Aliphatic Polyesters

1 Nonproprietary Names

See Table I.

2 Synonyms

See Table I.

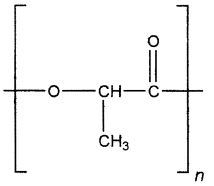
3 Chemical Name and CAS Registry Number

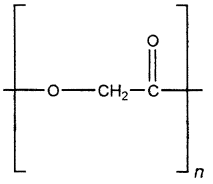
See Table I.

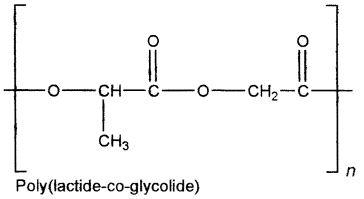
4 Empirical Formula Molecular Weight

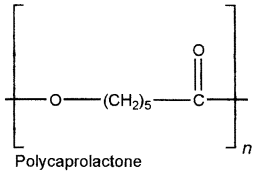
Aliphatic polyesters are synthetic homopolymers or copolymers of lactic acid, glycolic acid, and ε-hydroxycaproic acid. Typically, the molecular weights of homopolymers and copolymers range from 2000 to >100 000.

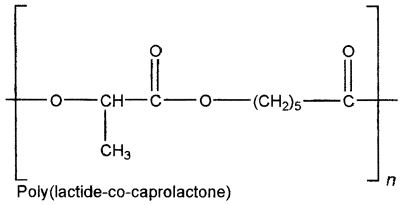
5 Structural Formula






Poly(lactide-co-glycolide)


Polycaprolactone


Poly(lactide-co-caprolactone)

6 Functional Category

Bioabsorbable, biocompatible, biodegradable material.

7 Applications in Pharmaceutical Formulation or Technology

Aliphatic polyesters are a group of synthesized, nontoxic, biodegradable polymers. In an aqueous environment, they undergo hydrolytic degradation, through cleavage of the ester linkages, into nontoxic hydroxycarboxylic acids. Aliphatic polyesters are eventually metabolized to carbon dioxide and water, via the citric acid cycle. Owing to their reputation as safe materials and their biodegradability, aliphatic polyesters are primarily used as biocompatible and biodegradable polymers for formulation of many types of implantable and injectable drug-delivery systems for both human and veterinary use. Examples of implantable drug delivery systems include rods, cylinders, tubing, films,[1] fibers,[2] pellets, and beads.[3] Examples of injectable drug-delivery systems include microcapsules,[4] microspheres,[5] nanoparticles, and liquid injectable controlled-release systems. The rate of biodegradation and drug-release characteristics from these systems formulated with the aliphatic polyesters can be controlled by changing the physicochemical properties of the polymers, such as crystallinity, hydrophobicity, monomer stereochemistry, copolymer ratio, and polymer molecular weight.

8 Description

Aliphatic polyesters are a group of synthesized homopolymers or copolymers. They are nontoxic and can easily be fabricated into a variety of novel devices, such as rods, screws, nails, and cylinders. The polymers are commercially available in varying molecular weights as both homopolymers and copolymers. Molecular weights of polyesters range from 2000 to greater than 100 000.

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

9 Pharmacopeial Specifications

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10 Typical Properties

For typical physical and mechanical properties of the aliphatic polyesters, *see* Table II.

Polymer composition and crystallinity play important roles in the solubility of these aliphatic polyesters. The crystalline homopolymers of glycolic acid are soluble only in strong solvents, such as hexafluoroisopropanol. The crystalline homopolymers of lactic acid also do not have good solubility in most organic solvents. However, amorphous polymers of DL-lactic acid and copolymers of lactic acid and glycolic acid with a low 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.

Table I: Chemical names and CAS registry numbers of the aliphatic polyesters.

