Biodegradable Polyglycol Succinates Used as Disposables

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ABSTRACT

The rapid development in the field of disposable polymers has brought about the important problem of their wastes and disposals. Although recycling is one way of using these wastes, but in some cases such as blood storage bags, the danger of contamination is a problem. Polyglycol succinates have been known for a long term for their use as biodegradable materials. It has been found that, in addition to their bioabsorbable character, polyglycol succinates are particularly well tolerated by the tissues in which they are implanted. Polyglycol succinates possess very good mechanical properties and they are insensitive to moisture. It was suggested that they can be used as biodegradable disposables due to their high mechanical properties as well as the ability to be adsorbed to the soil by the action of micro-organisms. A group of biodegradable polyesters, polyglycol succinates, were synthesized using polycondensation reaction with different diols. The biodegradation rate of these polymers was studied on thin films prepared from the polymer solution. The effects of different physical and chemical variables on the rate of their bioabsorption were also studied. Among all variables, it was shown that the pH of the soil and the chemical structure of the monomers used in the synthesis were the most important of all.

Key Words: biodegradable, polyglycol succinate, synthesis, soil burial, bioabsorption

INTRODUCTION

Polymer synthesis has grown rapidly in the research laboratories as well as in industry. The extended use of polymers as disposable materials in medicine and other applications has faced the researchers with the problem of their large volume of disposals. Recycling industry has eased the problem to some extent, but the danger of contamination, especially in the case of disposals from hospitals, made the scientists to investigate the possibility of synthesizing some biodegradable polymers.

Biodegradable polymeric systems have been used frequently in the development of advanced drug delivery systems. The use of biodegradable polymeric systems in controlled release of drug delivery is

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desirable, since the dosage forms will be degraded and eliminated from the body. This will avoid removal of the device from the body by surgery or other means when the device is no longer needed [1].

Biodegradable hydrogels have been used extensively in controlled drug delivery systems [2]. The poor mechanical properties played by these biodegradable polymers have limited their use as disposable devices. They possess very high compatibility in body environment and are, therefore, designed to be used extensively in many biomedical applications [3].

Recently, the term degradation or biodegradation, has become a key word in the development of new technologies not only for pharmaceutical and medical application but also for agricultural and environmental applications [4 and 5]. Degradability of polymers is relatively new, and no adequate definitions or test protocols exist. In reality everything degrades. The question is how fast it degrades. Poly-anhydrides or polyorthoesters can be hydrolyzed in a matter of hours, while polycarbonates may take many years to hydrolyze.

The world's growing concern about the waste disposals and the problem of large volume of polymeric materials used in everyday life, necessitates finding a wise solution to the persisting problem. The idea of replacing synthetic materials with disposable materials and, then, biodegradable disposable polymers is very young. It has been suggested that some disposable polymeric materials which should not be recycled for safety reasons, such as blood bags, syringes and the artificial artery used in dialysis, can be synthesized from poly(lactic acid), a biodegradable homopolymer of lactic acid (PLA) [6]. The material synthesized in this regard possesses very good mechanical and biodegradable properties but has not been tested in vivo.

Biodegradable polyglycolic acid (PGA) and copolymers of PLA/PGA were also synthesized in another study and their biodegradation rates were measured in vitro [7]. The in vivo studies in this respect should involve burying the polymer in a known soil environment and then measure the quantity remained after a defined period of time. In this work, a family of biodegradable polyglycol succinates were first synthesized and studied for their rate of biodegradation bearing in mind various factors affecting this degradation.

### The Concept of Biodegradation

With few exceptions, the common belief that polymers simply erode away like a slowly dissolving crystal while maintaining their initial strength and integrity in the residual mass is not correct. The polymers undergo four stages of biodegradation when inserted in the biological environment. These stages are summarized in Table 1, which show that biodegradation starts with the disruption of weak forces such as van der Waal's forces and hydrogen bonding ending to complete cleavage of the covalent bond in the backbone structure of the polymer. The last stage of biodegradation actually leads to complete solubilization of the whole polymer which is then easily absorbed into the living environment.

