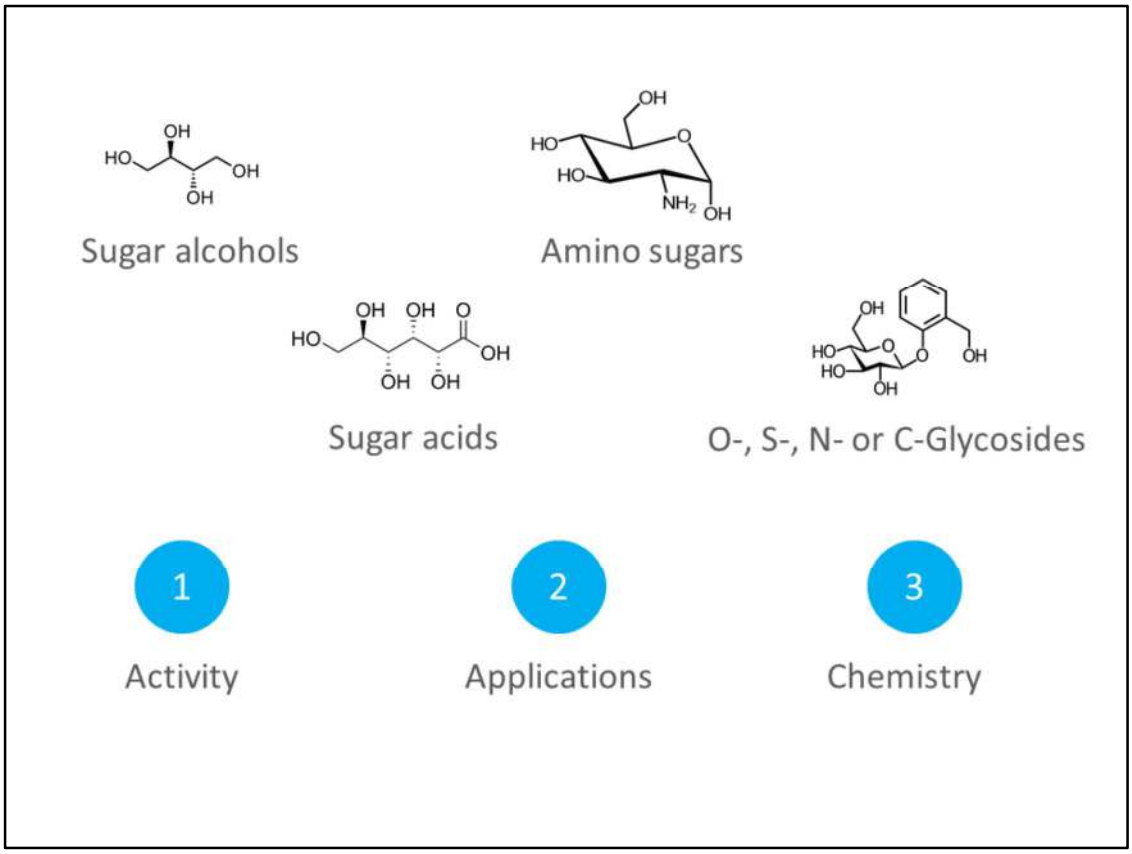

This presentation focuses on technical and material applications of sugar derivatives, food and pharmaceutical applications are excluded.

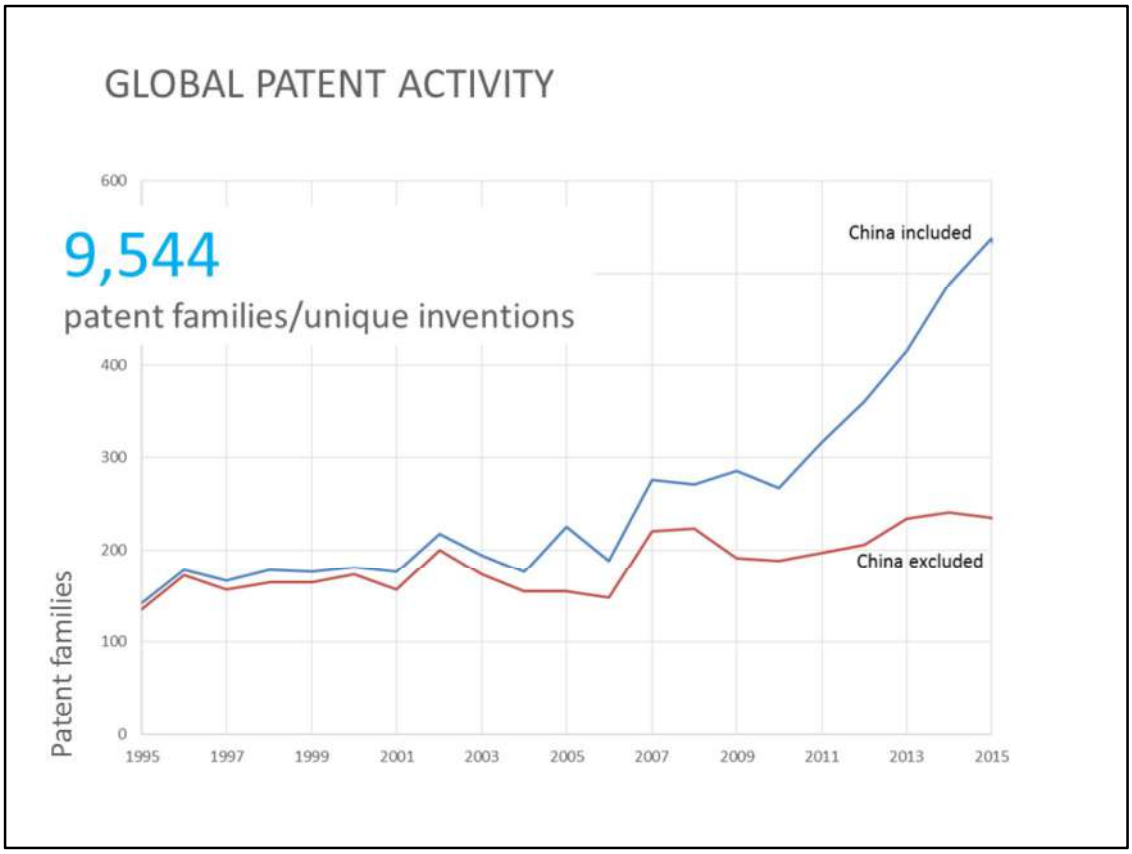
Sugar-based products
for
technical & material
applications?




Sugar derivatives can be categorized as following:

- Sugar-based alcohols (e.g. polyols, but also ethanol, propanediol),
- Sugar-based acids (e.g. lactic acid, levulinic acid),
- aminosugars (e.g. glycosamine),
- O-, S-, N- or C-glycosides (almost exclusively present in plants), which are composed of a glycon and an aglycon.

