Chapter 1

Biofuels and Co-Products Out of Hemicelluloses

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Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/52645

1. Introduction

Second generation biofuels are based on the utilisation of non-edible feedstock for the production either of ethanol to be inserted in the gasoline pool or of biodiesel to be inserted in the diesel pool. Ethanol is usually produced out of fermentation of C6 sugars (although other approaches does exist, see [1]) and the latter came, in first generation ethanol, from starch. In second-generation ethanol, the source of carbohydrate considered is usually cellulose, which, in turns, is obtained from lignocellulosic biomass. Recent work by Lavoie*et al*. [2] have depicted an overview of many types of lignocellulosic biomass and in most cases, cellulose, although a major component, is not the only one and is accompanied by lignin, hemicelluloses, extractives and, in case of agricultural biomass, proteins. High grade biomass (as wood chips, sugar cane or even corn) are usually very expensive (more than 100 USD/tonne) because, in most part, of the important demand related to those feedstock in industries and this is why cellulosic ethanol is more than often related to residual biomass. The latter includes but is not limited to residual forest and agricultural biomass as well as energy crops. In all cases, although the feedstock is rather inexpensive (60-80 USD/tonne), it is composed of many different tissues (leaves, bark, wood, stems, etc.) making its transformation rather complex [3]. Industrialisation of second-generation biofuel requires specific pre-treatment that should be as versatile as efficient in order to cope with the economy of scale that has to be implemented in order to make such conversion economical.

The whole economics of cellulosic ethanol relies first on ethanol, which has a commodity beneficiates from a quasi-infinite market as long as prices are competitive. Assuming average cellulose content of 45-55 % (wt) in the lignocellulosic biomass, the ethanol potential of lignocellulosic biomass would range between 313-390 L per tonne of biomass converted.

With an actual market price of 0.48 USD per liter the value of this ethanol would range between 150-187 USD per tonne of biomass processed. Since the latter is more expensive to process (first isolation of cellulose then hydrolysis of cellulose) and considering the fact that the feedstock is itself expensive, there is a necessity to get an added value out of the remaining 55-45 % (wt) content. This residual carbon source is composed mostly of hemicelluloses and of lignin. The latter is a very energetic aromatic-based macromolecule, that has a high calorific value explaining why many processes converting such biomass (as some pulp and paper processes) relies on the combustion of lignin to provide part of the energy for the industry. It could also serve as a feedstock for the production of added-value compounds and although the subject is very pertinent to the field, it is out of the scope of this review, which focuses mostly on C5 sugars derived from hemicelluloses.

Conversion of the carbohydrates is of course an important part of the process although; isolation of hemicellulose for the lignocellulosic matrix is also crucial for such an approach and in consequence should also be briefly assessed. For years now, the pulp and paper industry have worked with lignocellulosic substrates and they have over the year developed many techniques allowing isolation of hemicelluloses. Chemical processes as soda pulping and kraft pulping allows isolation of both lignin and hemicellulose whilst protecting the cellulosic fibres in order to produce the largest amount of pulp possible per ton of biomass. Nevertheless, in both chemical processes previously mentioned, the hemicellulose are rather difficult to reach since they are mixed with a variety of organic and inorganic compounds including lignin as well as the chemicals that were used for the pulping process. During the last decades, the pulp and paper industry have started to look toward other processes that could allow a preliminary removal of hemicelluloses in order to avoid a complicated and expensive isolation after a chemical pulping process.

Amongst the techniques used for prehydrolysis, treatments with hot water catalyzed or not have been investigated in details in literature. As an example, Schild*et al*. [4] performed a preliminary extraction with water (via auto-hydrolysis) or with alkaline water prior to soda pulping in order to recuperate the hemicellulose prior to pulping. Similar testing was also performed on northern spruce with pressurised hot water in the presence of sodium bicarbonate [5]. Hot water extractions were also performed at temperature around 170 ˚C at different pH (the latter were adjusted with a phthalate buffer) and these experiments showed that control of pH was crucial in order to extract more of the hemicelluloses (up to 8 % wt on original biomass) [6]. Hot water extractions at similar temperature range have also been performed on maple [7] as well as on sugarcane bagasse [8]. Overall the hot water pretreatment may be a very promising approach for isolation of hemicelluloses although reported rates did not go far over 10 % because of the necessity to preserve the cellulosic fibres in order to avoid losses for papermaking. Acid catalyst has also been used as pretreatment to remove hemicellulose prior to pulping as reported by Liu*et al*. [9]. Utilisation of sulphuric acid, although very efficient to remove hemicellulose may also have an impact on cellulose thus reducing the pulp production rates.

Another process that could lead to isolation of hemicellulose is the organosolv process, which is to a certain extent comparable to classical chemical pulping in that sense that the

technique allows simultaneous removal both for lignin and hemicelluloses. However, instead of using only an aqueous mixture of ions, the process relies on the utilisation of a combination of ions (usually alkaline) in a 50/50 mixture of aqueous organic solvent. In most cases, the solvent is methanol for obvious economic reasons although other solvents as butanol and certain organic acids have also been investigated to the same purposes. Recent work by Wang*et al*. [10]have shown that in an organosolv process using different solvent as well as different catalyst with poplar, sodium hydroxide was shown to be the best catalyst for hemicellulose removal from the pulp. Recent work by Brosse *et al*. [11] also showed that for *Miscanthus Gigantheus*, an ethanol organosolv process combined with an acid catalyst (sulphuric) lead to removal of most of the hemicelluloses and lignin from the original biomass.

Finally, another approach that could lead to isolation of hemicellulose from a lignocellulosic matrix is steam processes. This technique relies on impregnation of the feedstock with water (either catalyzed or not) then treatment under pressure at temperature ranging from 180-230 °C for a certain period of time after which pressure is relieved suddenly thus creating an "explosion" of the feedstock. Such process could lead, depending on the operating condition, to the isolation of either hemicellulose or lignin in two steps or in a single step. Our team has demonstrated the feasibility of both processes for different substrates [12-14].

Independently of the substrate or the technique used for the isolation of the hemicelluloses, conversion of lignocellulosic biomass, either for the production of paper or for the production of biofuels requires a complete utilization of the carbon compound found in biomass. Once the hemicelluloses are isolated from the original feedstock, they can undergo different types of transformation leading to different added value compounds that could lead to increase the margin of profit for the industries in the field.

Hemicelluloses account for 15-35 % of lignocellulosic biomass dry weight [2] and they are usually composed of different carbohydrates as well as small organic acids as acetic and formic acid. Glucose and xylose are often the most abundant sugars in hemicelluloses hydrolysis although mannose, arabinose and galactose might also be present in lower concentrations. The carbohydrate compositions of some lignocellullosic biomass are shown in Table 1. Whilst the C6 sugars could easily be fermented to ethanol following detoxification of the mixture, C5 sugars remains hard to convert to ethanol, mostly because classical yeasts don't metabolise them and the genetically modified organism that ferment C5 sugars are usually slower than classical organisms used in the production of etanol from C6 sugars. Nevertheless, even if ethanol production may remain a challenge, other alternatives could be considered, both on the chemical and on the microbiological point of view, to allow conversion of C5 sugar into added value products.

Carbohydrates tend to react in acidic, basic, oxidative or reductive mediums and therefore, numerous do arise for the conversion of C5 sugars. Although many options are available, this review will focus solely on 4 different pathways: acid, base, oxidative, and reductive. Each of these pathways could be inserted in an integrated biorefinery process where each of the fractions could be isolated and upgraded to high value compounds (see Figure 1).

Components (wt%)	Energy crops		Agricol residues		Forest residues	Coniferous
	Switchgrass [15]	Miscanthus [16]	Wheat Straw [15]	Corn Stover [17]	Aspen [18]	Loblolly Pine [19]
Glucan	38.5	55.5	39.2	36.2	52.4	36
Xylan	26.3	12.4	24.6	20.1	14.9	7.5
Galactan	1.16	-	-	1.45	2.2	2.5
Mannan	0.13	-	-	-	2.3	8.2
Arabinan	3.41	-	1.9	3.0	0.9	1.6

Table 1. Carbohydrate composition of some lignocellulosic biomass.

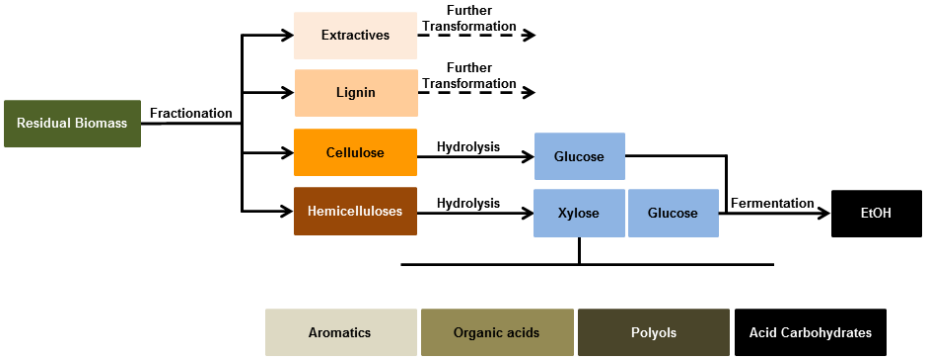

Figure 1. Potential utilization of hemicelluloses in an optimized conversion process for residual lignocellulosic biomass where C6 sugars are converted to ethanol, lignin and extractives to other added value products.

In this review, emphasis will be made on the recent work made for each of these conversion pathways both on the chemical and on the biochemical pathways. The review will focus on these 4 approaches also for their generally simple nature that would make them adaptable to an industrial context. These results will be compared to classical fermentation processes to produce ethanol with different types of organisms that can metabolise C5 sugars.

