INTRODUCTION AND AIM OF WORK

Open reduction and internal fixation have been used for decades for gaining the optimum result in the treatment of displaced fractures(1). Experiments with implants made of various available materials (e.g., bone from animals) were performed during the late 19th and early 20th centuries, but soon it became evident that these xenografts do not possess sufficient tissue compatibility for fixation purposes. With the development of metallurgic knowledge, it was possible to prepare implants made of different alloys (mainly steel), strong enough for fixation of unstable fractures. However, these implant materials had certain disadvantages : stress-protection with a risk of refractures(2), corrosion(3), allergy(4), late migration(5), artifacts to radiological examinations, necessity to remove it from weight-bearing young adult, and subjective discomfort due to sense of bulkiness. For these reasons, removal of the implants is often recommended(1), and patients have been shown to benefit from it(6).

Biodegradable implants were developed to avoid the above-mentioned problems(7), their indications have now expanded to cover most cancellous bone fractures and osteotomies as well as ligament injuries.

During the 1980's, simultaneously with the development of the knowledge on bioabsorbable materials, the pathophysiology of foreign-body infections was investigated(8). It was found that bacteria were able to adhere to the surfaces of implants and that the material of the implant may also have some effect on the bacterial adherence. The more concomitant findings proving that the degradation products of the polyglycolide and polylactide used for bioabsorbable implants may have some bacteriostatic or even bactericidal activity(9).

These implants theoretically eliminate the need for a second operation, reduce the risk of infection, provide adequate strength during the critical early stages of healing, and permit a progressive transfer of stress to bone(10).

The first usage of these materials in orthopaedic surgery was in 1984 by Rokkanen for internal fixation of ankle fractures. Since that time, various forms of implants have been designed in the form of screws, rods and interference screws(11).

Biodegradable screws and pins have been used to fix fractures, osteotomies(10), and graft fixation in ACL reconstruction(12). Polyglycolic Acid (PGA) and polylactic acid (PLLA) implants have been used in the treatment of cancellous bone fractures since 1985 and 1988 respectively. Only a few previous studies reported the use of absorbable fixation devices in osteochondritis dissecans(13). The biodegradable meniscus arrows have been used in repair tears of meniscus recently(14).

Biodegradable polymers, especially those belon-ging to the family of Polylactic Acid (PLA) and Polyglycolic Acid (PGA), play an increasingly important role in orthopedics. These polymers degrade by hydrolysis and enzymatic activity and have a range of mechanical and physical properties that can be engineered appropriately to suit a particular appli-cation. Their degradation characteristics depend on several parameters including their molecular structure, crystallinity and copolymer ratio(15).

Aim of Work:

The aim of this topic is to spotlight on orthopaedic uses of biodegradable materials; properties, body reaction to it, financial effect, disadvantages and advantages over the traditional methods of fixation.

BIODEGRADABLE MATERIALS AND THEIR MECHANICAL PROPERTIES

Biodegradable materials are derived by transforming compounds that are present in nature to structural plastics. Organic molecules are polymerized to form strong fibers and solid compounds. When these polymers are implanted in patients, they degrade and are eliminated from the body in a period of time. The first biodegradable material was made from animal intestines and used as a suture material by Galen.The first usage of these materials in orthopedic surgery was in 1984 by Rokkanen for the internal fixation of ankle fractures. Even since, various forms of implants have been designed in the form of screws, rods, interference screws(16).

SYNTHESIS

The following is an overview of the synthetic biodegradable polymers that are currently being used or investigated for use as wound closure or orthopaedic fixation device. Most of commercially avaliable biodegradable devices are polyesters composed of homopolymers or copolymers of glycolide and lactide. There are also products made from copolymers of acarpolactone and polydioxanone(17).

Copolymers include two different types of monomers i.e. -A-B-A-B

There are two types of copolymers:

Random copolymers: build up by a random sequence of two different monomers (-A-A-B-A-A-A-B-A-B-B-B-)

Block Copolymers: build up by long segments of alternating polymers (A-A-A-B-B-B-A-A-A-B-B-B-).

N.B: *The longer the polymers chain, the greater is the Molecular Weight (MW) and the strongest are the polymers*

Physical properties of the polymers include molecular weight, intrinsic viscosity, crystallinity, and melting temperature (TM) and glass transition temperature (Tg).

