

Investigation for Sustainable Polymers - Insights for the Use of Glycerol as a Biorefinery Product for the Synthesis of Monomers and Polymers

Daniel C. Assumpção^{a,b}, Maria Ingrid R. Barbosa^{*a,b}, Adriano P. Mariano^a, André Jardini^{a,b}, Maria Regina W. Maciel^a, Rubens Maciel Filho^{a,b}

^aUniversity of Campinas, School of Chemical Engineering, Laboratory of Optimization, Design and Advanced Process Control, Bioen division, Av. Albert Einstein, 500. Campinas SP – Brazil

^bNational Institute of Science and Technology in Biofabrication - BIOFABRIS, Av. Albert Einstein, 500. Campinas SP – Brazil

ingridrocha@feq.unicamp.br

The use of bio-based resources for the production of added value products has become a key element of sustainable development. In this regard, biorefinery is a recognized approach to transforming renewable feedstocks into fuels, chemicals, and materials. However, the integration of chemicals production into current biorefineries is challenging. This route is the least developed and most complex of all biorefinery operations and bio-based chemicals suffer from direct competition with oil-based counterparts. Additionally, the overabundance of targets makes difficult the decision making for companies. As such, there is a need to identify a core group of primary chemicals and secondary intermediates analogous to those in the petrochemical industry, including products with well-established value chains. To address some of these challenges, this work intends to contribute with ideas for the use of glycerol as a feedstock for polymers production. These polymers may be produced directly from glycerol or from some organic acid derived from glycerol. Such organic acids are in general flexible building blocks which may result in polymers for several applications, such as packaging materials and textile fibers, insulation foam, electronics and car parts. Among organic acids, succinic acid and lactic acid has a great potential to be used in the production of specialty polymers for medical implants because these materials can combine biodegradability with biocompatibility. Bearing this in mind, potential conversion routes of glycerol to lactic acid-derived specialty polymers are discussed in this work.

Key-words: Biorefinery; Glycerol; Organic acids; Sustainable polymers; Synthesis of polymers

1. Introduction

Changes on global environmental conscience have been reshaping the chemical industry. Companies are concentrating efforts on controlling pollutants emissions, minimizing residues generation and increasing process efficiency. Additionally, the seek for alternative raw materials, such as renewable and less toxic compounds, are not only reshaping but creating a new industrial niche: the *biorefinery* (Schulte *et al.*, 2013; Dube and Salehpour, 2014; BMEL, 2014; Sheldon, 2017). Biorefineries are fundamentally concerned to process biomass (animal and/or vegetable) into several bioproducts and bioenergy.

The concept of green chemistry has been essential to boost biorefineries development. It gained importance during the 90's when the American Pollution Prevention Act from the Environmental Protection Agency (EPA) entered into force. As one of its consequences, the law required companies to use raw material more effectively, minimizing residues production – CO₂ included. This was an effective strategy to reduce waste treatment costs and strengthen companies' competitiveness. Biorefineries, then, became an important economic player, producing bio-based chemicals derived from biomass, such as lignocellulosic materials (USDOE, 2004; Schulte *et al.*, 2013; Dube and Salehpour, 2014; BMEL, 2014; Sheldon, 2017).

A common biorefinery byproduct is Glycerol (1,2,3-propanetriol, also glycerin or glycerine), easily obtained from biodiesel production. It is a polyol, with three hydroxyl groups, abundant in nature, since it is the structural component of many lipids. It is non-toxic, edible, and biodegradable (Silva *et al.*, 2009; Amaral *et al.*, 2009; Gallezot, 2012; Mazumdar *et al.*, 2013). In the last decade, its global production increased 13.3 times fold, following renewable fuels market growth. Consequently, crude glycerol price dropped from US\$ 0.330 / kg (2001) to US\$ 0.088 / kg (2012) (Hejna *et al.* 2016). This low market price is a positive feature considering the gamut of products that derive from glycerol. Glycerol is an important building block for biorefineries, once it is one of the twelve molecules that convertible into high-value bio-based chemicals or materials according to USDOE (2004). It is a building block to produce primary chemicals and intermediates widely used in paint, automotive, food, cosmetic, and pharmaceutical industries among other applications (Wang *et al.*, 2001; Pagliaro *et al.*, 2007; Silva *et al.*, 2009; Amaral *et al.*, 2009).

