acid and choline chloride, was reused. 80 mg of starch and 3.33 ml of organic solvent were added to the aqueous phase, as in the runs with fresh catalysts. When THF was used, no additional NaCl was added to the aqueous phase, since it was assumed that the NaCl would remain in the aqueous phase after extraction of HMF by the organic solvent.

5.3.3 Product analysis

The HMF yields were determined using an Agilent 1260 HPLC system fitted with a Zorbax Eclipse Plus C18 (4.6 × 100mm, 3.5 mm) column and a variable wavelength detector (VWD) set at 280 nm. A 20:80 (v/v) mix of methanol and water was used as the mobile phase at a flow rate of 0.6 mL/min, with the column temperature maintained at 25 °C.

The HMF yields were expressed in terms of the wt% yields calculated from a calibration curve plotting concentrations of pure HMF in the particular organic solvent against areas obtained under the HPLC curve. Since the molecular weights of anhydroglucose and HMF are 162 and 126 g/mol respectively, the following formula was used for calculating the HMF yields:

$$HMF\ yield\ (mol\%) = \frac{Weight\ of\ HMF\ produced\ (mg)}{Weight\ of\ starch\ fed\ (mg)} \times \frac{162\ g/mol}{126\ g/mol} \times 100\% \qquad (1)$$

5.3.4 Optimisation of HMF production

Response surface methodology (RSM) was employed to obtain the optimal reaction conditions for HMF synthesis. The factors tested were the reaction time, the reaction temperature, the ChCl concentration and the BA concentration. To enable optimisation based on these factors, and to keep the required number of experiments within practical limits, other factors such as substrate loading, organic solvent used and ratio of organic phase to aqueous phase were kept constant. Initially, a Central Composite Design (CCD) was used to arrive at the optimal levels of the factors. The organic solvent used for the CCD runs was MIBK, and the ratio of MIBK to water was kept at 5:1, since this ratio had been judged to be the optimal in our earlier work [375]. Overall, 30 runs, comprised of 16 (2^4) factorial runs, 8 (2*4) axial runs and 6 centre-point runs, were conducted. Based on preliminary experiments, the range of experimental values was selected for each factor. The factor levels used for the CCD runs are given in Table 5-1. The JMP 11.2 (SAS Institute, USA) software was used to design and analyse the CCD runs.

Table 5-1: Levels of factors used in Central Composite Design (CCD) runs

Factor \ **Level**	**-2**	**-1**	**0**	**1**	**2**
Time (min)	20	40	60	80	100
Temp (°C)	135	150	165	180	195
ChCl (mM)	0	1	2	3	4
BA (mM)	0	2	4	6	8

The optimal conditions arrived at for MIBK (as discussed in Section 5.4.1) were then tested with THF as the organic solvent, with 100 mg of NaCl being added to each tube to enable phase separation between the aqueous and organic phases. The NaCl concentration chosen corresponded to 15 wt% of the aqueous phase, since a minimum concentration of 10 wt% is required to produce phase separation, while the NaCl can precipitate out at concentrations above 20 wt% [376]. Other reaction conditions were kept the same as for the MIBK runs.

5.4 Results and Discussion

5.4.1 HMF production using fresh catalyst

Figure 5-1 shows the HPLC chromatogram of the HMF sample obtained after solvent extraction and syringe filtration.

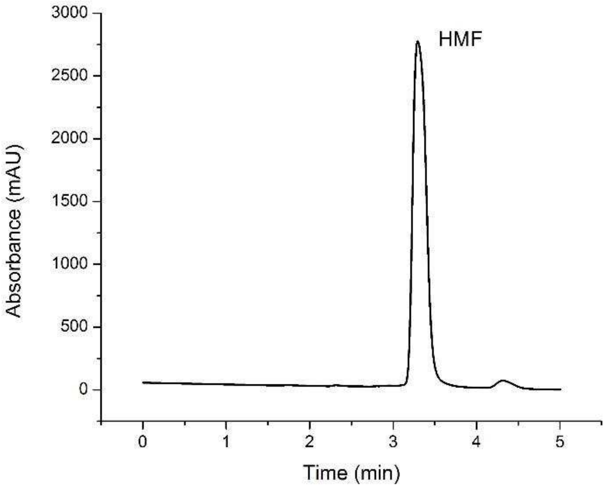


Figure 5-1: Sample HPLC chromatogram of filtered reaction product

Table 5-2: HMF yields obtained for different levels of the four factors

Run	Variable level				Yield (Mol%) (Error)
	Time	Temperature	ChCl	BA	
1	40 (-1)	150 (-1)	1 (-1)	2 (-1)	0.9 (0.1)
2	40 (-1)	150 (-1)	1 (-1)	6 (1)	2.6 (0.2)
3	40 (-1)	150 (-1)	3 (1)	2 (-1)	0.8 (0.1)
4	40 (-1)	150 (-1)	3 (1)	6 (1)	2.6 (0.2)
5	40 (-1)	180 (1)	1 (-1)	2 (-1)	9.8 (0.8)
6	40 (-1)	180 (1)	1 (-1)	6 (1)	14.3 (1.2)
7	40 (-1)	180 (1)	3 (1)	2 (-1)	11.4 (1.0)
8	40 (-1)	180 (1)	3 (1)	6 (1)	23.8 (2.2)
9	80 (1)	150 (-1)	1 (-1)	2 (-1)	1.0 (0.1)
10	80 (1)	150 (-1)	1 (-1)	6 (1)	1.0 (0.1)
11	80 (1)	150 (-1)	3 (1)	2 (-1)	1.2 (0.1)
12	80 (1)	150 (-1)	3 (1)	6 (1)	11.6 (1.1)
13	80 (1)	180 (1)	1 (-1)	2 (-1)	21.9 (2.0)
14	80 (1)	180 (1)	1 (-1)	6 (1)	33.9 (3.2)
15	80 (1)	180 (1)	3 (1)	2 (-1)	29.3 (2.9)
16	80 (1)	180 (1)	3 (1)	6 (1)	36.0 (3.2)
17	20 (-2)	165 (0)	2 (0)	4 (0)	3.1 (0.2)
18	100 (2)	165 (0)	2 (0)	4 (0)	22.8 (2.1)
19	60 (0)	135 (-2)	2 (0)	4 (0)	1.2 (0.1)
20	60 (0)	195 (2)	2 (0)	4 (0)	35.9 (3.4)
21	60 (0)	165 (0)	0 (-2)	4 (0)	6.2 (0.5)
22	60 (0)	165 (0)	0 (2)	4 (0)	14.9 (1.4)

23	60 (0)	165 (0)	2 (0)	0 (-2)	1.0 (0.1)
24	60 (0)	165 (0)	2 (0)	8 (2)	24.0 (2.2)
25	60 (0)	165 (0)	2 (0)	4 (0)	13.5 (1.3)
26	60 (0)	165 (0)	2 (0)	4 (0)	13.2 (1.1)
27	60 (0)	165 (0)	2 (0)	4 (0)	16.7 (1.4)
28	60 (0)	165 (0)	2 (0)	4 (0)	14.7 (1.4)
29	60 (0)	165 (0)	2 (0)	4 (0)	16.9 (1.6)
30	60 (0)	165 (0)	2 (0)	4 (0)	12.7 (1.2)

The results obtained from the CCD runs are given in Table 5-2. These were fitted to a second-degree standard least squares regression model using the software JMP. Figure 5-2 shows a plot showing a comparison of the actual and predicted HMF yields as per the model.

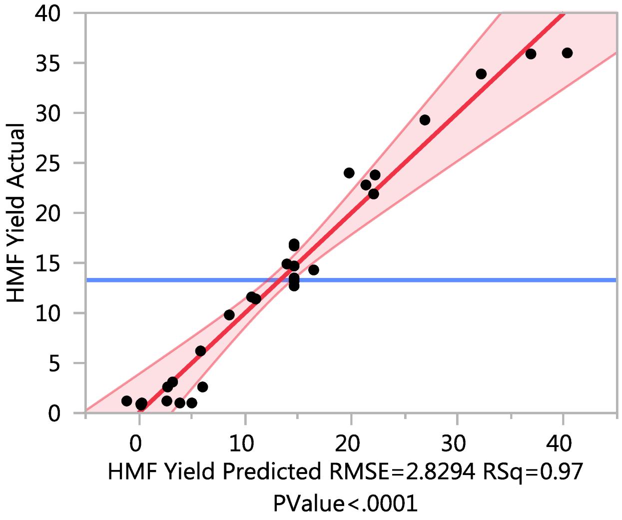


Figure 5-2: JMP plot of actual by predicted HMF yields

An initial analysis of the modelled experimental results indicated that the optimum values of the reaction parameters lay outside the tested region for reaction time, reaction temperature and BA concentration (Figure 5-3). This would initially appear to indicate that an increase in the values of time, temperature and boric acid will lead to higher yields.