The biodegradation of materials has been estimated by chemicals in vitro and long term in vivo implantation tests [9]. It has been shown that in the case of homo-biodegradable polymers, the rate of biodegradation could be varied only by changing molecular weights [10]. For applications of biodegradable materials, a better control of the rate of in vivo degradation is needed to meet the specific requirements [11]. In principle, the use of copolymers with different composition offers a possibility to establish an optimal rate of biodegradation.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Structural bond changes</th>
</tr>
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<tbody>
<tr>
<td>Hydration</td>
<td>Disruption of van der Waal's forces and hydrogen bonds.</td>
</tr>
<tr>
<td>Loss of strength</td>
<td>Initial cleavage of backbone covalent bonds.</td>
</tr>
<tr>
<td>Loss of integrity</td>
<td>Further cleavage of covalent bonds to polymer molecular weight levels insufficient for mass coherence.</td>
</tr>
<tr>
<td>Loss of mass</td>
<td>Dissolution of low molecular weight species and phagocytosis of small fragments.</td>
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Table 1. Four stages of polymer biodegradation [8].
Polyglycol Succinates

Polyglycol succinates have been known for a long term for their use as a stationary phase in the gas chromatography of n-paraffins, fatty acid methyl esters, fatty alcohols and dicarboxylic acid methyl esters [12, 13]. The biodegradable character shown by these polyesters is unexpected because it is known that polyesters such as polyethylene glycol terephthalate are not resorbed by human or animal tissues [14, 15]. The structural similarity of these polyesters with polyglycol succinates shows that there must be more to their biodegradation character than merely their chemical composition.

It has been found that, in addition to their bioabsorbable character, polyglycol succinates are particularly well tolerated by the tissues in which they are implanted [15]. Polyglycol succinates possess very good mechanical properties and insensitivity to moisture. Their filaments are easy to handle and do not necessitate the use of special storage device. They have been used in many fields of medicine especially as filaments which are used as bioabsorbable sutures in the internal surgery [16]. They erode away during the healing period and leave no poisonous material.

Polyglycol succinates are polyesters of succinic acid which can be prepared by a polycondensation reaction of succinic acid with various length diols. They all have the following general formula:

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\left\langle \text{O} - \text{C} - (\text{CH}_2)_n - \text{C} - \text{OR} \right\rangle_	ext{n}
\end{align*}
\]

in which R is a linear or branched alkylene radical, e.g. ethylene glycol, butane-1,4 diol and hexane-1,6 diol.

Polyglycol succinates have been used as biodegradable materials in an attempt to microencapsulate insulin to be administrated orally [17]. Most of the research on polyglycol succinates have employed these polymers as well as PGA and PLA in the drug delivery systems [18, 19]. We suggested that, polyglycol succinates can be suitable as polymeric materials to be used as disposable devices, because the rate of their biodegradation is in the range of days [17] and the products of their degradation are not toxic to the micro-organisms which live in the soil [20].

The idea of using polyglycol succinates as biodegradable disposable came to our mind for many reasons including their high bioabsorbability, good mechanical properties and their ability to be made as thin films. Therefore, a group of polyglycol succinates were synthesized and we called them the green polyesters. Their biodegradation rates and many factors influencing the degradation were studied after they were buried for a known period of time in well defined conditions.

Our results proved that many factors affected the rate of anaerobic degradation of these polymer. The aerobic degradation rates which are influenced by oxygen as well as micro-organisms, were higher than the anaerobic degradation rates. Some other factors such as the polymer's chemical structures, which are determined by the diol length, pH of the soil and the physical shape of the polymer were examined in this work and the results are discussed in the appropriate section.

