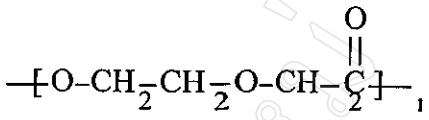
CHAPTER 6

DISCUSSION AND CONCLUSIONS

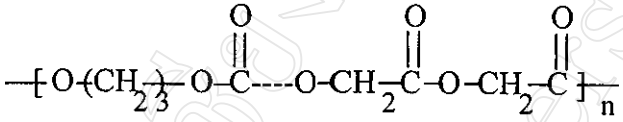
6.1 Property Changes from *In Vitro* Biodegradation

The weight and tensile strength changes in the MONOCRYL, MAXON, PDS II and PLCG samples during the *in vitro* biodegradation are shown in Fig. 5.2 and 5.7 respectively. As expected, it was found that weight retention and tensile strength of the PLCG fiber and the three commercial sutures decreased with hydrolysis time. On the basis of these results, an insight into the biodegradation mechanism is provided.

The differences in the property loss-time profiles of the PLCG fiber and the three commercial sutures demonstrate the sensitivity of biodegradability to even slight changes in chemical microstructure and semi-crystalline morphology. MONOCRYL, MAXON and PLCG samples are copolymers of glycolide, which is more vulnerable to hydrolysis than p-dioxanone (the monomer of PDS II), thus during the *in vitro* experiments they lose mass and tensile properties faster than PDS II. Since the composition of glycolide in MONOCRYL is higher than that in MAXON, consequently MONOCRYL shows a higher reduction rate in mass and tensile properties. Also, PDS II is a genuine homopolymer which means that it has a more regular structure than the rest and can therefore crystallize more readily. This would also contribute to its slower degradation rate.

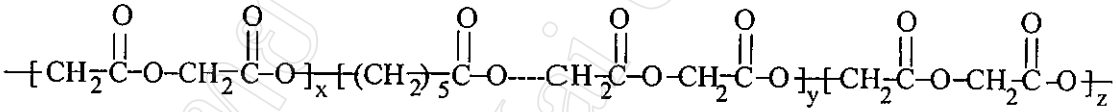


PDS II



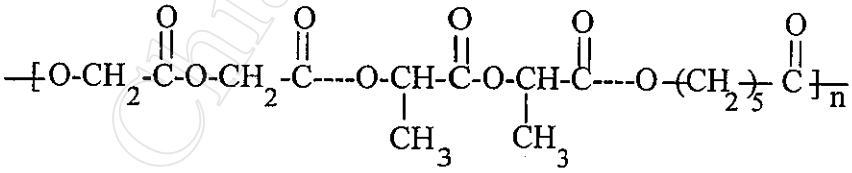
MAXON

(Glycolide : Trimethylene carbonate ≈ 67 : 33 mol%)



MONOCRYL

(Glycolide : ε-caprolactone ≈ 75 : 25 mol%)



Poly ((L-lactide)-*ran*-(ε-caprolacone)-*ran*-glycolide): PLCG

(L-lactide : ε-caprolactone : glycolide ≈ 70 : 20 : 10 mol%)

Although chemical microstructure is the dominant factor for hydrolytic degradation, matrix morphology (%crystallinity and crystalline orientation) is also important [19]. Hollinger [12] reported that the amorphous polyesters degrade faster than semi-crystalline polyester. This is because of the amorphous phase of the polymer is much more accessible to water than crystalline phase. In this research project, it was believed that the PLCG fiber should have much more structural irregularity than the 3 commercial sutures, as seen in the lowest heat of fusion, as shown in Table 5.6. Consequently, the PLCG fiber degraded faster than PDS II and MAXON and was comparable to the MONOCRYL sutures.

In all cases, the onset of weight loss occurred some time after the onset of tensile strength loss. The significant delay in mass degradation is a universal phenomenon for the synthetic absorbable sutures [12]. Hydrolytic degradation starts in the amorphous regions, as the tie-chain segments, free chain ends and chain folds in these regions degrade into fragments. The scissions of tie-chain segments would result in the loss of tensile breaking strength. As the degradation proceed, the size of the fragments reaches the stage where they can be dissolved into the buffer medium. This dissolution removes the fragments from the amorphous regions and loss of material results. Because the percent of tie-chain segments is relatively low and depends on the molecular weight and fiber spinning conditions, these synthetic absorbable sutures would lose most of their strength without significant mass loss.

From Figs. 5.16-5.19, it was found that the fracture surfaces of all of the samples showed evidence of ductile rather brittle fracture after *in vitro* hydrolysis. Ductile fracture characterized by failure at relative high strain with rough fracture surfaces. This is in contrast to brittle fracture surfaces which tend to be much smoother in appearance [20]. Ductile fracture is as would be expected since the fibers are all above their glass transition temperatures, T_g, and are therefore in their so-called "rubbery" states. This enables the samples to stretch more under tensile stress due to their inherent flexibility.