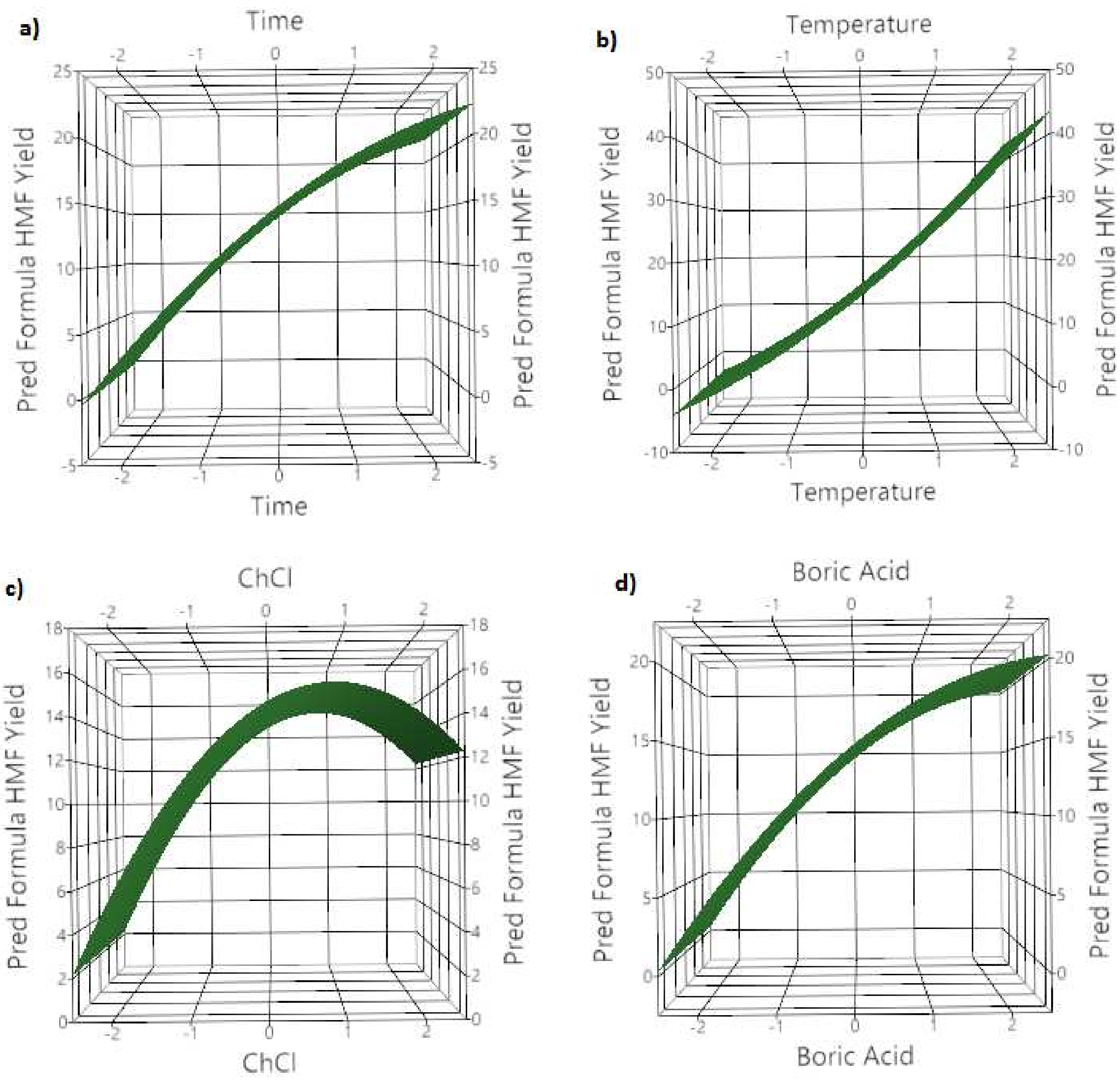


Figure 5-3: Predicted optimal values of factors in Central Composite Design

However, a statistical analysis of the parameter estimates (Table 5-3) showed that the time*temperature interaction is statistically significant at the 99% level, and temperature*boric acid is significant at the 90% level. This means that increasing the three factors simultaneously may actually lead to a decrease in yield.

Table 5-3: Statistical significance of parameter estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Temperature	9.504167	0.577549	16.46	<.0001
Time	4.545833	0.577549	7.87	<.0001
Boric Acid	3.979167	0.577549	6.89	<.0001
Time*Temperature	3.36875	0.70735	4.76	0.0003
ChCl	2.029167	0.577549	3.51	0.0031
ChCl*ChCl	-1.18438	0.540247	-2.19	0.0445
Temperature*Boric Acid	1.35625	0.70735	1.92	0.0744
Temperature*Temperature	0.815625	0.540247	1.51	0.1519
Boric Acid*Boric Acid	-0.69688	0.540247	-1.29	0.2166
ChCl*Boric Acid	0.81875	0.70735	1.16	0.2652
Time*Time	-0.58438	0.540247	-1.08	0.2965
Temperature*ChCl	0.61875	0.70735	0.87	0.3955
Time*ChCl	0.58125	0.70735	0.82	0.4241
Time*Boric Acid	0.54375	0.70735	0.77	0.454

This was borne out by additional runs conducted for reaction times of 120-170 minutes, in the temperature range of 185-210 ^{o}C, and for boric acid concentrations of 7-15 mM. The maximum HMF yield obtained in this range was only 21.5 mol%, which is considerably lower than the highest yields that had been obtained during the original CCD runs. Hence, the optimised yield was decided based on the values from the CCD runs.

From Table 5-2, it is clear that the maximum HMF yields were obtained for Run 16 and Run 20. The optimum conditions are therefore either: reaction time = 80 minutes, reaction temperature = 180 ^{o}C, ChCl concentration = 3 mM and boric acid concentration = 6 mM; or reaction time = 60 minutes, reaction temperature = 195 ^{o}C, ChCl concentration = 2 mM and boric acid concentration = 4 mM. Of these, the latter option is preferable owing to the shorter reaction time and lower amount of catalyst used, despite the higher reaction temperature employed.

When THF was used as the co-solvent in place of MIBK, it was observed that the HMF yield obtained increased to 60.3 mol%, which is significantly higher than the yields obtained using MIBK. This can be attributed to the higher partition coefficient of HMF in a water:THF system as compared to a water:MIBK system [372, 377]. Addition of NaCl to the water-MIBK system did not impact HMF yields significantly, with a yield of 34.2 mol% being observed in this case.

5.4.2 Catalyst recycle runs

The results of the catalyst recycle runs are shown in Figure 5-4. It can be seen that for THF, there was a sharp drop in the HMF yield obtained using the recycled catalyst. The first run using the recycled catalyst only resulted in a 37.5 mol% yield, and further runs with the reused catalyst led to a continued decline, with the sixth run yielding only 19 mol%. For MIBK, the decrease in the obtained HMF yields is less significant, with a yield of 31 mol% obtained even for the ninth round of use. It is only for the tenth round that the yield dropped to 21.7 mol%.

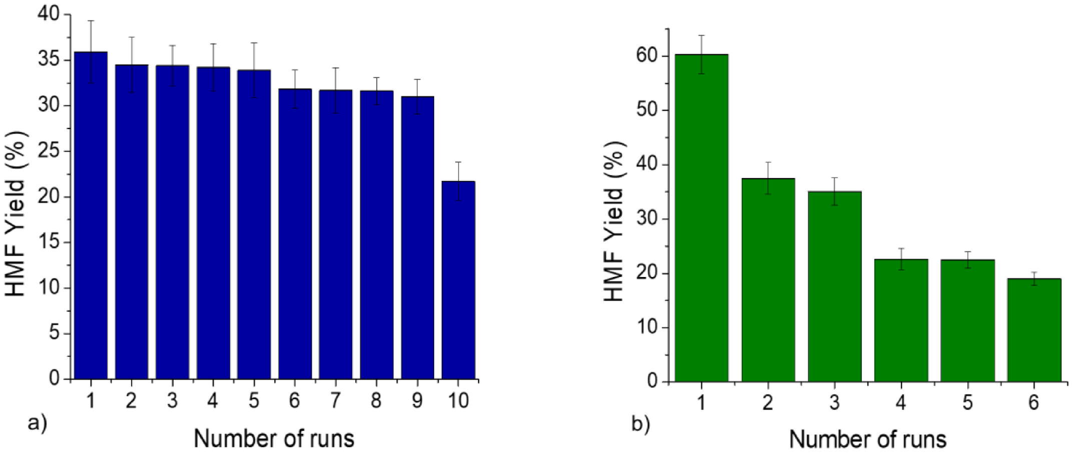


Figure 5-4: HMF yields obtained for catalyst recycle a) using MIBK solvent; b) using THF solvent

One possible reason for the faster decrease in yield when THF is used may be the entrainment of the NaCl in the organic phase during extraction, which would increase the miscibility of THF with water, and reduce the advantage of using a biphasic system. To test this, the THF recycling experiments were redone with 100 mg of NaCl being added to the system between runs. The resulting yields were, however, almost identical to those obtained during the original runs (within 1 mol% of the earlier results). This suggests an alternative possibility, which is that the traces of used THF that remained in the system between the runs adversely affected its recyclability, even after the addition of fresh THF. This occurs because THF degrades at temperatures beyond 180 °C, restricting its usability in high temperature systems [372, 378].

