Corn-Based Chemistry and its Applications

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Corn is the largest crop grown in the USA, occupying some 70 million acres. The U.S. produces 44% of the world's corn. It is a versatile, natural, biodegradable and renewable resource for many commercial applications. Corn as a raw material is replacing petroleum in many industrial applications, from plastic containers to clean-burning ethanol. One current goal is to produce 5 billion gallons of ethanol from corn annually. Corn components can be found in thousands of products ranging from food products, drugs, cosmetics and cleansers to adhesives and shoe polish. For example, corn oil is used in emollient creams and toothpaste while corn syrup is often used as a texturing and carrying agent in cosmetics. The current article will focus on new technologies arising from corn-based chemistry and their application in different fields e.g. the polymer industry, biomedicals, drug delivery systems and pharmaceuticals etc.

APPLICATION OF CORN PRODUCTS IN POLYMER INDUSTRY

The development of biodegradable polymers is one of the many important and urgent targets from the standpoint of environmental preservation. Biodegradable polymers from corn chemistry offer a number of advantages over other synthetic materials. Polymers derived from starch or other carbohydrates are of great interest since these materials are made from entirely renewable resources [1]. They have been used for manufacturing quality plastics, packaging materials and fabrics and also are very widely used in biomedical applications e.g. bioMEMs, biochips, bioscaffolds, etc.

Starch-based Biodegradable Polymers

Starch is one of the major components of corn. It is a linear polysaccaride made up of repeating glucose groups linked by glycosidic linkages in the 1-4 carbon positions and its chain length varies between 500 and 2000 glucose units. There are two major polymer molecules in starch – amylose and amylopectin. The alpha linkage of amylose starch allows it to be both flexible and digestible. As the starch content increases, starch based polymer composites become more biodegradable and leave fewer intractable residues. Biodegradation of starch-based polymers is due to enzymatic attack at the glycosidic linkages between the sugar groups, leading to a reduction in chain length and splitting out lower molecular weight sugar units (monosaccharides, disaccharides and oligosaccharides) that are readily utilized in biochemical pathways. Biodegradable starch-based polymers have recently been put forward as having potential for several applications in the biomedical field such as bone replacement implants [2], bone cements [3], drug delivery systems [4] and tissue engineering scaffolds [5]. The development of new processing technique and the reinforcement with various fillers results in materials with mechanical properties matching those of bone [6].

Thermoplastic Starch Products

Thermoplastic starch biodegradable plastics (TPS) have starch (amylose) content greater than 70% and with the use of specific plasticizing solvents, can produce thermoplastic materials having good performance properties and inherent biodegradability. High starch content plastics are very hydrophilic and readily disintegrate on contact with water. This can be overcome through blending and chemical modification, as the starch has free hydroxyl groups which readily undergo reactions such as acetylation, esterification and etherification. Starch-based polymers are often plasticized, destructured, and/or blended with other high-performance polymers (e.g. aliphatic polyesters and polyvinyl alcohols) to form useful mechanical properties for different applications.

Starch Aliphatic Polyester Blends

Blends of biodegradable synthetic aliphatic polyesters and starch are often used to produce high quality sheets and films for packaging. Approximately 50% of the synthetic polyester (costing approximately $4.00/kg) can be replaced with natural polymers such as starch (approximately $1.50/kg), leading to a significant reduction in cost. Furthermore, the polyesters can be modified by incorporating functional groups capable of reacting with natural starch polymers. Several starch-based plastics are currently available in the market. The major applications of these starch-derived polymers are generally films, such as shopping bags, bread bags, bait bags, over wrap, ‘flushable’ sanitary product backing materials, and mulch film. One of these is the ‘BioBag’, which is produced from the Novamont (Italy) resin that has been around since 1994, and is made from corn starch in combination with fully biodegradable plastics or polylactic acid. Foamed polystyrene can be replaced by starch foams. A well-known example is replacement of polystyrene foam packaging beads with water-soluble beads made from potato starch. Such starch products are readily soluble and biodegradable and have become an early market for biodegradable plastics.

Starch and PBS/PBSA Polyester Blends

Other polyesters can be blended with starch to improve material mechanical properties. Examples are polybutylene succinate (PBS) and polybutylene succinate adipate (PBSA). Starch and PBS or PBSA blends are used to produce biodegradable plastic sheet which can be thermoformed into products such as biscuit trays or film products. The tensile strength of the blends was somewhat lower than that of the polyester alone, but there was little significant further drop in strength with increasing starch content. At high starch contents (>60%), such sheets can become brittle. For this reason, plasticizers are often added to reduce the brittleness and improve flexibility.