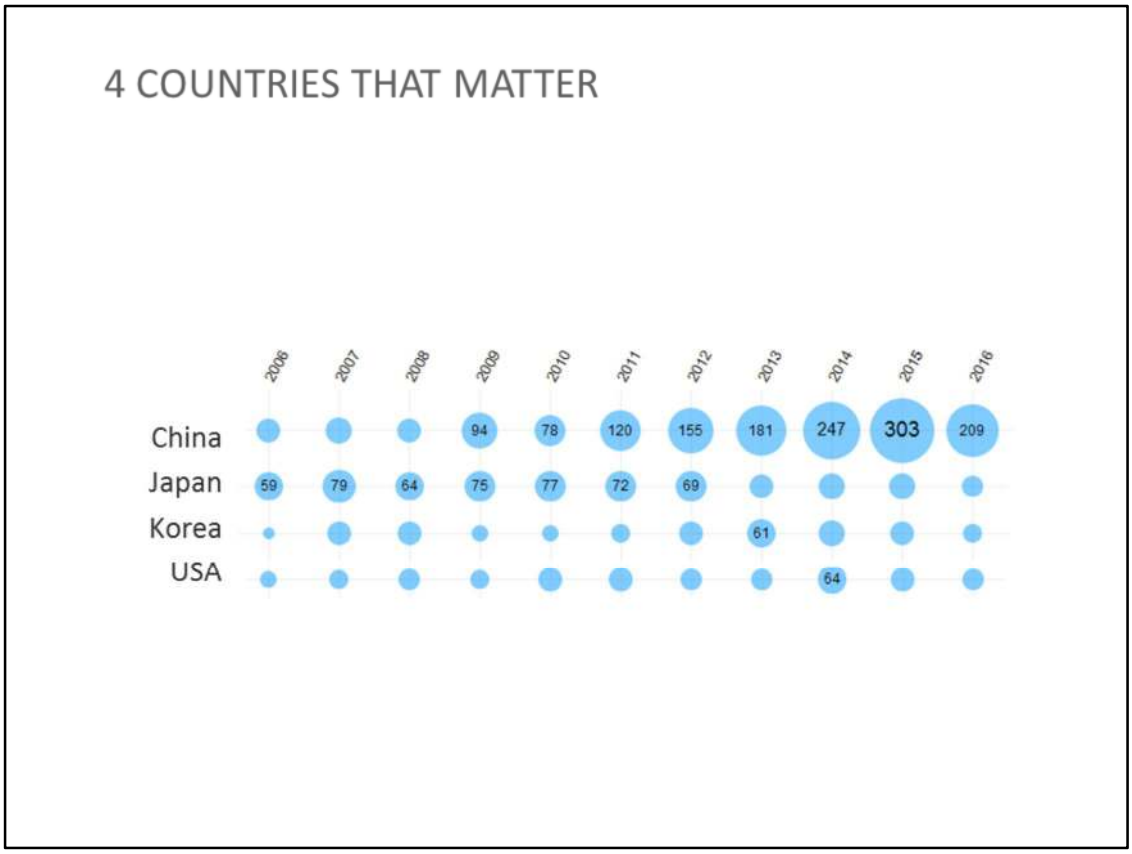

We will discuss global patent activity in sugar derivatives, the patent activity per country and the business expectations.




We have identified 19,425 patent families/unique inventions about sugar-based products, if we exclude medical and food domains (codes A21, A23 and A61) but keep cosmetic (code A61K8 and A61Q), it makes 9,544 patent families/unique inventions.

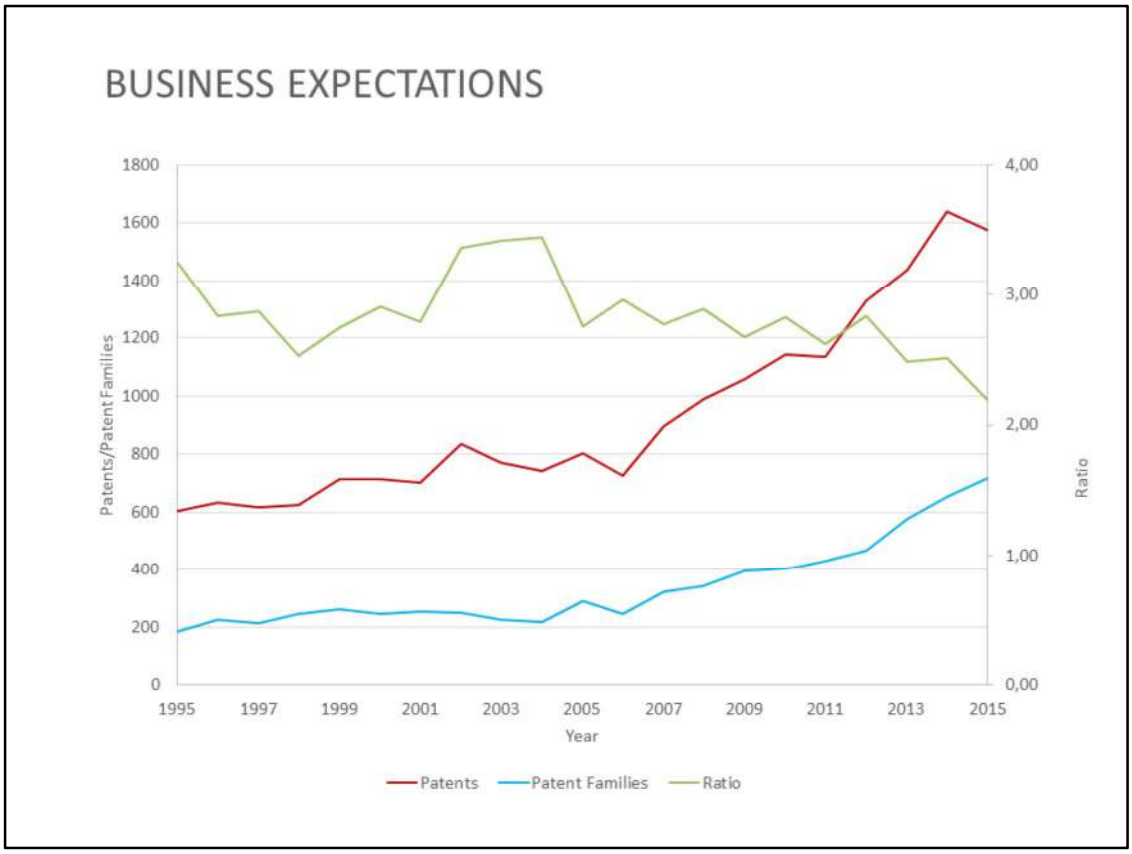
We clearly see a similar trend in global patent activity.

Patent activity in sugar-based products is increasing, but when China is excluded, global patent growth is rather marginal, but still significantly higher than the global patent activity china excluded. We can conclude that sugar-based products is more dynamic in IP than average IP.




China is the most important player in the field of sugar derivatives, followed by Japan, USA and Korea.

Important side note #patents/patent family (business expectation) is lower in China!