5.5 Conclusion

In this study, the applicability of a choline chloride-boric acid system to HMF synthesis from waxy corn starch was investigated with the aim of developing an inexpensive and eco-friendly method of producing a biorefinery chemical from renewable feedstock. A biphasic system of water and an organic solvent was utilised to achieve higher product yields by reducing HMF rehydration, with MIBK and THF being the organic solvents tested. Response Surface Methodology, based on Central Composite Design and other runs, showed the optimum reaction conditions to be reaction time = 60 minutes; reaction temperature = 195 ^{o}C; ChCl concentration = 2 mM and boric acid concentration = 4 mM. The maximum HMF yield for this system was 35.9 mol%. If THF was used as the organic solvent under these reaction conditions, the HMF yield rose to 60.3 mol%. However, catalyst recycle runs showed a sharper drop in yields in the THF system, which may be due to traces of residual THF degrading and affecting system recyclability. The MIBK system showed better recyclability, and hence offers more promise for further research.

Connecting Statement 4

The work in Chapters 3, 4 and 5 has focussed on the use of starch as feedstock. Cellulose is another widely available polysaccharide, and hence lignocellulosic biomass needs to be considered as a potential feedstock for HMF and LA synthesis. This is particularly true in the Canadian context, since the pulp and paper industry is a major sector in this country. Therefore, the use of hardwood and softwood pulp for HMF synthesis is the focus of Chapter 6.

First, preliminary experiments were conducted with hardwood pulp using the optimal reaction conditions found in Chapter 5 for boric acid-choline chloride co-catalysts in water-MIBK. It was found that the HMF yield was only 14.5 mol%, with a large proportion of the pulp remaining unconverted. It was therefore evident that a different catalyst would have to be used. Since ferric sulphate has in the past been used for cellulose depolymerisation, and also fulfils other necessary criteria such as being a Lewis acid, inexpensive, non-toxic and environment-friendly, it was decided to use it as a catalyst for the work presented in Chapter 6. This chapter is based on a manuscript to be submitted for publication with Dr Marie-Josée Dumont as co-author.

Chapter 6 : Synthesis of hydroxymethylfurfural from hardwood and softwood kraft pulp using ferric sulphate as catalyst

6.1 Abstract

Hydroxymethylfurfural (HMF) and furfural are promising chemicals for the creation of a bio-based economy. The development of an inexpensive and eco-friendly catalytic system for converting cellulosic biomass into these chemicals is an important step in this regard. Ferric sulphate is a common, cheap and non-toxic Lewis acid that has been used to catalyse reactions such as wood depolymerisation. In this work, ferric sulphate was used to help the production of HMF and furfural from hardwood and softwood pulps. It was found that for hardwood pulp, the use of ferric sulphate alone gave a maximum HMF yield of 31.6 mol%. The addition of the ionic liquid [BMIM]Cl or HCl as co-catalysts did not lead to an increase in the yields obtained. Softwood pulp was harder to depolymerise, with the maximum HMF yield of 37.9 mol% obtained using a combination of ferric sulphate and dilute HCl. It was thus concluded that ferric sulphate is a promising catalyst for HMF synthesis from cellulosic biomass.

6.2 Introduction

Chemicals derived from fossil fuels have been a pillar of the modern economy for over a century. In recent years, intense research focus has been placed on biomass-derived chemicals as a means of tackling fossil fuel depletion and climate change. The creation of a bio-based economy as a replacement for the present petroleum-based economy will require the conversion of lignocellulosic feedstock into 'platform chemicals'. These are chemicals which can be converted into a range of products, in a similar fashion to those employed in petrochemical refineries. Among the candidates that have been postulated as platform chemicals, 5-hydroxymethylfurfural (HMF) is one of the most promising [379]. This is because of the large number of chemicals that can be synthesised from HMF, for use in the chemical, polymer, pharmaceutical, biofuel, and other industries [332]. While HMF can be produced from polysaccharides like starch, cellulose and inulin, whose constituent monomers are 6-carbon sugars like glucose and fructose, 5-carbon sugar-containing polysaccharides like xylan can be used for the synthesis of furfural by analogous methods [9]. Like HMF, furfural is a heterocyclic aldehyde, differing from HMF in not having an alcohol group, and one fewer carbon atom. It is another potential platform chemical, which can be used for synthesising a range of products such as furfuryl alcohol, furan, tetrahydrofuran, furoic acid, etc. [380]. As lignocellulosic biomass typically contains both C5 and C6 sugars, furfural and HMF are generally co-produced from it.

HMF is produced by the loss of three water molecules from a hexose sugar. This means that the cellulose in lignocellulosic feedstock has to be hydrolysed into its constituent hexose monomers before the conversion to HMF can occur. This is generally accomplished by acid hydrolysis of the cellulose into glucose. While glucose can be converted to HMF via production of the HMF precursor 3-deoxyglucosone, higher yields are obtained if an isomerisation reaction to fructose occurs first, as the production of HMF from fructose occurs much more readily than from glucose [381]. This isomerisation step is usually carried out using Lewis acid catalysts such as $AlCl_3$, $CrCl_3$, $GeCl_4$, $ZrCl_4$, etc. [114, 317, 370, 382]. To obtain high HMF yields, a suitable catalyst needs to be able to depolymerise cellulose while minimising the decomposition of HMF to by-products. These include levulinic acid (LA), formic acid, and humins, which are dark insoluble byproducts formed via degradation of glucose and HMF during acid hydrolysis of carbohydrates [354]. Figure 6-1 shows a simplified reaction scheme for the conversion of cellulose to HMF [97, 270, 383], with a similar scheme existing for furfural.

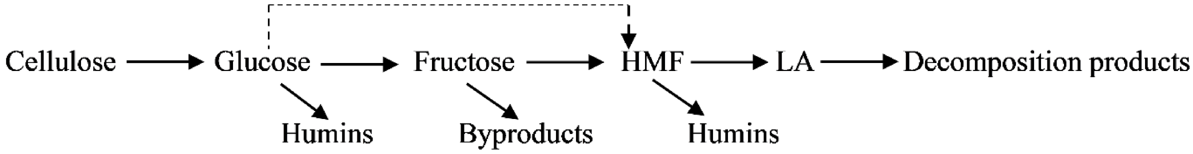


Figure 6-1: Reaction scheme for conversion of cellulose to HMF

Ferric sulphate hydrate ($Fe_2(SO_4)_3.xH_2O$) is a Lewis acid catalyst that has in recent years found application in a range of organic reactions [384-386]. This interest has arisen since it is eco-friendly, non-toxic, inexpensive and recyclable. However, its use as a catalyst for HMF synthesis has been neglected so far. Ferric sulphate has been shown to act as an acid catalyst for both cellulose depolymerisation and the subsequent dehydration steps [387]. Therefore, the use of ferric sulphate as a catalyst to depolymerise holocellulose and to synthesise HMF and furfural is a potential alternative that merits investigation.

In this work, the efficacy of ferric sulphate as a catalyst for HMF and furfural synthesis from eucalyptus hardwood and mixed softwood pulps has been examined under a range of reaction conditions. Given the higher concentration of cellulose in the wood pulp sample, the HMF yield was the primary focus of the runs, although the furfural concentrations have also been reported. In addition, this paper reports on the effect of combining catalyst ferric sulphate (Lewis acid) with a Brønsted acid catalyst (hydrochloric acid) or with an ionic liquid (1-butyl-3-methylimidazolium chloride). Lastly, a preliminary investigation of the effect of microwave heating on the hydrolysis of the wood pulp has been presented.

6.3 Materials and methods

6.3.1 Chemicals

Eucalyptus hardwood pulp, containing 86% glucan and 14% xylan, and mixed softwood kraft pulp (spruce, pine, fir, 1:1:1), containing 84.8% glucan, 7.7% xylan and 5.6% mannan, were provided by FPInnovations, Canada. The high performance liquid chromatography (HPLC) mobile phase was prepared using HPLC-grade methanol (99.8%) and HPLC-grade water, both purchased from Sigma-Aldrich Co. LLC, USA. Methyl isobutyl ketone (MIBK) (≥ 99%, Sigma-Aldrich), iron (III) sulphate hydrate (97%, Sigma-Aldrich), and 1-butyl-3-methylimidazolium chloride ([BMIM]Cl) (≥ 98%, Aldrich) were used as purchased without further purification. The hydrochloric acid (HCl) catalyst was prepared by diluting 12.1 N HCl purchased from Thermo Fisher Scientific, USA. 5-hydroxymethylfurfural (≥ 99%) and furfural (99%) were purchased from Sigma-Aldrich and were used as standards for the HPLC calibration runs.

