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Review Article

A BRIEF REVIEW: BIOMATERIALS AND THEIR APLLICATION

AMOGH TATHE, MANGESH GHODKE AND ANNA PRATIMA NIKALJE *

Pharmaceutical Chemistry Department, Y. B. Chavan College of Pharmacy, Aurangabad-431001,Maharashtra, India. Email: ana@k.st

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ABSTRACT

The development of biomaterials is not a new area of science, having existed for around half a century. The study of biomaterials is called biomaterial science. It is a provocative field of science, having experienced steady and strong growth over its history, with many companies investing large amounts of money into the development of new products. Biomaterial science encompasses elements of medicine, biology, chemistry, tissue engineering and materials science.

Keywords: Biomaterials, Review

INTRODUCTION [1]

A biomaterial is essentially a material that is used and adapted for a medical application. Biomaterials can have a benign function, such as being used for a heart valve, or may be bioactive; used for a more interactive purpose such as hydroxy-apatite coated hip implants (the Furlong Hip, by Joint Replacement Instrumentation Ltd, Sheffield is one such example – such implants are lasting upwards of twenty years). Biomaterials are also used every day in dental applications, surgery, and drug delivery **.**

While a definition for the term 'biomaterial' has been difficult to formulate, more widely accepted working definitions include: "A biomaterial is any material, natural or man-made, that comprises whole or part of a living structure or biomedical device which performs, augments, or replaces a natural function".

Applications

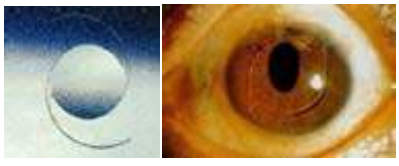
Biomaterials are used in:

- Joint replacements
- Bone plates
- Bone cement
- Artificial ligaments and tendons
- Dental implants for tooth fixation
- Blood vessel prostheses
- Heart valves
- Skin repair devices
- Cochlear replacements
- Contact lenses

Following are the Examples [2]

1) Intra ocular lens

Basic materials: - PMMA (acrylic), Silicone



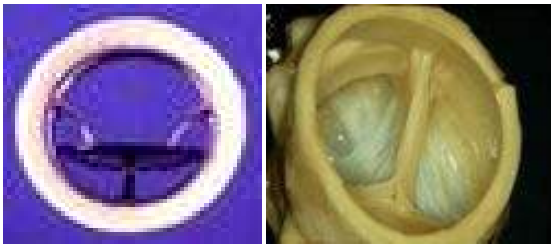
Challenge: - Combining long term biocompatibility with optical properties.

2) Artificial hip joints

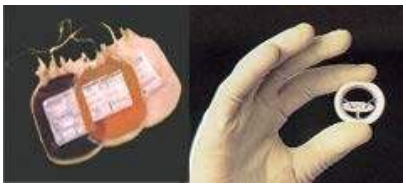
Basic materials: - Stainless steel, titanium & its alloys & UHMWPE.

Challenges: - Prevention of wear & loosening over extended periods (10-15 years).

3) Substitute heart valves



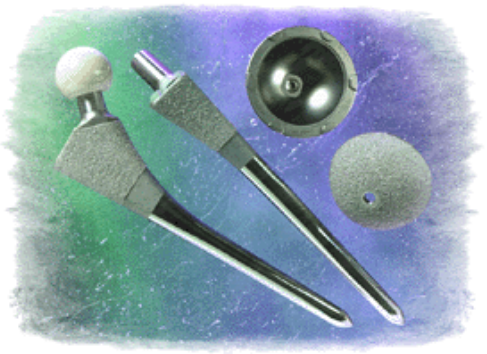
4) Indian chitra heart valve



5) Vascular grafts

Basic materials: - Polyurethane, Teflon & Dacron.

Challenges: - Maintenance of mechanical integrity, Long term blood compatibility (avoidance of blood clotting)



6) The human total hip system shown below offers titanium, dual tapered stem design which provides a physiologic proximal load transfer, thus greatly reducing the chance of calcar resorption and distal hypertrophy. No fooling! The system provides an anatomic fit coupled with a straight stem design. The role of cartilage is played by polyethylene in this application. The reference source URL is Biomet Corporation. For more about hip replacement and conditions under which this is done, please link to the Medline plus website and learn more about hip joint replacement (many great illustrations).