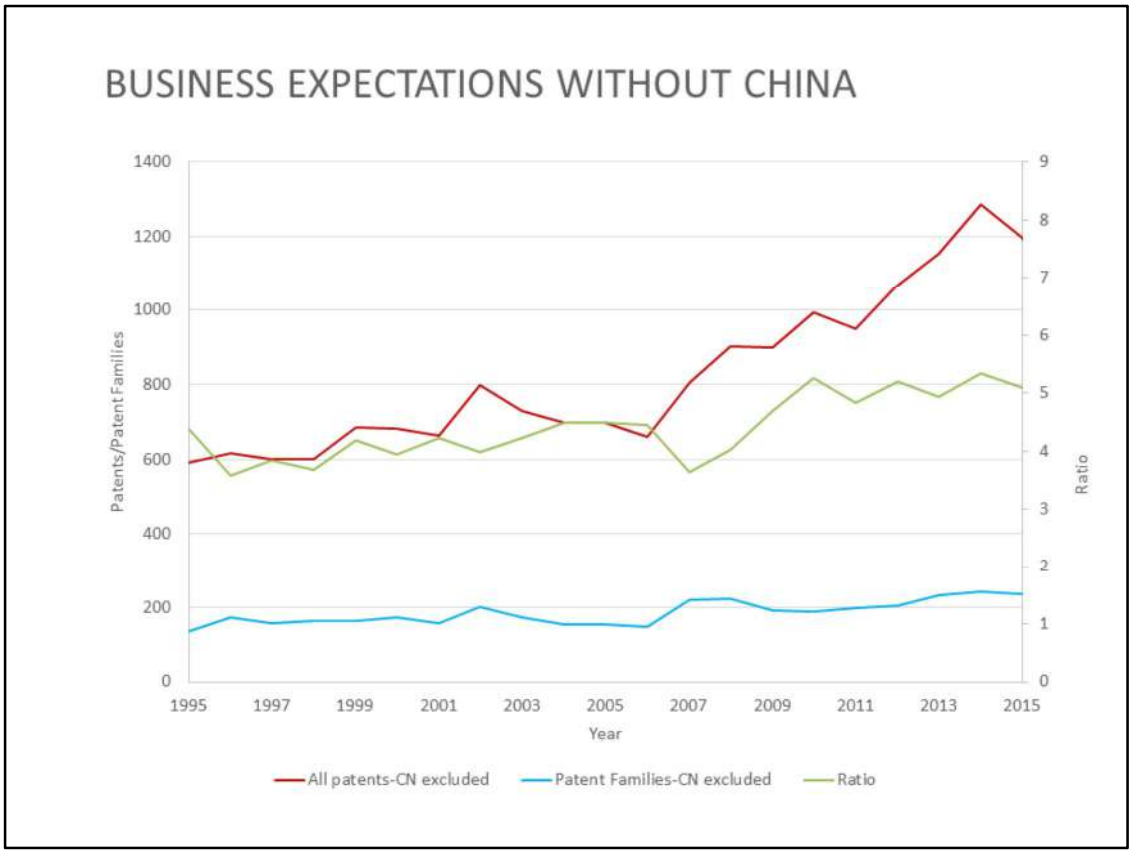



An important parameter to study the impact of a specific patent family is to check the number of patents per patent family, this parameter gives a glimpse of the business expectation.

Globally we see a decrease in business expectation, this indicates a reduction in number of patents applied outside the land of origin.

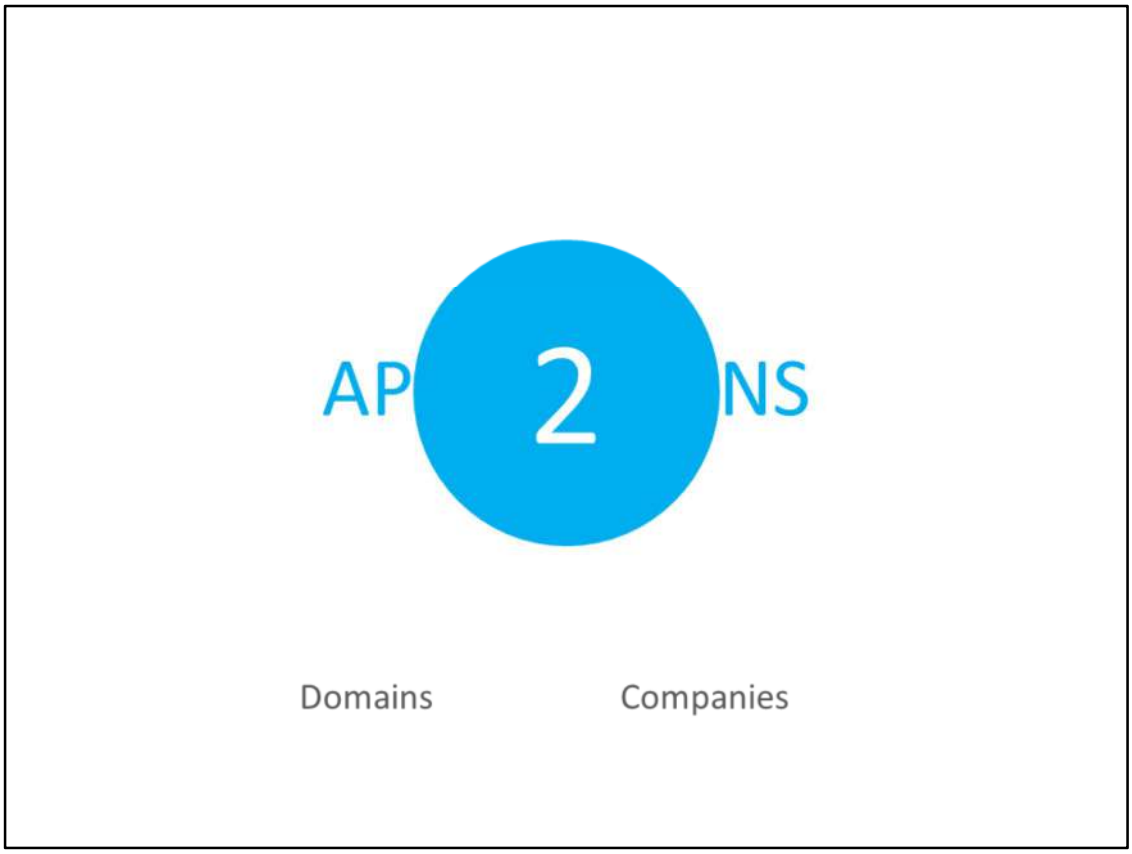
The decrease is due to China!

Patent/family ratio data is not relevent for the last 3 years (2013-2016) because of the 18-months lagtime before publication but also because daugther patents are published years after the mother patent.




When China is excluded we clearly see a significant growth in the patents/patent families ratio: it means the business expectation of patent applicants is increasing in the domain of sugar-based products.

While the ratio drops to 2 when China is included. This is because many Chinese patents are only patented in China, which moves the ratio closer to 1.