2. Conversion of xylose under an acid catalyst

2.1. The chemical pathway

Either in cyclic or aliphatic form, xylose then tends to dehydrate thus leading to the production of furfural whilst losing three molecules of water. Although this approach could explain the formation of furfural, it is not the sole options and many detailed reports have shown, by correlating the intermediaries with the actual structure, could be formed by many ap-

proaches depending on the reactant as reported by Marcotullio *et al*. [20] using halogen ions and proceeding only via the aliphatic form or as reported by Nimlos *et al*. [21] either via an aliphatic or a cyclic pathway (D-xylopyranose). Many different types of acid catalyst, either Brønsted or Lewis have been tested for the production of furfural. Although most of the acids reported in literature have been efficient so far for the production of the targeted molecule, one of the major side-reaction of furfural is polymerisation which influences the conversion rates and the selectivity of most of the processes reported in literature. An example of the abundance of research on this specific conversion is shown in Table 2 for different dehydration reactions under acid catalyst..

Catalyst	Conversion	Reference
H-Mordenite	98%	[22]
Sulphonic acid/Silica surface	99%	[23]
1-methylimidazole	91%	[24]
KI, KCl (dilute acid)	88%	[20]
NaCl, H_2SO_4	83%	[25]
1-alkyl-3-methylimidazolium	84%	[26]
NaCl, HCl	78%	[27]
Aluminium chloride Hexahydrate	76%	[28]
Amberlyst 70	75%	[29]
Zeolite H-Beta	74%	[30]
MCM-22, ITQ-2	70%	[31]
$FeCl_3$	71%	[32]
Nafion	60%	[33]
Keggin type acids	62%	[34]
Vanadyl pyrophosphate	53%	[35]

Table 2. Molar conversion to furfural in relationship with the catalyst used for the dehydration of xylose to furfural under acid catalyst.

For these reactions, the temperature is generally between 140-240 °C under proportional pressure allowing the mixture to remain liquid. Many researches also use a co-solvent, often toluene in order to isolate furfural from the aqueous mixture. The reason why toluene is so popular to this purpose is mostly related to the fact that toluene has affinity for fufural thus inhibiting its polymerization.

Heterogeneous catalyst has been proven to be very efficient for the process [22,23] although polymerisation tend to reduce the surface activity thus leading to a short-term deactivation of the catalyst. On the other hand, homogeneous catalyst was also shown to be efficient but at this point the whole technique relies on how the organic solvent is dispersed in the aqueous mixture. Reducing the size of the organic solvent particles in water (or vice-versa) to the maximum should allow the best transfer between the aqueous phase to the organic phase,

assuming of course that furfural has suitable affinity for the solvent and that the partition coefficient favours the solvent.

Production of furfural itself is of course of significant interest because, amongst many factors, this chemical is commonly used in the industry as a solvent (mostly in oil chemistry). The average world production for furfural is 250 000 t/y and the actual market price evolves around 1000 USD/t [36] with recent market value reported to be closer to 1600 USD/tonne [37]. Furfural can also be a gateway to other products that could be used either as biofuels or as biomolecules. Example of such would be furfuryl alcohol via partial reduction of furfural (see Figure 2 below).

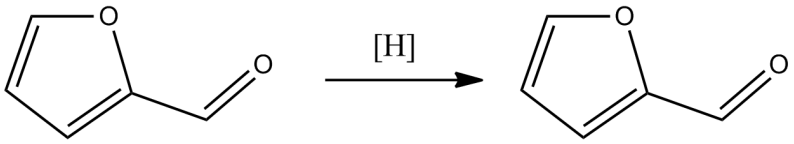

Figure 2. Reduction of furfural to furfuryl alcohol.

Furfuryl alcohol is also of interest since it is used as resins, adhesives and wetting agent, it has been mentioned that most of the 250 Kt/y of the furfural production is oriented toward production of furfuryl alcohol. The market value of this compound has been reported to be around 1800-2000 USD/tonne [38] and many reports in open literature mentions high selectivity for the conversion of furfural with iridium and ruthenium catalyst [39], rhodium [40], iron [41] and with zirconium oxide [42].

Another possible target for the transformation of furfural is for the production of 2-methyltetrahydrofuran (Me-THF) (see Figure 3). The latter is actually accredited as an additive for fuel and therefore, the possible market is virtually very important. It is also used in the petroleum industry to replace tetrahydrofuran (THF) that usually comes from non-renewables.

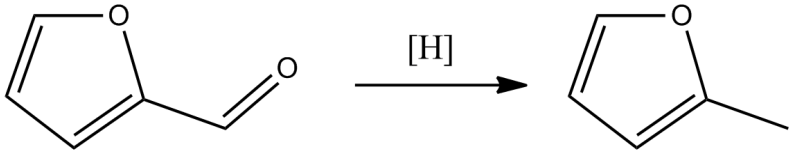

Figure 3. Reduction of furfural to 2-methyltetrahydrofuran.

Reduction of furfural to Me-THF seems to represent an important challenge since there is fewer reports mentioned in literature on the subject, as compared, as an example, to the reduction of furfural to furfuryl alcohol. Wabnitz *et al*. [43, 44] patented a one and two step process allowing conversion of furfural to Me-THF under a palladium-based catalyst and a mixture of palladium and copper oxide and chromium oxide as for the two step process.

Lange [45] patented a process using palladium and titanium oxide whilst Zheng et al. [46] worked with a copper alloy. Value for Me-THF could be estimated from the price of THF which is around 3000 USD/tonne [47] and the gap between the value of furfural and Me-THF could justify the process although hydrogen value can be estimated to be around 4.5 USD/Kg (estimated with the actual price of natural assuming reforming of the latter).

Another potentially interesting approach for a transformation of furfural would be decarboxylation to furan. The general process is depicted in Figure 4 below.

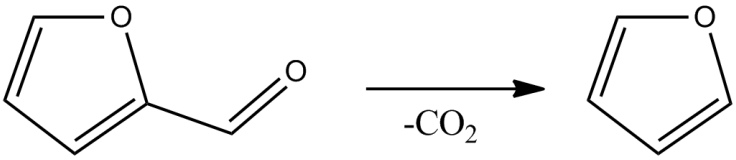

Figure 4. Decarboxylation of furfural to furan.

Many researches have focused on decarboxylation including work by Zhang *et al*. [48] who mentioned decarboxylation with potassium-doped palladium, and Stevens *et al*. [49] who reported conversion with copper chromite in supercritical CO_2.

Results reported in literature show that xylose, under an acid catalyst, tend invariably to dehydrate to furfural thus limiting the possibilities for side-products in such specific conditions. The acids could be Brønsted or Lewis type, all lead to the production of furfural furthermore when temperature are raised above 150 ˚C.

2.2. The biological pathway

Although furfural is a very common route for the conversion of xylose under an acid catalyst, furfural itself is rarely related to microorganisms in that sense that it is often considered as an inhibitor instead of a metabolite. Nevertheless, to the best of our knowledge, no report mentioned a biological conversion of xylose to furfural.

3. Conversion of xylose under a base catalyst

3.1. The chemical pathway

The interaction between xylose and bases, either Brønsted or Lewis, is rather less reported in the literature when compared to the acid conversion of xylose to furfural indicated in the previous section. Many very different reactions have been reported as in the case of Popoff and Theander [50] that have quantified the cyclic compounds produced after a base-catalyzed reaction of pure D-xylose at 96 ˚C for 4 hours. The produced compounds are rather peculiars in comparison to other work made on the subject (see Figure 5) since most of the reported compounds are aromatics. The presence of aromatics may be a result that the reac-

tion time was long and the isomerisation that was required in order to induce such reaction was efficient. Johansson and Samuelson [51] tested the effect of alkali treatments (NaOH) on birch xylan and contrarily to the previous research; they found that the treatment led to the production of a variety of organic acids. Testing on untreated xylene showed that most of the organic acids were already obtained from xylans and the most distinctive impact was observed after a 2 day test at 40 °C where the concentrations of L-galactonic and altronic acids increased significantly which could be related to a less severe treatment of xylans that also include C6 sugars.

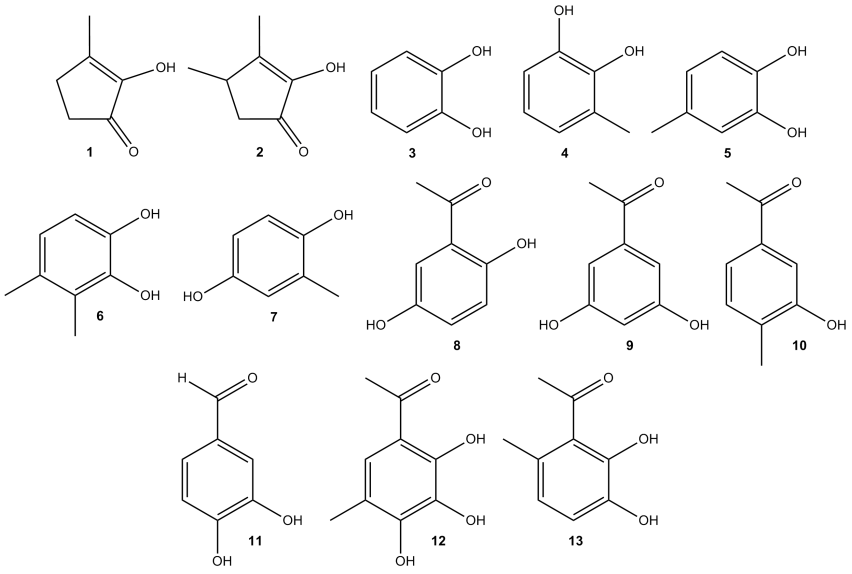

Figure 5. Cyclic and aromatics obtained from the based-catalysed treatment of D-xylose under a sodium hydroxide catalyst where (1) 2-hydroxy-3-methylcyclopent-2-enone; (2) 2-hydroxy-3,4-dimethylcyclopent-2-enone; (3) pyrocatechol; (4) 3-methylbenzene-1,2-diol; (5) 4-methylbenzene-1,2-diol; (6) 3,4-dimethylbenzene-1,2-diol; (7) 2-methylbenzene-1,4-diol; (8) 1-(2,5-dihydroxyphenyl)ethanone; (9) 1-(3,5-dihydroxyphenyl)ethanone; (10) 1-(3,4-dihydroxyphenyl)ethanone; (11) 3,4-dihydroxybenzaldehyde; (12) 1-(2,3,4-trihydroxy -5-methylphenyl)ethanone; (13) 1-(2,3-dihydroxy-6-methylphenyl)ethanone.