It was also suggested that other factors such as temperature, physical, biological, and chemical properties of the soil as well as the depth in which the polymer was buried will also affect the biodegradation rates. The type of micro-organisms whether they are aerobic or non-aerobic are determined by the soil environment and the depth in which the polymers are buried. In very deep garden soil it is less likely that aerobic degradation takes place as there are only very rare aerobic micro-organisms living in that depth. The existence of fresh air and oxygen are also very unlikely in the depths more than 50 cm. The studies on the degradation rates of similar polymers in the same sort of soil will, therefore, show a comparison between biodegradation in aerobic and non-aerobic conditions regardless of the type of soil.

Sources of Monomers and Reagents

The monomers (ethylene glycol, propane-1,3 diol, butane-1,4 diol, hexane-1,6 diol and diethyl succinate) were used as supplied by B.D.H. Chemicals. Catalysts (antimony trioxide and zinc acetate) supplied by B.D.H. Chemicals were used without further
purification. Chloroform was of S.L.R. purity and used without further purification. Methanol, as a solvent to reprecipitate the polymer, was also of S.L.R. purity and used as supplied without further purification. The environment used for in vivo biodegradation studies was a specified corner of the back garden with its natural micro-organisms.

EXPERIMENTAL

Synthesis of Polymers
In a typical experiment, a polymerization mixture consisting of 58 g of diethyl succinate, 45 g of butane-1,4 diol, 0.093 g of zinc acetate and 0.023 g of antimony trioxide were placed into a 250 mL split resin flask equipped with a mechanical stirrer, a nitrogen inlet tube, a thermometer and a condenser provided with a receiving container.

The contents of the flask were heated, using an isomantle, to 180 °C over a period of 45 min with stirring and under a stream of nitrogen. The conditions were maintained for 2 h. During this period, butanol was distilled over and collected in the receiver and weighed. The nitrogen bleed was then disconnected and the temperature was raised to 270 °C over a period of 2 h, and the apparatus was connected to a vacuum pump. The pressure was reduced to 0.1 mm Hg over a course of 50 min. These conditions were maintained for 7 h. During this period, the excess of butane-1,4 diol distilled over and was collected and weighed. The reaction mixture was then left to cool down. The solid light brown product was dissolved in 150 mL of chloroform.

The light brown solution was then added dropwise to 1500 mL of vigorously stirred methanol to reprecipitate the polymer. The product obtained was filtered off and dried at 45 °C in a vacuum oven. Other polyglycol succinates were also synthesized using a similar procedure with some slight variations. Melting points of the polymers were obtained using a Perkin-Elmer differential scanning calorimeter. A heating rate of 10 °C/min was used, and the melting point was conventionally taken as the point where the melting process was completed.

Biodegradation Studies
The films of 1–5 mm from the polyesters were prepared using 10% (w/v) solution of the polymer in chloroform and pouring it onto glass petri dishes to allow the solvent to evaporate slowly at room temperature. Then, they were annealed at 90 °C before being removed, for testing.

The samples were then weighed and buried in the depth of 20 cm in the corner of a garden. The films were taken out every 2 days, washed, dried and weighed carefully. The rate of anaerobic biodegradation was measured as the weight of the film remained during these periods in g/day (Figure 1).

RESULTS AND DISCUSSION

The effect of different factors on the rate of biodegradation were studied. Using different polymers synthesized from various diols condensed with succinic acid, the effect of length of the diol on the bioabsorption rate was examined. It was shown that other variables such as pH of the soil and the thickness of the polymer film have significant effects on the biodegradation of the polymer. The results are summarized in Figures 2–4.

Figure 2 shows that the rate of polymer bioabsorption depends on the thickness of the disposable film. The thicker the film the slower the biodegradation rate. This is predictable as the hydration process

![Figure 1. The bioabsorption rate of a typical polyglycol succinate.](image-url)
Film thickness (mm)

Figure 2. The effect of polymer thickness on the biodegradation rate.