As shown, glycerol is intrinsically a versatile molecule. However, its potential is further increased when used to produce polymers. It is easily converted to several organic acids, which are the basis to different polymers (Figure 1). This brief review is concerned to present the main synthesis and processing routes of polymers obtained from glycerol or its derived organic acids. Additionally, insights on how glycerol has been shaping biorefinery industry are presented.

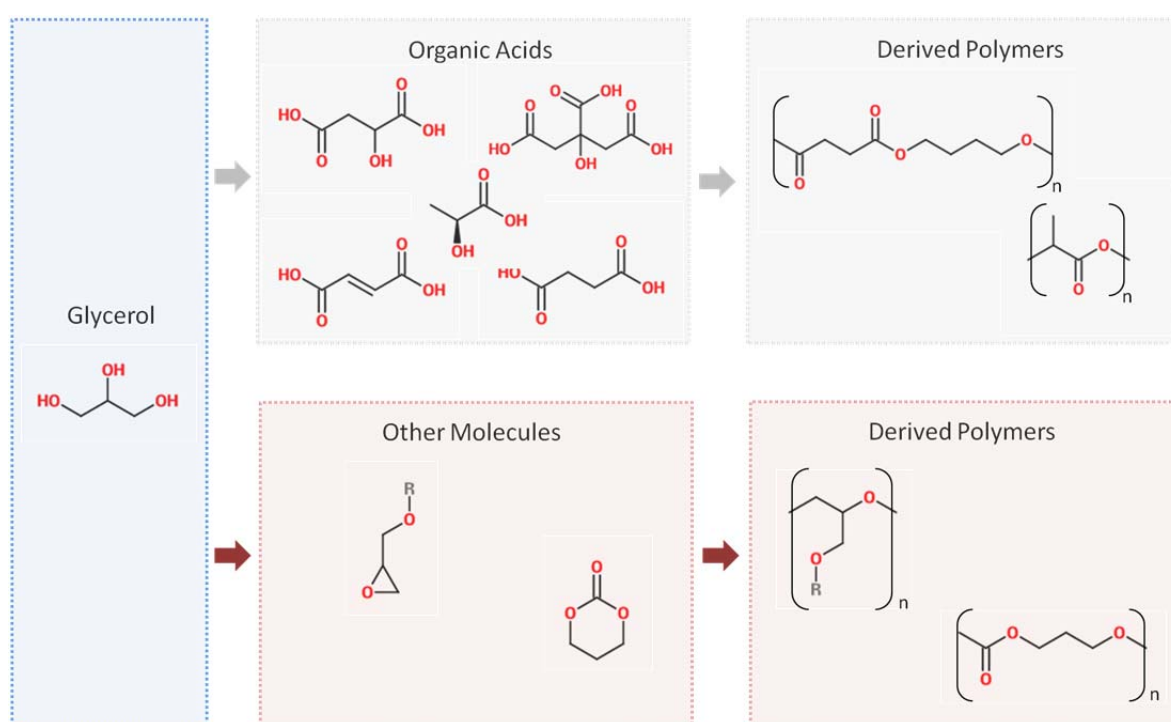


Figure 1: Glycerol potentiality as a building block: monomers and polymers from glycerol.

2. Organic Acids from Glycerol as Potential Monomers

The production of organic acids from glycerol is more likely to be a chosen route to produce biobased polymers for two reasons: (1) glycerol is a raw material to several organic acids production and, (2) one organic acid usually originates more than one polymer, by combining it with different molecules, increasing business flexibility. Glycerol conversion to organic acids may occur through chemical and biological routes. Chemical catalyzed routes frequently have higher productivity if compared to biological routes. Nevertheless, biological routes result in optically pure molecules. Literature reports a considerable amount of studies regarding organic acid production from glycerol. Nevertheless, the chosen synthesis route depends on the material application.