El Khadem *et al*. [52] studied the effect of xylose conversion in an alkali medium at low temperatures (room) and for long periods (1-4 weeks) and one of the interesting features of his work was that the process did lead to the epimerization of sugars, but furthermore, it leads to the production of C6 sugars most probably from a reverse aldol reaction. Among the sugars that were formed during the reaction, conversion of xylose was shown to be more efficient to lyxose (18 %) and arabinose (15 %) with a decrease observed for most of the compounds between 1 and 4 weeks (see Figure 6). A vast majority (more than 50 %) of xylose remains on its original form and the reaction leads to the production of 1 % glucose and 2.5 % of sorbose, both are C6 sugars.

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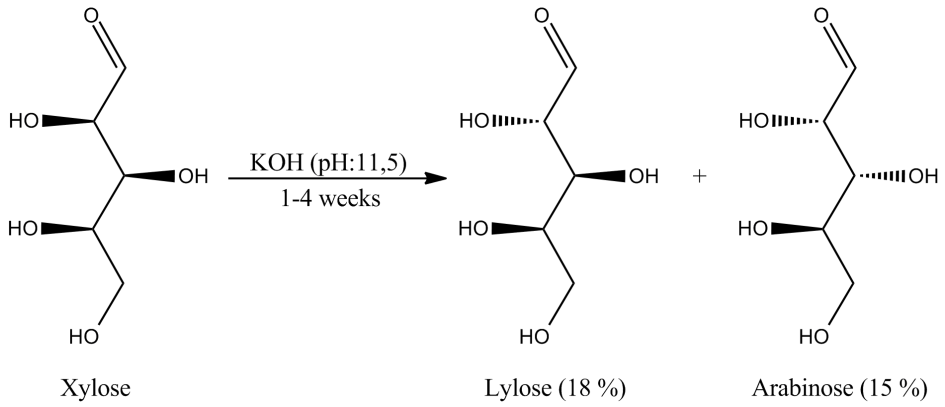

Figure 6. Major epimerisation products from 1-4 week reaction of D-xylose in a pH 11.5 KOH solution at room temperature.

Xylose, as the other carbohydrates, is converted to smaller organic acids when reacted with a strong alkali medium. As an example, Jackson *et al*. [53] have demonstrated that the conversion of xylose to lactic acid could reach 64 % (molar) accompanied by glyceric acid. Although they did not used xylose but rather ribose and arabinose, they were able to reach conversions between 35-43 % into lactic acid using potassium hydroxide as catalyst under microwave irradiation [54]. Rahubadda *et al*. [55] have provided a mechanism for the conversion of xylose to lactic acid under a base catalyst. The simplified pathway is depicted in Figure 7 below.

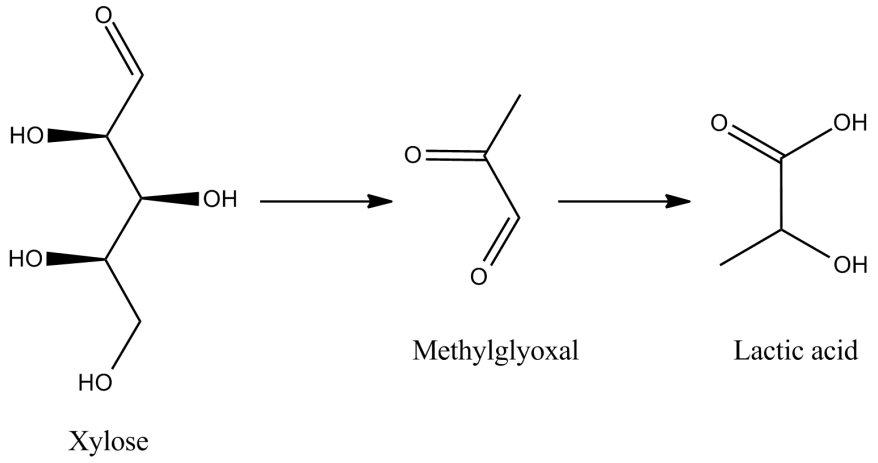

Figure 7. Conversion of D-xylose to lactic acid via the methylglyoxal pathway.

They mentioned in this report that methylglyoxal is most probably derived from glyceraldehyde as depicted in Figure 8 below. The possible reaction leading to methylglyoxal may involve an E2 reaction on C2 leading to removal of the hydroxyl group on C3 then a keto-enol rearrangement to methylglyoxal.

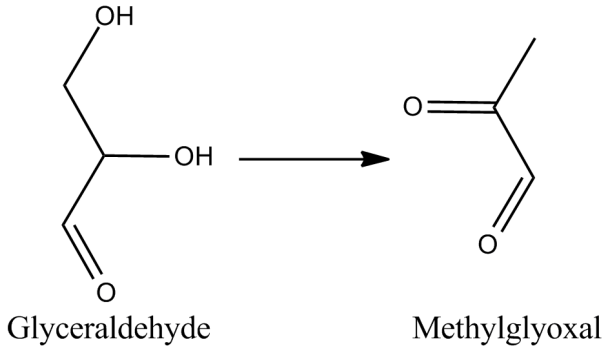

Figure 8. Conversion of glyceraldehyde to methylglyoxal.

Onda *et al*. [56] achieved a conversion rate of more than 20 % when using xylose as a feedstock with a carbon-supported platinum catalyst in alkali solution. In a recent report by Ma *et al*. [57], it was shown that using model compounds, different carbohydrates tend to convert into lactic acid at different levels. Fructose was shown to be more effectively converted to lactic acid than glucose and finally than xylose. The work also showed a correlation between the amount of catalyst (varying from 1-3 % wt.) of NaOH, KOH and $Ca(OH)_2$ respectively. Part of the work by Aspinall *et al*. [58] was aimed at the non-oxidative treatment of xylans from different substrates using sodium hydroxide as solvent. The reaction was performed at room temperature for 25 days and amongst the products that emerged from this reaction, a majority was acidic and lactic acid as well as formic acid were the two major products. Other work by Yang *et al*. [59] showed that higher temperature treatments of xylose (200 °C) in a $Ca(OH)_2$ solution produced about 57 % (mol.) of lactic acid with 2,4-dihydroxybutanoic acid in second with 10 % (mol.). The same conversion patterns were observed by Raharja *et al*. [60] with production rates for lactic acid above 50 %.

3.2. The biological pathway

Amongst the different options for the conversion of xylose reported in the previous chapter, production of lactic acid via the microbial route is a vastly studied field [61-63] since currently, all of the production of lactic acid at an industrial scale in the world is biologically based. Traditionally, the concept evolves around fermenting carbohydrate-based syrup by homolactic organisms, mostly lactic acid bacteria (LAB). The most common carbohydrate-based substrates used to this purpose may be molasses, corn syrup, whey, sugarcane or even beet bagasse. Highly efficient LAB includes *Lactobacillus delbrueckii*, *L.*

amylophilus, *L. bulgaricus* and *L. leichmanii*. Mutant *Aspergillus niger* has also been reported to be effective at an industrial scale [64]. LAB have the particularity to possess an homofermentative metabolism producing only lactic acid as extracellular waste product, instead of the heterofermentative pathway yielding by-products such as aldehydes, organic acids and ketones. The catabolic pathway yielding lactic acid is essentially the same across all organisms; the pyruvate intermediate is converted to lactic acid by a lactate dehydrogenase (LDH). Thus for hexose sugars, the theoretical yield is 2 moles of lactate per mole of sugar (or 1g sugar for 1g lactate). This enzymatic catalysis has the advantage over its chemical counterpart to be stereospecific: both L-lactate-dehydrogenase (L-LDH) and D-lactate-dehydrogenase (D-LDH) exist, generating either L-lactate or D-lactate respectively [65]. Both are NAD-dependant (nicotinamide adenine dinucleotide) and may be found alone or together in wild lactate-producing microbial strains. Since optical purity of lactate is a major requirement for the lactate industry, research focuses on stereospecificity as much as yields and productivity [61,66-70].

An efficient lactate producer has to display specific attributes, mainly the adaptability to low-cost substrates, high selectivity of desired enantiomer (L, D or both), high optimal temperature for decreased contamination risks, low pH tolerance and high performances (yield and productivity). LAB display appreciable performances, but lack a low pH tolerance, which implies uses of a pH control apparatus during the fermentation process. LAB optimal pH is near neutral, but the pKa of lactic acid being 3.8, an alkali agent, usually $Ca(OH)_2$, must be used thus generating calcium lactate. After typical batch fermentation, the medium is acidified with H_2SO_4 therefore regenerating and purifying the lactic acid [64]. Another drawback of LAB is their requirement for a complex growth medium, since they are auxotroph for certain amino acids and vitamins [71]. In order to overcome this problem, many fungi were also investigated for lactate production. Strains of *Rhizopus*, *Mucor* and *Monilla sp.* have shown potential whilst other fungi even displayed amylolytic activity, which could lead to a direct starch-to-lactate conversion [72-74].

