

## 1 Nonproprietary Names

None adopted.

## 2 Synonyms

DL-PLA; DL-PLGA; *Lactel*; poly(lactic acid); poly(DL-lactic-co-glycolic acid); poly(DL-lactide); poly(DL-lactide-co-glycolide); *Purasorb*; *Resomer*; *Resomer Select*.

See also Table I.

## 3 Chemical Name and CAS Registry Number

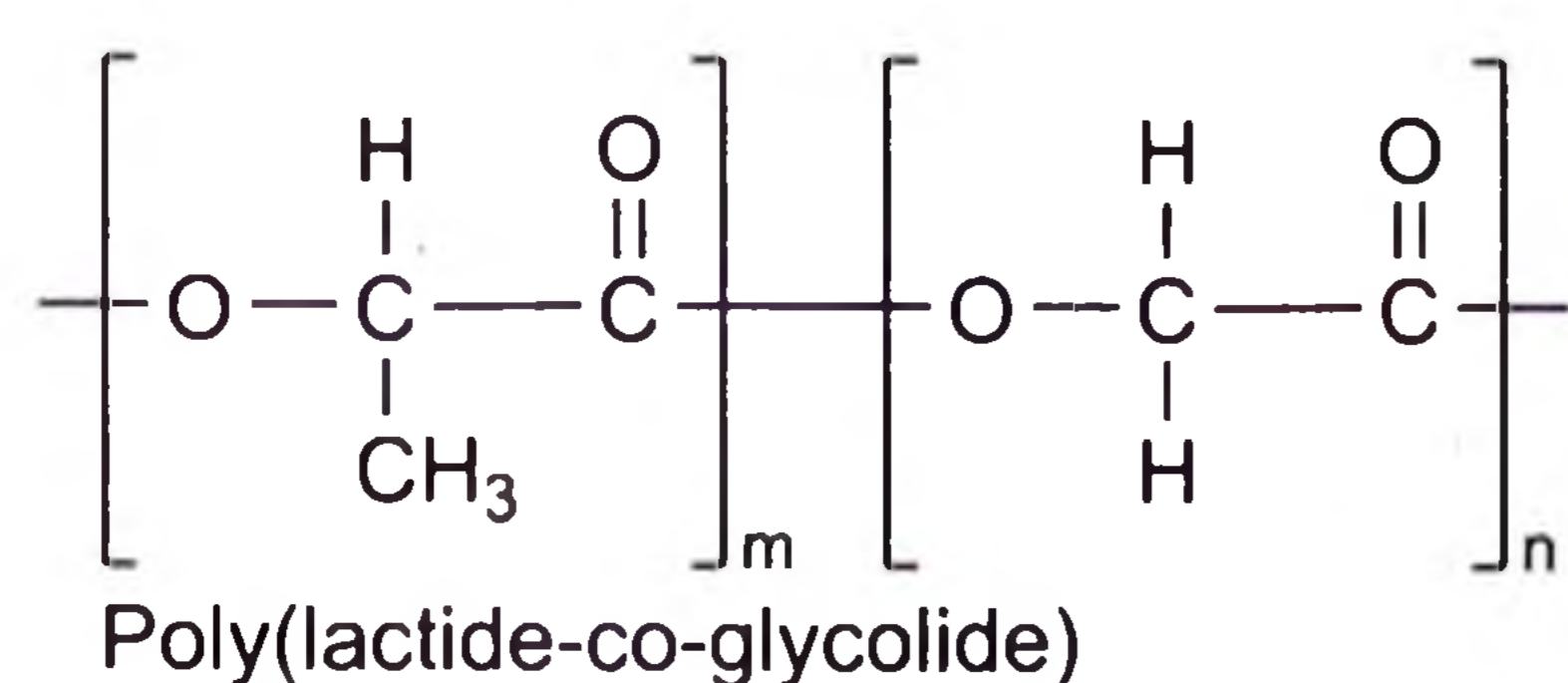
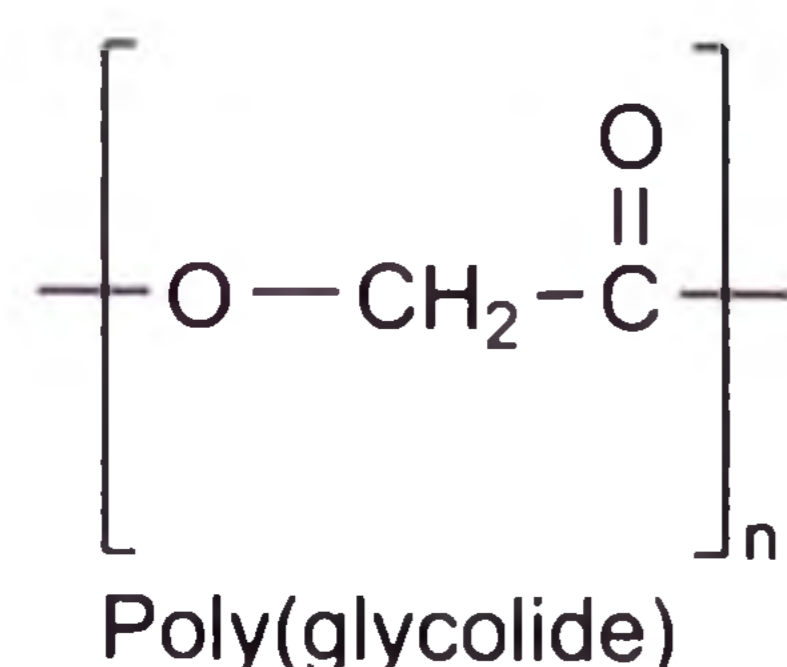
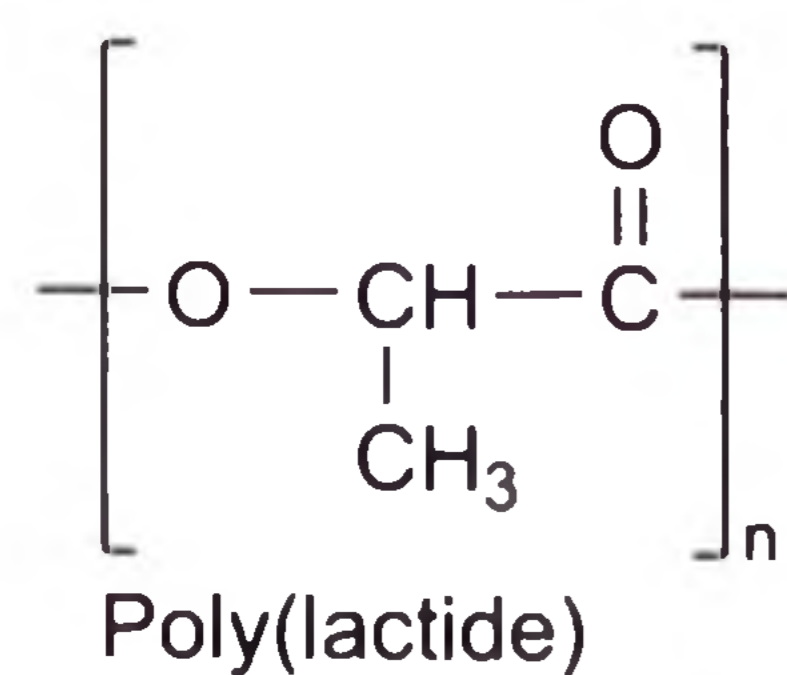
See Table I.