In a patent, Yocum *et al.* (2014) demonstrated that is possible to produce succinic acid, fumaric acid, L-malic acid, L-lactic acid or D-lactic acid through biological catalysis, using genetic modified *Escherichia coli* and glycerol as carbon source. Among these, this paper focuses on succinic and lactic acids.

Succinic, fumaric and malic acids are obtained from similar biochemical processes. These organic acids are potential building blocks that may originate commodities and chemical specialties (USDOE, 2004). Succinic

acid or succinate is an organic acid used as solvents, pharmaceutical products or as monomers in biodegradable polymer synthesis (Chen and Liu, 2016). The presence of two carboxylic acids in the molecule, as well as its partial solubility in water, turns this molecule an important compound to be used as a building block (Serrano-Ruiz *et al.*, 2011).

Lee *et al.* (2001) reported a high yield of glycerol fermentation to succinic acid by *Anaerobiospirillum succiniciproducens* (ATCC 29305). From 6.5 g/L of glycerol, the microorganism produced 4.9 g/L, above the maximum theoretical yield. In this case, is probable that another unmeasured carbon source was used by the microorganism. Sholten *et al.* (2009) tested continuous glycerol fermentation to succinic acid using the bacteria *Basfia succiniciproducens* DD1. Using 5.0 g/L of glycerol in the feed, fermentation performance parameters increased with dilution rates increase (as expected). The best performance was obtained at a dilution rate of 0,018 h⁻¹, resulting in the succinic acid concentration of 5.21 g/L, the succinic acid productivity of 0.094 g/L.h, succinic acid to glycerol yield of 1.02 g/g and specific productivity of succinic acid to glycerol of 0.375 g/gh. Again, the succinic acid yield is above the theoretical maximum. Sholten and Dägele (2008), obtained 8.4 g/L of succinic acid from glycerol, with a productivity of 0.9 g/L.h and yield of 1.2 g/g using *Pasteurellaceae sp.* Carvalho *et al.* (2014) surprisingly reached 49.62 g/L of succinic acid when using *Actinobacillus succinogenes* as microorganism and DMSO as an electron acceptor.

Lactic acid is the carboxylic acid derived from biomass most studied and can be used directly in pharmaceutical and food industries, as a surfactant, in polymer synthesis, and other basic chemical compounds. It is possible to obtain lactic acid via glycerol dehydrogenation under a nitrogen atmosphere, catalyzed by iridium in basic medium. Sharninghausen *et al.*(2014) produced lactic acid through the mentioned chemical route obtaining selectivities as high as 95%, resulting in one of the most promising studies for lactic acid via homogeneous catalysis.

Isomers L-lactic and D-lactic acid are obtained biologically from glycerol oxidation similarly to 2,3-butanediol (Chen and Liu, 2016). Depending on the microorganism and culture medium composition, different yields are obtained. For instance, genetically modified *Escherichia coli* produced L-lactic acid reaching a yield of 0.89 g/g (Mazumdar *et al.*, 2014); *Enterococcus faecalis* reached 0.98 g/g (Doi, 2015); *Escherichia coli* AC-521 produced 85.8 g/L of lactic acid after 88h, (productivity of 0.97 g/Lh) and a yield of 0.9 mol/mol (Hong *et al.*, 2009).

Optically pure lactic acid is reported in the literature as well. Glycerol (30 g/L) and acetic acid (10 g/L) were converted to pure L-lactic acid (55.3 g/L) by *Enterococcus faecalis* (Murakami *et al.*, 2016); 32 g/L of D-lactic acid was produced by genetically modified *Escherichia coli* from 40 g/L of glycerol, reaching 85% of the maximum theoretical yield (Mazumdar *et al.*, 2010).