Most researches still focuses on hexose conversion, and research group have optimized strains and process strategies in order to obtain high lactate titers, yields and productivities. Ding and Tan [75] developed a glucose fed-batch strategy using *L. casei* and generating up to 210 g/L of lactic acid with a 97 % yield. Chang *et al.* [76] proposed a continuous high cell density reactor strategy yielding a titer of 212.9 g/L and productivity of 10.6 g/L/h with *Lb. rhamnosus*. Dumbrepatil *et al.* [77] created a *Lb. delbrueckii* mutant by ultraviolet (UV) mutagenesis producing 166 g/L with productivity of 4.15 g/L/h in batch fermentation. Genetically engineered non-LAB biocatalysts yet have to match the performances of highly efficient wild LAB. In fact, *C. glutamicum*, *S. cerevisiae* and *E. coli* recombinant have been developed, but with limited success [61].

The search for lignocellulose-to-lactate biocatalysts have led to the discovery of many strains of pentose-utilizing LAB. *Lb. pentosus ATCC8041* [78, 79], *Lb. bifermentans DSM20003* [80], *Lb. brevis* [81], *Lb. Plantarum* [82], *Leuconostoc lactis* [83, 84], and *E. mundtii QU 25* [85, 86]. Lactic acid produced from xylose per say has been investigated by few [84,85, 87, 88], but with mitigated results, mainly due to the fact that the pentose-utilizing

LAB do not perform as well in pentoses as in hexoses-rich metabolism. This phenomenon is most likely due to the fact that pentoses are metabolized in the PK pathway (phosphoketolase), thus for a given strain, even if hexoses are fermented through an homofermentative route, pentose will yield heterofermentative products (i.e. acetic and lactic acid) [78, 89]. Nevertheless, Tanaka *et al.*[84] have shown that in addition to the PK, *L. lactis* could metabolize xylulose-5-phosphate (X5P), an intermediate pentose catabolite, through the pentose phosphate pathway (PPP). The theoretical yield through the PPP is 5 moles of lactate for 2 moles of pentoses, but through the PK it decreases to 1:1 [61], thus, the conversion advantage of the PPP is obvious. Okano *et al.* [87,89] demonstrated this approach by creating a pentoses-utilizing *Lb. plantarium* recombinant in which the native L-lactate dehydrogenase (L-LDH) gene was disrupted, leaving only the homologous D-lactate dehydrogenase (D-LDH) active. However, this strain produced both acetic and D-lactic acid; hence the PK gene (*xpk1*) was substituted by a heterologous transketolase (*tkt*) from *L. lactis*, thereby shifting heterolactic fermentation to a homolactic one.

Modification of yeast strains in order to achieve xylose-to-lactate conversion has also been investigated, as an example Ilmen *et al.* [90] expressed the L-LDH gene from *L. helveticus* in *P. stipitis* and was able to reach a titer of 58 g/L of lactate with a yield of 58 %. These results were obtained despite the fact that no effort had been made to silence the native PDC/ADH (pyruvate decarboxylase/alcohol dehydrogenase) ethylic pathway, consequently 4.5 g/L of ethanol was simultaneously produced as the endogenous PDC rivalled against the recombinant L-LDH for pyruvate. Tamakawa *et al.* [88] went further by transforming *C. utilis*, disrupting the native *pdc1* gene, and expressing heterologous LDH, XR (xylose reductase), XDH (xylitol dehydrogenase) and XK (xylulokinase) enzymes. Furthermore, to prevent the redox imbalance, they increased the XR's NADH (reduced nicotinamide adenine dinucleotide) affinity by site-directed mutagenesis. In batch culture this recombinant was able to yield titers up to 93.9 g/L of lactate at a yield of 91 %. Table 3 shows the most recent and most efficient strains developed for lactic acid production, both from hexoses and pentoses.

Strain	Gen Eng Str	Medium	Process	LA (g/L)	Tf (h)	Yield (g/g)	Prd (g/L/h)	Ref
E. mundtii QU 25	-	Cellobiose	Batch	119	106	0.83	1.12	[86]
	-	Xylose	Batch	86.7		0.84	0.9	[85]
	-	Glucose/ cellobiose	Batch	35.1	15	0.91	2.99	[86]
Lactobacillus sp. RKY2	-	Wood hydrolysates*	Continuous w/cell recycling	27	-	0.9	6.7	[91]

Strain	Gen Eng Str	Medium	Process	LA (g/L)	Tf (h)	Yield (g/g)	Prd (g/L/h)	Ref
Lb. bifermentas DSM 20003	-	Wheat bran hydrolysates	Batch	62.8	60	0.83	1.17	[80]
Lb. casei NCIMB 3254	-	Cassava bagasse	Batch SSF**	83.8	60	0.96	1.4	[92]
Lb. delbrueckii Uc-3	UV mutagenesis	Cellobiose	Batch	90	40	0.9	2.25	[93]
		Molasse	Batch	166	40	0.95	4.15	[77]
Lb. lactis RM 2-24	UV mutagenesis	Cellobiose	Batch	80	48	0.8	1.66	[94]
		Cellulose	Batch SSF	73	48	0.73	1.52	
Lb. plantarum ΔldhL1-xpk1::tkt	Disruption of endogenous LDH gene. Replacment of endogenous PK (*xpk1*) gene with heterologous *tkt* to redirect the PK pathway to the PPP.	Arabinose	Batch	38.6	28	0.82	1.37	[89]
Lb. plantarum ΔldhL1-xpk1::tkt-Δxpk2	Idem as above. Disruption of 2nd PK gene (*xpk2*) to terminate acetate production.	Xylose	Batch	41.2	60	0.89	0.67	[87]
Lb. rhamnosus ATCC 7469	-	Paper Sludge	Batch SSF	73	168	0.97	0.45	[95]
Lb. rhamnosus ATCC 9595 (CECT288)	-	Apple pomace	Batch	32.5	6	0.88	5.41	[96]
L. lactis IO-1	-	Xylose	Batch	33.3	-	0.68	-	[84]
S. cerevisiae recombinant	Replacement of native *pdc1* and *pdc5* by heterologous bovine L-LDH gene.	Glucose	Batch	82.3	192	0.83	0.43	[97]

Strain	Gen Eng Str	Medium	Process	LA (g/L)	Tf (h)	Yield (g/g)	Prd (g/L/h)	Ref
S. cerevisiae recombinant	Disruption of *pcd1* and *adh1* genes. Expression of bovine L-LDH.	Glucose	Batch	71.8	65	0.74	1.1	[98]
K. lactis	Disruption of PDC and PDH genes. Expression of bovine L-LDH gene.	Glucose	Semi-Batch	60	500	0.85	0.12	[99]
C. utilis	Disruption of endogenous PDC gene.Expression of heterologous LDH, XR, XDH and XK. XR gene site-specific mutation for preferential NADH cofactor utilization	Xylose	Batch	66.7	78	0.79	1.62	[88]
			Batch	93.9	78	0.91	2.18	
P. stipitis	Expression of LDH from *L. helveticus.*	Xylose	Batch	58	147	0.58	0.39	[90]

** No xylose consumption occurred*

***SSF = simultaneous saccharification and fermentation*

Table 3. Lactic acid concentration (LA), time of fermentation (Tf), yield and production rate for the most common microorganisms used for the biological conversion of xylose to lactic acid

Lactic acid seems to be, on the biological as well as on the chemical point of view the best possible compound that could be derived from a based-catalysed reaction of xylose. Racemic mixtures of lactic acid (most probably derived from chemical synthesis) can be evaluated to 1150 USD/tonne [100] whilst the pure isomer was reported to have a price market around 1750 USD/tonne [101]. As in many cases, the price will vary proportionally with purity of the compound. Utilisation of lactic acid on the market is mostly related to polymers, food, pharmaceutical and detergents. The annual world demand for the compound should reach a little more than 367 Ktonnes/year by 2017 [102].

4. Conversion of xylose under reducing conditions

4.1. The chemical pathway

Xylose, as all the other carbohydrates that can be isolated from lignocellulosic biomass, has a carbonyl function that is susceptible to transformations, including reduction. One of the most common compounds that can be derived from xylose is xylitol, a pentahydroxy chiral compound as depicted in Figure 9.

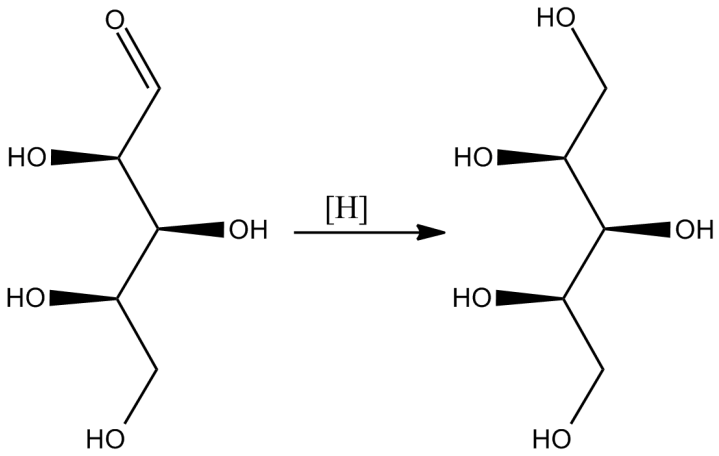

Figure 9. Simplified conversion of D-xylose to D-xylitol.

