

Chapter 2

Degradation Process

Keywords Degradation mechanism • Hydrolytic degradation • Autocatalytic degradation • Bulk erosion • Surface erosion • Strength and mass loss profile • Critical device dimension • Hydrolysis

2.1 Degradation Mechanism for Bioresorbable Polymers

A typical resorption profile of a material consists of four steps, namely water sorption, reduction of mechanical properties, reduction of molar mass, and finally complete loss of weight, as shown in (Fig. 2.1) [1]. Initially, water and/or biological fluids diffuse into the material, followed by a reduction in the mechanical properties. Loss in strength and modulus is initially due to the plasticizing effect of the fluids and later due to the reduction in molar mass. Change in shape and weight loss are the final stages before the material is completely resorbed [2].

Different resorbable polymers have different strength and mass loss profiles. However, all of them have one common characteristic, i.e., strength loss always occurs much earlier than mass loss. Initially, hydrolysis takes place in the amorphous regions of the polymer, converting long polymer chains into shorter fragments. This causes a reduction in molecular weight without a loss in physical properties as the matrix is still held together by the crystalline regions. Reduction in molecular weight is soon followed by a reduction in physical and mechanical properties as more and more chains are converted to smaller fragments. At the later stages, the fragments are metabolized and converted to oligomers which are either absorbed or excreted by the body. The metabolization of the fragments results in a rapid mass loss for the polymer [3, 4].

The process of bioresorption can be initiated by any of the following four ways:

Fig. 2.1 Typical changes in the properties during bioresorption of a material [2]

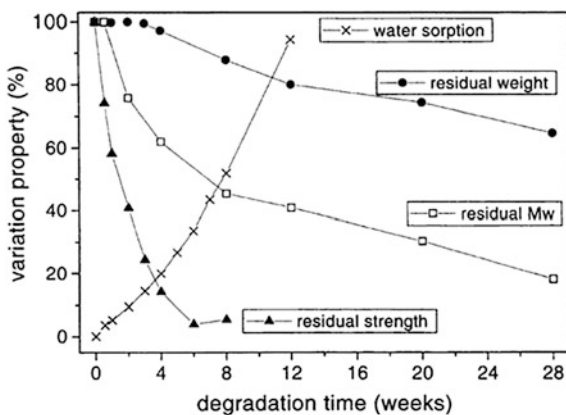
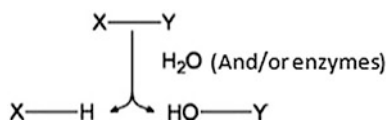


Fig. 2.2 Hydrolysis of a chemical bond



1. **Solubilization** (e.g., dextran, polyvinyl alcohol, and polyethylene oxide);
2. **Ionization followed by solubilization** (e.g., polyacrylic acid and polyvinyl acetate);
3. **Enzymatically catalyzed hydrolysis** (e.g., polysaccharides and polyamides);
4. **Simple hydrolysis** (e.g., aliphatic polyesters).

Simple hydrolysis and enzymatically induced hydrolysis are the two main mechanisms for bioresorption of various resorbable implantable materials. Both the mechanisms involve cleavage of bonds that are susceptible to hydrolysis in the polymer backbone, causing fragmentation of the whole polymeric structure and producing low molecular weight oligomers that can be absorbed or excreted by the body, as shown in Fig. (2.2).

2.2 Bulk Erosion Versus Surface Erosion

The resorption process of a biomaterial is also classified according to its erosion mechanism [5]. Bulk erosion is the mechanism when water diffuses rapidly into a polymer structure, leading to hydrolysis. The subsequent mass loss then occurs throughout the bulk of the material, as shown in (Fig. 2.3c). In this case, the rate of diffusion of water into the substrate is higher than the rate of hydrolysis. And as a result, the water that penetrates the substrate leads to hydrolysis from the inside out. A characteristic behavior of bulk eroding polymers is the sudden and rapid loss of strength and structural integrity as the resorption continues over time.