The polymer's Molecular Weight (MW) affect its mechanical properties and also degradation behavior and is therefore a critical property to evaluate, fabrication processing can change the MW. The intrinsic viscosity, which correlates with the MW, is a measure of the polymer's resistance to flow and is an indication of the average size of the polymer's molecular chains. Arrangement of the polymer's molecular chains determines its crystallinity.

Polymers can have none to some crystallinity and can accordingly be described as either amorphous (chains are randomly oriented with respect to each other) or semi crystalline (regions bearing chains lie parallel and in close proximity to each others and also contain amorphous regions). Factors that influence the crystallinity include molecular chain structure, molecular chemistry, temperature and the rate of cooling during solidification(15).

Glass transition temperature (Tg): this is the temperature below which the polymer is stiff and hard and above which is flexible, soft and rubbery. The value of the Tg will vary with the chemical identity of the polymer and MW(18).

Mechanical properties of the biodegradable polymers must be well-characterized both initially and during degradation as biodegradable implants used in orthopeadic applications and are subjected to significant loads. These prosperties include ductility, elastic modulus and mechanical strength. The modulus of elasticity which measures the stiffness of the polymer, depends primarily on the crystallinity. Ductility measures the amount of plastic strain the polymer can withstand before fracturing and is expressed as percent elongation. The mechanical strength of the polymer include tensile strength and flexural strength, and to improve both of them, the polymer can be reinforced with fibers and so the biodegradable implant degrades relatively slowly and therefore retain their strength for long time(15).

1. **Poly Glycolic Acid (PGA): (**Fig. 1**)** Polyglycolide is the simplest linear aliphatic polyester. PGA was used to develop the first totally synthetic absorbable suture, marketed as Dexon in the 1960s PGA is highly crystalline (45-55%), with a high melting point (220-225°C) and a glass-transition temperature of 35-40°C.

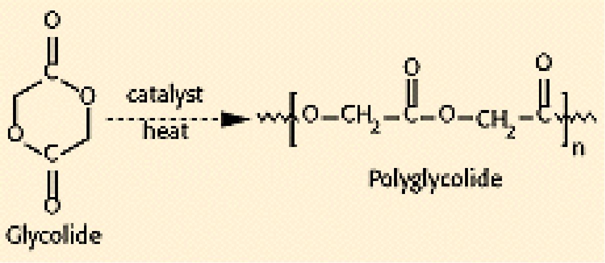

Fig. (1): Synthesis of polyglycolide (PGA).

2. Poly Lactic Acid (PLA): (Fig. 2) Lactide is the cyclic dimer of lactic acid that exists as two optical isomers, D (Dextro) and L (Levo) L-lactide is the naturally occurring isomer, and dl-lactide is the synthetic blend of d-lactide and l-lactide. The homopolymer of l-lactide (LPLA) is a semi-crystalline polymer. These types of materials exhibit high tensile strength and low elongation, and consequently have a high modulus that makes them more suitable for load-bearing applications such as in orthopedic fixation and sutures. Poly (dl-lactide) (DLPLA) is an amorphous polymer .This

material has lower tensile strength, higher elongation, and a much more rapid degradation time, making it more attractive as a drug delivery system. Poly(l-lactide) is about 37% crystalline, with a melting point of 175-178°C and a glass-transition temperature of 60-65°C. The degradation time of LPLA is much slower than that of DLPLA. Copolymers of l-lactide and dl-lactide have been prepared to disrupt the crystallinity of l-lactide and accelerate the degradation process.

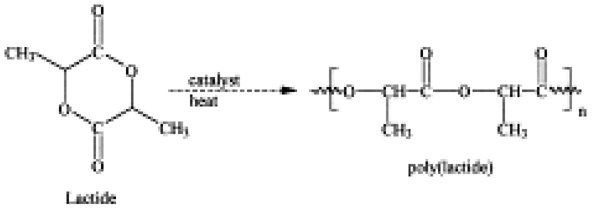

Fig. (2): Synthesis of polylactide (PLA)

3. Poly (dioxanone): (Fig3). The ring-opening polymerization of *p*-dioxanone resulted in the first clinically tested monofilament synthetic suture, known as PDS (marketed by Ethicon). This material has approximately 55% crystallinity, with a glass-transition temperature of -10 to 0°C. The polymer should be processed at the lowest possible temperature to prevent depolymerization

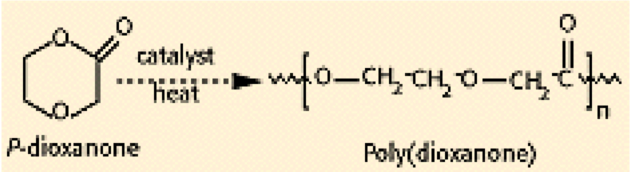

Fig. (3): Synthesis of poly (dioxanone).

