

## NANOBIMATERIALS-NOVEL TRENDS IN BIOTECHNOLOGY: A REVIEW

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### Abstract

Biomaterials, especially those in the nanoscale, have sparked immense research interest in recent times. New developments in the field of nanotechnology have led to the discovery of nanobiomaterials that are totally bio-compatible, non-toxic and essentially biodegradable. These materials, often described as smart biomaterials, have the potential to be used over a wide range of applications ranging from tissue regeneration, stem cell differentiation, drug delivery to biosensors and biomedical diagnostic equipment. The present review focuses on some of the biomaterials that have gained importance in biomedicine and pharmaceuticals, in the past decade. We also present a general discussion on the current developments in the field and some of the emerging next-generation applications.

**Key Words:** Nanobiomaterials, Hydrogels,  $\beta$ -Tricalcium phosphate, Chitosan, Fibrin.

### INTRODUCTION

Nanotechnology has been playing a pivotal role in the development of new materials in the past decade. Combining the applied knowledge of biomaterials along with the fundamentals of nanoscience has paved the way for the creation of smart biomaterials that possess several trivial applications especially in nanomedicine and cancer therapy. A single biomaterial may not meet all the requirements for a specific application. Often two or more biomaterials are selected and their physical, chemical and mechanical properties optimized and advanced fabrication procedures are carried out before their final utilization. Several natural and synthetic nanobiomaterials have been used widely in neural interfaces, scaffolds for tissue engineering, matrix, implant forms etc.

Development of neural interfaces, that bridge the gap between neurons lost in an injury and external devices, has generated great interest in the last decade. Existing interfaces use electronic neural electrodes that are often not bio-compatible and do not form a proper communication channel between the nervous system and the outer world. Nanobiomaterials including functionalized graphene and carbon nanotubes, conducting polymers etc, have now enhanced the performance of the neural interfaces by manifold.

Recent advances in controlled-release drug delivery systems, has resulted in improvised drug forms that have been obtained by altering the pharmacokinetics and pharmacodynamics of existing drugs. The new strategies developed have improved the efficacy and safety of targeted drug delivery systems.

Nanobiomaterials form an indispensable part of tissue engineering. The

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advent of scaffolding matrices for tissue regeneration, have revolutionized nanobiotechnology. Current research in the field seeks to achieve smart biomaterials as matrices that trigger or stimulate target cell responses, which are vital in the tissue regeneration process.

Research on biomaterials has mainly focused on development of biocompatible, non toxic and biodegradable materials for various applications. This article aims to provide an insight into some of the latest innovations in nanobiomaterials, the use of nanoscale technologies for their modification and their potential applications that offer a promising future.

### **Hydrogels**

Polymer chains, cross-linked physically or chemically, and are able to retain large amounts of water or biological fluids are termed as hydrogels. Ever since its discovery in 1960s, hydrogels have found use in a variety of applications in pharmaceutical and medical industry. During the past few years, hydrogel-based materials have gained huge importance owing to their bio-compatible and non toxic nature. The water-retaining capacity of hydrogels makes them the best alternative to plastic matrix and scaffolds, as they resemble living tissues.

In 2010, Qigang Wang et al. described about high-water-content mouldable hydrogels by mixing clay and a dendritic molecular binder, as a step towards replacing plastic matrices by water-based gels. Biopolymer-based hydrogels as scaffolds for tissue engineering applications was reviewed by S.V. Vlierberghe et al. in 2011 and in 2012, Allan.S. Hoffman provided an in-depth overview of hydrogels for biomedical applications, which gave an insight into the synthesis procedures and the various properties of hydrogels.

Peptide hydrogels assembled from nonionically-polypeptide amphiphiles

prepared by ring-opening polymerization by Chonyi Chen et al. in 2013 and assembly of viral hydrogels for three-dimensional conducting nanocomposites by Po-Yen Chen et al. in 2014 highlights the latest developments in hydrogels that are likely to revolutionize the pharmaceutical industry.

### **$\beta$ -Tricalcium Phosphate**

$\beta$ -Tricalcium phosphate is a biocompatible material that finds use as clinical substitute for bone deformations. Although osteoconductive, it lacks growth factors and cellular components and does not possess osteoinductive properties. It is also highly resorbable and supports new bone formation in animals.

Osteoconductive properties of poly(96L/4D-lactide)/beta-tricalcium phosphate in long term animal model by Guy Dalcusi et al. in 2011 studied the effect of calcium phosphate mineral on the bone ingrowth at the expense of a co-polymer. Osteoconductive action of alendronate after implantation of beta tricalcium phosphate in rat adjuvant-induced arthritis by Takahiri Netsu et al. in 2012, was an attempt to study the effect of alendronate on  $\beta$ -TCP resorption and bone formation in rats with adjuvant-induced arthritis.

Recombinant human platelet-derived growth factor-bb and beta-tricalcium phosphate (rhpdgf-bb/ $\beta$ -tcp): an alternative to autogenous bone graft, by Christopher W DiGiovanni et al. in 2013 proposed an alternative to autograft technique through his celebrated work on  $\beta$ -TCP. Much research is to be done in the case of beta tricalcium phosphate which has opened up new avenues of interest amongst the scientists of the current era.

### **Chitosan**

Chitosan is the deacetylated product of the polysaccharide chitin- which forms the hard exoskeleton of most arthropods. It is non-toxic, biocompatible, bio degradable and

possesses antibacterial properties that make it an excellent nanobiomaterial for drug delivery, wound healing and tissue engineering applications.