3. Major Polymers from Succinic Acid and Lactic Acid

A large number of polyamides, polyesters and poly(ester amide)s can be produced by polycondensation of succinic acid or succinic acid diesters with diamines or diols (Isikgor and Becer, 2015).For instance: polyamide-5,4and, poly(butylsuccinate) (PBS), a biodegradable thermoplastic and can be composted even though it is not transparent (Harmsen and Hackmann, 2003). It is suitable for extrusion, injection molding, thermoforming, and film blowing, developed by Amber Works, an alliance by Nature Works and Bio Amber, to explore the development of 100% renewable polyester copolymers of 1,4-butanediol (1,4-BDO) and succinic acid (PBS) (Adkins *et al.*, 2012).

PBS, an aliphatic polyester (Okada, 2002), resembles polypropylene (PP) in terms of mechanical properties. Compared to many other biopolymers such as poly(lactic acid) or PLA, PBS has a higher heat deflection temperature (HDT) and is much tougher (Harmsen and Hackmann, 2003). Due to their properties, PBS and its copolymers have been receiving much attention. They can be used in several applications like, disposable products, films (compost bag, shopping bag, packaging film etc.), agriculture or horticulture (mulch film, plant pot, rope etc.), fishing gear (fishing net, fishing trap, fishing line etc.), containers (tray, food containers, bottles etc.) (Isikgor and Becer, 2015).

Lactic acid is a monomer of poly(lactic acid) (PLA). There are two major chemical ways to synthesized PLA: polycondensation of lactic acid or ring-opening polymerization (ROP) of its cyclic dimer (lactide) (Isikgor and Becer, 2015). By direct polycondensation reaction, a low to intermediate molecular weight PLA is produced, due to the water formed during the polymerization reaction. This reaction generally uses solvents and/or catalysts and occurs under high vacuum and temperatures for the removal of water produced in the condensation (Lasprilla *et al.*, 2012). Water formation during the reaction polymerization can lead to other side reaction, like transesterification, producing lactide, which lowers the overall molecular weight and the removal of the lactide formed reduces the first pass yield of the process. The formation of lactide cannot be excluded, but to suppress the lactide formation and increase the first pass yield of the polycondensation reaction of the lactic acid, the lactide can be returned back to the reaction mixture (Södegard and Stolt, 2010) and increase

the molecular weight of the PLA. ROP is more widely used for the preparation of high molecular weight PLA. This reaction proceeds in the presence of catalysts and it allows the control of molecular weight and stereotacticity of PLA in comparison with polycondensation. Depending on the isomer, L-lactic acid, D-lactic acid or meso form, used to synthesized PLA, different properties of the polymers are expected. Poly-L-lactide (PLLA) is a semi-crystalline polymer, with glass transition temperature (T_g) between 60 and 65° C, and a melting temperature (T_m) of around 175° C. PDLLA is an amorphous polymer resulting of polymerization of the racemic mixture of D- and L-enantiomers (Isikgor and Becer, 2015). PLA is currently the most important biobased polyester and one the most attractive examples of a fully biobased material (Harmsen and Hackmann, 2003). Due to its versatility (Lasprilla *et al.*, 2012), PLA can be used in medical and others applications like, packaging, textile, agriculture, electronics, automobile and other segments.

4. Glycerol and Glycerol Polymers

So far, this paper presented several organic acids obtained from glycerol, which can be used as monomers. Nevertheless, glycerol may not necessarily be converted into organic acids to originate polymers. Glycerol (without or with minor chemical changes) may be used as raw material to a variety of polymers. The three hydroxyls present in its structure are responsible for the broad range of structure possibilities (Zhou *et al.*, 2008).