6.3.2 Experimental procedure

6.3.2.1 Wood pulp impregnation with ferric sulphate

The procedure used for impregnating the wood pulp with ferric sulphate was based on the ‘adsorption method’ outlined by Dobele, et al. [387]. The original procedure resulted in a high water content remaining in the treated wood pulp samples. In the modified procedure, 0.8 g of sample was suspended in 14 mL of ferric sulphate solution of specified concentration, and the mixture was stirred for 6 hours at 80 °C using a magnetic stirrer. The weight of the final sample obtained using this method was found to be within 5% of the combined weight of the dry wood pulp and the added ferric sulphate. The ferric sulphate concentrations tested during the runs were 2, 20, 50 and 100 mg/mL, which correspond to concentrations of 80, 800, 2000 and 4000 mg ferric sulphate/g dry wood pulp. The first three values correspond approximately to the range studied by Dobele, et al., with the fourth value added to widen the range of this investigation.

6.3.2.2 Synthesis of HMF and furfural using an oil bath

The conversion of the wood pulp to HMF and furfural using conventional heating was carried out in a Fisher Scientific High Temp Bath 160-A. The heating medium was silicone oil purchased from Acros Organics, Morris Plains, NJ, USA. An amount of treated wood pulp sample equivalent to 40 mg of dry wood pulp was added to each Pyrex tube fitted with a high temperature seal. For the runs involving HCl as co-catalyst, 670 µL of 0.05M or 0.1M HCl was added to the sample. For all other runs, 670 µL of distilled water was used as the aqueous phase. When [BMIM]Cl was used as co-catalyst, the amount added was equal to 2% of the weight of dry wood pulp in the sample. Finally, 3.33 mL of MIBK were added to each tube as the organic phase. The 1:5 v/v ratio of the aqueous to organic phases was used since it was found to be optimal in our earlier work [375]. The tubes were then inserted into the oil bath and heated at the set temperature for the desired reaction time. The oil bath temperature was monitored using a K-type thermocouple, with deviations maintained within ±1 °C. At the end of the reaction time, the tubes were removed and immediately placed in an ice bath to stop the reaction. Subsequently, the organic phase of each tube was first removed and then the aqueous phase was extracted six times with MIBK. The pooled MIBK was filtered using a 0.2 µm syringe filter into 2 mL autosampler vials for HPLC analysis. All runs were conducted in triplicate, with the standard deviation for a particular run maintained at below 12%.

6.3.2.3 Synthesis of HMF and furfural using microwave heating

The microwave experiments were conducted in a reactor operating at 2.45 GHz (MiniWAVE digestion module, SCP Science, Canada). The heating profile in the microwave involved a heating time of 10 minutes, an isothermal hold time specific to each run, and a cooling time of 10 minutes. For every run, treated wood pulp sample corresponding to a dry wood pulp weight of 200 mg was inserted into three quartz reaction tubes (maximum tube volume 50 mL), along with 3.3 mL of distilled water as the aqueous phase. Finally, 16.7 mL of MIBK was added to each tube as the organic phase. The tubes were then sealed using Teflon caps and mounted in the reactor. The desired reaction temperature and time were programmed, and the reaction was allowed to proceed for the appropriate duration. After the reaction, the contents of the tubes were filtered using a syringe filter (0.2 µm) into 2 mL autosampler vials for HPLC analysis. All runs were conducted in triplicate, with the standard deviation for each run maintained at below 12%.

6.3.3 Analysis of substrates and products

The thermal behaviour of the wood pulp samples was determined by thermogravimetric analysis (TGA) (Q50, TA Instruments, New Castle, DE, USA). Around 30 mg of sample was used for each run, and the analyses were carried out under a stream of nitrogen at a flow rate of 60 mL/min, with the samples heated from 25 °C to 800 °C at a constant rate of 5 °C/min. All the runs were conducted in duplicate.

The HMF yields were determined using an Agilent 1260 HPLC system fitted with a Zorbax Eclipse Plus C18 (4.6 × 100mm, 3.5 mm) column and a variable wavelength detector (VWD) set at 280 nm. A 20:80 (v/v) mix of methanol and water was used as the mobile phase at a flow rate of 0.6 mL/min, with the column temperature maintained at 25 °C.

The HMF yields were expressed in terms of the wt% yields calculated from a calibration curve plotting concentrations of pure HMF in MIBK against areas obtained under the HPLC curve. Equation 1 was used to calculate the HMF yield. This equation takes into account that the hardwood pulp contained 34 wt% holocellulose (Section 6.4.1), of which 86 wt% was the glucan portion, and that the molecular weight of anhydroglucose and HMF are 162 and 126 g/mol respectively.

$$HMF\ yield\ (mol\%) = \frac{Weight\ of\ HMF\ produced\ (mg)}{Weight\ of\ wood\ fed\ (mg)} \times \frac{162\ g/mol}{126\ g/mol} \times \frac{1}{0.34 \times 0.86} \times 100\% \qquad (1)$$

For softwood, 28 wt% of the pulp is holocellulose, with the sum of the glucan and mannan portions being 90.4 wt%, and hence those terms are substituted in Equation 1. It should be noted that mannan is a component of softwood hemicellulose, but being a polymer of the aldohexose mannose, it is included in the calculations for HMF yield. The furfural yields were similarly calculated using Equation 2, with the molecular weights of anhydroxylose and furfural being 132 and 96 g/mol respectively.

$$Furfural\ yield\ (mol\%) = \frac{Weight\ of\ furfural\ produced\ (mg)}{Weight\ of\ wood\ fed\ (mg)} \times \frac{132\ g/mol}{96\ g/mol} \times \frac{1}{0.34\times0.14} \times 100\%$$

(2)

6.4 Results and Discussion

6.4.1 TGA analysis of wood pulp sample

In this study, since the reactions involved the hydrolysis of wood pulp at high temperature, it is important to examine the thermal stability of the samples using TGA. Figure 6-2 shows the TGA curve obtained for the hardwood and softwood pulp samples.

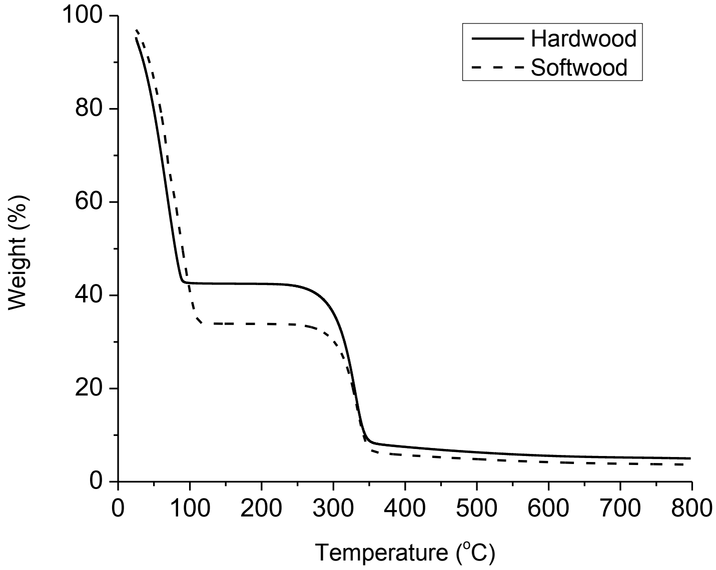


Figure 6-2: TGA of hardwood and softwood pulp

The TGA profiles of both wood pulp types followed a similar pattern. The first weight loss was in the range of 25 to 100 °C, and represented the moisture loss. The moisture content was 57 wt% for the hardwood and 63 wt% for the softwood pulp samples. The second phase of weight loss, which occurred between 250 and 360 °C, was the primary devolatilisation region and represented the volatilisation of the holocellulose present in the wood [388]. This accounted for about 34 wt% of the total wood for the hardwood pulp, and 28 wt% for the softwood pulp.

6.4.2 HMF synthesis from hardwood pulp using only ferric sulphate

When ferric sulphate alone was used as the catalyst for runs conducted in the oil bath at 170 °C, the HMF yields obtained were below 6 mol% for all concentrations of ferric sulphate used, even for run times of 90 minutes (Figure 6-3 a). Furfural yields were more significant ((Figure 6-3 b), with a maximum yield of 56 mol% being obtained for ferric sulphate concentration of 800 mg/g dry wood pulp after 90 minutes.