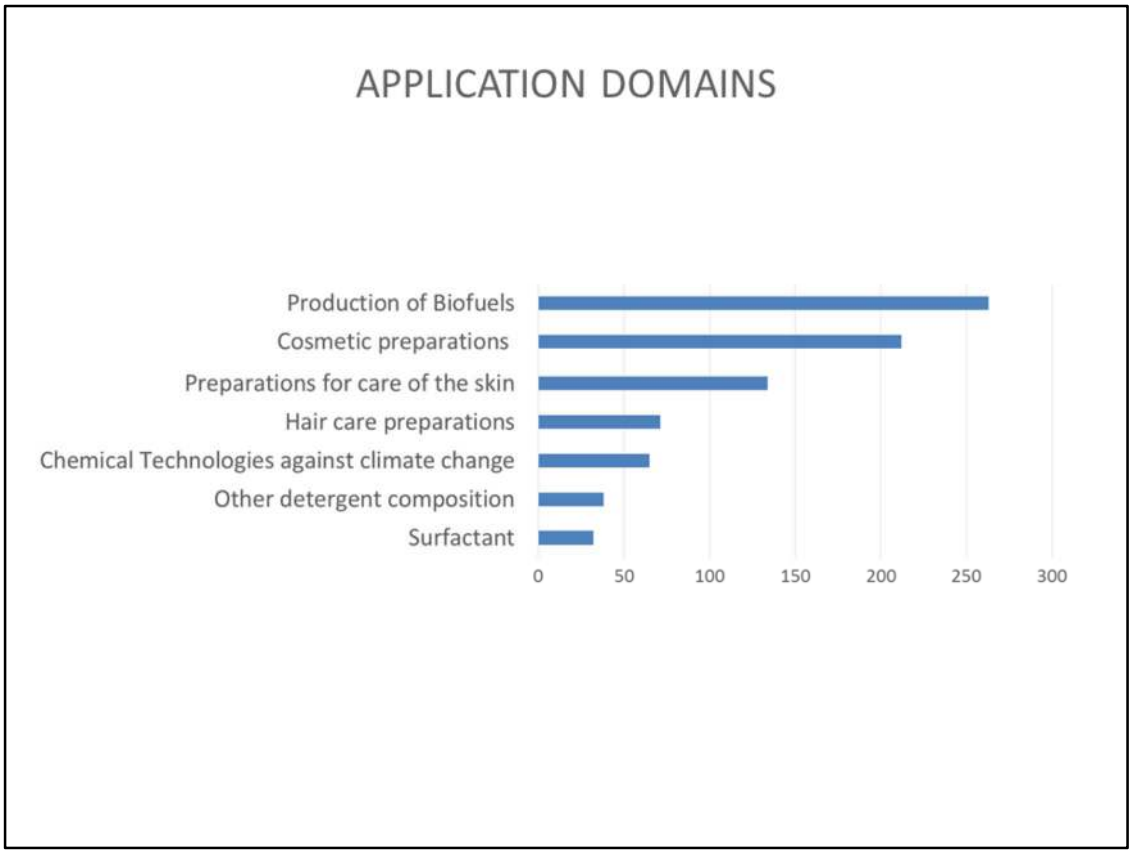

AP
2
NS
Domains
Companies


Conclusion: biofuels, cosmetics and surfactants are the most popular application domain in sugar derivatives

Surfactantia = C-glycosides! Linear and cyclic *C*-glycosides as surfactants, http://pubs.rsc.org/en/content/articlelanding/2011/gc/c0gc00407c/unauth#!div Abstract

Cosmetics: hyaluronic acid and sugar alcohols = skin care; xylose or xylobiose = haircare;

Biofuels = Ethanol and other sugar alcohols

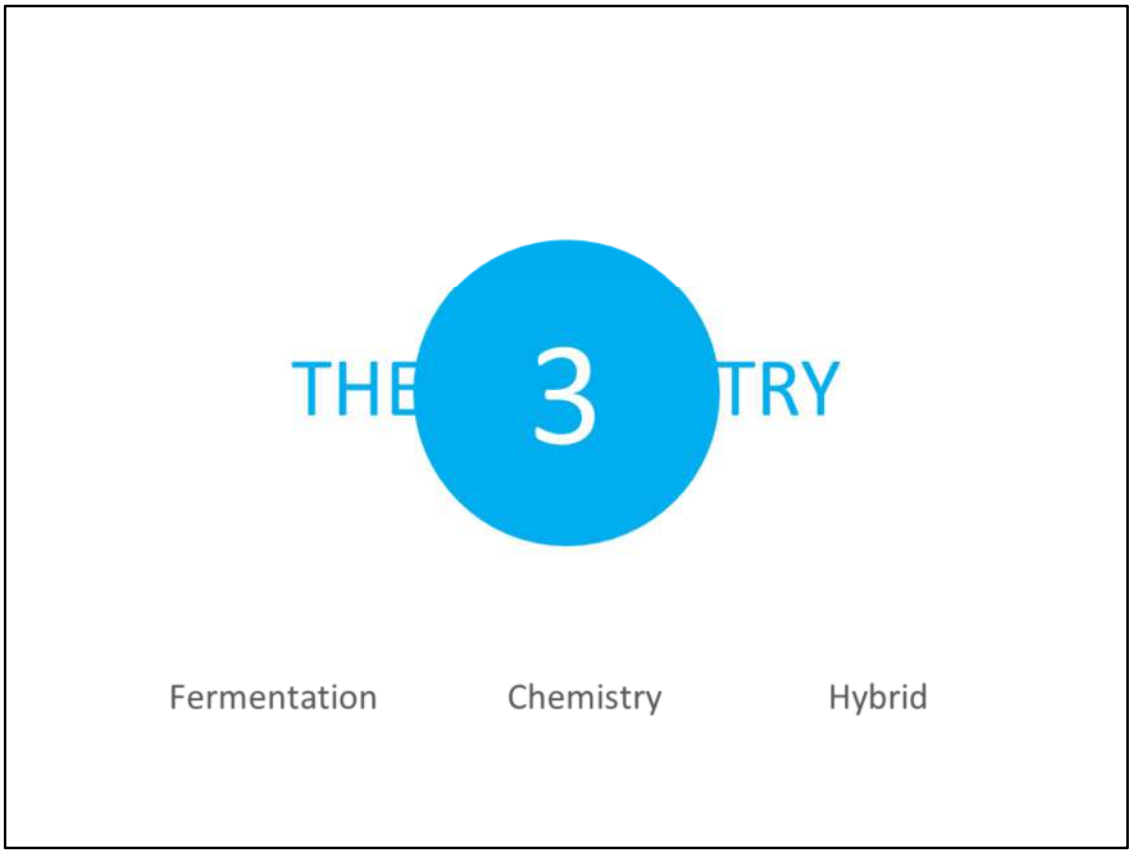



Chemical technologies against climate change = biofuels


A carbon snake can also be seen as a sugar derivative, a carbon snake results from the dehydration of table sugar catalyzed by high concentrated sulfuric acid.


Conclusion: the most dynamic companies in sugar derivatives over the period 2005-2015 are L'Oréal, Kao Corporation, Toray Industries, Sumitomo and BASF.

**China Petrochemical Corporation is a newcomer since the last 5 years.**




Oxidation, reduction, dehydration and coupling are the most important chemical reactions, these can be applied in chemical synthesis or via fermentation.

Some sugar derivaties are mainly produced via either fermentation or chemical synthesis, however sugar acids are produced equally by both routes.