Glycerol polymers may be linear, branched or dendritic, depending on the synthesis route chosen. Among linear polymers, research has been focusing on 1,2-Linear Poly(Glycerol Ether), 1,2-Linear Poly(Glycerol Carbonate), 1,3-Linear Poly(Glycerol Carbonate) and polyesters obtained from polycondensation reactions (Zhang and Grinstaff, 2014). Each polymer is obtained in different conditions, through different chemical routes and presents a variety of physical and biological properties. This broad range of properties determines which medical application is more suitable for each polymer. Considering that medical uses for glycerol polymers, some routes using radioactive or heavy metals catalysts (such as Caesium, Cobalt or Chromium) must be avoided (Geschwind and Frey, 2013). Yet, alternative routes using safe catalyst have already been developed.

Glycerol polymers have reached several medical fields of application. Liu *et al.* (2012) developed a glycerol and ϵ -caprolactone polymer coupled with a diversity of fatty acids to be used as a drug delivery system to avoid lung cancer recurrences after extirpation surgery. Grinstaff (2002) also presented dendritic glycerol polymers from methacrylate and poly(glycerol-co-succinic acid) for ophthalmologic healing purposes. The material was in vivo tested, completely healing eye wounds, tolerating eye blood pressure. Putnam *et al.* synthesized a polymer appropriated to be used as seroma coating, avoiding the accumulation of corporeal fluids after ablative medical procedures. Poly(ethylene glycol-co-dihydroxyacetone carbonate) (MPEG-pDHA) was synthesized varying blocks molecular weights and the resulting polymer was a cross-linked hydrogel upon hydration and applicable through a syringe (Zawaneh *et al.*, 2010). Despite recent developments and applications of glycerol polymers, no applications for skin purposes were reported.

5. Conclusions

Glycerol and organic acids may be a key factor to increase biorefineries competitiveness. Although commodities may dictate the production capacity, high-value products, such as medical polymers may be the responsible for positive economic results in biorefineries economy. Therefore, the development of chemical and biological routes to convert glycerol into organic acids and/or polymers is interesting for biomass companies.

Acknowledgments

We thank the National Council for Scientific and Technological Development (CNPq process number 465624/2014-6) and São Paulo Research Foundation (FAPESP process number 2015/20630-4) for funding the research.

Reference

- Adckins J., Pogh S., McKenna R., Nielsen D. R., 2012, Engineering microbial chemical factories to produce renewable "biomonomers", *Frontiers in Microbiology*, 3: 313, 1-12, DOI: 10.3389/fmicb.2012.00313
- Amaral P. F. F., Ferreira T. F., Fontes G. C., Coelho M. A. Z., 2009, Glycerol valorization: New biotechnological routes, *Food and Bioproducts Processing*, 87, 179–186, doi:10.1016/j.fbp.2009.03.008
- BMEL (Federal Ministry of Food and Agriculture), 2014, National Policy Strategy on Bioeconomy, Renewable resources and biotechnological processes as a basis for food, industry and energy, <www.bmel.de> accessed 28.06.2017.