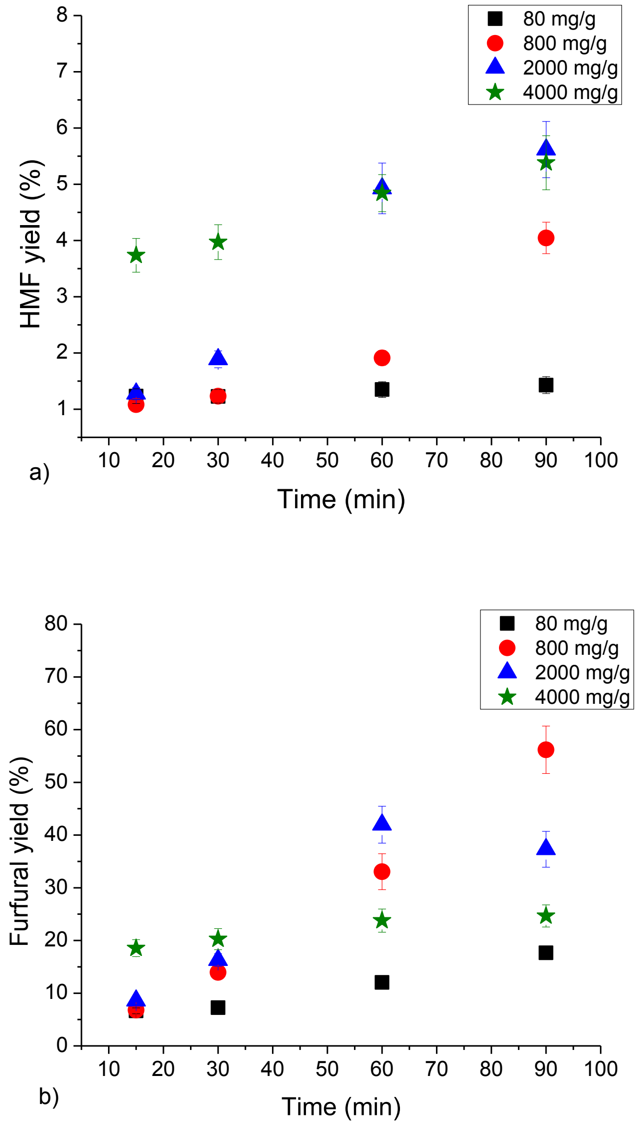


Figure 6-3: Yields of a) HMF and b) furfural for different ferric sulphate concentrations obtained at 170 °C

To increase HMF yields, the reaction temperature was raised to 200 °C, which is the maximum temperature attainable by the system. The results obtained are shown in Figure 6-4.

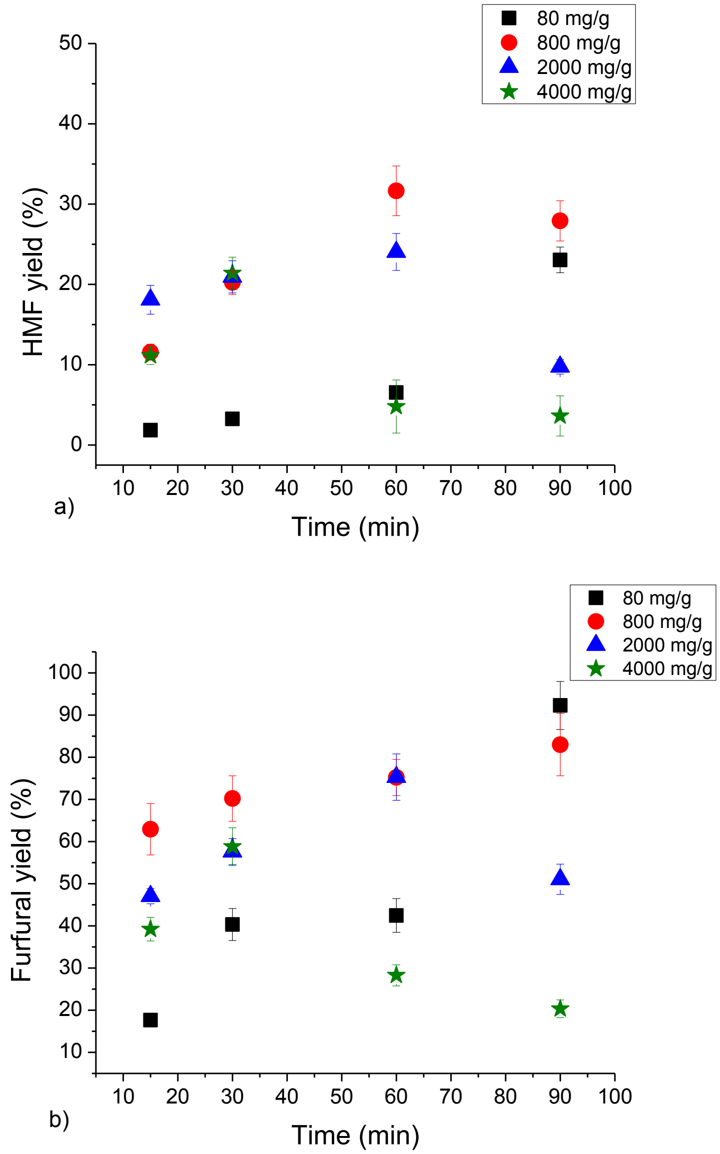


Figure 6-4: Effect of ferric sulphate concentration on a) HMF and b) furfural yields from hardwood pulp obtained at 200 °C.

It can be observed from Figure 6-4 that for a ferric sulphate concentration of 80 mg/g dry wood pulp, the HMF yield continued to increase until a reaction time of 90 minutes. However, further runs showed that if the reaction time was increased to 105 minutes, the yield dropped sharply to 12.5 mol%. The highest HMF yield was obtained for a ferric sulphate concentration of 800 mg/g dry wood pulp and a reaction time of 60 minutes, at 31.6 mol%.

Blank runs, conducted for wood pulp samples not impregnated with ferric sulphate, did not lead to HMF or furfural formation in perceptible quantities, at either 170 or 200 °C. On the other hand, if ferric sulphate (800 mg/g dry wood pulp) was added directly at the time of the reaction and without prior impregnation, then the yield obtained after 60 minutes increased to 20.3 mol%. However, this yield was still considerably lower than what was obtained for the impregnated samples. It is therefore clear that ferric sulphate impregnation can catalyse HMF synthesis.

A comparison of HMF and furfural yields clearly shows that the yields of furfural obtained from xylan are considerably higher than HMF yields from cellulose. This can be attributed to the structural differences between these two biopolymers. It is well known that hemicellulose is hydrolysed more readily than cellulose, and more dilute acid concentrations are suitable for hemicellulose hydrolysis than is the case for cellulose [389, 390]. For instance, it has been shown that xylan can be completely converted while leaving behind 85% of the cellulose when dilute H_2SO_4 is used as the catalyst [391]. In cellulose, the hydroxymethyl group of the glucose molecules participate in an extensive network of intra- and inter-chain hydrogen bonds [392]. This makes cellulose a highly crystalline material that is resistant to hydrolysis [393]. In xylan, the hydroxyl groups are substituted with 4-0-methylglucuronic acid, arabinose and acetyl groups, which leaves the xylans unable to form a hydrogen bonding network [392, 393]. Hemicellulose, therefore, is amorphous, and more easily depolymerised and converted to dehydration products like furfural.

There are three major conclusions that can be drawn from Figure 6-4 (a). Firstly, HMF yields initially rise and then decrease with an increase in reaction time for all ferric sulphate concentrations. The second aspect is that the peak HMF yields occur at progressively shorter reaction times for higher ferric sulphate concentrations. Finally, HMF yields increase when ferric sulphate concentration is raised from 80 to 800 mg/g dry wood pulp, but further increase in ferric sulphate concentration leads to a drop in yields.

These results can be explained based on the fact that the conversion of cellulose to HMF and the conversion of xylan to furfural are both chain reactions, as shown in Figure 6-1. For any catalyst concentration, a specific time period is necessary for the cellulose to be depolymerised and transformed to HMF. The ferric sulphate catalyses these reactions by forming an adduct between the metal cation and the saccharide molecules. The intra-molecular bonds of cellulose are weakened by the polarising action of the cations, accelerating the hydrolysis process [394]. An increased presence of ferric cations, therefore, leads to a more rapid cellulose depolymerisation, which is why the HMF peak occurs earlier when ferric sulphate concentration is increased.

At prolonged reaction times, the formation of byproducts like LA, humins and decomposition products increased, leading to a decrease in HMF yields observed at the end of the reaction. This effect is especially pronounced at higher ferric sulphate concentrations, since HMF is formed at shorter reaction times, which leaves more time for byproduct formation.