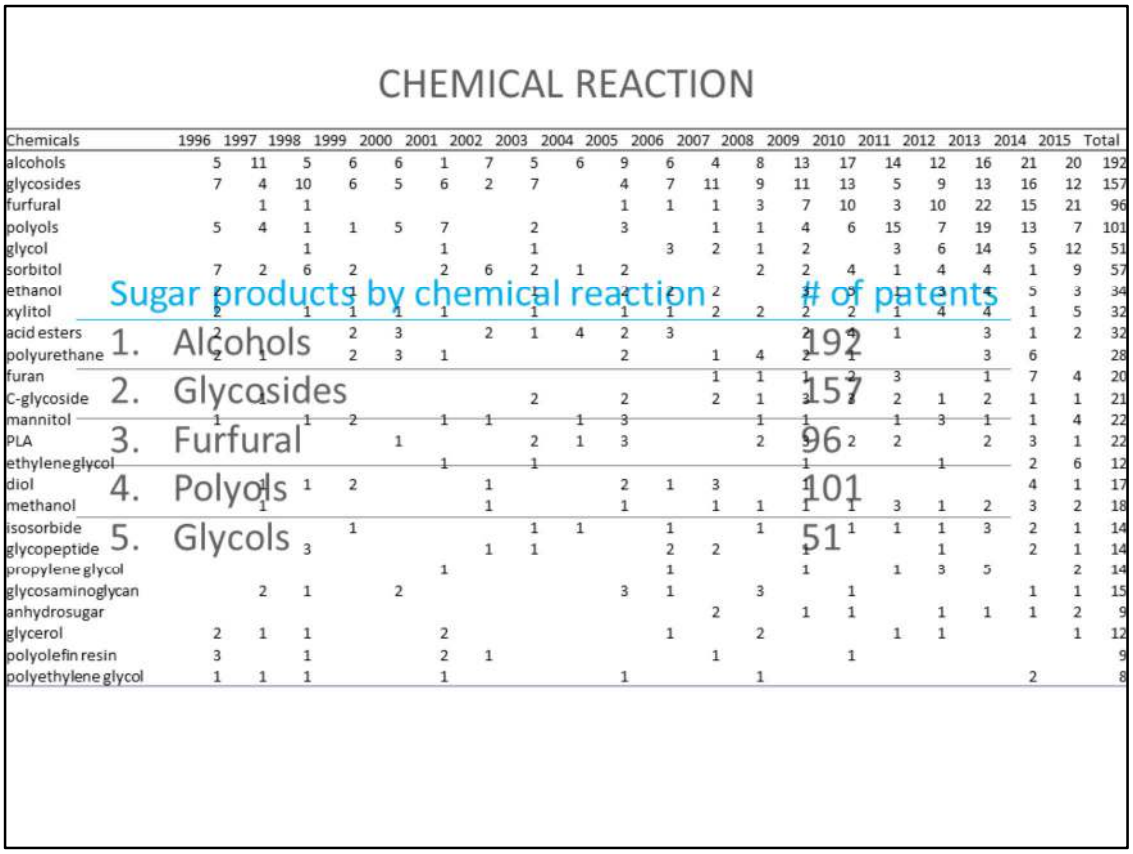
## FERMENTATION

| Product kind | CPC code | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ethanol, i.e. non-beverage | C12P7/06 | | | | 1 | 1 | 2 | 4 | 2 | | | 1 | | 1 | 4 | 6 | 1 | 5 | 4 | 5 | 1 | 39 |
| Polyol e.g. glycerol, butanediol | C12P7/18 | | | 1 | | 2 | 1 | | 1 | 1 | 1 | | 2 | 1 | 1 | 1 | 4 | 2 | 1 | 4 | 2 | 27 |
| Lactic acid | C12P7/56 | 1 | | | | | 1 | 1 | | 2 | | 1 | 1 | 2 | | 3 | 2 | 3 | 1 | 4 | 1 | 24 |
| Butanols | C12P7/16 | | | | | | | | | | | | 1 | 2 | 1 | 3 | | 2 | 1 | 4 | 1 | 16 |
| Produced by the action of an isomerase, e.g. fructose | C12P19/24 | | | | 1 | 3 | | | 1 | 1 | | | | 1 | | 1 | | 1 | 1 | 2 | | 12 |
| Hydroxy-carboxylic acids | C12P7/42 | | | | 1 | | 2 | 1 | | 1 | | | | | | | 2 | 1 | 2 | 2 | | 12 |
| O-glycosides | C12P19/44 | | | | | 1 | | | | | | | | | | 1 | | 2 | 2 | | 3 | 10 |
| Containing a carboxyl group, including Peroxycarboxylic acids | C12P7/40 | | | | | | | | 1 | | | 1 | 2 | 1 | | | 1 | 1 | | 1 | 1 | 10 |
| Disaccharides | C12P19/12 | | 2 | | | | | | | | | | 1 | | | | | 2 | 1 | 1 | | 9 |
| Nitrogen-containing carbohydrates | C12P19/26 | | | | 1 | | 1 | | 1 | | | 1 | | 1 | 1 | | | | 2 | 1 | | 9 |
| Glycopeptides & glycoproteins | C12P21/005 | | | | | | | | | | 2 | | 2 | | | | 1 | 1 | 1 | | 1 | 8 |
| Acyclic oxygen-containing compounds | C12P7/04 | | | 1 | | | | | | | | | | | 1 | 1 | 1 | 1 | 1 | 2 | | 8 |
| Dicarboxylic acids having <5 carbons, e.g. fumaric acid, maleic acid | C12P7/46 | | | | | | | | | | | 1 | 2 | | | | 1 | 1 | | 1 | | 6 |
| Polyesters of hydroxy-carboxylic acids, e.g. PHA | C12P7/625 | | | 1 | | | | | | | | | | 1 | 1 | 1 | | | 1 | | | 6 |
| N-glycosides | C12P19/28 | 1 | | | | | | | | | | 1 | | | | | | | 2 | | 1 | 5 |
| Methane | C12P5/023 | | | | | | 1 | | | | | | | 1 | | 1 | 1 | | 1 | | | 5 |
| Propionic acid;Butyric acid | C12P7/52 | | | 1 | | | | | | | | | | | | | | 2 | | | | 5 |
| 2-Ketogulonic acid | C12P7/60 | | | | | 1 | | 1 | | 1 | | | | 1 | | | | | | | | 5 |
| Ketones | C12P7/26 | | | | | | | | | | | | | 1 | 1 | | | | | 2 | | 4 |
| Acetone-containing products | C12P7/28 | | | | | | | | | | | | 1 | | | 1 | | 1 | 1 | | | 4 |
| Carboxylic acid esters | C12P7/62 | | | | | | 1 | | | 1 | | | | | | | | | | | | 4 |
| Hydroxy-containing compounds | C12P7/02 | | | | | | | | | | | 1 | 1 | | | | | | | | 1 | 3 |
| Glycerol | C12P7/20 | | | | | 1 | | | | | | | | | | | | 2 | | | | 3 |
| Aldonic, keto-aldonic or saccharic acids | C12P7/58 | 1 | | | | | | | | | | | | | | | 1 | 1 | | | | 3 |
| Produced by the action of a beta-amylase, e.g. maltose | C12P19/22 | | | | | | | | | | | 1 | | | | | | | | | | 2 |