Fracture mechanics is a complex subject and is beyond the scope of this project. However, taking a simplified view, the cracking formation in PLCG sample does suggested that there are internal stress present inside the samples from the processing (hot-drawing and annealing) operations. These stresses and the chain hydrolysis mechanism combine to induce crack formation [19]. This opens up an interesting further study which should form the subject of a future project.

From Fig. 5.12, it was found that the melting point for MONOCRYL and MAXON during the *in vitro* studies decreased sharply after 3 and 10 weeks respectively. Thus, hydrolysis had no significant effect on the crystal structure of MONOCRYL and MAXON up to 3 and 10 weeks respectively. Before 3 weeks (for MONOCRYL) and 10 weeks (for MAXON) the hydrolysis had destroyed the tie-chain segments in the amorphous regions, resulting in decreasing in %tensile strength retention. Up to 3 and 10 weeks for MONOCRYL and MAXON respectively, the amorphous regions progressively decreased in molecular weight until the %tensile strength retention decreased toward to zero. Therefore, most of the hydrolytic chain scission during the first 3 and 10 weeks for MONOCRYL and MAXON respectively, was believed to occur in the noncrystalline regions. At the later stage of hydrolysis (after 3 and 10 weeks for MONOCRYL and MAXON respectively), most of hydrolytic chain scission occurred in the crystalline regions and gradually destroyed this regions, resulting in significantly decrease in melting point.

However, PDS II doesn't show any significantly decrease in melting point within 30 weeks of *in vitro* biodegradaion.

The data in Fig. 5.13 indicate clearly that the time where the maximium heat of fusion locates varies with the type of suture materials. The position of the peak could be used as an indicator to predict the rate of hydrolytic degradation [12]. From the weight loss and tensile strength profiles, it is suggested that MONOCRYL suture degrade faster than MAXON suture. This agree with the data obtained from Fig. 5.13. The MONOCRYL suture has the maximium heat of fusion appearing at 9 weeks of hydrolysis, while MAXON suture locate at 14 weeks.

The molecular weight reduction by *in vitro* hydrolysis of PLCG fibers is shown in Fig. 5.15 as a function of immersion time. It is apparent that the reduction rate of the molecular weight is very similar to that of the tensile strength shown in Fig. 5.7. In contrast to the change in strength and molecular weight with hydrolysis time, PLCG fibers exhibited slower reduction rate for their weight during hydrolysis (shown in Fig. 5.2). No significant weight change was noticed, at least within 5 weeks of hydrolysis. This must be because the low molecular weight fragments, formed as a results of hydrolysis, are still unable to diffuse out of the degrading matrix. This is presumably due to the fact that they are still too large compared with the small water molecules which can easily diffuse in [3].

6.2 A Mechanistic View of The Biodegradation Process

In vitro testing under conditions designed to simulate various aspects of the human body can provide useful and often quite accurate indications of the rate at which biodegradation will occur in the physiological environment. This is especially true of **simple hydrolysis** reactions in which agents such as enzymes and bacteria are not specifically required for catalysis, although they may have an effect.