The mechanism of ferric cation-catalysed cellulose depolymerisation also helps understand the reason for the decrease in HMF yields when ferric sulphate concentrations are higher than 800 mg/g dry wood pulp. As stated in Section 6.2.1, ferric sulphate is a Lewis acid. However, in aqueous media, it dissociates into ferric and sulphate ions. The sulphate ions react with the aqueous media to form dilute sulphuric acid (H_2SO_4). Additionally, free ferric ions are solvated by water to form complex ions like $Fe.(H_2O)_6^{3+}$. These complex ions undergo successive hydrolysis reactions as presented in equation (3) and (4) [395]:

$$Fe(H_2O)_6^{3+} + H_2O \rightarrow Fe(H_2O)_5OH^{2+} + H_3O^+ \quad (3)$$

$$Fe(H_2O)_5OH^{2+} + H_2O \rightarrow Fe(H_2O)_4(OH)_2^+ + H_3O^+ \quad (4)$$

This decrease in pH is analogous to what has been obtained for other Lewis acid catalysts like $CrCl_3$ [22]. It leads to an increase in the formation of humins and other by-products, as evidenced by visual inspection of the reaction mixtures, and corroborated by the results obtained in Section 6.4.4.

After analysing the above results, it was concluded that increasing HMF yields above what has been obtained using ferric sulphate alone may require using a co-catalyst that could depolymerise cellulose more quickly, without abetting byproduct formation. In this regard, the effects of adding an ionic liquid to the reaction mixture were investigated, since ionic liquids have been stated to be useful in depolymerising cellulosic biomass [396].

6.4.3 HMF synthesis from hardwood pulp using ferric sulphate and ionic liquid

The ionic liquid [BMIM]Cl has been used previously for dissolving cellulose [396, 397]. It was also used in our previous work for depolymerising corn starch [375]. In that work, it was found that a [BMIM]Cl concentration of 2 wt% led to optimal results, since an increase in ionic liquid concentration led to a rise in the system viscosity. Accordingly, the same concentration was used in this work.

From Figure 6-5, it can be observed that the HMF yields when [BMIM]Cl was used followed a similar trend to what was observed in its absence. The yields were, however, slightly lower than the values that were obtained using ferric sulphate alone. For instance, the maximum yield was still obtained for ferric sulphate concentration of 800 mg/g of dry wood pulp and a reaction time of 60 minutes, but the value was only 26.7 mol%.

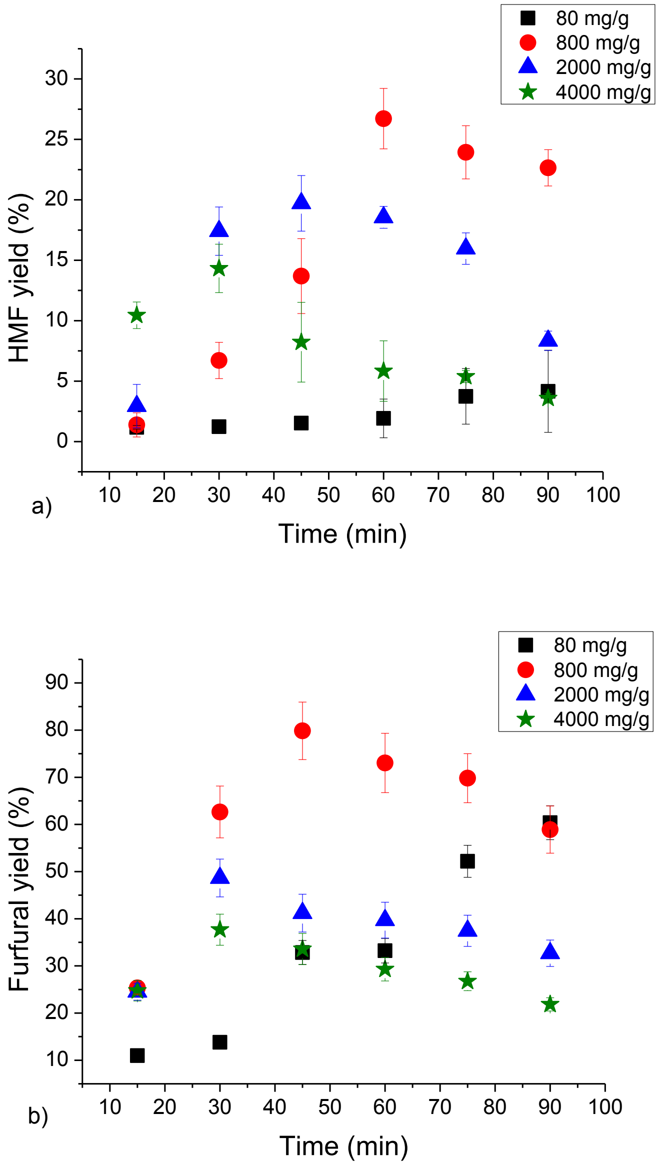


Figure 6-5: Effect of ferric sulphate concentration on a) HMF and b) furfural yields from hardwood pulp obtained at 200 °C using [BMIM]Cl as co-catalyst

Therefore, it is clear that the addition of [BMIM]Cl did not increase the HMF yields for hardwood pulp. On the contrary, the increased viscosity of the aqueous phase owing to [BMIM]Cl

[398] led to increased mass transfer limitations, accounting for the drop in yield. This lack of effectiveness of [BMIM]Cl can be attributed to the fact that long reaction times, of the order of several hours, are needed for substantial cellulose dissolution to occur in [BMIM]Cl [397]. The alternative is the addition of mineral acids like H_2SO_4 and HCl to [BMIM]Cl to induce depolymerisation [399, 400]. Under the reaction conditions employed in this study, [BMIM]Cl did not increase the depolymerisation of hardwood pulp.

Since mineral acids have been used by several researchers for lignocellulose depolymerisation [279, 283, 401], another strategy to enhance the depolymerisation of the wood pulp is the addition of HCl (Section 6.4.4).

6.4.4 HMF synthesis from hardwood pulp using ferric sulphate and HCl

Preliminary experiments using 0.5 and 2 M HCl, and a ferric sulphate concentration of 800 mg/g dry wood pulp, indicated that high HCl concentrations lead to excessive humin formation even at short reaction times. Low HCl concentrations and short reaction times gave higher yields. Therefore, the combination of ferric sulphate and dilute HCl was further investigated. The HCl concentrations used were 0.05 and 0.1 M. The HMF and furfural yields obtained are shown in Figures 6-6 and 6-7.

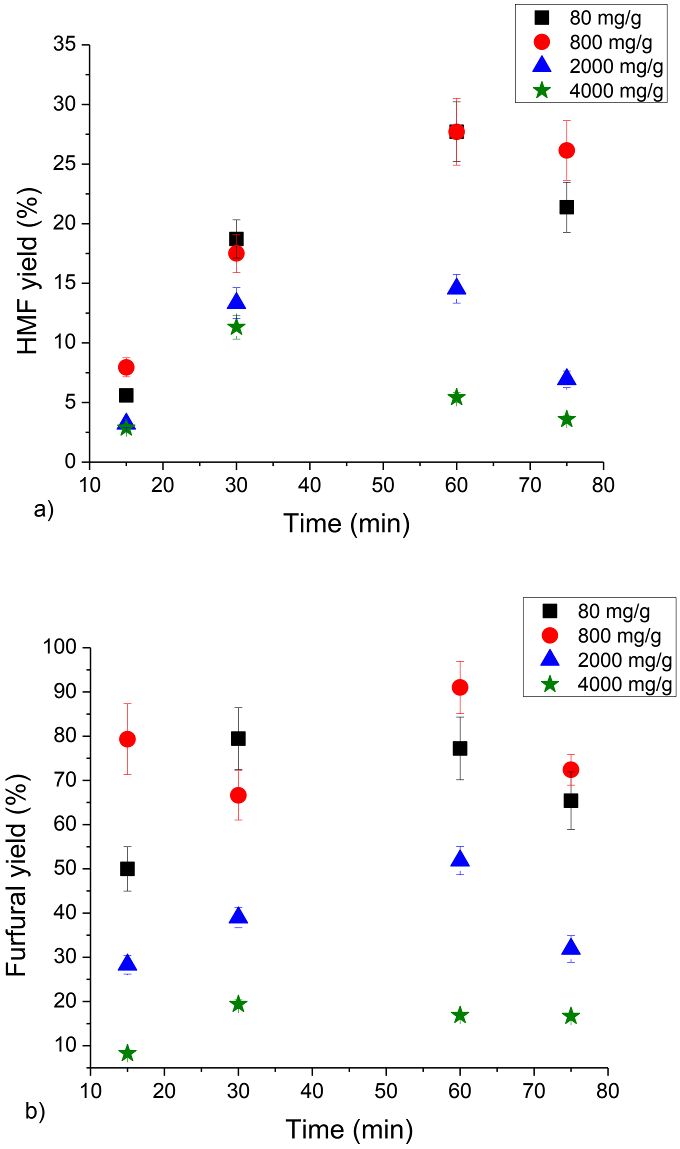


Figure 6-6: Effect of ferric sulphate concentration on a) HMF and b) furfural yields from hardwood pulp obtained at 200 ºC with 0.05 M HCl co-catalyst