Sugar based fermented products # of patents

1. Bio-ethanol 39
2. Polyols 27
3. Lactic acid 24
4. Butanols 16
5. Produced by the action of an isomerase 12

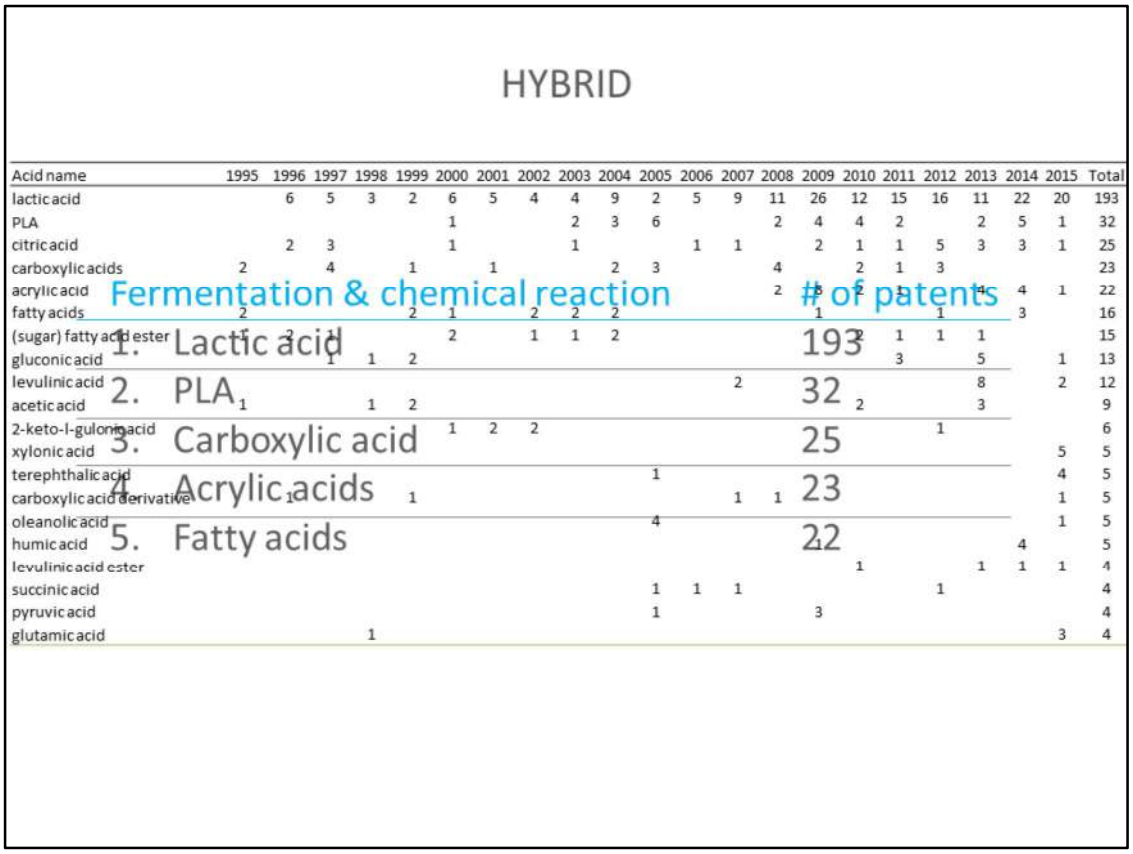
Bio-ethanol attracts the highest patent activity, but polyols like butanediol, propanediol, glycerol are also popular topics in patents. Hydroxycarboxylic acid includes the “famous” 3-hydroxy propionic acid”.




| Chemicals | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| alcohols | 5 | 11 | 5 | 6 | 6 | 1 | 7 | 5 | 6 | 9 | 6 | 4 | 8 | 13 | 17 | 14 | 12 | 16 | 21 | 20 | 192 |
| glycosides | 7 | 4 | 10 | 6 | 5 | 6 | 2 | 7 | | 4 | 7 | 11 | 9 | 11 | 13 | 5 | 9 | 13 | 16 | 12 | 157 |
| furfural | | 1 | 1 | | | | | | | 1 | 1 | 1 | 3 | 7 | 10 | 3 | 10 | 22 | 15 | 21 | 96 |
| polyols | 5 | 4 | 1 | 1 | 5 | 7 | | 2 | | 3 | | 1 | 1 | 4 | 6 | 15 | 7 | 19 | 13 | 7 | 101 |
| glycol | | | 1 | | | 1 | | 1 | | | 3 | 2 | 1 | 2 | | 3 | 6 | 14 | 5 | 12 | 51 |
| sorbitol | 7 | 2 | 6 | 2 | | 2 | 6 | 2 | 1 | 2 | | | 2 | 2 | 4 | 1 | 4 | 4 | 1 | 9 | 57 |
| ethanol | 6 | 5 | 1 | 3 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | | 3 | 3 | 2 | 1 | 1 | 5 | 3 | 34 |
| xylitol | 2 | | 1 | 1 | 1 | 1 | | 1 | | 1 | 1 | 2 | 2 | 2 | 2 | 1 | 4 | 4 | 1 | 5 | 32 |
| acid esters | 2 | | | 2 | 3 | | 2 | 1 | 4 | 2 | 3 | | | 2 | 4 | 1 | | 3 | 1 | 2 | 32 |
| polyurethane | 2 | 1 | | 2 | 3 | 1 | | | | 2 | | 1 | 4 | 2 | 1 | | | 3 | 6 | | 28 |
| furan | | | | | | | | | | | | 1 | 1 | 1 | 2 | 3 | | 1 | 7 | 4 | 20 |
| C-glycoside | | 1 | | | | | | 2 | | 2 | | 2 | 1 | 1 | 1 | 2 | 1 | 2 | 1 | 1 | 21 |
| mannitol | 1 | | 1 | 2 | | 1 | 1 | | 1 | 3 | | | 1 | 1 | | 1 | 3 | 1 | 1 | 4 | 22 |
| PLA | | | | | 1 | | | 2 | 1 | 3 | | | 2 | 3 | 2 | 2 | | 2 | 3 | 1 | 22 |
| ethylene glycol | | | | | | 1 | | 1 | | | | | | 1 | | | 1 | | 2 | 6 | 12 |
| diol | 1 | | 1 | 2 | | | 1 | | | 2 | 1 | 3 | | 1 | | | | | 4 | 1 | 17 |
| methanol | | 1 | | | | | 1 | | | 1 | | 1 | 1 | 1 | 1 | 3 | 1 | 2 | 3 | 2 | 18 |
| isosorbide | | | | 1 | | | | 1 | 1 | | 1 | | 1 | 3 | 1 | 1 | 1 | 3 | 2 | 1 | 14 |
| glycopeptide | 3 | | | | | | 1 | 1 | | | 2 | 2 | | 1 | | | 1 | | 2 | 1 | 14 |
| propylene glycol | | | | | | 1 | | | | | 1 | | | 1 | | 1 | 3 | 5 | | 2 | 14 |
| glycosaminoglycan | | 2 | 1 | | 2 | | | | | 3 | 1 | | 3 | | 1 | | | | 1 | 1 | 15 |
| anhydrosugar | | | | | | | | | | | | 2 | | 1 | 1 | | 1 | 1 | 1 | 2 | 9 |
| glycerol | 2 | 1 | 1 | | | 2 | | | | | 1 | | 2 | | | 1 | 1 | | | 1 | 12 |
| polyolefin resin | 3 | | 1 | | | 2 | 1 | | | | | 1 | | | 1 | | | | | | 9 |
| polyethylene glycol | 1 | 1 | 1 | | | 1 | | | | 1 | | | 1 | | | | | | 2 | | 8 |

