PAH polyanhydride

PARAMETER	UNIT	VALUE	REFERENCES
GENERAL			
Common name	-	polyanhydride	
IUPAC name	-	e.g., poly(oxydecanedioyl)	
CAS name	-	poly[oxy(1,6-dioxo-1,6-hexanediyl)] (adipic); poly[oxy(1,10-dioxo-1,10-decanediyl)] (sebacic); poly[oxy(1,9-dioxo-1,9-nonanediyl)] and 2,10-oxecanedione, homopolymer (azelaic)	
Acronym	-	PAH	
CAS number	-	26913-47-3 (sebacic polyanhydride); 26968-29-6 (adipic polyanhydride); 26968-31-0 and 27306-28-1 (azelaic polyanhydride)	
HISTORY			
Person to discover	-	Bucher and Slade; Carothers & Hill; Rosen, Wnek, Linhardt, Langer	Jain, J P; Chirkara, D; Kumar, N, Expert Opin. Drug Deliv., 5, 8, 889-907, 2008; Carothers, W H, US Patent 2,071,250, DuPont, Feb. 16, 1937.
Date	-	1909; 1930-32; 1983	
Details	-	first report on synthesis of aromatic polyanhydride (1909); aliphatic polyanhydrides were reported in 1930-1932; in 1983 polyanhydrides were studied for drug delivery	
SYNTHESIS			
Monomer(s) structure	-	acids: 5-(p-carboxyphenoxy) valeric, 8-(p-carboxyphenoxy) octanoic, 1,3-bis(p-carboxyphenoxy) propane,1,6-bis(p-carboxyphenoxy) hexane, 1,6-bis(o-carboxyphenoxy) hexane, adipic, azelaic, dodecanedicarboxylic, dodecanedioic, fumaric, isophthalic, p-carboxyphenoxy acetic, pimelic, sebacic, suberic, terephthalic; other: erucic acid dimer, ricinoleic acid maleate, ricinoleic acid succinate, 12-hydroxystearic acid succinate; photopolymerizable monomers, e.g., methacrylated sebacic acid	Goepferich, A; Tessmar, J, Adv. Drug Delivery Rev., 54, 911-32, 2002; Jain, J P; Chirkara, D; Kumar, N, Expert Opin. Drug Deliv., 5, 8, 889-907, 2008.
Monomer ratio	-	20/80 to 80/20	Kipper, M J; Hou, S-S; Seifert, S; Thiyagarajan, P; Schmidt-Rohr, K; Narashimhan, B, Macromolecules, 38, 8468-72, 2005.
Method of synthesis	-	polyanhydrides can be prepared by melt condensation polymerization in which dicarboxylic acid monomer reacts with excess of acetic anhydride	
Temperature of polymerization	^oC	150-200	
Catalyst	-	cadmium acetate	
Propagation rate constant	s^{-1}	0.002-0.077	Young, J S; Gonzalea, K D; Anseth, K S, Biomaterials, 21, 1181-88, 2000.
Number average molecular weight, M_n	dalton, g/mol, amu	10,000-15,000 (microspheres)	
Mass average molecular weight, M_w	dalton, g/mol, amu	1,200-5,000 (commercial); 19,000-75,000 (micropsheres); 10,000-65,000 (experimental)	
Polydispersity, M_w/M_n	-	2-4.9 (microspheres); 1.2-2.2 (experimental)	
Radius of gyration	nm	1.51-2.27 (sebacic)	Kipper, M J; Hou, S-S; Seifert, S; Thiyagarajan, P; Schmidt-Rohr, K; Narashimhan, B, Macromolecules, 38, 8468-72, 2005.