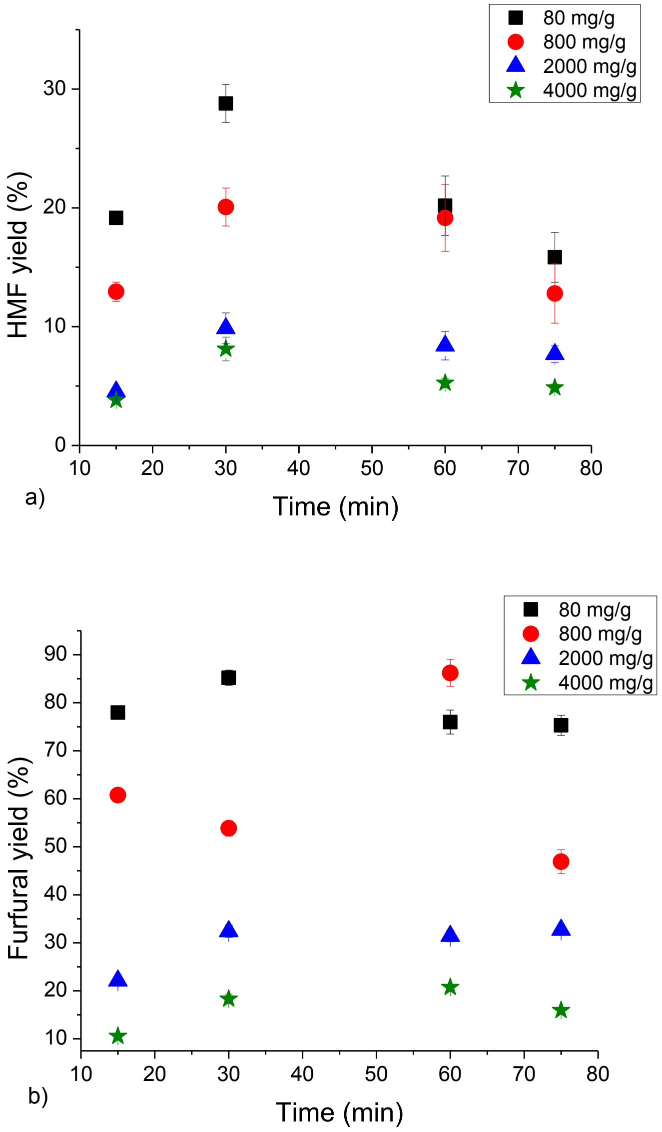


Figure 6-7: Effect of ferric sulphate concentration on a) HMF and b) furfural yields from hardwood pulp obtained at 200 °C with 0.1 M HCl co-catalyst

When 0.05 M HCl was used, the maximum HMF yield was 27.7 mol%. This was obtained after a reaction time of 60 minutes at ferric sulphate concentrations of 80 and 800 mg/g of dry wood pulp. At the end of the runs, the reaction mixtures were darker than when ferric sulphate alone was used, which indicated a greater extent of humin formation. For 0.1 M HCl, it was observed that the maximum HMF yield was 28.8 mol%, which was slightly lower than the highest yield obtained using ferric sulphate alone. This was, however, obtained after a reaction time of only 30 minutes as opposed to 60 minutes without HCl co-catalyst. The yields obtained for the same time interval when HCl alone was used as catalyst were lower than for the combination of HCl and ferric sulphate, at 24.0 and 25.0 mol% for 0.05 and 0.1 M HCl. It was observed that for runs of 30 minutes and longer, using 0.1 M HCl, the wood pulp had been converted completely, but there was an increasing amount of black residue left in the reaction mixture.

This showed that while the presence of HCl helped to depolymerise the wood pulp, as evidenced by the absence of wood pulp residues obtained at the end of the reaction, it also resulted in the excessive formation of byproducts, especially humins. The increased conversion was therefore cancelled out by the loss in selectivity. This tallies with the findings of Section 6.4.2, where higher ferric sulphate concentrations increased humin production and a drop in HMF yields due to a decrease in pH. The lower HMF yields obtained when HCl alone was used is attributed to the fact that HCl is a Brønsted acid, in whose presence HMF is formed from glucose via the 3-deoxyglucosone route [361]. HMF yields are lower if this route is followed instead of the fructose intermediate route [381].

It is clear from the results obtained in Sections 6.4.2, 6.4.3 and 6.4.4 that for hardwood pulp, the use of ferric sulphate alone gave the highest HMF yields with minimal humin formation. It was also showed that the use of a ferric sulphate concentration of 800 mg/g of dry wood pulp did generally give the highest HMF yields. It was therefore decided to use this ferric sulphate concentration for HMF synthesis from softwood pulp.

6.4.5 HMF synthesis from softwood pulp

The HMF and furfural yields obtained from softwood pulp are given in Figure 6-8. For each catalytic system used, the HMF yields from softwood pulp attained a peak value at longer reaction times than for the hardwood pulp. For instance, the maximum HMF yield obtained using ferric sulphate alone was 28.7 mol%. This value was obtained after 90 minutes, which is considerably longer than the 60 minutes time period that was required for the hardwood pulp sample. Likewise, the peak HMF value when ferric sulphate and 0.1 M HCl were used occurred at 75 minutes, as compared to only 30 minutes for hardwood pulp.

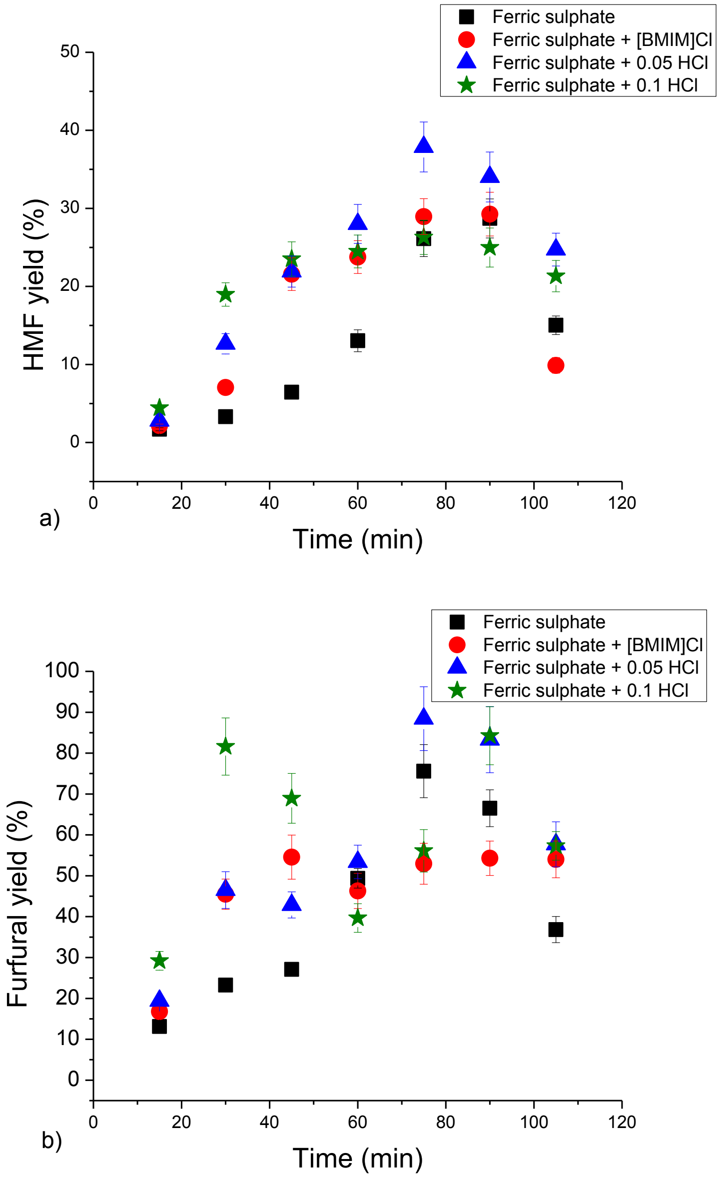


Figure 6-8: a) HMF and b) furfural yields obtained from softwood pulp

Another difference from hardwood pulp is that the maximum HMF yield (37.9 mol%) was obtained when the ferric sulphate was combined with 0.05 M HCl. The combination of ferric sulphate and [BMIM]Cl also gave a higher yield (29.3 mol%) than when ferric sulphate was used alone. This showed that longer reaction times and harsher reaction conditions were necessary to depolymerise softwood pulp. The resistance to depolymerisation also resulted in lower byproduct formation, as evidenced by the lesser amount of humins present at the end of the reaction. This explains why for softwood pulp, the use of a mild co-catalyst, such as [BMIM]Cl or 0.05 M HCl, alongside ferric sulphate raised HMF yields as compared to the use of ferric sulphate alone. However, when a stronger mineral acid was used, the problem of greater byproduct formation remained, which is why the maximum HMF yield was only 26.3 mol% for 0.1 M HCl.