Starch-based Superabsorbent Polymers (SAPs)

Superabsorbent polymers (SAPs) are a unique group of materials that can absorb over a hundred times their weight in liquids and do not easily release the absorbed fluids under pressure. Superabsorbents were first developed by the United States Department of Agriculture in 1970s in the form of starch/acrylonitrile/acrylamide based polymers that were called "superslurpers". The applications for these products were originally focused in the agriculture/horticulture markets where they were used as hydrogels to retain moisture in the surrounding soil during growing and transportation [7]. There are two primary types of superabsorbent polymers: starch-graft polymers and those based on cross-linked polyacrylates. These polymers are prepared by graft-polymerizing acrylonitrile onto a starch substrate [7,8]. Saponification of the graft polymer with an alkali yields a final product with nitrile, amide, and carboxyl functionalities (**Figure 1**). The hydrophilic groups on the composite can be adjusted by controlling the amount of NaOH and reaction time during saponification process; it is found that the collaborative absorbent effect of $-CONH_2$, $-COONa$ and $-COOH$ groups is superior to that of single $-CONH_2$, $-COONa$ or $-COOH$ group [9].

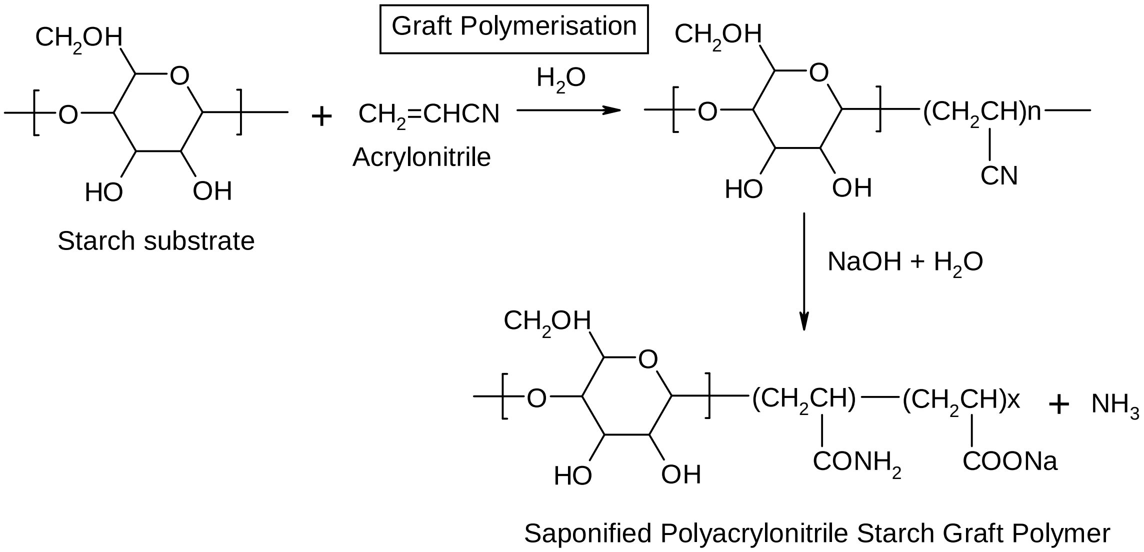


Figure 1: Synthesis of Starch-Graft Polymers

Cross-linking during polymerization is important as it yields a networked polymer, which will not dissolve in water, and can absorb and retain water under low load. A typical cross-linking agent is trimethylolpropane triacrylate in concentrations of 0.05 mol percent relative to the monomer. Cross-linking is also possible with ethylene glycol diglycidyl ether which reacts with carboxyl groups on the polymer molecules to crosslink them.

Global demand for SAP totaled an estimated 1.05 million tons in 2003; demand growth for 2003-2008 is forecast to average 3.6 percent per year. Globally, baby diapers account for an estimated 81% of SAP demand as shown in **Figure 2** (http://nexant.ecnext.com/coms2/gi_0255-3047/Super-Absorbent-Polymers-SAP.html). Adult incontinence is the next largest sub-segment (8%), followed by other applications (6 percent) and then feminine hygiene (5 percent). The “other applications” category includes such widely-varying uses as de-watering agents for sewage sludge, and drying agents for china clay slurries and pulverized coal slurries. [10]