Some commonly used biomaterials [2]

1. Silicone rubber
2. Dacron
3. Cellulose
4. Poly(methyl methacrylate)
5. Polyurethanes
6. Hydrogels
7. Stainless steel
8. titanium
9. Alumina
10. Hydroxyapatite
11. Collagen (reprocessed)

Applications

- Catheters, tubing
- Vascular grafts
- Dialysis membrane
- Intraocular lenses, bone cement
- catheters, Pacemaker leads
- Opthalmological devices, Drug delivery
- Orthopedic devices, stents
- Orthopedic & Dental devices
- Orthopedic & Dental devices
- Orthopedic & Dental devices
- Ophthalmologic applications, wound dressings

Literature Survey

1) Biomaterials: Protein-Surface Interactions[3]

Protein-surface interactions are fundamentally responsible for the bio compatibility of medical devices, or the lack thereof. When a solid material (e.g., a catheter, stent, hip joint replacement, or tissue engineering substrate) comes in contact with a fluid that contains soluble proteins (e.g., blood, interstitial fluid, cell culture media), proteins rapidly adsorb onto the surface of the material, saturating the surface within a time frame of seconds to minutes. Therefore, when living cells (which are much larger than proteins and thus much more slowly moving) approach the biomaterial surface, they do not actually contact the molecular structure of the material surface itself, but rather they contact and interact with the molecular structure of the adsorbed protein layer. Cells, of course, cannot "see" the adsorbed protein layer, but rather they interrogate their surroundings by way of membrane-bound receptors that can bind to specific bioactive features presented by the adsorbed proteins. Then, through a series of orchestrated molecular mechanisms, these receptor-protein binding events are transduced through the cell membrane in a manner that stimulates specific intracellular processes that then determine a cell's response. Accordingly, at the most fundamental level the key to controlling cellular response is to control the type of bioactive sites that are presented by the adsorbed layer of proteins. This, in turn, can be controlled by controlling the amounts and the types of proteins that are adsorbed and their orientation, conformation, and packing arrangement on the biomaterial surface. While this is conceptually simple to understand, the numerous types of soluble proteins contained in physiological fluids combined with their structural complexity has made, and continues to make, this an extremely challenging problem

Attention will be focused on highlighting several of the most interesting relatively recent techniques that have been developed and applied to further our understanding of the submolecular-level mechanisms involved in how surface chemistry influences the orientation, conformation, and organization of adsorbed proteins. The continued development of our understanding of these processes is critical if we are to get beyond the current era of surface design largely by trial and error, and move into an era where surfaces are proactively designed to directly control adsorbed protein bioactivity, and thereby control cellular response.

2) Computer Simulation of Protein Adsorption to a Material Surface in Aqueous Solution: Biomaterials Modeling of a Ternary System[4]

Biomaterials are often in contact with the body or body fluids, so interfacial phenomena, especially protein adsorption, control essential parameters, such as biocompatibility and bioreactivity. In addition, optimization of biotechnology tools such as DNA/protein micro arrays and micro fluidic systems will also require a mechanistic understanding of how biological macromolecules interact with materials surfaces. Thus, atomistic characterization of structure function relationships at the interface between biological macromolecules and materials surfaces will be crucial to the future development of an enormous range of bioengineering and biotechnology applications. They used standardized computer modeling software to simulate protein adsorption to a materials surface in water. Molecular dynamics and local minimization were employed to simulate a multi component system in which a hydrated protein, bovine pancreatic trypsin inhibitor (BPTI), encounters an MgO surface in pure water. It is known that soluble proteins bind to charged materials surfaces in water and in vivo. The simulations show adsorption of BPTI to MgO in water with binding energies of 242, 350, and 241 kcal/mol for three different initial protein orientations. Importantly, our results show that in this aqueous system there is very little interaction between the atoms of the protein and those of the surface. Crucial binding events at the surface are mediated by the solvation layer in the interphase (double-layer) region. This result is expected on the basis of classical electrochemical theory but is usually not explicitly considered in the protein adsorption literature.

