

## Chapter 2

# Application of Biomaterials

The main applications of biomaterials can be classified into the categories below and described later:

- Cardiovascular medical devices (stents, grafts and etc.)
- Orthopedic and dental applications (implants, tissue engineered scaffolds and etc.)
- Ophthalmologic applications (contact lenses, retinal prostheses and etc.)
- Bioelectrodes and biosensors
- Burn dressings and skin substitutes
- Sutures
- Drug delivery systems

**Cardiovascular medical devices.** Heart valves, endovascular stents, vascular grafts, stent grafts and other cardiovascular grafts are common medical devices in cardiovascular applications. There are several major forms of valvular heart disease, most involving the aortic and/or the mitral valve. The most common type of valve disease and most frequent indication for valve replacement overall is calcific aortic stenosis obstruction at the aortic valve secondary to age-related calcification of the cusps of a valve that was previously anatomically normal. In case of vascular pathologies, stents and vascular graft is used. Different polymers and metals with or without coating can be applied in this category (titanium, polytetrafluoroethylene and etc.) [1].

**Tissue engineering scaffolds.** Tissue engineering is one of the most important ways to achieve tissues for repair or replacement applications. Its goal is to design and fabricate reproducible, bioactive and bioresorbable 3D scaffolds with tailored properties that are able to maintain their structure and integrity for predictable times, even under load-bearing conditions. Scaffolds can be applied in different tissues. It is only important to note that it only in designing the scaffold, type of fabrication and biomaterial selection depending on the target organ and its cells that can be affected on final application. Chemistry, architecture, porosity and rate of degradation should provide a sufficient mechanical environment and should facilitate cell attachment, proliferation and migration, waste nutrient exchange, vascularization and tissue ingrowth. Also there should be a proper ratio between degradation of the scaffold and tissue ingrowth [2].

There are various types of scaffold fabrication methods. At first, only polymeric scaffolds were used but gradually composite scaffolds and especially ceramic/polymer scaffolds have been used. The main important scaffold fabrication methods are: fiber bonding, solvent casting and particulate leaching, compression molding, extrusion, freeze-drying, phase emulsion, solid free form fabrication and electrospinning. Differences between these methods are temperature, pressure, solvent type, porogen (which is responsible for making pores) and etc.

Recently researchers used mesostructured materials in scaffolds to supply drug and biological agents in situ during degradation of scaffold and growing new tissue.

**Ophthalmologic applications.** Vision impairment/low vision, blindness, refractive error (Myopia and Hyperopia), astigmatism, presbyopia, cataracts, primary open-angle glaucoma, age-related macular degeneration (AMD) and diabetic retinopathy are common ophthalmologic diseases. To improve the life of these patients, many implants have been applied. The main biomaterials which are used in this category are summarized in Table 2.1 [1].

**Bioelectrodes and biosensors.** Bioelectrodes are sensors used to transmit information into or out of the body. Surface or transcutaneous electrodes used to monitor or measure electrical events that occur in the body are considered monitoring or recording electrodes. Typical applications for recording electrodes include electrocardiography, electroencephalography, and electromyography information into or out of the body. Various parameters influence the material selection of electrodes (see Table 2.2).

These bioelectrodes are mainly applied in cardiology and neurology applications. A biosensor is a sensor that uses biological molecules, tissues, organisms or principles to measure chemical or biochemical concentrations. Biosensors can

**Table 2.1** Ophthalmic implant materials commonly used [1]

Implant	Materials which used
Contact lenses	Poly(methyl methacrylate) (PMMA), 2-hydroxyethyl methacrylate (HEMA) copolymers, silicone hydrogels
Inlays or onlays	Hydrogels, collagen, permeable membranes
Intraocular lenses	Optic: PMMA, hydrophobic acrylic, silicone, hydrophilic acrylic Haptic: polypropylene, PMMA, polyimide, polyvinylidene fluoride (PVDF)
Ophthalmic viscosurgical device (OVD)	Chondroitin sulfate, sodium hyaluronate, hyaluronic acid, hydroxypropyl methylcellulose (HPMS), polyacrylamide, collagen, or combinations of these materials
Glaucoma shunts	Plates: silicone (impregnated with barium), polypropylene Tubing: silicone
Vitreous replacements	Silicone oil, gases

**Table 2.2** Parameters influencing the material selection of electrodes [1]

Electrode	Surface area, geometry, and surface condition
Electrical	Potential, current, and quantity of charge
Environmental	Mass-transfer variables and solution variables
Engineering	Availability, cost, strength, and fabricability

be used in many medical and non-medical applications. Biomedical sensors are sensors that detect medically relevant parameters; these could range from simple physical parameters like blood pressure or temperature, to analyses for which biosensors are appropriate (e.g. blood glucose). Biosensors can work by changes in pH, ions, blood gases ( $O_2$ ,  $CO_2$  and etc.), drugs, hormones, proteins, viruses, bacteria, tumors and etc. [1].