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STRUCTURE			
Crystallinity	%	40-66	Goepferich, A; Tessmar, J, Adv. Drug Delivery Rev., 54, 911-31, 2002; Mathiowitz, E; Amato, C; Dor, P; Langer, R, Polymer, 31, 547-55, 1990.
COMMERCIAL POLYMERS			
Some manufacturers	-	Chevron Phillips; MGI Pharma	
Trade names	-	PA-18; Gliadel	
PHYSICAL PROPERTIES			
Density at 20°C	g cm^{-3}	0.97-1.07	
Color	-	white	
Melting temperature, DSC	°C	50-90 (aliphatic); >100 (up to 240) (aromatic)	
Erosion rate		70% in 48 h (short chain aliphatic); 20% in 48 (long chain aliphatic); 5% in 17 days (aromatic)	Goepferich, A; Tessmar, J, Adv. Drug Delivery Rev., 54, 911-31, 2002.
Decomposition temperature	°C	195-322	
Storage temperature	°C	-12	deRonde, B M; Carbone, A L; Uhrich, K, Polym. Deg. Stab., 95, 1778-82, 2010.
Glass transition temperature	°C	41-65	Jaszcz, K; Lukaszczyk, J, Reactive Functional Polym., 70, 630-38, 2010.
Long term service temperature	°C	150	
Heat deflection temperature at 0.45 MPa	°C	39	
Contact angle of water, 20°C	degree	69-71.5	
MECHANICAL & RHEOLOGICAL PROPERTIES			
Tensile strength	MPa	35 (azelaic polyanhydride)	
Tensile modulus	MPa	640-1,400 (crosslinked); 800-2,100 (tricarballylic acid for orthopedic applications)	Muggli, D S; Burkoth, A K; Anseth, K S, J. Biomed. Mater. Res., 46, 271-78, 1999; Young, J S; Gonzalea, K D; Anseth, K S, Biomaterials, 21, 1181-88, 2000.
Elongation	%	14.9 (azelaic polyanhydride)	
Compressive strength	MPa	0.0018-0.121; 32-40 (crosslinked)	Muggli, D S; Burkoth, A K; Anseth, K S, J. Biomed. Mater. Res., 46, 271-78, 1999.
Young's modulus	MPa	1.3	Gunatillake, P; Mayadunne, R; Adhikari, R, Biotech. Ann. Rev., 12, 301-47, 2006.
Shore D hardness	-	65-75 (azelaic polyanhydride)	
Intrinsic viscosity, 25°C	dl g^{-1}	0.3	
Mooney viscosity	-		
Melt viscosity, shear rate=1000 s^{-1}, 60°C	Pa s	800-1,000	
CHEMICAL RESISTANCE			
Alcohols	-	poor (reaction of esterification)	
Alkalis	-	poor	
Aromatic hydrocarbons	-	poor	

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PARAMETER	UNIT	VALUE	REFERENCES
Esters	-	poor	
Halogenated hydrocarbons	-	poor	
Ketones	-	poor	
Good solvent	-	acetone, benzene, carbon tetrachloride, 1,2-dichloroethane, ethyl acetate, MIK, sodium and potassium hydroxides aqueous solutions	
Non-solvent	-	ethanol, methanol	
FLAMMABILITY			
Ignition temperature	°C	104-302	
BIODEGRADATION			
Typical biodegradants	-	hydrolysis of anhydride linkage causes surface erosion degradation	Williams, D F; Zhong, S P, Int. Biodet. Biodeg., 34, 2, 95-130, 1994; Lucas, N; Bienaime, C; Belloy, C; Queneudec, M; Silvestre, F; Nava-Saucedo, J-E, Chemosphere, 73, 429-42, 2008.
Stabilizers	-	generally not required in this biocompatible polymer	
TOXICITY			
NFPA: Health, Flammability, Reactivity rating	-	1-3/0-1/0	
Carcinogenic effect	-	not listed by ACGIH, NIOSH, NTP	
Oral rat, LD_{50}	mg kg^{-1}	>8,000	
Skin rabbit, LD_{50}	mg kg^{-1}	>2,000	
ENVIRONMENTAL IMPACT			
Aquatic toxicity, *Daphnia magna*, LC_{50}, 48 h	mg l^{-1}	>100	
PROCESSING			
Typical processing methods	-	coating, compounding, forming, spraying	
Applications	-	adjuvants, bone replacement, controlled drug delivery, corrosion protection, chemotherapy, curing agent, implants (e.g., antibiotic delivery), microspheres (protein delivery), paper, vaccine delivery	
Outstanding properties	-	biocompatible, bioerodible, easily metabolized	
BLENDS			
Suitable polymers	-	PEG, PLA	
ANALYSIS			
FTIR (wavenumber-assignment)	cm^{-1}/-	C=C – 1640; anhydride double peak – 1810 and 1740	Young, J S; Gonzalea, K D; Anseth, K S, Biomaterials, 21, 1181-88, 2000.
Raman (wavenumber-assignment)	cm^{-1}/-	PSA – 1739, 1803; P(CPP) – 1712, 1764	Kumar, N; Langer, R S; Domb, A J; Adv. Drug Delivery Rev., 54, 889-910, 2002.
x-ray diffraction peaks	degree	17, 18-28 (four peaks)	Gopferich, A, Biomaterials, 18, 397-403, 1997.