3) Carbohydrate derived protein resistant biomaterial [5]

Carbohydrate-derived side-chain polyethers that may be synthesized by condensation polymerization of monomers derived from natural occurring carbohydrates. These compounds are protein resistant, biodegradable and may be functionalized at location other that the chain ends. Various devices, apparatus and articles of manufacture may be formed, at least in part, of the compounds of the present invention to achieve desirable protein resistance, biodegradability and/or functionalization.

4) Hard Tissue: Biomaterial Interactions [6]

Bone and cartilage are vulnerable to injury and replacement of these tissues by biomaterials, synthetic and treated natural materials used to replace and/or regenerate functioning tissues, has been successfully used for years. Recent advancements in science elaborated the Tissue Engineering concept where regeneration of injured tissues is intended by the combined application of: a) biomaterial-based scaffolds; b) cells grown in culture; c) systemic and/or local hormones/mediators; and recently d) genetic modulators. Tissue engineering products and basically biomaterials of various shapes and forms have been widely used in musculoskeletal diseases and disorders for decades. Metals of steel, cobalt-chrome, and titanium in pure and/or alloy form, ceramics of hydroxyapatite (HA) and calcium phosphate, and polymers such as polymethyl-methacrylate are currently used in bone, cartilage, and joint replacement. Biocompatibility of biomaterials is simply defined as the in vivo functioning of the implant without causing local and/or systemic intolerable responses. Implants used for hard tissue replacement should also possess appropriate mechanical properties as load bearing of bone and lubrication in joints are among the basic physiological functions of these tissues. Research to improve the biocompatibility of biomaterials and tissue engineering products is still going on as bone and cartilage will, nevertheless, cause a response even when "inert" materials are implanted. Local and systemic responses elaborated by biomaterials depend on various factors including surface topography, heterogeneity, and chemical and physical properties. The tissue-implant interface is, therefore, the hot spot of research for the better understanding of the response to biomaterials and tissue engineering products. Industry has also focused on improving biomaterial surfaces, the front line of tissue-implant interactions.

5) Modeling and simulation of biomaterials [7]

Modeling and simulation are becoming increasingly accepted components of materials research. In this review the authors discuss application of modeling and simulation in the developing field of biomaterials. To restrict the discussion somewhat, authors focus primarily on the structure and properties of biomaterials and do not discuss biochemical or biomedical applications. A discussion of how atomistic-level simulation can be used to study molecules and collections of molecules. We then focus on mesoscale simulations of structure and properties, followed by a brief review of continuum-scale approaches.

6) Nano Biomaterials [8]

Detergent manufacturers have long used enzymes in their formulations for fighting really tough dirt. Jonathan Dordick, a chemical engineer at Rensselaer Polytechnic Institute in Troy, NY, is taking the battle against dirt a step further, using nanotechnology to design a self-cleaning plastic in which the enzyme molecules are an integral part of the material. When the plastic comes into contact with bacteria or other pathogens, the enzymes attack the microbes and destroy their ability to bind to its surface.

7) Bioengineering of Improved Biomaterials Coatings for Extracorporeal Circulation Requires Extended Observation of Blood-Biomaterial Interaction under Flow [9]

Extended use of cardiopulmonary bypass (CPB) systems is often hampered by thrombus formation and infection. Part of these problems relates to imperfect hemocompatibility of the CPB circuitry. The engineering of biomaterial surfaces with genuine long-term hemocompatibility is essentially virgin territory in biomaterials science. For example, most experiments with the well-known Chandler loop model, for evaluation of blood-biomaterial interactions under flow, have been described for a maximum duration of 2 hours only. This study reports a systematic evaluation of two commercial CPB tubing's, each with a hemocompatible coating, and one uncoated control. The experiments comprised (i) testing over 5 hours under flow, with human whole blood from 4 different donors; (ii) measurement of essential blood parameters of hemocompatibility; (iii) analysis of the luminal surfaces by scanning electron microscopy and thrombin generation time measurements. The dataset indicated differences in hemocompatibility of the tubing's. Furthermore, it appeared that discrimination between biomaterial coatings can be made only after several hours of blood-biomaterial contact. Platelet counting, myeloperoxidase quantification, and scanning electron microscopy proved to be the most useful methods. These findings are believed to be relevant with respect to the bioengineering of extracorporeal devices that should function in contact with blood for extended time.