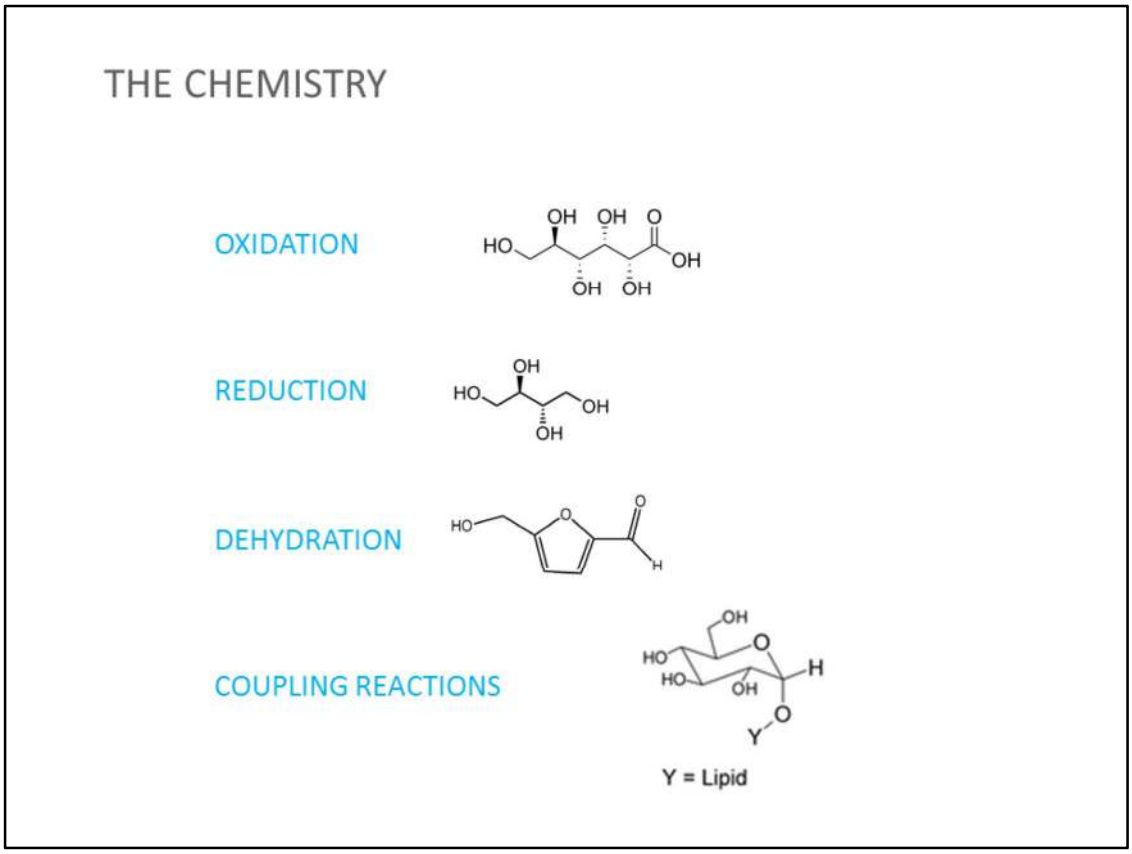
The polyols mentioned here are made **from reduction of sugar** (eg to form sorbitol) or from **dehydration of sugar**.

Sugar-based furan is of high interest for the production of **2,5-Furandicarboxylic acid**, which is a possible **building block for bio-based polyester**, Du Pont and BASF are quite active on that.




| Acid name | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| lactic acid | | 6 | 5 | 3 | 2 | 6 | 5 | 4 | 4 | 9 | 2 | 5 | 9 | 11 | 26 | 12 | 15 | 16 | 11 | 22 | 20 | 193 |
| PLA | | | | | | 1 | | | 2 | 3 | 6 | | | 2 | 4 | 4 | 2 | | 2 | 5 | 1 | 32 |
| citric acid | | 2 | 3 | | | 1 | | | 1 | | | 1 | 1 | | 2 | 1 | 1 | 5 | 3 | 3 | 1 | 25 |
| carboxylic acids | 2 | | 4 | | 1 | | 1 | | | 2 | 3 | | | 4 | | 2 | 1 | 3 | | | | 23 |
| acrylic acid | | | | | | | | | | | | | | 2 | 13 | 2 | 1 | | 4 | 4 | 1 | 22 |
| fatty acids | 2 | | | | 2 | 1 | | 2 | 2 | 2 | | | | | 1 | | | 1 | | 3 | | 16 |
| (sugar) fatty acid ester | 1 | 3 | 1 | | | 2 | | 1 | 1 | 2 | | | | | | 2 | 1 | 1 | 1 | | | 15 |
| gluconic acid | | | 1 | 1 | 2 | | | | | | | | | | | | 3 | | 5 | | 1 | 13 |
| levulinic acid | | | | | | | | | | | | | 2 | | | | | | 8 | | 2 | 12 |
| acetic acid | 1 | | | 1 | 2 | | | | | | | | | | | 2 | | | 3 | | | 9 |
| 2-keto-l-gulonic acid | | | | | | 1 | 2 | 2 | | | | | | | | | | 1 | | | | 6 |
| xylonic acid | | | | | | | | | | | | | | | | | | | | | 5 | 5 |
| terephthalic acid | | | | | | | | | | | 1 | | | | | | | | | | 4 | 5 |
| carboxylic acid derivative | | 1 | | | 1 | | | | | | | | 1 | 1 | | | | | | | 1 | 5 |
| oleanolic acid | | | | | | | | | | | 4 | | | | | | | | | | 1 | 5 |
| humic acid | | | | | | | | | | | | | | | | | | | | 4 | | 5 |
| levulinic acid ester | | | | | | | | | | | | | | | | 1 | | | 1 | 1 | 1 | 4 |
| succinic acid | | | | | | | | | | | 1 | 1 | 1 | | | | | 1 | | | | 4 |
| pyruvic acid | | | | | | | | | | | 1 | | | | 3 | | | | | | | 4 |
| glutamic acid | | | | 1 | | | | | | | | | | | | | | | | | 3 | 4 |

Acids are commonly **made either by fermentation or by chemical modification**, so it makes **more sense to keep all the acids together**. **Acrylic acid** is often based on lactic acid dehydration, and since acrylic and methacrylic acid are key **building block for many polymers** (plexiglas, superabsorbing polymers), this is quite an intersting application for lactic acid.




Oxidation, reduction, dehydration and coupling → O-glycoside

Oxidation → sugar acids

Reduction → sugar alcohols

Dehydratation → sugar alcohols, furane derivatives

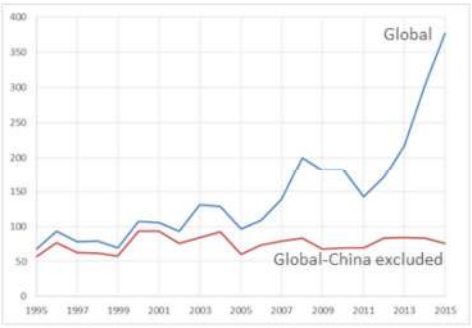
Coupling reactions → Glycosides

## FOCUS ON PROPANEDIOL

- 1,3-Propanediol can be formulated into a variety of industrial products, including, adhesives, laminates, polyesters, polyurethane, solvents…
- Can be produced from petrochemical or by fermentation from glucose or glycerol.
- Du Pont and Tate & Lyle commercialize fermentation-based propanediol for 10 years.


Top 5 companies in patents over the period 2010-2015
- China Petrochemical Corporation
- DU PONT
- Metabolic Explorer SA
- BASF
- DAICEL Chemical

Global patent activity for propanediol:
Patent activity increases mostly in China




Reference:
2014, ABENGOA BIOENERGIA NUEVAS TECNOLOGIAS SA, WO2014207105A1
Du Pont and Tate & Lyle

CREAX

| CASE STUDY 19

Propanediol is used in adhesives, laminates, polyesters, polyurethanes and solvents.

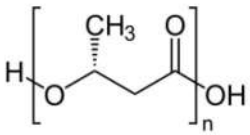
It's also a building block in the production of polymers.

In contrast to the rest of the world, China presents an increase in patent activity, also CNPC is in the top 5 companies.

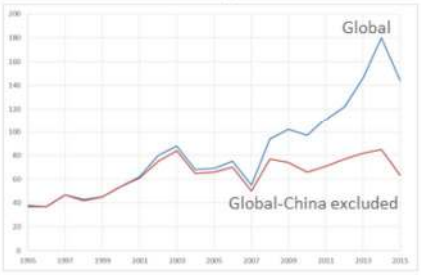
Noteworthy is that glycerol can be an alternative for sugars, glycerol is abundant since it's a side product of biodiesel production.

## FOCUS ON POLYHYDROXYALKANOATES (PHA)

- Polyhydroxyalkanoates or PHAs are linear polyesters produced in nature by bacterial fermentation of sugar or lipids.
- These polymers are biodegradeable and are used in the production of bioplastics.
- Lots of research dedicated to lower production costs, still too high for large scale commercialization.