Generic name	Composition (%)			Synonyms	Trade name	Manufacturer	CAS name	CAS number
	Lactide	Glycolide	Caprolactone					
Poly(D-lactide)	100	0	0	D-PLA	*Purasorb PD*	PURAC	(3*R*-cis)-3,6-Dimethyl-1,4-dioxane-2,5-dione homopolymer	[25038-75-9]
Poly(L-lactide)	100	0	0	L-PLA	*Lactel L-PLA*	BPI	Propanoic acid, 2-hydroxy-, homopolymer	[26161-42-2]
					Medisorb 100 L	Alkermes		
					Purasorb PL	PURAC		
					Resomer L 206, 207, 209, 210, 214	BI		
Poly(DL-lactide)	100	0	0	DL-PLA	*Lactel DL-PLA*	BPI	Propanoic acid, 2-hydroxy-, homopolymer	[34346-01-5]
					Medisorb 100 DL	Alkermes		
					Pursasorb PDL	PURAC		
					Resomer R 202, 202H, 203, 206, 207, 208	BI		
Poly(glycolide)	0	100	0	PGA	*Lactel PGA*	BPI	Acetic acid, hydroxy-, homopolymer	[34346-01-5]
					Medisorb 100 PGA	Alkermes		
					Purasorb PG	PURAC		
					Resomer G 205	BI		
Poly(L-lactide-co-glycolide)	75	25	0	L-PLGA (75 : 25)	*Pursasorb PLG*	PURAC	1,4-Dioxane-2,5-dione, polymer with (3*S*-cis)-3,6-dimethyl-1,4-dioxane-2,5-dione	[30846-39-0]
Poly(L-lactide-co-glycolide)	50	50	0	L-PLGA (50 : 50)	*Purasorb PLG*	PURAC	1,4-Dioxane-2,5-dione,polymer with (3*S*-cis)-3,6-dimethyl-1,4-dioxane-2,5-dione	[30846-39-0]
Poly(DL-lactide-co-glycolide)	85	15	0	Polyglactin; DL-PLGA (85:15)	*Lactel 8515 DL-PLGA*	BPI	Propanoic acid, 2-hydroxypolymer with hydroxyacetic acid	[26780-50-7]
					Medisorb 8515 DL	Alkermes		
					Resomer RG 858	BI		
Poly(DL-lactide-co-glycolide)	75	25	0	Polyglactin; DL-PLGA (75 : 25)	*Lactel 7525 DL-PLGA*	BPI	Propanoic acid, 2-hydroxypolymer with hydroxyacetic acid	[26780-50-7]
					Pursasorb PDLG	PURAC		
					Resomer RG 752, 755, 756	BI		
Poly(DL-lactide-co-glycolide)	65	35	0	Polyglactin; DL-PLGA (65 : 35)	*Lactel 6535 DL-PLGA*	BPI	Propanoic acid, 2-hydroxypolymer with hydroxyacetic acid	[26780-50-7]
Poly(DL-lactide-co-glycolide)	50	50	0	Polyglactin; DL-PLGA (50 : 50)	*Lactel 5050 DL-PLGA*	BPI	Propanoic acid, 2-hydroxypolymer with hydroxyacetic acid	[26780-50-7]
					Medisorb 5050 DL	Alkermes		
					Purasorb PDLG	PURAC		
					Resomer RG 502, 502H, 503, 503H, 504, 504H, 505, 506	BI		
Poly-ε-caprolactone	0	0	100	PCL	*Lactel PCL*	BPI	2-Oxepanone, homopolymer	[24980-41-4]
Poly(DL-lactide-co-caprolactone)	75	0	25	DL-PLCL (75 : 25)	*Lactel 7525 DL-PLCL*	BPI	1,4-Dioxane-2,5-dione,3,6-dimethyl-, polymer with 2-oxepanone	[70524-20-8]
Poly(DL-lactide-co-caprolactone)	25	0	75	DL-PLCL (25 : 75)	*Lactel 2575 DL-PLCL*	BPI	1,4-Dioxane-2,5-dione,3,6-dimethyl-, polymer with 2-oxepanone	[70524-20-8]

Alkermes, Alkermes Inc.; BI, Boehringer Ingelheim; BPI, Birmingham Polymers Inc.; PURAC, PURAC America.