Amongst the most reported catalysts in the literature are nickel and Raney nickel. According to Wisniak *et al*. [103] they are good catalysts for the production of xylitol from xylose with total conversion at 125 °C and 515 psi. In the same year, the authors published the use of ruthenium, rhodium and palladium for the reduction of xylose [104] concluding that the efficiency of those metals was declining in the order Ru>Rh>Pd at temperatures around 100-125 °C under pressure. Mikkola *et al*. [105, 106] also used nickel as a catalyst by ultrasonic process that generated close to 50 % conversion of xylose to xylitol. From this process was reported that an important problem was the deactivation of the catalyst. Utilisation of nickel also led to the publication of two patents, one in 2003 [107] and another in 2007 [108]. In the case of the first, the concept relied on the isomerization of D-xylose to L-xylose prior to catalytic reduction under a nickel catalyst.

Ruthenium as well as ruthenium-based compounds has also been reported as catalysts for the reduction of xylose to xylitol. Ruthenium has been operated at temperatures between 90 °C and 110 °C under pressure using ruthenium supported either on silica [109] or on carbon [110]. Conversion rates for the latter have been reported to reach 35 % to xylitol for the latter with coproduction of glycerol and ethylene glycol. Ruthenium chloride ($RuCl_3$) has also been reported as a catalyst for the reduction of xylose to xylitol [111, 112].

Treatment of carbohydrates at a higher severity leads to the hydrogenolysis, implying not only the carbonyl compounds being reduce to alcohol but a breakage of the carbon-carbon bonds in the original carbohydrate. Recent work [113] shows that temperature above 250 ˚C and pressure between 600-1000 psi, can lead to conversion of xylose to ethylene glycol, propylene glycol and glycerol, as depicted in Figure 10 below.

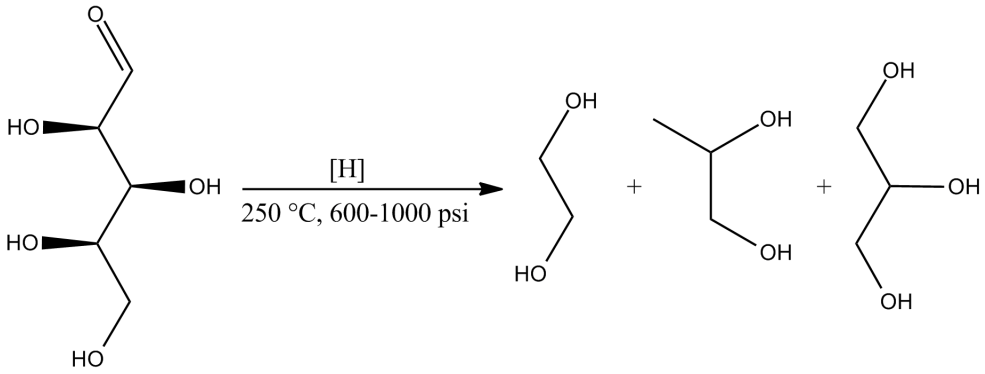

Figure 10. Simplified conversion of D-xylose to ethylene glycol, propylene glycol and glycerol as reported by Crabtree *et al*. [113].

Production of ethylene glycol and glycerol has also been reported by Guha *et al*. [110] as a side product of their xylitol production. Hydrogenolysis of xylitol is a logical suite for reduction of xylose and specific work has been reported using different catalytic systems and experimental setups. As an example, it was recently reported [114] that xylitol could be converted into a mixture of polyols and different other products as formic acid and lactic acid as well as xylitol, which, according to the previously mentioned work in this chapter, is given when xylose is submitted to a noble metal catalyst under hydrogen. In this specific case, the catalyst was platinum supported on carbon under a base-catalyzed matrix. Chopade *et al*. [115] also presented a patent reporting the conversion of carbohydrates (including xylose) into polyols using a ruthenium catalyst as did Dubeck and Knapp in 1984 [116].

In 2010 it was reported the use of nickel as a catalyst for hydrogenolysis of xylose [117] whilst Kasehagen [118] reported hydrogenolysis of carbohydrates under a nickel-iron-copper catalyst using a matrix of alkali salts with glycerol as the main product. The effects of nickel was studied by Wright [119] but this time using tungsten as a co-catalyst. Finally, there is a report about hydrogenolysis of carbohydrates under a rhenium catalyst [120].

4.2. The biological pathway

Only a few bacteria have been shown to naturally produce xylose as a metabolite. It has been showed [121] that a bacteria belonging to the genus *Gluconobacter* was able to produce xylitol from arabitol by way of a membrane-bound D-arabitol deshydrogenase (AraDH), followed by a soluble XDH. Rangaswamy *et al*. [122] isolated strains of *Serratia*, *Cellulomonas*

and *Corynebacterium* species that were able both to grow and produce xylitol with xylose as sole carbon source, although the reported yields were very low. In early work [123, 124], it was found that both *Corynebacterium* and *Enterobacter liquefaciens* strains were able to grow and produce xylitol from xylose although gluconate had to be present as cosubstrate. Nevertheless, studies using wild bacterial strains for xylitol production are scares [122, 125-127]. In most metabolic pathways, bacteria go through direct xylose to xylulose conversion via isomerisation, bypassing the xylitol intermediate. Subsequently, xylulose is phosphorylated in X5P and can be metabolized by most prokaryotes and eukaryotes via the PPP, or the PK pathway in the case of heterolactic bacteria (Figure 11) [128].

Although the fact that yeast and fungi are generally more efficient xylitol producers than bacteria is widely recognized [129], certain highly productive species such as *Candida* are actually known for their pathogenic nature [130]. Moreover, construction of recombinant yeasts by introduction of xylose reduction pathway in GRAS species such as *S. cerevisiae* have been accomplish, although these recombinant still have to match the productivities found using non-GMO organisms (genetically modified *organisms*) [131-134]. Bacterial species on the other hand present high yields, fast metabolism and many GRAS (generally recognized as safe) species with recombinant strains often display higher efficiencies than their non-altered counter-part [135].

It was found that the catabolic rate of xylose is usually enhanced by the presence of a co-substrate such as glucose [136, 137]. However, most organisms preferentially use glucose to any other sugars due to allosteric competition in sugar transport and/or repression of other carbon catabolites [138, 139]. Thus, a suitable biocatalyst would have to simultaneously metabolize both substrates. This functionality was achieved in *E. coli* [140]by replacing the putative cAMP-dependent receptor protein (CRP) with a cAMP-independent mutant, which also expressed a plasmid-based xylose transporter. Similarly, some authors [125] used this approach as well as inserting the heterologous XR gene and silencing the endogenous xylose isomerase (XI). Alternatively, heterologous XR and XDH may be introduced and the putative XK (*xylB* gene) silenced.

Other well suited candidates for such a bioconversion would be LAB, offering the advantage of an energy metabolism completely independent of their limited biosynthetic activity, thus their glycolysis pathways may be engineered without disturbing other key structural pathways [129]. By introduction of yeast XR gene, as well as a heterologous xylose transporter in *L. lactis,* they showed that bacterial productivity and yield might reach those of the best yeasts. Even if all xylose is not consumed when in high initial concentration, the non-pathogenic and anaerobic nature of *L. lactis* is a notable advantage.

Early work done on *Corynebacterium glutamicum* showed another alternative for the production of xylitol but the necessity of inserting gluconate as co-substrate for NADPH (nicotinamide adenine dinucleotide phosphate) regeneration rendered the application non economical [122,124]. Sasaki *et al.* [141] developed a *C. glutamicum* recombinant achieving simultaneous co-utilization of glucose/xylose. This was done by introducing the pentose transporter area in *C. glutamicum* chromosomal DNA (deoxyribonucleic acid). *C. glutamicum* is a noticeable candidate for its non-pathogenic and gram-positive nature, as well as its ex-

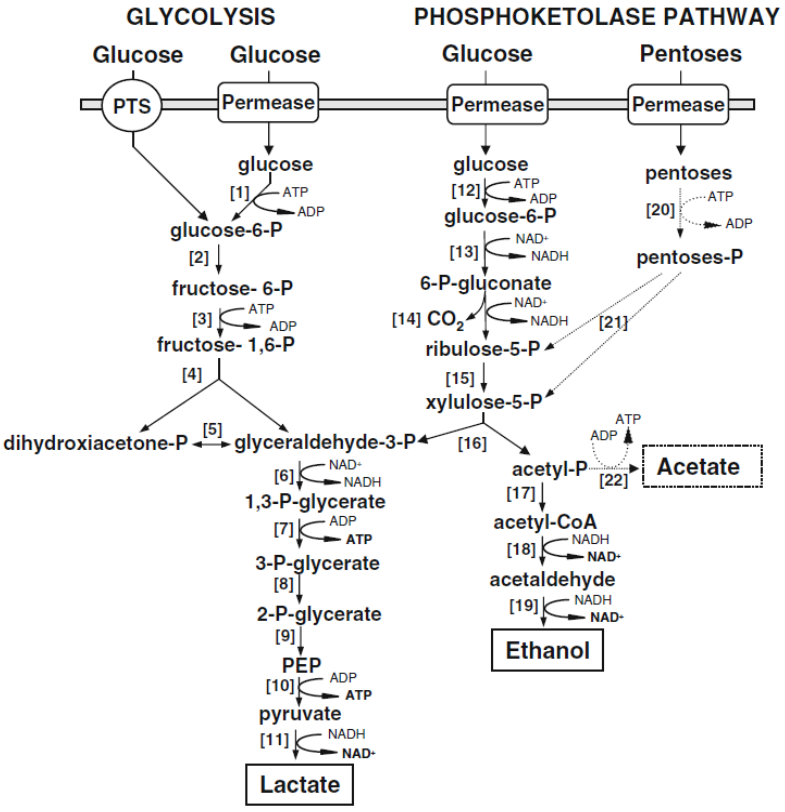

Figure 11. Glycolysis and phosphoketolase (pentose phosphate) pathways in lactic acid bacteria (1) glucokinase, (2) phosphoglucose isomerase, (3) phosphofructokinase, (4) fructose 1,6-bisP aldolase, (5) triose-phosphate isomerase, (6) glyceraldehyde-3P dehydrogenase, (7) phosphoglycerate kinase, (8) phosphoglycerate mutase, (9) enolase, (10) pyruvate kinase, (11) lactate dehydrogenase, (12) hexokinase, (13) glucose-6P dehydrogenase, (14) 6-phosphogluconate dehydrogenase, (15) ribulose-5P 3-epimerase, (16) xylulose-5P phosphoketolase, (17) phosphotransacetylase, (18) acetaldehyde dehydrogenase, (19) alcohol dehydrogenase; (20) pentose kinase, (21) pentose phosphate epimerase or isomerase, (22) acetate kinase. *CoA* coenzyme A.

