

Biomaterials in Regenerative Medicine

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ABSTRACT

Physiological regenerative system of human body is incapable of restoring the function when an injury exceeds its normal limits. Conventional methods previously being used for repair and rejuvenation of tissues had certain limitations that have brought the biomaterials to the forefront in the area of regenerative medicine. Biomaterials provide optimal support to the tissue during the process of healing and remodeling. Numerous classes of biomaterials are focused on specific applications; most prominent among them are polymers. Biomaterials are now being used in several areas such as fabrication, hematology and blood cell substitutes, tissue engineering, extracorporeal artificial organs, bone and vascular regeneration, stem cell differentiation and soft tissue repair. However, for the success of biomaterials in regenerative medicine, the focus should not only be on the physical, mechanical and chemical properties of the materials but also the fundamental principles of biological interactions and biocompatibility.

Keywords: Biomaterials, Polymers, Regeneration, Regenerative medicine, Tissue engineering

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Introduction:

The term “regeneration” refers to the process of replacement of lost non-functional specialized tissues with healthy specialized cells.(1) Naturally, human body functions to regenerate whenever an injury occurs. However, the regenerative capacity is limited by numerous factors such as type of tissue or any structural defect (physical size of tissue). Need of an external support is necessary whenever the type of injury reaches beyond the normal physiological capacity of the internal regenerative system.(2) Conventional methods in regenerative medicine have numerous limitations and for this reason great emphasis has been laid down on the need of biomaterials in repair and regeneration of tissues.(3) For example in the transplantation of cells, tissues and organs, major limitations were inadequate availability of donor tissues and cultivation of extra tissue in human body.(4) Combining the concepts of cellular biology, biomaterials and molecular signaling led to the advancement of tissue engineering field as well as de-novo synthesis of organs and limbs.(5) Likewise, damaged articular cartilage was previously replaced with metal and plastic implants. Some of the major drawbacks of this treatment strategy were wear particle formation, inflammation, and limited life-time. With the improvement in field of biomaterials, autologous chondrocyte transplantation was developed with proven benefits in healing.(6) Therefore, in order to

regenerate human tissues and organs with better functioning, regenerative medicine utilizes the basic concepts of various disciplines including materials science, life sciences and medicine.(7)

Materials used in the regenerative medicine are characterized by numerous properties including density, tensile strength, degradability, modulus and porosity along with many other material and mechanical properties.(8) Certain prerequisites have been proposed by various scientists that must be kept in focus while utilizing any biomaterial in regenerative medicine; the most important of them is the biocompatibility of the material under in-vivo and in-vitro conditions.(3) The material must be able enough to carry out optimal cellular activity for tissue regeneration without stimulating any inflammation or adverse systemic responses in the host body.(9) Furthermore, assessment of a cytotoxicity of the biomaterial is also a key point to consider in regenerative medicine.(3)

The objective of the current study is to highlight numerous applications of biomaterials in the field of regenerative medicine. Additionally, role of carbohydrate polymers in tissue engineering will also be discussed.

Methods & Results:

A mini review was conducted by carrying out an online search using key words such as regenerative medicine, biomaterials, advanced biomaterials, tissue engineering, implants, polymers etc. Boolean operators were used to combine the key words. Literature search was done using search engines and databases including PubMed, Google Scholar, Cochrane and Pakmedinet and the studies related to the topic were identified.

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Latest approaches in regenerative medicine:

Artificial red blood cells substitutes are now used clinically for pre-operative blood dilution or for post hemorrhage resuscitation.(10) Different types of raw materials are used for this purpose depending upon the type of artificial blood being made. For example, Perfluorocarbons (PFC) are used as blood substitute and are chemically inert. Also, their products involve polymerization reaction. Evidence suggests some proven benefits of PFCs to be used as artificial blood substitute as they do not allow the oxygen to react with the other gases and also allows smooth gaseous exchange between cells and tissues.(11) Biomaterials are also being used in the development of mechanical and biological cardiovascular valves and also in cardiovascular stents.(12, 13) Devices used as extracorporeal artificial organs like bio artificial livers, are used to assist the patients with acute hepatic failure.(14) In case of hollow fiber system, Synthetic or natural polymers like collagen are used to design such kind of devices.(15)

In case of skeletal muscle repair, electro spun chitosan microfibers are used as biomaterials.(16) These three dimensional scaffolds help the muscles to regain their normal function that are otherwise subjected to scar tissue formation as a result of normal healing process.(17) Tissue engineering is another area of regenerative medicine that utilizes combination of cells within biomaterials with the overall goal to generate viable and long lasting tissues with fast neovascularization. Several natural and synthetic polymers are used in cartilage tissue engineering such as silk, col and col etc.(18) Both synthetic and naturally occurring polymers can be used in regenerative medicine, and scaffold fabrication from natural polymers such as alginate, collagen, agarose, hyaluronan, fibrin etc. as well as synthetic polymers include polyglycolic acid, poly hydroxy ester, polylactic acid (PLA) and their copolymers is used.(19) Studies have shown significant regenerative results of corneal implants composed of methacryloyloxyethyl phosphorylcholine (MPC) cross linked collagen in corneal tissue regeneration as well.(20) Furthermore, substantial role of biomaterials can also be seen in nerve regeneration for axonal growth,(21, 22) hepatocytes regeneration,(23) bone and vascular regeneration, stem cell differentiation, and soft tissue regeneration.(24)

Carbohydrate polymers in regenerative medicine:

Tissue engineering is one of the most prominent tools and an active field of research in regenerative medicine.(25) Moreover, polymers are

the most popular biomaterial used for the purpose of regeneration of the damaged tissues. Evidence suggests that carbohydrate polymers not only play an active role in drug delivery and hydrogels but also in tissue engineering.(26) Linear glycosaminoglycan hyaluronic acid has a significant role in extracellular matrix formation as well as in tissue morphogenesis.(27) Studies have shown that hyaluronic acid is effective for the prophylactic treatment of knee pain and also for surgical adhesions.(28) Several modifications in the structures of relatively simple carbohydrate polymers can enhance their activity to promote efficient migration, spreading and multiplication of cells.(25, 29)

Future Challenges:

Numerous issues are imperative for consideration regarding the progression of regenerative medicine as a field. Creation of big engineered replacement tissues will necessitate equipment and technology that allows fully vascularized grafts to be anastomosed with the host vasculature at the instance of transplantation, permitting optimum graft survival.(30) Furthermore, enhanced knowledge of the role of the host immune system is integral for the success of regenerative medicine. An improved knowledge of the role of age and state of disease state of the host is also important in terms of progressing in the field of regenerative medicine.(31-33) Lastly, the use of three dimensional human tissue culture models are very integral as they would allow experimentation with polymers and other biomaterials in a human biological environment in contrast to animal models that are commonly used, but the two environments may have important differences.(34)

Conclusion:

It is evident from the above mentioned examples that the role of biomaterials in regenerative medicine is immense. However, for the success of the use of biomaterials in regenerative medicine, the focus should not only be on the physical, mechanical and chemical properties of the materials but also the fundamental principles of biological interactions and biocompatibility.

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Author Contribution:

Malik RJ: Conception of the idea, literature search and manuscript writing