- Carvalho M., Matos M., Roca C., Reis M. A. M., 2014, Succinic acid production from glycerol by *Actinobacillus succinogenes* using dimethylsulfoxide as electron acceptor, *New Biotechnology*, 25, 133-139, DOI: 10.1016/j.nbt.2013.06.006
- Chen Z., Liu D., 2016, Toward glycerol biorefinery: metabolic engineering for the production of biofuels and chemicals from glycerol, *Biotechnology for biofuels*, 9:205, DOI: 10.1186/s13068-016-0625-8
- Doi Y., 2015, L-lactate production from biodiesel-derived crude glycerol by metabolically engineered *Enterococcus faecalis*: cytotoxic evaluation of biodiesel waste and development of a glycerol-inducible gene expression system, *Applied Environmental Microbiology*, 81, 2082-2089, DOI: 10.1128/AEM.03418-14
- Dube M. A., Salehpour S., 2014, Applying the Principles of Green Chemistry to Polymer Production Technology, *Macromolecular Reaction Engineering*, 8, 7–28, DOI: 10.1002/mren.201300103.
- Gallezot P., 2012, Conversion of biomass to selected chemical products, *Chemical Society Reviews*, 41, 1538–1558, DOI: 10.1039/c1cs15147a
- Geschwind J., Frey H., 2013, Poly(1,2-glycerol carbonate): a fundamental polymer structure synthesized from CO₂ and glycidyl ethers. *Macromolecules*, 46, 9, 3280-3287, DOI: 10.1021/ma400090m
- Grinstaff, M. W., 2002, Biodendrimers: New Polymeric Biomaterials for Tissue Engineering, *Chemistry - A European Journal*, 8, 13, 2838–2846. DOI: 10.1002/1521-3765(20020703)8:13<2838::AID-CHEM2838>3.0.CO;2-I
- Harmsen P., Hackmann M., 2003, Green building blocks for biobased plastics - Biobased processes and market development. Propress, Wageningen, ISBN 978-94-6173-610-9
- Hejna A., Kosmela P., Formela K., Piszczyk L., Heponiuk J. T., 2016, Potential applications of crude glycerol in polymer technology – Current state and perspectives, *Renewable and Sustainable Energy Reviews*, 66, 449 – 475, DOI: 10.1016/j.rser.2016.08.020
- Hong A.-A., Cheng K.-K., Peng F., Zhou S., Sun Y., Liu C.-M., Liu D.-H., 2009, Strain isolation and optimization of process parameters for bioconversion of glycerol to lactic acid, *Journal of Chemical Technology and Biotechnology*, 84, 10, 1576-1581, DOI:10.1002/jctb.2209
- Isikgor F. H., Becer R., 2015, Lignocellulosic biomass: a sustainable platform for the production of bio-based chemicals and polymers, *Polymer Chemistry*, 2015, 6, 4497, DOI: 10.1039/c5py00263j
- Lasprilla A. J. R., Martinez G. A. R., Lunelli B. H., Jardini A. L., Maciel Filho R., 2012, Poly-lactic acid synthesis for application in biomedical devices – A review, *Biotechnology Advances*, 30, 321-328, DOI:10.1016/j.biotechadv.2011.06.019
- Liu, R., Wolinsky, J.B., Catalano, P.J., Chiriac L. R., Wagner A. J., Grinstaff M. W., Colson Y. L., Raut C. P., 2012, Paclitaxel-Eluting polymer film reduces locoregional recurrence and improves survival in a recurrent sarcoma model: a novel investigational therapy, *Annals of Surgical Oncology* (2012) 19, 1, 199-206, DOI: 10.1245/s10434-011-1871-4
- Mazumdar S., Clomburg J. M., Gonzalez R., 2010, *Escherichia coli* Strains Engineered for Homofermentative Production of D-Lactic Acid from Glycerol, *Applied and Environmental Microbiology*, 76, 13, 4327-4336, DOI: 10.128/AEM.00664-10
- Mazumdar S., Blankschien M. D., Clomburg J. M., Gonzalez R., 2013, Efficient synthesis of L-lactic acid from glycerol by metabolically engineered *Escherichia coli*, *Microbial Cell Factories*, 12:7, DOI:10.1186/1475-2859-12-7
- Murakami N., Oba M., Iwamoto M., Tashiro Y., Noguchi T., Bonkohara K., Abdel-Rahman M. A., Zendo T., Shimoda M., Sakai K., Sonomoto K., 2016, L-Lactic acid production from glycerol coupled with acetic acid metabolism by *Enterococcus faecalis* without carbon loss, *Journal of Bioscience and Bioengineering*, 121, 1, 89-95, DOI: 10.1016/j.jbiosc.2015.05.009
- Okada M., 2002, Chemical synthesis of biodegradable polymers, *Progress in Polymer Science*, 27, 1, 87-133, DOI: 10.1016/S0079-6700(01)00039-9
- Pagliaro M., Ciriminna R., Kimura H., Rossi M., Pina C. D., 2007, From Glycerol to Value-Added Products, *Angewandte Chemie International Edition*, 46, 4434 – 4440, DOI: 10.1002/anie.200604694
- Rico-Ramirez V., Napoles-Rivera F., Gonzalez-Alatorre G., Diwekar U., 2010, Stochastic optimal control for the treatment of a pathogenic disease, *Chemical Engineering Transactions*, 21, 217-222, DOI: 10.3303/CET11226001
- Schulte P. A., McKernan L. T., Heidel D. S., Okun A. H., Dotson G. S., Lentz T. J., Geraci C. L., Heckel P. E., Branche C. M., 2013, Occupational safety and health, green chemistry, and sustainability: a review of areas of convergence, *Environmental Health*, 12:31, DOI:10.1186/1476-069X-12-31
- Serrano-Ruiz J. C., Luque R., Sepúlveda-Escribano A., 2011, Transformations of biomass-derived platform molecules: from high added-value chemicals to fuels via aqueous-phase processing, *Chemical Society Review*, 40, 5266–5281, DOI: 10.1039/c1cs15131b