4. Poly (ε-Caprolactone) (PCL): (Fig. 4) The ring-opening polymerization of ε-caprolactone yields a semi-crystalline polymer with a melting point of 59-64°C and a glass-transition temperature of -60°C. The polymer has been regarded as tissue compatible. Copolymers of ε-caprolactone with dl lactide have yielded materials with more-rapid degradation rates. A block copolymer of ε-caprolactone with glycolide, offering reduced stiffness compared with pure PGA, is being sold as a monofilament suture under the trade name Monacryl.

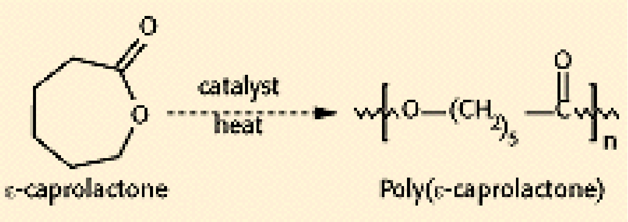

Fig. (4): Synthesis of poly (ε-caprolactone)

5. Poly (Lactide-co-Glycolide) (PLG): (Fig. 5) Using the polyglycolide and poly(l-lactide) properties as a starting point, it is possible to copolymerize the two monomers to extend the range of homopolymer properties. Copolymers of glycolide with both l-lactide and dl-lactide have been developed for both device and drug delivery applications. It is important to note that there is not a linear relationship between the copolymer composition and the mechanical and degradation

properties of the materials. For example, a copolymer of 50% glycolide and 50% dl-lactide degrades faster than either homopolymer. Copolymers of l-lactide with 25-70% glycolide are amorphous due to the disruption of the regularity of the polymer chain by the other monomer. A copolymer of 90% glycolide and 10% l-lactide was developed as an absorbable suture material under the trade name Vicryl. It absorbs within 3-4 months but has a slightly longer strength-retention time.

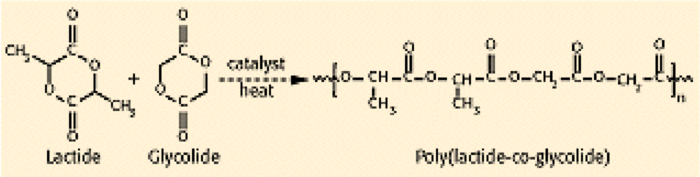

Fig. (5): Synthesis of poly(lactide-co-glycolide).

6. Polyglyconate: (Fig. 6) Copolymers of glycolide with Trimethylene Carbonate (TMC), have been prepared as both sutures, (Maxon) and as tacks and screws (Acufex Microsurgical). Typically, these are prepared as A-B-A block copolymers in a 2:1 glycolide:TMC ratio pure . These materials have better flexibility than pure PGA and are absorbed in approximately 7 months(19).

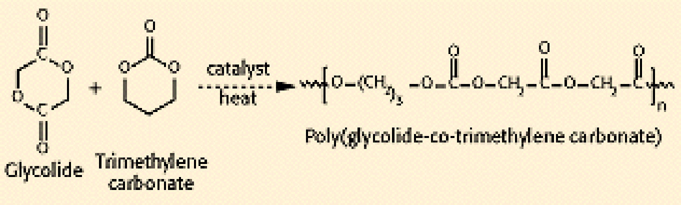

Fig. (6): Synthesis of polyglyconate.

Polymer Processing

Polymer processing consists of:

I. Injection moulding: Pellets are melted and the polymer is forced into metal cavity under pressure.

II. Extrusion: A polymer bar is ejected and pulled through a dye.

III. Orientation: By heating an extruded bar of polymer to render it soft but not melted, the polymer can be pulled in a controlled fashion through a dye to align the polymer chains in the direction of pulling.