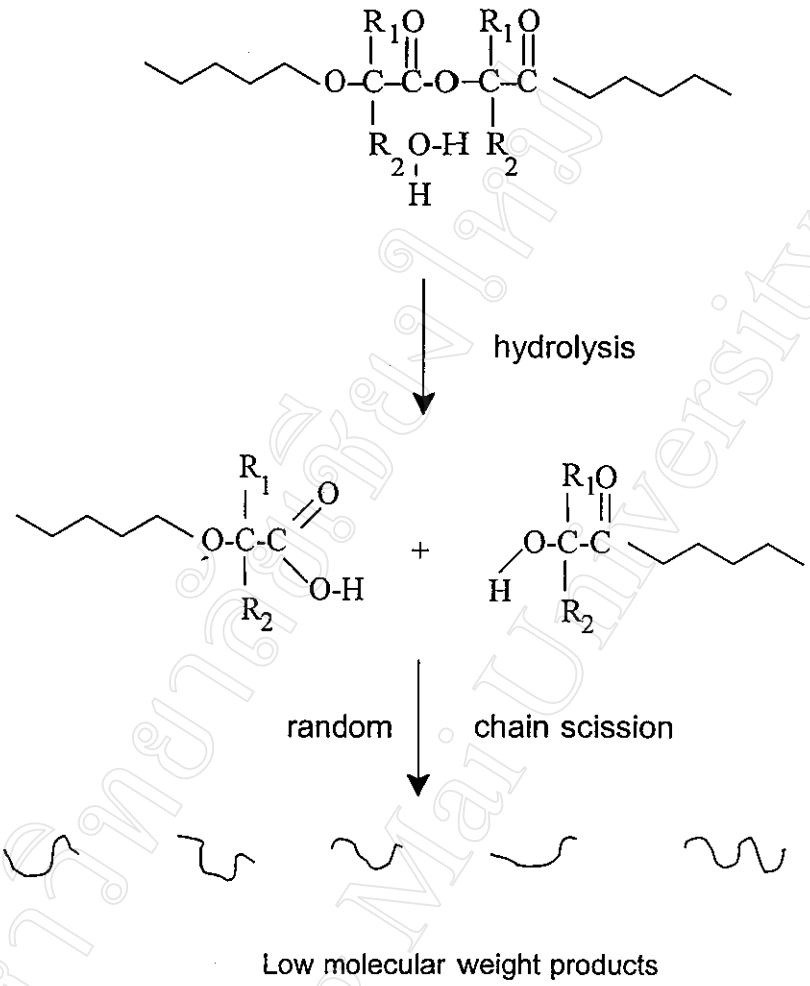


Fig. 6.1 Simple hydrolysis of a poly-∝-ester

Absorbable synthetic sutures are degraded by hydrolysis process which generally lead to low molecular weight products [21]. This implies that, for this type of suture, the degradation process depends on the chemical structure of the polymer. For the degradation to happen, the polymer should have hydrolytically unstable functional groups, e. g., ester groups. When these biodegradable sutures are placed in contact with the physiological environment, water penetrates the polymer matrix and facilitates the hydrolytic chain cleavages, leading to biodegradation. The degradation of this polymer is believed to be a **random chain scission** which may take place through hydrolysis in the main chain, side chain or both (illustrated in Fig. 6.1).

The simple hydrolysis reaction can be base-catalysed in an aqueous medium of pH > 7 (as in this case where the pH = 7.4) or acid-catalysed in the event that the new COOH end groups formed causes the pH of the medium to drop below 7. When these generated groups act as a catalyst, the hydrolytic degradation is called an **autocatalytic** process [12, 22].

Biodegradability is a polymer property dependent not only on the chemical structure but also on various physical characteristics such as geometric configuration, surface-to-bulk ratio, porosity, molecular weight and its distribution and matrix morphology [8, 12, 23].

The first step in hydrolytic degradation process is the adsorption of water and wetting at the polymer surface. The efficiencies and, therefore, the rate of these physical processes depend primarily on the hydrophilicity of the polymer and the amount of surface area available for interaction. Since the commercial sutures and the PLCG fiber are simple aliphatic polyesters, adsorption and wetting can be expected to occur easily and quickly.

This is then followed by ester hydrolysis at the surface leading to the formation of micro-defects which facilitate the diffusion of water into the bulk interior of the polymer matrix. The exact nature of these surface defects (i. e., whether they are pore or crack, etc.) has apparently not yet been studied systematically. As water diffuse into the polymer's semi-crystalline matrix, as shown in Fig. 6.2, the ester hydrolysis occurs preferentially in the amorphous regions where the chains are more loosely packed than in highly-ordered crystalline regions. Then, as hydrolysis proceeds, the polymer molecular weight decreases until the degradation products are small enough in size to diffuse out the matrix, resulting in mass loss.

In vitro, the degradation products simply dissolve in the immersion medium, often causing the pH to change, whereas in the human body, i. e., *in vivo*, the products would be removed by the body's natural process of metabolism and excretion [3].