- Sharninghausen L. S., Campos J., Manas M. G., Crabtree R. H., 2014, Efficient selective and atom economic catalytic conversion of glycerol to lactic acid, *Nature Communications*, 5:5084, DOI: 10.1038/ncomms6084
- Sheldon R. A., 2017, The E factor 25 years on: the rise of green chemistry and sustainability, *Green Chemistry*, 19, 18, DOI: 10.1039/c6gc02157c
- Sholten E., Dägele D., 2008, Succinic acid production by a newly isolated bacterium, *Biotechnology Letters*, 30, 12, 2143-2146, DOI: 10.1007/s10529-008-9806-2
- Sholten E., Renz T., Thomas J., 2009, Continuous cultivation approach for fermentative succinic acid production from crude glycerol by *Basfia succiniciproducens* DD1, *Biotechnology Letters*, 31:1947, DOI: 10.1007/s10529-009-0104-4
- Silva G. P., Mack M., Contiero J., 2009, Glycerol: A promising and abundant carbon source for industrial microbiology, *Biotechnology Advances*, 27, 30-39, DOI: 10.1016/j.biotechadv.2008.07.006
- Södergard A., Stolt M., 2010, Industrial Production of High Molecular Weight Poly(Lactic acid), POLY(LACTIC ACID) – Synthesis, Structures, Properties, Processing, and Applications, Eds. Auras R., Lim L.-t., Selke S. E. M., Tsuji H., John Wiley & Sons, Inc., Hoboken, New Jersey, United States
- USDOE (U.S. Department of Energy), 2004, Top Value Added Chemicals from Biomass Volume I - Results of Screening for Potential Candidates from Sugars and Synthesis Gas, <www.nrel.gov/docs/fy04osti/35523.pdf> accessed 22.06.2017
- Wang Z.-X., Zhuge J., Fang H., Prior B. A., 2001, Glycerol production by microbial fermentation: A review, *Biotechnology Advances*, 19, 201–223, DOI: 10.1016/S0734-9750(01)00060-X
- Yocum R. R., Hermann T., Hu X., 2014, Fermentation of glycerol to organic acids, US 20140234923 A1.
- Zawaneh P. N., Singh S. P., Padera R. F., Henderson P. W., Spector J. A., Putnam D., 2010, Design of an injectable synthetic and biodegradable surgical biomaterial, *Proceedings of the National Academy of Science of the United States of America*, 107, 24, 11014-11019, DOI:10.1073/pnas.0811529107
- Zhang H., Grinstaff M. W., 2014, Recent advances in glycerol polymers: chemistry and biomedical applications, *Macromolecular rapid communication*, 35, 22, 1906-1924. DOI: 10.1002/marc.201400389
- Zhou C. H. C., Beltramini J. N., Fan Y. X., Lu G. Q. M., 2008, Chemoselective catalytic conversion of glycerol as a biorenewable source to valuable commodity chemicals, *Chemical Society Reviews*, 37, 527-549, DOI: 10.1039/B707343G