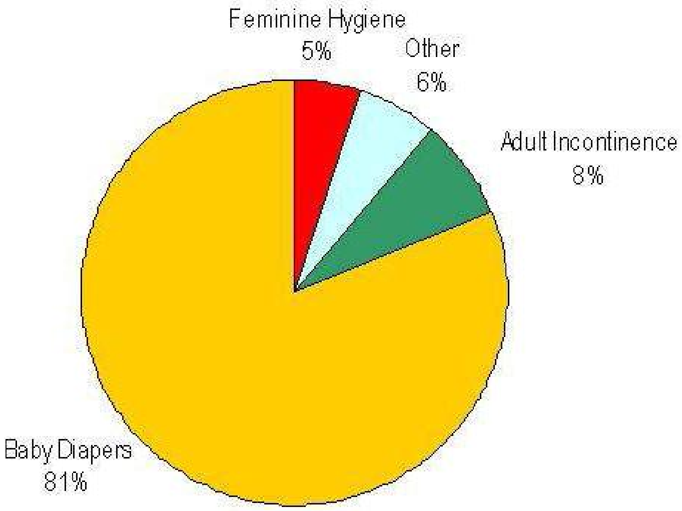


Figure 2: Global SAP end-use pattern, 2003, Total = 1.05 million tons.

Polylactic acid or Polylactide (PLA)

Polylactide is a biodegradable polymer based on renewable resources with a similar application range as PET. Uhde Inventa-Fisher, a Germany based company has been developing its PLA process for last 10 years (http://www.uhde-inventa-fischer.com). In the USA, Cargill is also investing in large scale production facilities for PLA manufacture, and Teijin in Japan are likewise active. The feedstock for these processes is glucose, which can be produced from hydrolysis of starch. In this process, glucose first undergoes fermentation to give sodium lactate, along with other impurities such as. proteins and cellular mass etc. After a number of purification steps, the sodium lactate is transformed into lactic acid, which is then concentrated to remove residual water. Next comes a thermal polymerization (self-condensation) to give a low molecular weight polyactide prepolymer which is then thermally depolymerised to give the distillable cyclic dimer, dilactide or (simply) lactide. The purified dilactide, on ring-opening polymerization with a suitable catalyst, often a tin salt such as stannous octoate, produces high molecular weight polylactide (**Figure 3**). The final polymer is granulated and further processed for various desired applications. Due to its good mechanical properties, PLA is used as packaging materials (film, sheet, and bottles), textiles (filament and fibers), engineering plastics and medical polymers (surgical threads and implants).

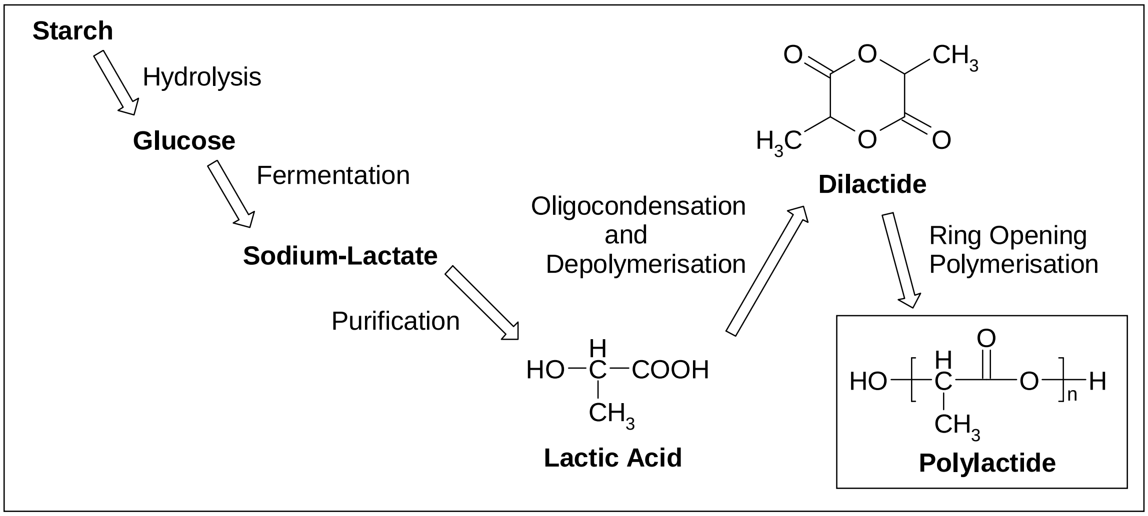
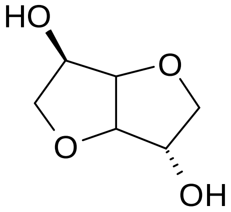
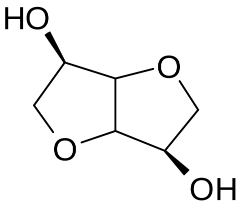


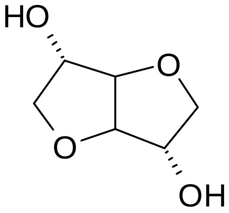
Figure 3: Process of making Polylactide from Starch (Uhde Inventa-Fisher).