**Burn dressing and skin substitutes.** Skin is the largest organ that protects body from microorganisms and external forces, integrates complex sensory nervous and immune systems, controls fluid loss, and serves important aesthetic function. Deep skin injuries due to deep cuts, burns or degloving injuries can cause significant physiological derangement, expose the body to a risk of systemic infection, and become a life threatening problem. So the need of skin substitutes depending on wound depth is felt. An ideal skin substitute must be inexpensive, long lasting, a bacterial barrier, semipermeable to water, elastic, easy to apply, painless to the patient, non-antigenic and non-toxic and has durable shelf-time. Today a lot of commercial skin substitutes are applied [1].

**Sutures.** Suture is any strand of material that is used to ligate blood vessels or approximate tissue. Ligatures are used to achieve hemostasis or to close a structure to prevent leakage. The suture device is comprised of: the suture strand; the surgical needle; and the packaging material used to protect the suture and needle during storage. The ideal suture must be biocompatible, sterile, compliant, adequate knot/straight strength, secure and stable knot, strength and mass loss profiles adequate for proposed usage, low friction, adequate needle attachment strength, atraumatic needle design, non-electrolytic, non-capillary, non-allergenic, non-carcinogenic, minimally reactive, uniform and predictable performance. Silk, nylon, polyester, cotton, polypropylene, ultra-high molecular weight polyethylene (UHMWPE), stainless steel and synthetic absorbable polymers such as poly glycolic acid (PGA), p-dioxanone (PDO) and etc. are the main materials that are used as sutures yet [1].

**Drug delivery systems (DDS).** Drug delivery systems introduced as formulations or instruments which enable to control the release rate of a biological agent (especially a drug) in the target site. Drug delivery systems are an interface between patient and drug. Drugs can be introduced to the organ by different anatomical routes due to disease and drug type: Digestive system (oral, anal), oral, rectal, parenteral (subcutaneous, intramuscular, intravenous, arterial), mucous membranes, respiratory tract by inhalation, subcutaneous or intraosseous are man anatomical routes.

By increasing the size the dosage in single dose administration, side effects would appear so in order to reduce these side effects, coatings with varying thickness, are

**Table 2.3** DDS systems [1]

Macroscale DDS (“zero order” constant delivery rate DDS) <ul style="list-style-type: none"> <li>• Implants (e.g. subcutaneous or intramuscular)</li> <li>• Inserts (e.g. vaginal, ophthalmic)</li> <li>• Ingested DDS (e.g. osmotic pumps, hydrogels)</li> <li>• Topical DDS (e.g. skin patches)</li> </ul>
Macroscale and microscale DDS (site-specific, sustained delivery rate DDS) <ul style="list-style-type: none"> <li>• Surface-coated DDS (e.g. oral tablets, catheters, drug-eluting stents)</li> <li>• Injected DD depots (e.g. degradable microparticles and phase separated masses)</li> </ul>
Nanoscale DDS (targeted DDS) <ul style="list-style-type: none"> <li>• Injected nanocarrier DDS (e.g. PEGylated drugs, polymer-drug conjugates, PEGylated liposomes, PEGylated polymeric micelles, and drug nanoparticles, sometimes targeted by monoclonal antibodies or cell membrane receptor ligands)</li> </ul>

applied. Such formulations are now known as “sustained release” or “prolonged release” products. However, the pharmacokinetics of such products depended greatly on the local in vivo patient environment and as such, vary from patient to patient. These systems are called “zero order” systems because they release drug during time in a constant rate. These reasons were among the most important driving forces that led to the birth of the field of “controlled drug delivery” (CDD) in the mid to late 1960s that became known as “macro-scale devices” that exhibit constant or zero order drug delivery rates, leading to constant plasma drug concentrations over long time durations of drug delivery. By the rapid growth of nanoscale materials, injectable targeting drug delivery systems appear (see Table 2.3) [1].

**Dental materials.** Restorative materials have been used as tooth crowns and root replacements. Four groups of materials which are used in dentistry today are metals, ceramics polymers and composites. Despite recent advances in material science and dentistry, there still is not a proper material for restorative dentistry. Characteristics of an ideal restorative material are listed below:

- Be biocompatible
- Bond permanently to tooth structure or bone
- Match the natural appearance of tooth structure and other visible tissues
- Exhibit properties similar to those of tooth enamel, dentin and other tissues
- Be capable of initiating tissue repair or regeneration of missing or damaged tissue

Dental materials can be classified in two categories: preventive materials, restorative material. Preventive dental materials include pit and fissure sealants, sealing agents that prevent leakage, materials that are used primarily for the antibacterial effects, liners, bases, cements and restorative materials that are used primarily because the release fluoride, chlorhexidine or other therapeutic agents used to prevent or inhibit the progression of tooth decay. This type of materials used for short-term application. Restorative dental materials consist of all synthetic components that can be used to repair or replace tooth structure, including primes, bonding agents, liners, cement bases, amalgams, resin based composites, compomers, metal-ceramics, hybrid ionomers, cast metals and denture polymers. Restorative materials can be used for both

short and long-term applications. Restorative materials can be classified as *direct restorative materials* and *indirect restorative materials* dependent on whether they are used. Direct fabricated intraorally and indirect fabricated extraorally [3].