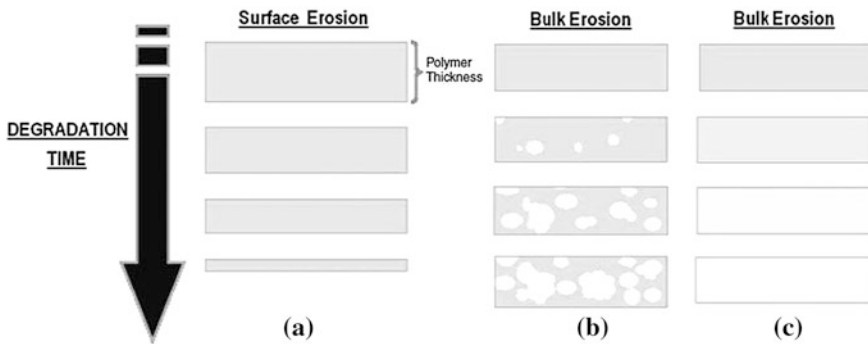


Fig. 2.3 Schematic illustration of erosion mechanisms: **a** surface erosion, **b** bulk erosion with autocatalysis, and **c** bulk erosion without autocatalysis [10]

Another mechanism is surface erosion, in which the mass loss occurs at the water/implant interface, causing the implant to resorb from its outer surface toward its center while maintaining its bulk integrity. This is sometimes referred to as ‘device thinning,’ as shown in (Fig. 2.3a). In this case, the rate of hydrolysis is higher than the rate of diffusion of water. Most of the enzymatically resorbable polymers show surface erosion. Surface-eroding polymers have a better ability to achieve zero-order release kinetics and are therefore ideal candidates for developing drug delivery devices [6].

It has been proposed that all resorbable polymers can undergo both surface erosion and bulk erosion. The option followed in a particular situation is governed not only by the rate of hydrolysis of the functional groups in the backbone chain and the rate of diffusion of water inside the matrix, but also by the dimensions of the matrix. A critical device dimension (L_{critical}) can be calculated for each resorbable polymer. If the thickness of a matrix is larger than L_{critical} , then it will undergo surface erosion. However, if it is smaller, then bulk erosion will occur [7]. L_{critical} values for some of the resorbable polymers are given in Table 2.1.

Another factor that complicates the resorption behavior of resorbable polymers is the phenomenon called autocatalytic degradation [8]. Autocatalysis occurs when the reaction product is itself the catalyst for the same reaction. In the case of bulk eroding polymers, the oligomeric hydrolysis products (usually carboxylic and other acids) are retained within the material, causing a localized decrease in pH which accelerates the rate of degradation [5]. As a result of this self-catalyzed hydrolysis, hollow structures are formed within the polymer, which leads to a rapid deterioration of the mechanical properties and sudden loss of structural integrity, as shown in (Fig. 2.3b). For example, in the case of poly(lactide) (PLA), when the thickness of the substrate is larger than 2 mm, the entrapment and accumulation of acidic oligomers and monomer result in autocatalytic degradation [9]. It should be noted that even though polymers such as PLA and poly(lactide-co-glycolide) (PLGA) are being widely studied as scaffold materials for tissue regeneration, the by-products and the acidic condition generated by the rapid autocatalytic

Table 2.1 Critical thickness (L_{critical}) values for selected resorbable polymers above which the hydrolytic resorption mechanism changes from bulk erosion to surface erosion [7]

Polymer	L_{critical}
Poly(anhydride)	75 μm
Poly(ketal)	0.4 mm
Poly(ortho esters)	0.6 mm
Poly(acetal)	2.4 cm
Poly(ϵ -caprolactone)	1.3 cm
Poly(α -hydroxy esters) (PLA)	7.4 cm
Poly(amides)	13.4 m

degradation of these polymers might be detrimental for the growth of certain cell lines. The effect of an autocatalytic degradation mechanism on the growth of cells should be considered when selecting the resorbable scaffold material.

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