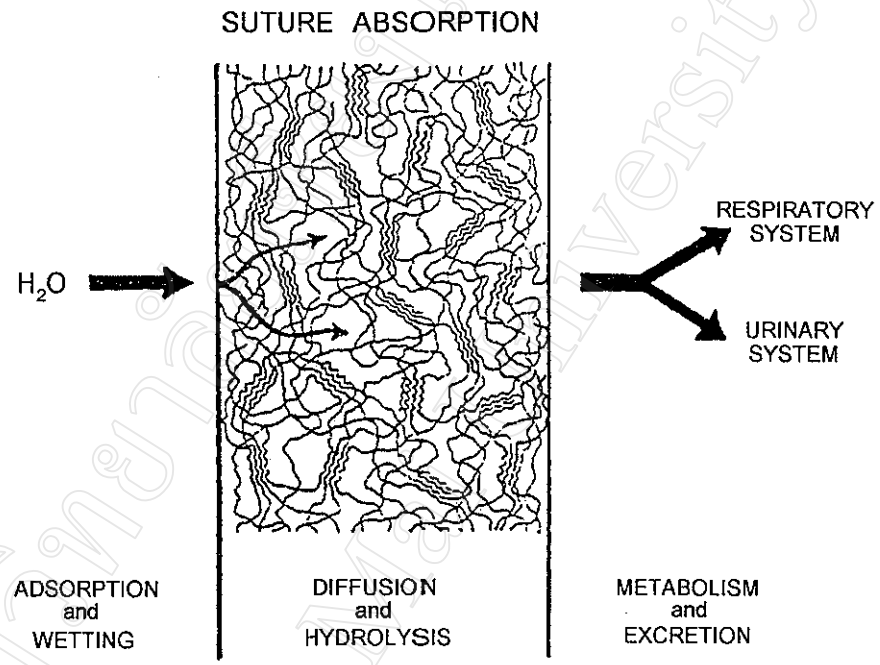


Fig. 6.2 The various physico-chemical processes involved in suture absorption

Although Fig. 6.2 presents what is obviously a very simplified picture of polymer absorption, it does at least give some idea of the complex balance of the various physical, chemical and biological processes involved. These processes are all interrelated with each other and with all aspects of the polymer/copolymer' microstructure. Even slight variations in copolymer characteristics such as molecular weight, %crystallinity, composition and monomer sequence distribution can have quite marked effects on the rate of absorption. This places great demands on the degree of control required in both copolymer synthesis and fiber spinning.

Research on semicrystalline polymers have given rise to many models of fiber structure, such as the model proposed by Bonart and Hosemana, the fringed micelle fibrillar model suggested by Hess, Mahl and Guter and finally the microfibrillar model proposed by Peterlin. Among all the models proposed, the microfibrillar one which combines the concepts of the folded chain and fringed micelle models has taken account of the space requirement for the accommodation of tie-chain segments as well as the anisotropy of mechanical properties [20, 24, 25].

On the basis of this microfibrillar model, the basic element is the microfibrils in which alternative crystalline and amorphous regions arrange in the direction of fiber axis. The crystalline regions are composed of chain sequences in ordered of preferred conformation. The amorphous regions containing chain folds and tie-chain segments are in disordered conformations. In this model, two types of tie-chain segments can be formed: interfibrillar and intrafibrillar. Their major function is to tie crystalline blocks and to support and transmit tensile loads to the crystalline regions.

This model of fiber structure provides the basis for the proposed degradation mechanism of the three commercial sutures and the PLCG fiber. It is believed that degradation proceeds through two main stages: the first stage takes place in the amorphous regions; the second in the crystalline regions. Within the first stage, the tie-chain segments in the amorphous regions degrade into fragments. This chain scission results in a lesser degree of entanglement of long-chain molecules located in the amorphous regions. Therefore, the remaining undegraded chain segments can move and reorganize themselves from a disordered to an ordered state. Further crystallization is induced and an increase in the heat of fusion is thus observed. Therefore, two competing processes, hydrolysis and induced crystallization, were observed in the hydrolytic degradation. In addition, the weight loss of the polymer samples first occurs in the amorphous regions

can lead to an apparent increase in crystallinity [8]. Along the scission of the chain segments which connect the crystal blocks along the axis direction, lower axial elastic moduli and tensile strength should be found. This is exactly found in this research project.

When all of the amorphous regions have been removed by the hydrolysis, the second stage of degradation starts. The heat of fusion profile for all samples would reach a maximium at the end of the first stage degradation; and it would then start to decrease when hydrolysis destroyed the crystalline lattice. From the observed changes of the heat of fusion, the first stage degradation for MONOCRYL and MAXON was predominant during the 9 and 14 weeks immersion period respectively, while second-stage degradation became important after the 9 and 14 weeks degradation period respectively.

In conclusion, simple hydrolysis had significant effects on the change of MONOCRYL, MAXON, PDS II and PLCG fiber morphology and properties. These included: tensile property, mass, thermal property and surface structure. The property loss-time profiles for PLCG fiber was comparable with MONOCRYL but the initial tensile strength was much lower. The differences in the property loss-time profiles of the 3 commercial sutures and the PLCG fiber can be ascribed to their differences in chemical microstructure and semi-crystalline morphology. The property loss-time profiles obtained from this *in vitro* studies can be used as the key to the elucidation of degradation mechanism.

SUGGESTIONS FOR FURTHER WORKS

In continuation of the research described in this thesis, the following suggestions for further work are made.

1. The *in vitro* biodegradation experiment for the 3 commercial sutures and the PLCG fiber should be repeated. This would provide a more accurate indication of their likely *in vivo* performance.

2. Other parameters determined as a function of degradation time should also be studied using additional techniques such as gel permeation chromatography (GPC) for determining the changes of molecular weight and the molecular weight distribution and X-ray diffraction which can determine the changes of the %crystallinity during the period of *in vitro* biodegradation.

3. Other immersion medium such as blood plasma, citrate-phosphate buffer and the physiological saline solution should be used instead of phosphate buffer saline solution to study the effect of immersion medium on the biodegradation behavior of absorbable sutures.

4. To better understand the hydrolytic degradation of biodegradable sutures, some kinetic studies should also be considered.