tensive use for amino and nucleic acid industrial synthesis [142, 143]. It was established [135] that xylitol productivity may be improved by disabling the xylitol import system (ptsF gene) and suggested that more work done on xylitol export system and redox balance may yield further improvements. Nevertheless, their CtXR7 *C. glutamicum* recombinant attained a productivity of 7.9 g/L/h and final xylitol concentration of 166 g/L after 21 h (see Table 4). This was achieved by (to date this is considered the best xylitol bacterial producer):

- introduction homologous pentose transporter (*araE*);
- disruption of the native lactate deshydrogenase (*ldhA*);
- expression of single-site mutant XR from *C. tenuis*;

- disruption of XK native gene (*xylB*);
- disruption of phosphoenolpyruvate-dependent fructose phosphotransferase (*ptsF* gene; PTS^{fru}).

Strain	Genetic Engineering Strategy	Yield g/g	Xylose g/L	Xylitol (g/L)	Tf (h)	Prd (g/l/h)	Process Strategy	Reference
Candida athensensis SB18	-	83%	250	207.8	175	1.15	Batch limited O_2	[144]
		87%	300	256.5	250	0.97	Fed Batch limited O_2	
		79%	200	151.71	156	0.97	Batch limited O_2	
C. tropicalis ASM III	-	93%	200	130	120	1.08	Batch limited O_2	[145]
Candida sp. 559-9	-	99%	200	173	121	1.44	Batch limited O_2	[146]
C. tropicalis KCTC 10457	-	87%	200	172	48	3.66	Batch limited O_2	[147]
C. tropicalis KFCC 10960	-	93%	270	251	55	4.56	Fed Batch	[148]
C. tropicalis KCTC 10457	-	90%	260	234	48	4.88	Fed Batch	[147]
C. guilliermondii	-	73%	250	-	-	-	Fed Batch limited O_2	[149]
C. tropicalis	-	82%	750	189	58	4.94	Fed Batch/ Cell recylcing/ Glucose cosubstrate/ limited O_2	[150]
C. tropicalis	-	69%	100	-	-	5.7	Cell recycling/ limited O_2	[151]
C. tropicalis	-	85%	214	182	15	12	cell recycling/ limited O_2	[147]
S. cerevisiae	Expression heterologous XR gene from *P. stipitis*.	95%	190	-	-	0.4	Fed batch/ Glucose cosubstrate	[152]
Corynebacterium glutamicum CtXR7	Expression of *araE* pentose transporter gene. Disruption of *ldhA*. Single site mutation of heterologous XR gene. Disruption of *xylB*& PTS^{fru} genes.	-	120	166	21	7.9	Fed batch/ Glucose cosubstrate/ 40g/L dry cell	[135]
D. hansenii NRRL Y-7426	-	38%	45	19.7	72	0.274	Batch/ Detoxified grape marc hydrolysates	[153]
S. cerevisiae	Overexpression ALD6 & ACS1 genes.Expression of *P. stipitis* XR gene.	~100%	20	91.3	60	1.76	Fed batch/ Glucose cosubstrate	[154]
Lactobacillus brevis NZ9800	Expression of *P. stipitis* XR gene.Expression of *Lb. brevisxylT* symporteur.	~100%	160	75	41	2.72	Fed batch/ Glucose cosubstrate	[129]

Strain	Genetic Engineering Strategy	Yield g/g	Xylose g/L	Xylitol (g/L)	Tf (h)	Prd (g/l/h)	Process Strategy	Reference
C. tropicalis	-	83%	80	96.5	120	1.01	Fed batch/ Corn Cob hydrolysates/limited O_2	[155]
C. tropicalisSS2	Xylitol-assimilation deficient strain by chemical mutagenesis.	93%	100	220	70	3.3	Fed batch/ aerobic	[156]
C. trolpicalis JH030	-	71%	45	31.1	80	0.44	Batch/ Rice straw hydrolysates	[157]

Table 4. Overview of the different strains allowing conversion of xylose to xylitol including yields, fermentation time (Tf), production (Prd) and the process strategy.

As previously discussed for ethanol, the redox imbalance that often occurs from XR/XDH preferential use of NADPH/NAD+ cofactors is a key factor for xylitol accumulation in the cell. In most yeast studied, it has been shown that XR has a marked preference for NADPH, while XDH has a quasi-unique specificity for NAD+ [126]. The main exception being *P. stipitis* who shows a nearly by-specificity for NAD(P)(H) for its XR and *P. tannophilus* whose XDH shows a higher activity with NADP+ than NAD+ [158] proposed a theoretical maximum xylitol yield in yeasts of 0.905 mol of xylitol per mol of xylose when NADH was efficiently used as cofactor by the XR or under aerobic condition where the NADH can be oxidized back to NAD+ in the respiratory chain. Otherwise, under anaerobic conditions, the theoretical yield drops to 0.875. These yields follow the equations (1) and (2) below respectively:

$$126\ \text{xylose} + 3\ O_2 + 6\ \text{ADP} + 6\ P_i + 48\ H_2O \rightarrow 114\ \text{xylitol} + 6\ \text{ATP} + 60\ CO_2 \quad (1)$$

$$48\ \text{xylose} + 15\ H_2O \rightarrow 42\ \text{Xylitol} + 2\ \text{ethanol} + 24\ CO_2 \quad (2)$$

Owing the better yield both in xylitol and ATP (adenosine triphosphate) under oxygen-limited xylitol production, aeration is a crucial parameter. As a general trend, xylitol production increases when oxygen is allowed in the medium under a certain threshold concentration [159]. This preference is yeast specific since for *P. stipitis* it is reported that the absence of dissolved oxygen is needed for optimal xylitol production; while *P. tannophilus* reaches maximum yields under anoxic conditions [160, 161].

Many strains of *S. cerevisiae* have been transformed for xylose utilization in the early 90's. As for xylose-to-xylitol, Hallborn *et al.* [152] reported a highly efficient conversion of xylose to xylitol (95 % of theoretical). It has been suggested that the incapacity of *S. cerevisiae* to rapidly replenish its NADPH pool from its PPP during xylose metabolism is what causes the metabolic bottleneck [162, 163]. This is mainly due to the fact that xylose is a

non-preferred carbon substrate for *S. cerevisiae* and do not provide sufficient energy for growth and metabolism [164].

C. tropicalis is a candidate of choice for xylitol production among the few native strains reported as the best xylitol producers to date (see Table 4) and this research for native strains and genetically engineered recombinant is still under way today [155-157]. As in *S. cerevisiae*, the PPP is the major NADPH biosynthesis pathway and efforts have been made to increase its flux. Ahmad *et al.* [165] recently successfully increased the metabolic flux toward PPP for NADPH regeneration, thereby enhancing xylitol production of the original strain by 21 %. This was done by disrupting XDH putative gene, and over-expressing homologous glucose-6-phosphate dehydrogenase (G6PDH) and 6-phosphogluconate dehydrogenase (6-PGDH). Table 4 summarize the best xylitol producing strains found in the literature up to date.

Reduction of xylose either at low or at high severity thus producing either xylitol or polyols (including glycerol) is a process driven by the price of hydrogen. On the other hand, the market for small polyols as ethylene or propylene glycol may generate more opportunity than the xylitol market. Xylitol market value is between 3650 and 4200 USD/tonne [166] whilst ethylene glycol is reported at a market price of 980-1500 USD/tonne [167] and propylene glycol at 1500-1700 USD/tonne [168]. The market for each of the previously mentionned compound is around 100 Ktonnes/y for xylitol [169], 19 Mtonnes/y for ethylene glycol [170] and 1.4 Mtonnes/y for propylene glycol. Although the market for smaller polyols may seem to be larger, as an example conversion of xylose to ethylene glycol and propylene glycol would require 3 times as much hydrogen if compared to xylitol. Since the price for hydrogen can be estimated roughly at 4.5-5 USD/Kg, the very concept of polyols production relies on the efficiency of the hydrogenolysis process therefore explaining why many of the reported litterature in this chapter are patents.

5. Conversion of xylose under oxidizing conditions

5.1. The chemical pathway

Oxidation of xylose has been numerously reported in the literature although focus interest, both on the biological as well as chemical point of view has been focused toward a simple oxidation of xylose to xylonic acid (see Figure 12).

Oxidation of xylose has been reported for a variety of different metallic catalyst including gold for high conversion rates [171]. Using a process performed a little higher than room temperature in a basic pH for 1 hour, they were able to reach a 78 % conversion of xylose to xylonic acid. Using comparable catalyst, Pruesse *et al*. [172] were able to reach 99 % selectivity with a conversion rate of 21 mmol/min/g (Au) in a continuous reactor. Nevertheless, contrarily to Bonrath, Pruesse and co-worker used a mixture of gold and palladium to perform this oxidation and temperature slightly higher (60 ˚C as compared to 40 ˚C).