Global patent activity for PHA:
Outside China, steady patent activity over the last 20 years




Top 5 companies in patents over the period 2010-2015

- Metabolix
- Kaneka
- BASF
- TEPHA
- LG Chemical

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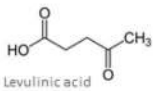
| CASE STUDY 20

According to some market reports, the market for PHA is going to increase within the next 5-10 years, but today it's still a niche product

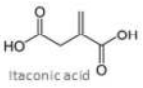
Again China shows a boom in patent activity, however there's a drop after 2014.

## LEVULINIC AND ITACONIC ACID

- Levulinic acid is a precursor to pharmaceuticals, plasticizers, various additives and biofuels (such as methyltetrahydrofuran, gamma-valerolactone, and ethyl levulinate).
- Bio-based levulinic acid is made from fermentation of sugar or chemical modification of furfuryl alcohol.
- Itaconic acid is a precursor of many industrially relevant compounds in pharmaceutical and chemical industries, especially of interest for polymers, as potential substitute for acrylic and methacrylic acid.
- Current fermentation processes for the production of itaconic acid from sugar are executed aerobically using oxygen as the terminal electron acceptor.



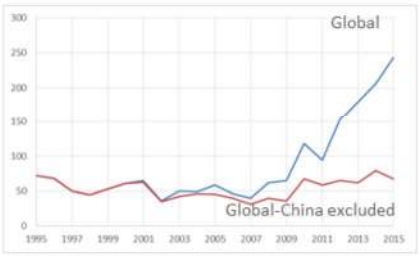
Levulinic acid



Itaconic acid

Top 5 companies in patents over the period 2010-2015
- China Petrochemical Corporation
- DSM
- Jinan Huaming Biochemistry
- BASF
- Qingdao Langyatai Group

Global patent activity for levulinc acid and itaconic acid
Growing mostly in China




CREAX

| CASE STUDY 21

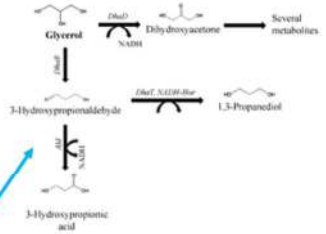
Those two compounds are promising, but the fact that most patent activity is happening in China raises some questions, like is it just a buzz. On the other hand, DSM and BASF are quite active here

Levulinic acid is used in nylon, synthetic rubber and plastics

Itaconic acid is produced via distillation of citric acid, and there's interest to use this compound for the production of polymers.

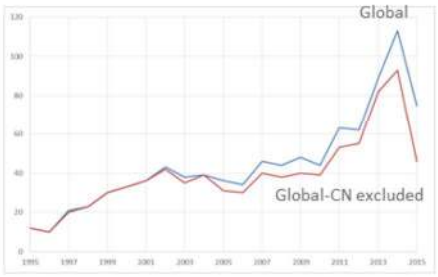
# HYDROXYPROPIONIC ACID

- 3-hydroxypropionic acid (3-HP) identified by the U.S. Department of Energy as one of the top 12 high-potential building block chemicals that can be made by fermentation.
- 100% theoretical yield from glucose
- Attention: glycerol, from biodiesel production waste, is a competition for sugar in the production of hydroxypropionic acid.




Top5 companies in patents over the period 2010-2015

- SAMSUNG ELECTRONICS
- OPX Biotechnologies
- Du Pont
- Nippon Catalytic Chemical Industries
- Invista North America




Reference:
Bioconversion of glycerol into hydroxypropionic acid
2014, SAMSUNG ELECTRONICS CO, KR20140003262A
2011, SNU R&DB FOUNDATION, KR20110018122A, (glycerol and glucose are fermented together)
2016, NOVOZYMES, WO2016100894A1

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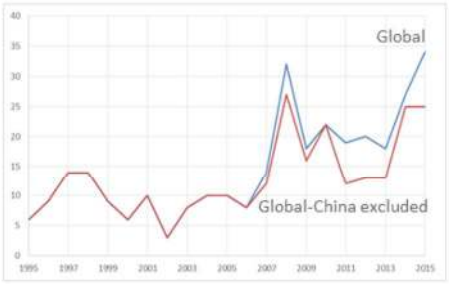
| CASE STUDY 22

Hydroxypropionic acid is definitively a very interesting sugar-based product, the only big risk is the competion with glycerol-based hydroxypropionic acid.

## C-GLYCOSIDE CHEMISTRY

- C-Glycosides often rely on green chemistry and facile methodology for their synthesis.
- Glycosides are commonly used as pharmacophores, biomaterials and green surfactants.
- C-Glycosides are considered to be best alternatives for O-, N-, S-glycosides.
- Other applications of C-glycoside are biomolecules, green surfactants and self-assembled soft-materials.


Global patent activity about C-glycoside




Top5 patent applicants over the period 2010-2015

- L'Oréal
- Tianjin Institute for Pharmaceutical Research
- Centre National de la Recherche Scientifique
- Henan College for Traditional Chinese Medicine
- Shanghai Institute of Materia Medica

Reference:
K. Lalithaa et al., Recent Developments in β-C-Glycosides: Synthesis and Applications, Carbohydrate Research, Volume 402, 30 January 2015, Pages 158–171

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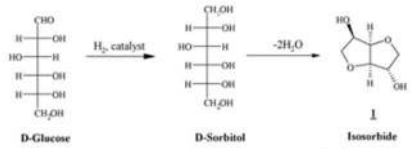
| CASE STUDY 23

C-glycosides are typically used for bio-based surfactant, with a sugar polar head and fatty acid apolar tail. They also find applications as pharmaceutical intermediate and building blocks for hydrogels.

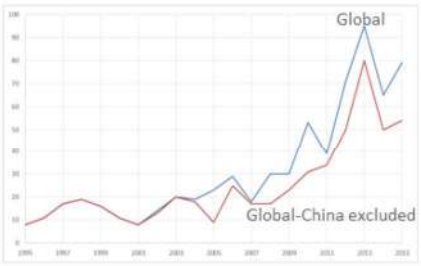
## DIANHYDROHEXITOL-BASED POLYMERS/MATERIALS

- Obtained by double dehydration of hexitols such as mannitol and sorbitol.
- The 1,4- and 3,6-dianhydrohexitols are well known under the names isosorbide, isoidide and isomannide.
- Isosorbide has been used in a wide variety of polymers, including polyesters, polycarbonates, polyethers, PEEK and polyurethanes and bio-based bisphenol A alternative.




isosorbide

Global patent activity about dianhydrohexitol:
Strong increase with or without china




Top 5 companies over the period 2010-2015

- SK Chemicals
- Roquette Frères
- Mitsubishi Chemical Corporation
- CLARIANT GmbH
- Archer Daniels Midland

Reference:
F. Fenouillot et al., Progress in Polymer Science, Volume 35, Issue 5, May 2010, Pages 578–622 (Funded by the Roquette company)

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| CASE STUDY 24

Ordinary sugar has too many hydroxyl groups. This double dehydration is ideal to form functional compounds that can replace other petrochemical intermediates. The Roquette companty is quite active for this compound.


- However, many other sugar-derived compounds are incoming, with higher value than biofuel
- Patents about propanediol, PHA, levulinic and itaconic acid are especially numerous in China (propaandiol, levulinezuur, PHA)
- Hydroxypropionic acid, C-glycoside and dianhydrohexitol are trendy topics in the world outside China (HPZ, C-, DianH)

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