1,4:3,6-Dianhydrohexitols Based Polymers and their Applications

The direct incorporation of simple carbohydrates into polymer structures is difficult because of the plethora of both primary and secondary hydroxyl functionalities in these compounds, which renders the synthesis of well-defined products difficult. This problem can be circumvented by using 1,4:3,6-dianhydrohexitols. Dianhydrohexitols are well-documented by-products of the starch industry, obtained by dehydration of D-hexitols [11] which are made by a simple reduction of hexose sugars. They are produced worldwide at a rate of 650,000 tons per annum [12]. These chiral biomass-derived products exist as three main isomers according to the relative configuration of their two hydroxyl functions. The three are isosorbide, isomannide and isoidide, derived from D-glucose, D-mannose and L-fructose, respectively).


Isosorbide


Isomannide


Isoidide

Isosorbide is the most widely-available dianhydrohexitol as it comes from glucose via sorbitol. The Iowa Corn Promotion Board (ICPB) in conjunction with the US Dept of Agriculture and the US Dept of Energy is supporting research into corn-derived products notably isosorbide. ICPB is partnering with NJIT to identify and assess potential polymer applications for isosorbide. Isosorbide is biodegradable and regarded by the FDA as a "generally recognized as safe" (GRAS) material.

In principle, isosorbide can be directly incorporated into commercial polyesters such as polyethylene terephthalate (PET). PET is widely used in a variety of food and beverage containers with a current market of 4.4 billion pounds. Due to the rigid molecular structure of isosorbide, it stiffens the PET chains and raises the glass-rubber transition temperature ($T_{g)}$ of PET resin to 85-90 °C, depending on the level of incorporation, which allows bottles made from the modified resins to be filled hot with food products that need to be pasteurized, or are so viscous that they need heating to reduce the filling time. Normal unmodified PET bottles simply distort when hot-filled in this way.

The preliminary cost estimates show that isosorbide from this technology is competitive with petroleum-based building blocks used to make plastics [13,14]. As well as modifying PET, there are many potential uses for isosorbide in the polymer industry. The use of renewable corn-derived isosorbide will potentially reduce the amount of petroleum necessary to make plastics. Already the synthesis of numerous polymers such as polyethers [15-17], polyesters [18,19], polyurethanes [20-22] and polycarbonates[23], has been examined. Some potential applications for these dianhydrohexitol-based polymeric products are:

(a) Isosorbide diglycidyl ether resins to replace bisphenol-A epoxies, used as food and beverage can liners. Bisphenol-A is suspected of being a xenestrogen and its replacement with a naturally-derived biodegradable diol has clear consumer advantages.

(b) Isosorbide and dianhydroiditol polycarbonate resins as molding plastics with high T_g, transparency and good UV-resistance. They could be potential candidates for replacing bis-A polycarbonates in CD blanks.

(c) Amorphous insoluble polyurethanes based upon isosorbide as chiral separation resins, potentially of great value in the pharmaceutical and fine chemicals market for resolving enantiomeric molecules. This exploits the basic chirality of the anhydrosugar molecules.

(d) Isosorbide/isoidide ester copolymers of controlled stereochemistry as potential high performance fibers and engineering resins. One can envision creating new classes of controlled performance, cost-effective polyesters through control of the polymer chirality along the chain.

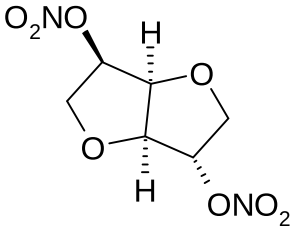
(e) Polyester resins from isosorbide with terephthalic and isophthalic acids, and copolymers with monomers such as L-lactide, caprolactone etc. for biomedical applications. Their applications vary from environmentally friendly molding resins to drug release and new degradable suture materials.