The first step in biodegradation, Table 1) is easier in a thin film than a thicker polymer. The thickness was not made less than 1 mm as it was difficult to handle and weigh the polymer especially after some days during which some of its strength was lost due to different stages of biodegradation.

As it is evident from Figure 3 the length of the diol used is another important factor which affects the rate of polymer bioabsorption. The longer the diol used in the synthesis process the lower is the rate of biodegradation. This is because the structure of the polymer is simpler and, therefore, easier to hydrate, when a smaller diol is used in the polymer backbone.

Figure 4 shows the effect of the pH of the soil in which the disposable polymer is buried. It can be seen that in both acidic and alkaline pH the rate is highest when the pH is moderate. This can be due to the polymer deterioration in strong acidic or alkaline environments.

The results of studies on the biodegradation rate of polyethylene glycol succinate buried in a corner of the garden showed that rate was higher as the polymer was buried deeper in the soil (Figure 5).

This observation led us to the conclusion that there may be much more micro-organisms in deeper soils which with the moisture also help the biodegradation of the polymer. This conclusion is regardless of the type of soil in terms of physical conditions.

Figure 3. The effect of diol length on the biodegradation rate.

Figure 4. The effect of the pH of the soil on the rate of bioabsorption.

Figure 5. The effect of the depth of the soil in which the polymer is buried on the biodegradation rate of polyethylene glycol succinate.
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Figure 6. Comparison between the rate of aerobic and anaerobic biodegradation of polyethylene glycol succinate buried in the same garden as in Figure 5.

texture and chemical composition. These factors are left to a later study to be published soon.

However, it should be noted that aerobic degradation has a much higher rate than the anaerobic biodegradation and this is proved in Figure 6. It can be seen from this figure that the rate of biodegradation decreases when the polymer is buried in the soil deeper than 50 cm. This observation brings about the conclusion that oxygen helps the degradation and that the aerobic micro-organisms have a better ability for the biodegradation of the polymer.

In this research, the effect of some variables such as the type of soil and its micro-organisms, the temperature and shape of the disposable polymer on the bioabsorption rate were not examined. Some studies are underway to further examine all these factors as well as synthesizing another family of biodegradable polyesters and exploring their effectiveness.

CONCLUSION

Based on the results obtained from our study on this group of biodegradable polyesters, the following general conclusions could be made.

In this group of polyesters, the length of the diol is an important factor in determining the strength of the polymer, i.e. the rate of its biodegradation. Diols with less number of carbon atoms between the hydroxyl groups have a stronger backbone and degrade more slowly.

The thickness and possibly the physical shape of the biodegradable waste is also important and, as is expected the thin polymeric films degrade more rapidly. This problem can be overcome by crushing the waste disposal before burying them.

An alternative method to dispose wastes is by burning the wastes in an open air or in a closed furnace. The danger of this route is the thick and carcinogenic fumes which are produced especially from the burning of synthetic polymers. These fumes and gases are of a very complicated composition and there is no efficient way to absorb them safely.

The nature of the soil in terms of pH is important in the bioabsorption process of polyglycol succinates. In both highly acidic and alkaline pH the rate decreases. This is mainly due to the fact that nearly neutral environments allow the growth of more micro-organisms which enhance the biodegradation processes.

The depth of the soil in which the wastes are disposed determines the type and number of micro-organisms as well as the amount of oxygen available to help the biodegradation. In very deep grounds the biodegradation occurs very slowly. It can be concluded from this observation that the aerobic degradation of the polymer is more important than anaerobic biodegradation. This is beneficial as there is no need to dig very deep holes to dispose the wastes. In fact they can be thrown into natural holes in the ground and covered with at least 10 cm of soil.

The type of micro-organism is very important and needs to be studied further and the possibility to add some specific organisms to the soil to achieve the desired aim. This is under research in our laboratory and will be published soon.

REFERENCES