Novel chitin and chitosan nanofibres for biomedical applications by R. Jayakumar et al. in 2010, gave a detailed analysis on the preparation and properties of the fibres (such as high surface area and porosity) due to which they find novel applications in the biomedical field. In 2011, M. Dash et al. presented a review on chitosan-a semi-synthetic polymer in biomedical applications, which provided a detailed summary of the chemical nature, biological properties and the uses of chitsan in regenerative medicine and drug delivery.

PEGylated chitosan derivatives: Synthesis, characterizations and pharmaceutical applications, by Luca Casatteri et al. in 2012 discusses the scope of PEGylated chitosan derivatives for medical use. Jackie-Stephen Haynes et al. in 2014 described the significance of chitosan in wound care in comparison with other biomaterials and discussed the peculiar properties of the substance that makes it a promising biomaterial for wound healing, in the near future.

### **Fibrin**

Fibrin is a tough, insoluble protein that forms a major component of blood clot. It is obtained by the polymerization of the protein fibrinogen under the enzymatic activity of thrombin.

The Effect of Platelet-Rich Fibrin Matrix on Rotator Cuff Tendon Healing: A Prospective, Randomized Clinical Study by Scott A. Rodeo et al. in 2011 was an important breakthrough in the case of fibrin. Engineered aprotinin for improved stability of fibrin biomaterials by K M Lorentz et al. in 2011, provided a detailed analysis on improving the stability of fibrin as a biomaterial for wound healing and other applications. Percutaneous

treatment of pseudoaneurysms using fibrin adhesive by M B Matson et al., in 2014, provided a firm footing on the research based on fibrin in many biomedical applications.

### **Applications**

In recent years, nanobiomaterials have come up with plenty of applications promising a healthy and safe life in future. In July 2013, Ryan F. Donnelly et al investigated the hydrogel forming micro arrays that can be inserted in the skin by self application. Basically, applications of hydrogels are divided into four main categories and they are drug delivery, tissue engineering, bioseperation and biosensors. In 2014, Wang Y et al reviewed the hydrogel solutions which were important in taking guard and using it for repairing the tissues under tissue engineering and also for the regeneration of tissues using it in regenerative medicine. Similarly for bone regeneration, Ana Catarina Lima et al. in 2013, showed the cell and protein based methodology by hydrogel spheres. The next potential role of hydrogel was demonstrated by Jiayang Li et al in 2013. They detailed the applications of hydrogels for Intracellular Imaging and Intratumoral Chemotherapy.

Another important nanobiomaterial discussed above is  $\beta$ -TCP which is a pioneer source of calcium, the main factor of bone and teeth. In 2014 G S Diogo et al manufactured  $\beta$ -TCP for its potential application in bone tissue engineering to incorporate it in bone related disease which is the most abundant in old age. Another tremendous target was achieved by Joshua Chou et al in 2014 itself when they evaluated the antibiotic potential of a marine structure-based new drug delivery system produced by hydrothermally converting foraminifer's exoskeletons to  $\beta$ -tricalcium phosphate ( $\beta$ -TCP). Several potential applications of  $\beta$ -TCP have come up in 2014 itself. Tomohiro Minagawa et al 2014 showed the osteoconductive and biodegradable properties of beta-tricalcium

phosphate in a rat calvarial defect model. Jinku Kim et al 2014 showed the combinations of autograft, demineralized bone matrix, and tricalcium phosphate and its effect in defected femoral of rabbit.

The advantages of nanobiomaterials will not be completed without discussing about chitosan. The key role at medicinal level was started in early 2000. J.-K Francis Suh et al in 2000 reviewed the role of chitosan in cartilage tissue engineering. Sara Vitalini et al 2014 reviewed (article submitted) the effect of chitosan in sensory attribute of wine. They showed that chitosan plays effective role in production of phytochemicals in plants which participate actively in the defense mechanism against pathogens. Hajer Aloui et al 2014 evaluated the treatments on the fruits' sensory characteristics under the effect of chitosan and Locust Bean Gum with different citrus essential oils to verify the complete absence of off-odours and off-flavours. Chitosan coatings have the potential to improve the post-harvest life of some fruits like raspberries by reducing water loss, respiration rate and decay incidence. Jaqueline Visoni Tezotto-Uliana et al 2014 studied the effect of different concentrations of chitosan, applied pre- or post-harvest, on the retention of quality attributes of fresh raspberries. Chitosan also serves as regenerative medicines. S.S. Silva et al 2013 examine issues concerning structural features, topography, enzymatic degradation behavior, antibacterial activity and cellular response of chitosan/aloe vera-based membranes. They hypothesized that the chitosan/aloe vera-based membranes might be promising wound dressing materials. G.L. Dotto et al 2013 studied role of chitosan to remove the food dye thermodynamically.

There are plenty of applications shown by fibrin in vivo and in vitro. Fibrin is one of those main blood clotting factors which are essential most in formation of a blood clot. Fibrin is also known as factor Ia and factor XIII is required for contraction and hardening

of fibrin by cross linking, leading to the formation of the blood clot. Many research work has been going on fibrin protein. Wilson et al 2014 studied the role of fibrin in to reduce pancreatic stump complications. Vipin Asopa et al 2014 reported the use of fibrin bioadhesive hip arthroscopy for articular cartilage lesions. Fibrin is also useful in alveolar defect treatment. Hideki Itano 2013 optimized the combined effect of fibrin sealant and bioabsorbable sheet against alveolar air leakage. Salvador Morales-conde et al 2013 quantified how fibrin adjusts the postoperative seroma and laproscopic repair of ventral hernia.

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