APPLICATIONS IN COSMETICS AND DRUG DELIVERY

Dimethyl isosorbide (DMI) is a water-white liquid with excellent solvent properties. It can easily be synthesized by methylation of isosorbide using dimethyl sulfate and aqueous alkali. It is used as a sustainable solvent in skin-care products and in drug formulation applications. (http://www.bulkactives.com/dimethylisosobide.htm). It enhances the penetration of actives through the epidermis layer of skin, enabling targeted delivery for products such as self-tanners, make-up removers and anti-acne treatments, etc. Not only does it reduce skin irritation, but it also lowers the required concentration level of aggressive active agents such as salicylic acid, Vitamin C, lactic acid, hydrocortisone and hyaluronic acid, serving to reduce the formulation cost of the finished product. Other product advantages include improved shelf stability (particularly those formulations susceptible to hydrolysis or trans-esterification), miscibility with most organic solvents and non-ionic surfactants, and compatibility with many product forms including clear gels. DMI is able to transport water-soluble actives into the skin, without recrystallization of the actives and can be formulated with standard equipment, without the need for special materials handling such as flammables. Most importantly, it does not promote penetration of the ingredients into the bloodstream. All these properties of DMI make it a potential choice for transdermal or topical drug delivery for a variety of drugs. Preliminary studies indicate that this solvent is practically nontoxic. When used internally, it is predicted that DMI will be metabolized to form isosorbide. It has been used successfully for the stable liquid formulation of aspirin [24], which is a classical formulation problem due to the instability of aspirin in various other solvents.

PHARMACEUTICAL IMPORTANCE OF DIANHYDROHEXITOLS

The mono- and dinitrate esters of isosorbide and isomannide are active NO-releasing drugs and widely used in the pharmaceutical industry as vasodilators. Isosorbide dinitrate (sold under the brand names Isordil® and Sorbitrate®) is widely used in various formulations and by different routes of administration as a basic vasodilator for the management of angina pectoris and congestive heart failure [25,26]. Many pharmaceutical preparations of these compounds are trade products.



isosorbide dinitrate

Isosorbide and isomannide have been explored as successful templates for RGD-mimetics (RGD is the single letter code for arginine-glycine-aspartate motif , which can be found in proteins of the extracellular matrix) in the development of integrin antagonists (integrins link the intracellular cytoskeleton of cells with the extracellular matrix by recognizing this RGD motif) [27] (**Figure 4**). These mimetics might be used as drugs against angiogenesis, inflammation and cancer mestastasis, since the RGD mimetics can inhibit cell attachment and consequently induce apoptosis.

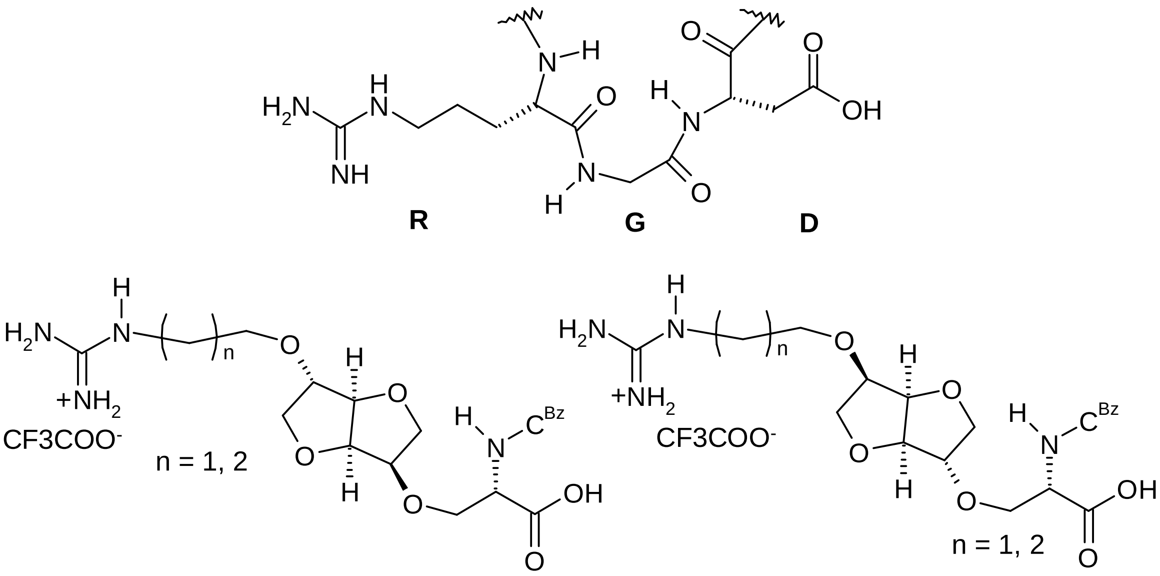


Figure 4: RGD-mimetics derived from isosorbide and isomannide

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