Table II: Typical physical and mechanical properties of the aliphatic polyesters.[a]

	50/50 DL-PLG	65/35 DL-PLG	75/25 DL-PLG	85/15 DL-PLG	DL-PLA	L-PLA	PGA	PCL
Molecular weight	40 000–100 000	40 000–100 000	40 000–100 000	40 000–100 000	40 000–100 000	>100 000	>100 000	80–150 000
Inherent viscosity (mPa s)	0.5–0.8[b]	0.5–0.8[b]	0.5–0.8[c]	0.5–0.8[c]	0.5–0.8[c]	0.9–1.2[c]	1.1–1.4[b]	0.7–1.3[c]
Melting point (°C)	Amorphous	Amorphous	Amorphous	Amorphous	Amorphous	173–178	225–230	58–63
Glass transition (°C)	45–50	45–50	50–55	50–55	55–60	60–65	35–40	–65 to –60
Color	White to light gold	White to light gold	White to light gold	White to light gold	White	White	Light tan	White
Solubility[d]	$MeCl_2$, THF, EtOAc, C_3H_6O, $CHCl_3$	$MeCl_2$, THF, EtOAc, C_3H_6O, $CHCl_3$	$MeCl_2$, THF, EtOAc, C_3H_6O, $CHCl_3$	$MeCl_2$, THF, EtOAc, C_3H_6O, $CHCl_3$,	$MeCl_2$, THF, EtOAc, C_3H_6O, $CHCl_3$	$MeCl_2$, $CHCl_3$	HFIP, HFASH	$MeCl_2$, $CHCl_3$, C_3H_6O
Specific gravity	1.34	1.30	1.30	1.27	1.25	1.24	1.53	1.11
Tensile strength (psi)	6000–8000	6000–8000	6000–8000	6000–8000	4000–6000	8000–12 000	10 000+	3000–5000
Elongation (%)	3–10	3–10	3–10	3–10	3–10	5–10	15–20	300–500
Modulus (psi)	$2–4 \times 10^5$	$2–4 \times 10^5$	$2–4 \times 10^5$	$2–4 \times 10^5$	$2–4 \times 10^5$	$4–6 \times 10^5$	1×10^6	$3–5 \times 10^4$

Note: DL-PLG: DL-poly(lactic-co-glycolic acid); DL-PLA: DL-polylactic acid; L-PLA: L-polylactic acid; PGA: polyglycolic acid; PCL: poly-ε-caprolactone.

[a] Specifications obtained from Birmingham Polymers, Inc.

[b] (HFIP) hexafluoroisopropanol.

[c] ($CHCl_3$) chloroform.

[d] Partial listing only: $MeCl_2$, methylene chloride; THF, tetrahydrofuran; EtOAc, ethyl acetate; HFIP, hexafluoroisopropanol; HFASH, hexafluoroacetone sesquihydrate; C_3H_6O, acetone.

11 Stability and Storage Conditions

The aliphatic polyesters are easily susceptible to hydrolysis in the presence of moisture. Hence, they should be properly stored, preferably refrigerated at below 0°C. It is necessary to allow the polymers to reach room temperature 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.

12 Incompatibilities

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13 Method of Manufacture

Generally, aliphatic polyesters can be synthesized via polycondensation of hydroxycarboxylic acids and catalytic ring-opening polymerization of lactones. Ring-opening polymerization is preferred because polyesters with high molecular weights can be produced. Moreover, the dehydration of hydroxycarboxylic acids to form lactones does not have to be carried to a high degree of completion. Lactones can easily be purified owing to the differences of their physical and chemical properties from those of the corresponding hydroxycarboxylic acid.

14 Safety

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

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Contact with eyes, skin, and clothing, and breathing the dust of the polymers should be avoided. Aliphatic polyesters produce acid materials such as hydroxyacetic and/or lactic acid in the presence of moisture; thus, contact with materials that will react with acids, especially in moist conditions, should be avoided.

16 Regulatory Status

GRAS listed.

17 Related Substances

Lactic acid.

18 Comments

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19 Specific References

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21 Authors

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