The reason for the lowered effectiveness of ferric sulphate in catalysing softwood pulp depolymerisation as compared to hardwood pulp is the difference in the structure and the composition of the two wood types. Of particular significance is the fact that softwood contains more extractives than hardwood [402, 403]. This higher extractive content forms complexes with the metal cations, reducing the catalyst's ability to bind with the cellulose molecules and depolymerise them [404].

An alternative to using a co-catalyst for cellulose depolymerisation is the use of microwave energy, since microwave energy has been demonstrated to depolymerise cellulose, even without the addition of acid catalysts [405]. Therefore, the use of microwave energy to convert hardwood and softwood pulp treated with ferric sulphate concentration of 800 mg/g dry wood pulp was tested.

6.4.6 HMF synthesis using microwave heating

Preliminary experiments indicated that the maximum temperature that the microwave system could reach was 180 °C, and hence this was the temperature initially used for converting both softwood and hardwood pulp to HMF. It was observed that running the system without an isothermal hold time gave the highest HMF yields for both types of wood pulp, with a yield of 22.5 mol% obtained for hardwood pulp and 26 mol% for softwood pulp. The absence of the isothermal phase meant that the reactor was operated for the minimum possible time period, that is, 10 minutes for the heating step and another 10 minutes for the cooling step. Increasing the reaction time by incorporating an isothermal heating phase of any duration resulted in increased humin formation and reduced HMF yields.

Since the reaction time could not be reduced, the only option for attempting to reduce humin formation was to lower the reaction temperature. Accordingly, runs were conducted at 170 °C. It was observed that in the absence of an isothermal heating phase, most of the wood pulp remained unconverted, with yields of only 3.3 and 6.6 mol% obtained for hardwood pulp and softwood pulp respectively. Adding an isothermal heating phase led to an increase in cellulose depolymerisation. The maximum HMF yield from hardwood pulp (27.1 mol%) was obtained for an isothermal heating time of 20 minutes. Under these conditions, the corresponding yield from softwood pulp was 25.1 mol%.

The values obtained using microwave heating are therefore comparable with those that were obtained using oil bath heating. However, it is well known that HMF yields are maximised at high temperatures and short reaction times [332]. Therefore, a microwave system that can attain higher reaction temperatures with shorter heating and cooling times could give higher HMF yields than the system used here.

6.5 Conclusion

This work demonstrated the potential of the eco-friendly catalyst ferric sulphate for synthesising HMF and furfural from cellulosic biomass. For the hardwood pulp, it was shown that the highest HMF yields, with minimum humin formation, were obtained using ferric sulphate alone. The addition of the ionic liquid [BMIM]Cl to the reaction system led to a slight drop in yields owing to increased mass transfer limitations in the system. When HCl was added, it caused increased humin formation, which also adversely affected the product yields. A ferric sulphate loading of 800 mg/g dry wood pulp was found to give the maximum HMF yields (31.6 mol%). Softwood pulp, however, proved to be harder to depolymerise, resulting in higher yields being obtained for both ferric sulphate-[BMIM]Cl and ferric sulphate-HCl systems than for ferric sulphate alone. The highest yield (37.9 mol%) was obtained for the combination of 0.05 M HCl and ferric sulphate concentration of 800 mg/g dry wood pulp. The use of microwave heating was trialled as another possible method of depolymerisation, and it was concluded that its use in conjunction with ferric sulphate merits further investigation.

Chapter 7 : General Conclusions and Recommendations

7.1 General conclusions and summary

This thesis examined HMF and LA synthesis predominantly from the standpoint of sustainability and environment friendliness. To reduce the carbon footprint of the process, it is necessary to minimise feedstock consumption, which can be done by selecting suitable feedstock based on their composition. In case of starch, it was shown that corn starch high in amylopectin content gave better results than normal or high amylose corn starch. This was first determined by fractionating starch into amylose and amylopectin and comparing the product distribution of their acid hydrolysis (Chapter 3). The hypothesis was then confirmed by constructing a kinetic model analysing the results of acid hydrolysis of waxy (high amylopectin), normal and high amylose corn starch (Chapter 4). Waxy corn starch is therefore a better feedstock for HMF and LA synthesis.

A comparison of conventional and microwave heating for LA synthesis using HCl catalyst showed that while final LA yields were similar, a shorter reaction time was required in microwave heating (Chapter 4). However, for a heterogeneous catalyst like boric acid, the mass transfer limitations occurring due to the larger tube size and long initial heating period meant that oil bath heating was more suitable.

A boric acid-choline chloride system was found to be a potential alternative to the metal salt Lewis acid-ionic liquid systems that are commonly used for converting polyglucans to HMF (Chapter 5). This system, when used with waxy corn starch, gave higher yields in a biphasic water-THF system than in water-MIBK, owing to the higher extraction coefficient of HMF in THF as compared to MIBK. However, THF also led to the degradation of the catalyst system, meaning that boric acid-choline chloride was more recyclable in water-MIBK.

Due to its ability to depolymerise cellulose and also act as a Lewis acid, ferric sulphate can be used as a catalyst to convert hardwood and softwood pulp to HMF and furfural (Chapter 6). For hardwood pulp, impregnation with ferric sulphate alone gives the highest HMF yields, while for softwood pulp, the addition of dilute HCl increases depolymerisation and thereby the product yields. The ionic liquid [BMIM]Cl does not significantly aid depolymerisation of either wood variety under the reaction conditions tested.

7.2 Contributions to knowledge

HMF and LA are two of the most promising biomass derived chemicals, whose large scale production depends on the development of reaction systems that are cost effective and eco-friendly. This work has helped advance the development of biorefineries by making the following major contributions to knowledge:

1. It was determined that the composition of starch plays an important role in the product yields obtained, addressing the gap in knowledge in this area. Specifically, high amylopectin corn starch was found to be acid hydrolysed more easily than normal and high amylose corn starches, and therefore to be a more suitable feedstock for HMF and LA synthesis.
2. For homogeneous catalysts like HCl, microwave heating was found to give yields equivalent to those obtained using conventional oil bath heating at shorter reaction times.
3. A kinetic model was developed for the first time for predicting HMF and LA yields from starches of different compositions for either conventional or microwave heating.
4. The effectiveness of a novel boric acid-choline chloride as a practical option for HMF synthesis from starch was evaluated, and the optimum reaction conditions were assessed when using either water-MIBK or water-THF as biphasic media.
5. The recyclability of the boric acid-choline chloride system in both water-MIBK and water-THF biphasic media was tested, and it was determined that the catalyst system shows excellent reusability in water-MIBK. This opens up the possibility of using boric acid-choline chloride as an inexpensive and green alternative to metal salt Lewis acid-ionic liquid systems.
6. Ferric sulphate, an inexpensive, non-toxic and eco-friendly Lewis acid, was found to be a novel and effective catalyst for HMF and furfural synthesis from both hardwood and softwood pulp.

7.3 Recommendations for future research

Based on the work performed in this thesis, certain avenues for further advances in this line of research are proposed:

1. The appeal of HMF lies in the fact that it can be readily converted into a wide range of compounds, but this is also a shortcoming, as its instability makes its synthesis, isolation and storage problematic. A possible option would be the conversion of HMF into a suitable derivative that is more stable than HMF. For this derivative to be useful as a platform chemical, it would need to retain some of the ease of conversion possessed by HMF, or be able to be transformed back readily to HMF. Some research has already been undertaken in this regard, with 5-acetoxymethyl furfural (AMF) [406], 5-bromomethyfurfural (BMF) [407, 408] and 5-chloromethyl furfural (CMF) [409] being some of the candidates proposed. It remains to be seen if these or other derivatives can help increase the commercial appeal of HMF.
2. This study has shown the relevance of starch composition in determining its suitability for HMF and LA synthesis. This can be used to identify non-edible and waste starches, such as from industrial processing, that can be utilised as sustainable feedstock.
3. It was seen in Chapter 6 that the combination of ferric sulphate impregnation and microwave heating is promising, but requires the reactor to be able to attain higher temperatures at a faster heating rate to fulfil its potential. Also, the reactor used in this study was a batch reactor, while industrial operation would most likely need a continuous flow system. These would potentially be areas of interest to future researchers in this field.
4. Since HMF is an intermediate in the formation of LA, at a commercial scale it would be desirable to operate a reaction system that could be tuned to produce either HMF or LA depending on requirements. This would be similar to petrochemical refineries, where the product mix can be altered based on feed characteristics, market demand, or other factors. A biorefinery like this requires a solvent and catalyst system that can favour either HMF or LA formation depending on the requirement, alongside precise control of the reaction parameters affecting product distribution- temperature, reaction time, water concentration, and pH. Development of such a reactor is an essential step to bridging the gap between lab-scale and commercial production of biomass platform chemicals.

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