IV. Compression moulding: The polymer preformed is rendered soft by heat and then pressed into a form between heated, movable plates.

V. Casting: The polymer preformed is machined on a milling machine where material is physically removed with a cutting tool.

Implants of more complex design, such as screw and small plates, became possible first in the late 1970s and early 1980s(20).

Degradation

Once implanted, a biodegradable device should maintain its mechanical properties until it is no longer needed and then be absorbed and excreted by the body, leaving no trace. Simple chemical hydrolysis of the hydrolytically unstable backbone is the prevailing mechanism for the polymer's degradation, this occurs in two phase:

In the first phase: water penetrates the bulk of the device, preferentially attacking the chemical bonds in the amorphous phase and converting long polymer chains into shorter water-soluble fragments. Because this occurs in the amorphous phase initially, there is a reduction in molecular weight without loss in physical properties, since the device matrix is still held together by the crystalline regions. The reduction in molecular weight is soon followed by a reduction in physical properties, as water begins to fragment the device (Fig. 7).

In the second phase: Enzymatic attack and metabolization of the fragments occurs, resulting in a rapid loss of polymer mass. This type of degradation is called bulk erosion at which the rate of penetration of the water to the device exceeds that at which the polymer is converted into water-soluble materials (resulting in erosion throughout the device). All of the commercially available synthetic devices and sutures degrade by bulk erosion(21).

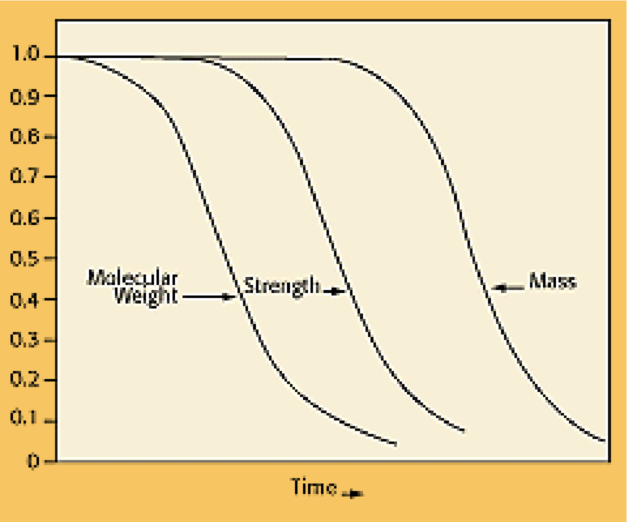

Fig. (7): Generic absorption curves showing the sequence of polymer molecular weight, strength, and mass reduction

A second type of biodegradation, known as surface erosion, occurs when the rate at which the water penetrates the device is slower than the rate of conversion of the polymer into water-soluble materials. This type of erosion occurs when the polymer is hydrophobic, but the chemical bonds are highly susceptible to hydrolysis. Surface erosion results in the device thinning over time while maintaining its bulk integrity. In general, this process is bioerosion rather than biodegradation(22).

Implants placed at sites exposed to stress degrade at a faster rate. It is possible that under the action of stresses the implants develop cracks, which increase the effective surface exposed to water and result in enhanced degradation. Also, stress cracks reduced the effective strength of the implants(15).

The difference in the final metabolism of the polymers are relatively slight Fig. (8) as for example:

I. PGA degrades to glycolic acid molecules which are acted upon by glycolate oxidase and are transformed into glyoxylate which react with glycine transminase and results in formation of glycine. The glycine can be used for protein synthesis or used to synthesize serine and subsequently transformed into pyruvic acid where it enters the tricarboxylic acid cycle (TCA) PGA absorbs very quickly in the body losing all strength within one month and all mass within about 6-12 months.

II. PLA is degraded to lactic acid which transformed to pyruvate. The pyruvate then converted to glucose and acetyl CoA. The later enters (TCA) cycle where H_2O and Co_2 are the end products. The degradation is much faster in presence of certain enzymes such as pronase proteinase and bromelain. The rate of degradation of poly-L lactic (PLLA) from 40 weeks to over 5 years and from 28 weeks to 18 months for poly-D-Lactic acid (PDLA).

III. Polydioxanon degrades by hydrolysis and the breakdown products excreted in urine (93%) faeces (2.9%) and exhaled carbon dioxide (3.19%)(23). The