8) Advances in Vascular Tissue Engineering Using Protein-Based Biomaterials [10]

The clinical need for improved blood vessel substitutes, especially in small-diameter applications, drives the field of vascular tissue engineering. The blood vessel has a well-characterized structure and function, but it is a complex tissue, and it has proven difficult to create engineered tissues that are suitable for widespread clinical use. This review is focused on approaches to vascular tissue engineering that use proteins as the primary matrix or "scaffold" material for creating fully biological blood vessel replacements. In particular, this review covers four main approaches to vascular tissue engineering: 1) cell-populated protein hydrogels, 2) cross-linked protein scaffolds, 3) decellularized native tissues, and 4) self-assembled scaffolds. Recent advances in each of these areas are discussed, along with advantages of and drawbacks to these approaches.

9) Biomaterials: Where We Have Been and Where We are Going [11]

Since its inception just over a half century ago, the field of biomaterials has seen a consistent growth with a steady introduction of new ideas and productive branches. This review describes where we have been, the state of the art today, and where we might be in 10 or 20 years. Herein, they highlighted some of the latest advancements in biomaterials that aim to control biological responses and ultimately heal. This new generation of biomaterials includes surface modification of materials to overcome nonspecific protein adsorption in vivo, precision immobilization of signaling groups on surfaces, development of synthetic materials with controlled properties for drug and cell carriers, biologically inspired materials that mimic natural processes, and design of sophisticated three-dimensional (3-D) architectures to produce well-defined patterns for diagnostics, e.g., biological microelectromechanical systems (bioMEMs), and tissue engineering.

10) Biomaterials for blood-contacting applications [12]

Consideration of biomaterials for blood-contacting applications should take into account blood-biomaterial interactions, factors influencing the blood response and evaluation procedures. Examination of blood-biomaterial interactions indicates that relevant features are protein adsorption, platelet reactions, intrinsic coagulation, fibrinolytic activity, erythrocytes, leucocytes and complement activation. Factors influencing the blood response to a biomaterial in clinical application are the biomaterial structure, the presence of an antithrombotic agent, the patient status as determined by the disease and drug therapy, and the nature of the application. Evaluation options for biomaterials are clinical, *in vivo*, *ex vivo* and *in vitro*, with *ex vivo* and *in vitro* procedures relevant for biomaterial development.

11) Biomaterials in Canada: The first four decades [13]

Biomaterials research in Canada began in the 1960s. Over the past four decades significant contributions have been made across a broad spectrum covering dental, orthopedic, cardiovascular, neuro

and ocular biomaterials. Canadians have also been active in the derivative area of tissue engineering. Biomaterials laboratories are now established in universities and research institutes from coast to coast, supported mainly by funding from the Federal and Provincial Governments. The Canadian Biomaterials Society was formed in 1971 and has played an important role in the development of the field. The Society played host to the 5th World Biomaterials Congress in Toronto in 1996. The work of Canadian researchers over the past four decades is summarized briefly. It is concluded that biomaterials and tissue engineering is a mature, strong area of research in Canada and appears set to continue as such into the future.

12) Future directions in biomaterials [14]

Biomaterials have made a great impact on medicine. However, numerous challenges remain. This paper discusses three representative areas involving important medical problems. First, drug delivery systems; major considerations include drug-polymer interactions, drug transformation, diffusion properties of drugs and, if degradation occurs, of polymer degradation products through polymer matrices developing a more complete understanding of matrix degradation in the case of erodible polymers and developing new engineered polymers designed for specific purposes such as vaccination or pulsatile release. Second, cell-polymer interactions, including the fate of inert polymers, the use of polymers as templates for tissue regeneration and the study of polymers which aid cell transplantation. Third, orthopedic biomaterials, including basic research in the behavior of chrondrocytes, osteocytes and connective tissue-free interfaces and applied research involving computer-aided design of biomaterials and the creation of orthopedic biomaterials.