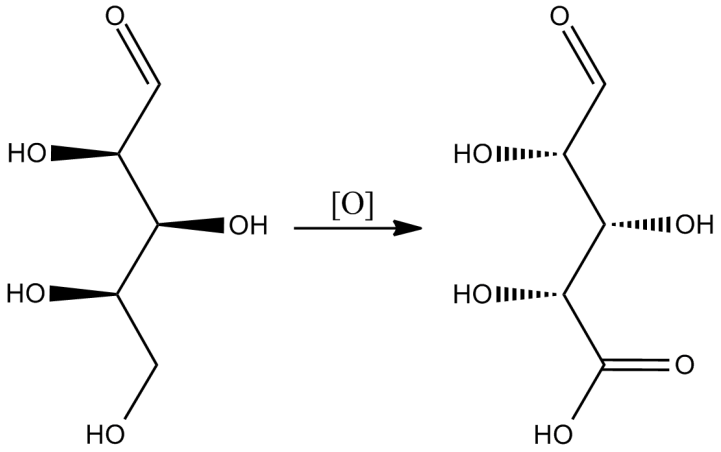

Figure 12. Simplified conversion of xylose to xylonic acid

Copper has also been indirectly investigated for the conversion of xylose to xylonic acid in that sense that Van der Weijden *et al*. [173] used C5 sugars (including xylose) for the reduction of copper sulfate in wastewater with very promising results. Although emphasis was not put on the carbohydrate itself, results showed that the reduction of copper from (II) to elemental was possible yet economical at larger scale. Xylonic acid was also observed as by-product of xylose oxidation using chlorine, as a side reaction of lignin oxidation. In this work [174], the concentration of xylonic acid increased by a factor of 40 after the chlorination process. Interesting enough, the xylitol concentration also increased, which might lead to the conclusion that oxidation, was probably not the sole factor here and that side reactions as the Cannizarro reaction between two xylose molecules could have been occurring. Jokic *et al*. [175] showed that it was possible up to an efficiency of 80 % to convert xylose simultaneously to xylonic acid and xylitol using electrotechnologies. Such process could be to a certain extent compared to the Cannizarro reaction where the original aldehyde is acting as redox reagent.

Further oxidation of xylose leads to a trihydroxydiacid, more specifically xylaric acid as depicted in Figure 13 below.

Conversion of C5 sugars and to a smaller extent of xylose into aldaric acids has been described in literature in a few reports. Kiely *et al*. [176] reported that a conversion up to 83 % xylose into 2,3,4-trihydroxyglutaric acid was achievable in a reaction mixture composed of nitric acid and $NaNO_2$. The side product of this reaction was reported to be disodium tetrahydroxysuccinate. Conversion of xylose to xylaric adic was also reported [177] using oxygen under a platinum catalyst all of this in an alkali promoted medium. Comparable conversion process [178] was obtained without any alkali, though still performed the reaction in water at 90 °C under 75 psi of oxygen. The conversion for this process was 29 %. Fleche *et al*. [179] reported a maximum conversion of 58% once again using platinum supported on alumina.

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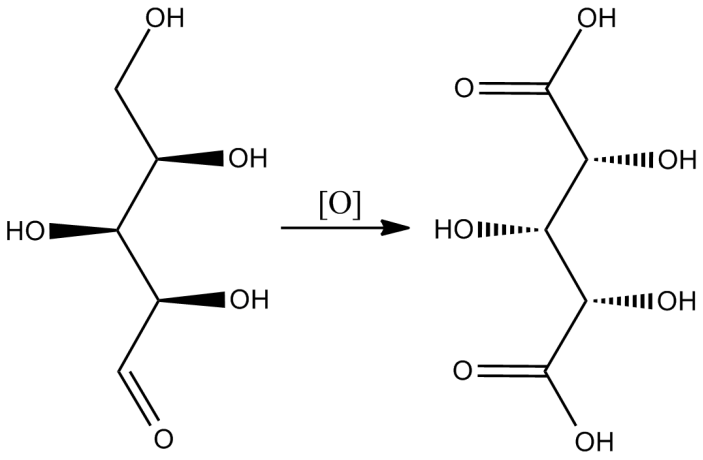

Figure 13. Simplified scheme for the conversion of xylose xylaric acid

Severer oxidizing conditions leads to a breakage of the carbon-carbon bonds in the carbohydrate molecule leading to the production, mostly, of small organic acids as formic and acetic acid on glucose [180]. A simplified scheme of such a reaction is presented in Figure 14 below:

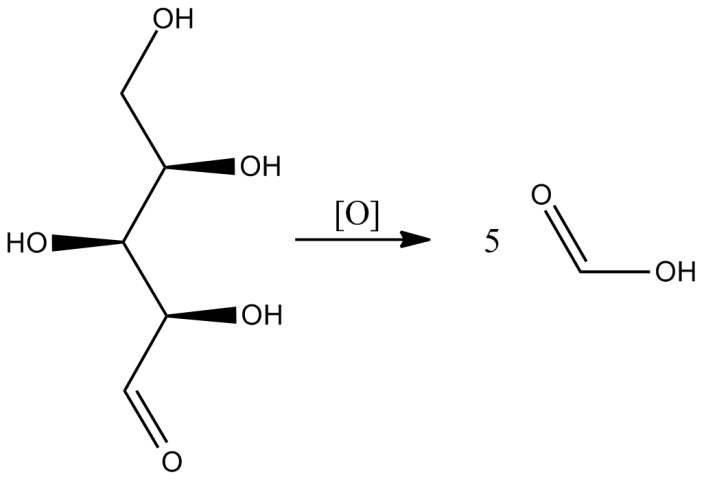

Figure 14. Simplified scheme for the conversion of xylose to formic acid under more severe oxidizing conditions.

An example of sever oxidation of xylose in a mixture of hydrogen peroxide and ammonium hydroxide have been recently reported [181] with a conversion of 96 % at room temperature for 1 h. Similar conversion of xylose was reported [182] for a process using oxygen and a molybde-

num and vanadium catalyst. The reaction was done for 26 h at 353 K and 30 bar for a conversion of up to 54 % into formic acid with carbon dioxide as by-product.

5.2. The biological pathway

Xylonic acid synthesis from xylose has been reported for *Acetobacter* sp. [183], *Enterobacter cloacea* [184], *Erwinia* sp. [185, 186], *Fusarium lini* [187], *Micrococcus* sp. [188], *Penicillium corylophilum*, *Pichiaquer cuum* [185], *Pseudomonas* sp. [189, 190], *Pullularia pullulans* [191], *Gluconobacter* and *Caulobacter* [192, 193].

In metabolic pathways, xylose is converted to xylonate via 2 key enzymes. First, a xylose dehydrogenase (XD) oxidizes xylose to D-xylono-1,4-lactone (xylonolactone) using either NAD + or NADP+ as cofactor. This reaction is followed by the hydrolysis of xylonolactone to xylonate either spontaneously or by an enzyme with lactonase activity [194, 195]. It is hypothesized that *Pseudomonas* and *Gluconobacter sp.* both carry a membrane-bound pyrroloquinoline quinine (PQQ)-dependent XD and a cytoplasmic one [195, 196]. Stephens *et al.* [193] recently proposed a full xylose catabolic pathway for *C. crescentus*. Note that a similar pathway was proposed for arabinose yielding L-arabonate [197]. As shown in Figure 15, the proposed metabolic pathway for *C. crescentus* shows that xylonate is an intermediate in catabolic reactions that is quite different from the XI or XR/XDH previously discussed which were more intensively studied.

Researches on highly efficient microbial xylonic acid production are scarce compared to biofuels or xylitol. Even if the identification of xylonate producing species began as early as 1938 [187], the first attempt to isolate a possible industrial biocatalyst was done by Buchert *et al.* [185], who identified *P. fragi ATCC4973* as a potentially high efficiency xylonate producer (92 % of initial sugar converted to xylonic acid with initial xylose concentration of 100 g/L). In further work, *P. fragi* and *G. oxydans* showed yields of over 95 % but the low tolerance of those native strains to inhibitors tends to be problematic for industrial uses [192]. As discussed above, the metabolic pathways implied by xylonate have been investigated in the recent years [193,196]. The first recombinant microorganism engineered for the industrial production of xylonate was done by Toivari *et al.* [198]. By introducing the heterologous *Trichoderma reesei xyd1* gene (coding for the NADP+ dependant XD) in *S. cerevisiae*, they were able to obtain up to 3.8 g/L xylonate with 0.036 g/L/h productivity and 40 % yield. Nygard *et al.* [195] engineered *K. lactis* by introducing *T. reesei xyd1* and deleting the putative *xyl1* gene coding for the XR. Up to 19 g/L xylonate where produced when grown on a xylose (40 g/L) and galactose (10.5 g/L) medium. The native ability of fast xylose uptake was an advantage, but high intracellular xylonate concentration was observed, which may indicate difficulties with product export. Liu *et al.* [199] used similar approach engineering *E. coli* by disrupting the native xylose metabolic pathways of XI and XK (as shown in Figure 16). The native pathway of xylonate was also blocked by disrupting xylonic acid dehydratase genes. The XD from *C. crescentus* was introduced and 39.2 g/L of xylonate from 40 g/L of xylose in minimal medium was obtained at high productivity 1.09 g/L/h. From these results it is clear that research is at its genesis and significant efforts will be required for the creation of a highly productive and effective xylonate production biocatalyst.

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At this point it is rather hard to verify the potential or the economic value of oxidation products from xylose. Complete oxidation to formic acid could be the most suitable approach at this point since the market for xylonic and xylaric acid is not as well defined as for the simple methanoic acid with its actual market value between 750-950 USD/tonne [200] and an annual world demand suspected to reach 573 Ktonnes in 2012 [201]. Conversion of xylaric acid into glutaric acid (pentanedioic acid) would lead to a very interesting market as a plasticizer but dehydration or reduction of the three central hydroxyl groups may be a challenge that could be winning at lab scale although a multiple synthesis pathway would be very difficult to reach economic at an industrial level.