## 4 Empirical Formula and Molecular Weight

Aliphatic polyesters that have been approved for drug delivery are synthetic homopolymers or copolymers of lactic acid, glycolic acid, lactide and glycolide. Typically, the molecular weights of homopolymers and copolymers range from 2 000 to >100 000 Da.

Co-monomer ratios of lactic acid and glycolic acid (or lactide and glycolide) for poly(DL-lactide-co-glycolide) range from 85:15 to 50:50. Table I shows the generic and trade names of different commercially available aliphatic polyesters.

## 5 Structural Formula



## 6 Functional Category

Biocompatible material; biodegradable material; gelling agent; microencapsulating agent; modified-release agent.

## 7 Applications in Pharmaceutical Formulation or Technology

Aliphatic polyesters are of special interest in pharmaceutical formulations because they are generally sensitive to hydrolytic degradation.<sup>(1)</sup> Owing to their reputation as safe materials and their biodegradability, aliphatic polyesters are primarily used as biocompatible and biodegradable carriers in many types of sustained-release implantable or injectable drug-delivery systems for both human and veterinary use, such as *in situ* gels and microspheres.<sup>(2-4)</sup> Properties of the polymer, such as degradation and water uptake, can be controlled by modifying the end-group chemistry (either acid or ester):<sup>(5)</sup> see also Table I.

See also Section 18.

## 8 Description

Aliphatic polyesters occur as white to off-white or light gold solid powders, pellets or granules, and are almost odorless.

## 9 Pharmacopeial Specifications

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## 10 Typical Properties

For typical resorption duration, physicochemical and mechanical properties of selected aliphatic polyesters, see Tables II, III.

Polymer composition and crystallinity play important roles in the solubility of these aliphatic polyesters. The crystalline homopolymers of glycolide or glycolic acid are soluble only in strong solvents, such as hexafluoroisopropanol. The crystalline homopolymers of lactide or lactic acid also do not have good solubility in most organic solvents. However, amorphous polymers of DL-lactide or DL-lactic acid and copolymers of lactide or lactic acid with a low glycolide or glycolic acid content are soluble in many organic solvents (Table II). Aliphatic polyesters are slightly soluble or insoluble in water, methanol, ethylene glycol, heptane, and hexane.

## 11 Stability and Storage Conditions

The aliphatic polyesters are easily susceptible to hydrolysis in the presence of moisture. Hence, they should be packaged under high-purity dry nitrogen and stored at 5°C in airtight containers with desiccant, preferably refrigerated at -10°C or below. It is necessary to allow the polymers to reach room temperature in a dry environment before opening the container. After the original package has been opened, it is recommended to re-purge the package with high-purity dry nitrogen prior to resealing. Protect from sunlight and keep away from sources of heat.

## 12 Incompatibilities

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## 13 Method of Manufacture

Aliphatic polyesters are mainly synthesized via polycondensation of hydroxycarboxylic acids and catalytic ring-opening polymerization of lactones. Ring-opening polymerization is preferred because polyesters with high molecular weights and specific end groups can be produced.<sup>(6)</sup>

Enzymatic polymerization is an alternative method carried out under mild conditions avoiding the use of toxic reagents, with the possibility to recycle the catalyst. Regional and stereo selectivity of enzymes provides attractive possibilities for the direct synthesis of functional polyesters, avoiding the use of protected monomers. Block copolymers may also be synthesized using enzymatic polymerization. However, the major drawback of this method is the relatively low molecular weight of the polymers obtained.<sup>(2)</sup>

## 14 Safety

Poly(lactic acid) or poly(lactide) and poly(lactic-co-glycolic acid) or poly(lactide-co-glycolide), are used in parenteral pharmaceutical formulations and are biodegradable, biocompatible, and bioabsorbable materials. Their biodegradation products are nontoxic, noncarcinogenic, and nonteratogenic. In general, these polyesters exhibit very little hazard.