13) Inflammatory responses to orthopedic biomaterials in the murine air pouch [15]

An in vivo model of the inflammatory response to orthopedic biomaterials was used to examine cellular and cytokine responses to polymer particles of ultra high molecular weight polyethylene (UHMWPE) and polymethylmethacrylate (PMMA), and metal particles of cobalt–chrome (Co-Cr) and titanium alloy (Ti-6Al-4V). Responses were determined separately and in combinations, to examine interactions between different forms of biomaterials. Murine air pouches were injected with particle suspensions, and reactions evaluated using histological, immunological, and molecular techniques. All particulate biomaterials caused significant increases in membrane thickness compared with control (saline) air pouches, with the highest reaction seen in response to Ti-6Al-4V particles. A synergistic increase in membrane thickness was observed when PMMA was combined with UHMWPE, suggesting that multiple biomaterial stimuli markedly increase the inflammatory reaction. Cellular analysis indicated that all particles increased the absolute number and the percentage of macrophages in the membrane over the control level, with the most pronounced increase due to individual biomaterial occurring with UHMWPE particles. Cytokine analysis revealed that biomaterials provoked a strong IL-1 response. Ti-6Al-4V stimulated the highest IL-6 gene transcription and the lowest IL-1 gene transcription. The data suggest that synergism in the inflammatory response to biomaterials may be important in adverse responses to orthopedic wear debris.

14) PEG-variant biomaterials as selectively adhesive protein templates: model surfaces for controlled cell adhesion and migration [16]

This study focused on the role of poly ethylene glycol (PEG) in actively regulating the biological responsiveness of protein-adsorbed biomaterials. To this end, they designed PEG-variant biomaterials from a family of tyrosine/PEG-derived polycarbonates to present surfaces ranging from low to intermediate levels of PEG concentration, below the PEG level requisite for complete abolition of protein adsorption. The effect of PEG concentration on the amount, conformation and bioactivity of an adsorbed model protein, fibronectin, and on the attachment, adhesion strength and motility of L929 fibroblasts were analyzed. The results demonstrate that low levels of PEG can regulate not only the extent but also the conformation and specific bioactivity of adsorbed fibronectin. As the PEG concentration was increased from 0 to 6 mol%, the amount of adsorbed fibronectin decreased linearly yet the fibronectin conformation was altered such that the overall bioactivity of adsorbed fibronectin was uncompromised. The degree of cell attachment varied with PEG concentration in a manner similar to the dependence of fibronectin bioactivity on PEG has been reported. In contrast, the nature of cell adhesion strength dependence on PEG paralleled the pattern observed for fibronectin surface concentration. Our studies also indicated that the rate of cell migration was inversely correlated with PEG concentration over a narrow range of PEG concentration. Overall, these results highlighted the striking ability of PEG-variant biomaterials to systematically regulate the behavior of adsorbed cell adhesion proteins and, consequently, effect cell functions.

15) Smart biomaterials design for tissue engineering and regenerative medicine [17]

As a prominent tool in regenerative medicine, tissue engineering (TE) has been an active field of scientific research for nearly three decades. Clinical application of TE technologies has been relatively restricted, however, owing in part to the limited number of biomaterials that are approved for human use. While many excellent biomaterials have been developed in recent years, their translation into clinical practice has been slow. As a consequence, many investigators still employ biodegradable polymers that were first approved for use in humans over 30 years ago.

16) Systemic effects of biomaterials [18]

Evaluation of the host response to implanted biomaterials usually focuses on the implant site tissue response. This may lead to erroneous conclusions in the same way that examination of battles outside of their historic context does. A broader view discloses a variety of possible and actual systemic effects of carcinogenic, metabolic, immunological and bacteriological nature. Recognition of these effects in patients is hampered by a lack of epidemiological studies.