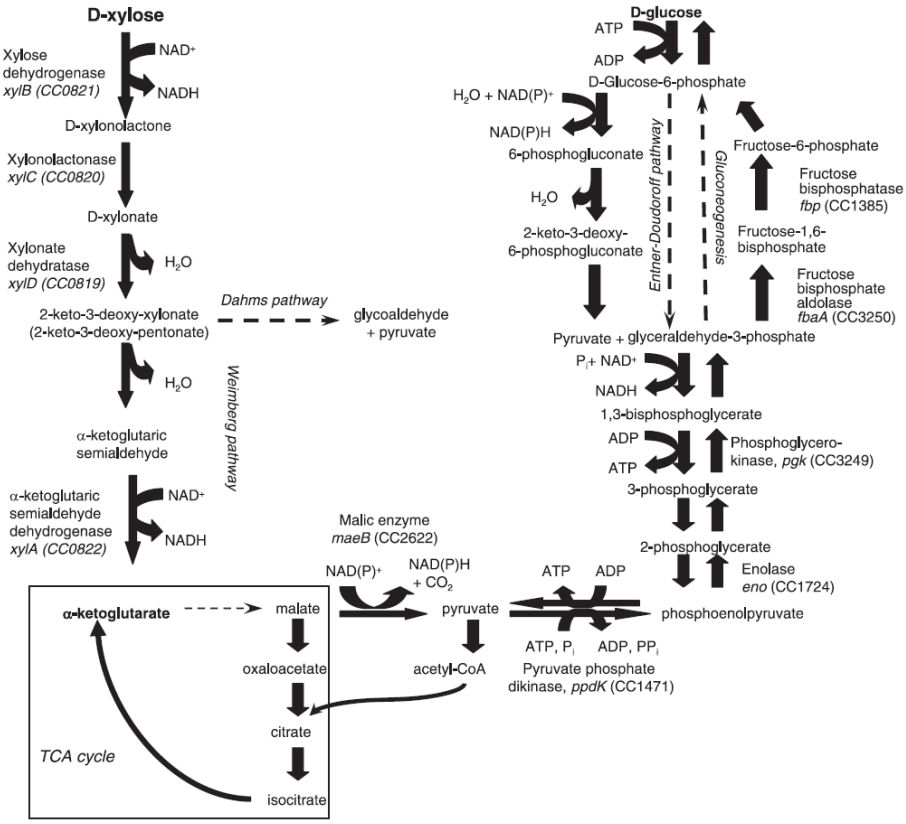

Figure 15. Proposed pathway ford-xylose metabolism in *C. crescentus* [193].

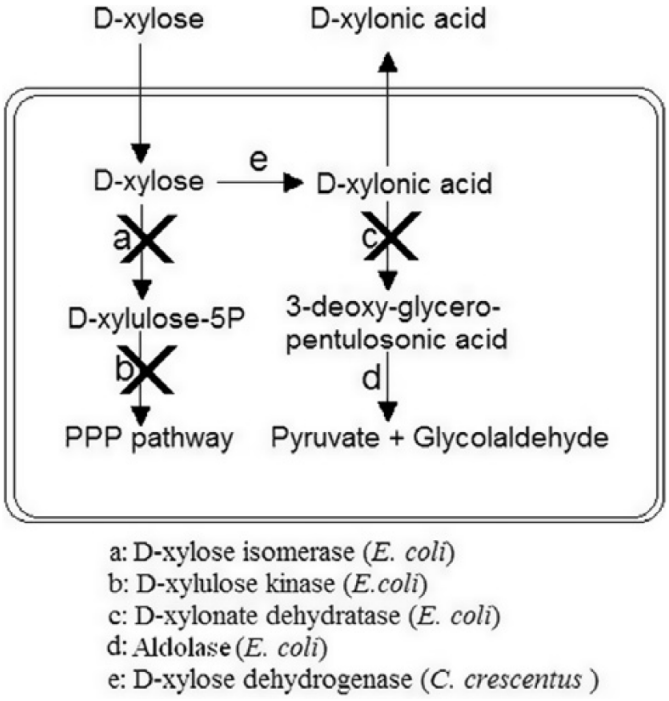

Figure 16. D-xylose and D-xylonic acid metabolic pathways in *E. coli*. The symbol X denotes that the gene is disrupted.

6. Conclusion

Second-generation ethanol or "cellulosic ethanol" relies on the utilisation of lignocellulosic biomass as a source of carbohydrates via the "bio" conversion route (keeping in mind that other pathway, as thermocatalytic pathways, may also lead to cellulosic ethanol). Production of ethanol thus requires isolation of cellulose from lignocellulosic matrix, then hydrolysis of cellulose to glucose prior to fermentation. Both of the previously mentioned steps represent challenges for industry, but the whole economic of the process is perhaps the most challenging part of cellulosic ethanol production. Cellulose is usually available in lignocellulosic biomass in the 45-60 % range which, assuming a perfect conversion implies production of 300-400 L/tonne of lignocellulosic biomass processed. At an actual price of 0.48 USD/L, each ton of biomass has a potential value of about 150-200 USD/tonne of biomass processed.

The conversion of lignocellulosic biomass is rather more complex and to a certain extent more expensive than starch-based feedstock as corn and therefore, one can assume that the

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conversion price is going to be higher than classical or first generation ethanol production. Keeping that fact in mind, the conversion of cellulose to glucose itself is a major technological challenge since it either requires enzymes, ionic liquids or strong acids that are rather expensive to buy or expensive to recycle and since it is of outmost importance for the production of the ethanol, technology is to a certain extent limited by this reality.

The remaining carbon content of lignocellulosic biomass is also an important factor to be considered. Since the maximum production of ethanol from the total feedstock could vary around 300-400 L per tonne, there is at this point a necessity to generate co-products from the biomass in order to make this whole process economic at the end thus coping for technological problem as conversion of cellulose to glucose. Lignin is one of the most abundant macromolecule on earth bested only by cellulose. The aromatic nature of lignin is a challenge for ethanol production but not for added value compounds as aromatic monomers that could displace actual monomers used in the polymer industry that are usually obtained from non-renewable materials.

Hemicelluloses are also an important part of the lignocellulosic biomass. Hemicelluloses, contrarily to cellulose that is characterized by an amorphous and a crystalline part, are highly ramified and easy to hydrolyse. Usually, a simple diluted alkali solution, acidic solution or even hot water can allow conversion of hemicellulose to simple sugars. The major problem with hemicellulose is the heterogeneous composition including but not limited to small acids and a variety of C6 and C5 sugars. Whilst the C6 sugars could be easily fermented to ethanol, pending reduction of the organic acids and other inhibitors, the C5 sugars require speciality yeasts for fermentation.

Other than the classical fermentative pathway, C5 sugars can as well be converted, biologically as well as chemically into a wide variety of added value products and "green" compounds. In this paper, we have identified 4 pathways for the conversion of C5 sugars but more specifically xylose, a common carbohydrate in biomass hemicelluloses.

Reaction of xylose under an acid catalyst is probably one of the most investigated fields in this domain. The target for this conversion being furfural, a well-known chemical as well as precursor for other compound as furan, Me-THF, THF and furfuryl alcohol, a reactant used in the polymer industry. The best approach for the conversion of xylose furfural, to the best of our knowledge, is chemical as no microorganism allowing conversion of C5 sugars to furfural has been identified so far. The conversion of xylose to furfural was reported to reach more than 95 % for both heterogeneous and homogeneous catalyst. On the other hand, the selectivity toward furfural is not always as efficient since the latter undergoes polymerisation in acidic medium, which often also leads to deactivation of the catalyst.

A basic catalyst leads to a conversion of C5 sugars to lactic acid although this pathway as not been deeply investigated in the literature. Lactic acid is a compound well in demand on the market but the limitations for the chemical transformation is the lack of stereospecificity of the products. Conversion of xylose under a base catalyst leads to the production of a racemic mixture of D- and L-lactic acid and thus reducing the market value of the product, particularly if the polymer industry is targeted. On the other hand, the biological conversion of

xylose to lactic acid is a well-known and extensively reported process for which the production was reported to reach 6.7 g/L/d for genetically modified organisms as, in this specific case, *Lactobacillus sp. RKY2*. According to the reports, the production of lactic acid would be more efficient by the biological approach since it can lead to a stereospecific and a higher market value.

Reduction of xylose can lead to many different products including xylitol for lower severity up to diols as ethylene glycol and propylene glycol at higher severity. It is ambiguous to determine at this point if either the chemical or the biological pathway is more efficient for the production of xylitol since reports on both pathways have shown promising results. The main problem with the xylitol market is that although it is increasing, it is fairly small and therefore it is harder to fit in a new production of xylitol. On the other hand, a more severe reduction of xylose, leading to diols, could be a very interesting opportunity for the production of ethylene glycol and propylene glycol, two very important products in the chemical industry. The downside of this approach would be the production of glycerol as a side-product.

Finally, oxidation of xylose is, at this point, the approach with the lower potential for a rapid commercialisation since the market for xylonic acid and xylaric acid is hard to size at present. The conversion process, both chemical and biological seems to have significant potential in terms of scalability but the end usage is not well defined at this point. The best option would be to produce glucaric acid from xylaric acid, which could be used as a plasticizer. On the other hand, such a process, overall rather complicated, would add a significant cost for a product that would land in the commodity range.

Acknowledgement

We would like to acknowledge Enerkem, Greenfield Ethanol, CRB Innovations and the Ministry of Natural Resources of Quebec for financial support of the Industrial Chair in Cellulosic Ethanol.

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