Because of importance of restorative dental materials, explain more about this part. Dental amalgam has been used traditionally for filling dental cavities. Amalgam is a mixture of copper, tin, zinc, mercury, silver and other trace metals. Later cement dental restorative materials were used as restorative materials. To achieve adhesive bonding in the general case of two rigid solids, such as a tooth enamel surface and an orthodontic bracket, it is necessary to apply a fluid adhesive between them.

Moreover, the fluid must be of appropriate chemical formulation to initially wet both surfaces, exhibiting a low contact angle. One or both surfaces may have been subjected to some form of pre-treatment or conditioning with an etchant or primer that, inter alia, may have modified surface porosity. In this case, the adhesive fluid may be drawn into the solid surface layers by capillary action. The presence of a suitable fluid between two solids greatly enhances the potential for intermolecular force interactions at each solid–fluid boundary.

Dental cements can be classified to:

- Conventional acid-base cements
- Poly-electrolyte cements: Zinc poly carboxylates and glass ionomers
- Resin-modified glass-ionomer cements
- Dual-setting resin-based cements

### ***Conventional acid-base cements***

Dental cements are, traditionally, fast-setting pastes obtained by mixing solid and liquid components. Most of these materials set by an acid-base reaction, and subsequently developed resin cements harden by polymerization. They have various compositions. This material is composed primarily of zinc oxide powder and a 50 % phosphoric acid solution containing aluminum and zinc. The mixed material sets to a hard, rigid cement by formation of an amorphous zinc phosphate binder. The bonding arises entirely from penetration into mechanically produced irregularities on the surface of the prepared tooth and the fabricated restorative material. Classifications of dental cements are summarized in Table 2.4.

### ***Poly-electrolyte cements: Zinc poly carboxylates and glass ionomers***

Poly (carboxylic acid) cements were developed in 1967 to provide materials with properties comparable to those of phosphate cements, but with adhesive properties of calcified tissues. This type of cement is composed of zinc oxide and aqueous poly (acrylic acid) solution. The metal ion cross-links the polymer structure via carboxyl groups, and other carboxyl group's complex to Ca ions in the surface of the tissue. Adequate physical properties, excellent biocompatibility in the tooth, and adhesion to enamel and dentin are main advantages of these cements being opaque is the main problem with these cements. The need for a translucent material led to the development of the glass-ionomer cements (GIC). GICs are also based on poly (acrylic acid) or its copolymers with itaconic or maleic acids, but

**Table 2.4** Classification of dental cements [1]

Dental cements	Components	Setting mechanism
Zinc phosphate	Zinc oxide powder, phosphoric acid liquid	Acid–base reactions; Zn complexation
Zinc polycarboxylate	Zinc oxide powder, aqueous poly(acrylic acid)	Acid–base reactions; Zn complexation
Glass ionomer (polyalkenoate)	Ca, Sr, Al silicate glass powder aqueous poly(acrylic acid-itaconic acid)	Acid–base reactions; Metal ion complexation
Resin modified glass ionomer	Dimethacrylate monomers. Aqueous poly(acrylic acid methacrylate) co-monomers. Silicate or other glass fillers	Peroxide-amine or photo-initiated polymerization
Resin-based	Aromatic or urethane dimethacrylates, HEMA	Photoinitiated addition polymerization
Dentin adhesive	Etchant: Phosphoric acid (aq.) Primer: HEMA in ethanol or acetone Bond resin: Dimethacrylate monomers	Photoinitiated addition polymerization

utilize a calcium aluminosilicate glass powder instead of zinc oxide. GICs set by cross-linking of the polyacid with calcium and aluminum ions from the glass, together with formations of a silicate gel structure.

### ***Resin-modified glass-ionomer cements***

Polyacid molecules contain both ionic carboxylate and polymerizable methacrylate groups. It is induced to set by both an acid-base reaction and visible light polymerization. Adhesive bonding but not complete sealing is obtained, because of the imperfect adaptation to the bonded surfaces under practical conditions.

### ***Dual-setting resin-based cements***

Dual-setting resin-based cements are fluid or paste-like monomer systems based on aromatic or urethane dimethacrylates. They are normally consisting of two-component materials that are mixed to induce setting. They may also be light-cured. These set materials are strong, hard, rigid, insoluble and cross-linked polymers [1].

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