17) Biomaterials and biomedical devices [19]

This review discusses the factors important in the incorporation or integration of biomaterials and devices by tissue. Methods for surface modification and surface-sensitive techniques for analysis are cited. In vitro methods to evaluate the biocompatibility or efficacy of certain biomaterials and devices are presented. Present and future directions in neural prostheses, cardiovascular materials, blood or bone substitutes, controlled drug delivery, orthopedic prostheses, dental materials, artificial organs, plasma and cytapheresis, and dialysis are discussed.

18) Biomaterials for healthcare [20]

Development of the prototype. Islets of animal origin were enclosed in a device formed by a support and a polycarbonate membrane, with an extra cellular matrix in the encapsulation chamber to prevent aggregation of the islets. By association of 20 devices in a plate-type support, it was possible to implant up to 20 000 pancreatic islets, as necessary for testing on a mini-pig. Sterile macro devices were implanted into normal mini-pigs and their biocompatibility studied after up to 92 days of implantation. Despite the induction of fibrosis, there was no observable inflammatory response, nor any significant effect on the peripheral immune system.

19) Optimization studies on the features of an activated charcoal-supported unease system [21]

The adsorption of urease onto a well-defined solid support, petroleum-based activated charcoal, has been achieved to provide the enzymatic hydrolysis of urea. In order to produce a biocompatible surface, the enzyme support system has been coated with hexamethyl disiloxane through plasma polymerization. The quality of the resulting coat was tested by electronic spectroscopy for chemical analysis and scanning electron microscopy techniques. Studies on the adsorption of urease, and activity and stability of the enzyme on the support have been in the direction to optimize the

features of the charcoal-supported urease and improve its availability for further use in clinical applications.

20) Bioactive specific biomaterials: Present and future [22]

Bioactive biomaterials made of synthetic or artificial polymers substituted with specific chemical functional groups carried by the macromolecular chain are designed to develop specific interactions with living systems. These soluble or insoluble polymers are derived from polystyrene and dextran. Such functional polymers may be endowed with anticoagulant heparin-like properties and, as a consequence, possess low thrombogenicity when they are in contact with flowing blood. Other functional polymers have been tailored specifically to interact with components of the immune system. Other polymers, in contact with cells can affect both cell growth and cell biological functions or only cell biological activity without necessarily undergoing change in all characteristics. Derived from the above concepts, it is possible to demonstrate that a random statistical distribution of chemical groups along the macromolecular backbone correlates with the biological properties of these polymers.

21) Macromolecular Engineering of Fluorinated Polymers and Hybrid Composites for Dental Resoration Application [23]

New polymeric materials with reduced polymerization shrinkage and low surface energy characteristics were investigated. New fluorinated ring-opening monomers were designed and synthesized and then used as starting materials for the corresponding polymers and composite resins. Properties, such as reactivity, chemical structure, thermal behavior and surface characteristics of different polymeric and co-polymeric systems were deeply studied. The polymers formed liquid crystalline mesophases due to the ordering of the fluorinated groups, even at very low contents of fluorinated chain side groups. Surface studies evidenced the presence of homogeneous well-ordered surfaces with low surface tension, due to the fluorine enrichment of the air-polymer interface. Dental composite resins incorporating fluorinated ring-opening monomers and cross linkers were formulated. Mechanical properties, surface composition and topography and bacterial adhesion were assessed as function of the components of the resin formulations. The insertion of fluorinated groups caused a significant reduction of volume shrinkage, without altering significantly the mechanical properties. A correlation between fluorine surface segregation, topography and surface energy was proposed.

22) Toward a suture less vasovasostomy: use of biomaterials and surgical sealants in a rodent vasovasostomy model [24]

With 500,000 to 800,000 vasectomies performed annually and a reversal rate of 3% to 8% vasectomy reversal has become a commonly performed procedure. Two-layer microsurgical vasovasostomy remains the gold standard for surgical reconstruction of the vas. However, the procedure is technically demanding and time-consuming. They determined the ability of biomaterials and surgical sealants to decrease the number of sutures used, enhance anastomosis water tightness and decrease operative time

CONCLUSION

A biomaterial is essentially a material that is used and adapted for a medical application. Biomaterials can have a benign function, such as being used for a heart valve, or may be bioactive. Used for a more interactive purpose such as hydroxy-apatite coated hip implants and such implants are lasting upwards of twenty years.

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