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EDITORIAL

Summary of the National Conference on Challenges in Biomaterials Research jointly organized by VIT and CSIR-CECRI

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Health care has become one of the highest priority research fields of this century owing to the dramatic increase in the number of people affected by various diseases. Health care costs and the high demand for biomaterials have placed tremendous pressure on government funding agencies and researchers to develop cost-effective, appropriate biomaterials to treat various diseases and to regenerate diseased and fractured organs. The field of biomaterials is projected to generate approximately $80 billion by the end of this decade. Thus, various funding organizations have allocated considerable funding for the development of the next generation of biomaterials. Despite the fact that certain global regions and countries (such as the US, Europe, Australia, Brazil, and the People's Republic of China) have considerable expertise in the manufacturing of various biomaterials, India has developed considerable expertise in specifically manufacturing cardiovascular and orthopedic implants over the past 3 decades.

There are several research and development institutes, universities, and colleges in India working toward developing novel biomaterials and unique characterization methods. Extensive research in the field of nanobiomaterials is being pursued all over India, with considerable effort toward generating new biomaterials with enhanced service and lifetime and superior biocompatibility. In order to provide young researchers a platform to interact with clinicians, industrialists, and researchers from and in India, and to showcase their talent to understand the current challenges in this field, a 2-day national conference on "Challenges in Biomaterials Research" was held at VIT University, Vellore, India from December 23–24, 2013. Challenges from the clinical, industrial, and academic researcher point of view were presented by speakers from numerous international and national universities. Clinicians were present from various medical hospitals, and scientists working in research labs also contributed toward the discussion. Topics such as problems encountered in surgical procedures, the design of biomaterials, toxicity of materials, development of orthopedic implants, surface engineering, corrosion and wear, and biocompatibility were presented by both researchers and students.

This supplement issue of the *International Journal of Nanomedicine* comprehensively presents the peer-reviewed research presented at this unique conference. As various topics were covered, the papers are categorized under categories: "Novel materials for bone tissue engineering", "Novel materials for wound healing and nerve applications", "Novel nanomaterials for antibacterial applications", "Novel calcium phosphate-based biomaterials", "Novel non-calcium phosphate-based biomaterials",

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"Silver-based and calcium-based anti-toxicity studies", and "Mechanical properties and surface engineering of orthopedic implants".

We hope you enjoy reading this issue and learning about all of the wonderful research presented at this conference as we continue to forge a path forward developing improved biomaterials to meet health care challenges in the decades ahead.

Category 1

Novel materials for bone tissue engineering

As bone is the second most transplanted tissue in the body, concerns have consistently arisen for the development of improved synthetic bone graft substitutes. The most popular bone graft substitutes available in the market are versions of demineralized allogenic or xenogeneic bones. These substitutes, although successful, are not without risk of microbial contamination and immunorejection. Alternatively, in vitro-constructed bone tissue from the patient's own cells and porous–bioactive tissue-engineering biomaterials offer a potential risk-free future for bone graft substitutes. Biomaterials used in bone tissue engineering have varied from biopolymeric, polymeric, ceramic, metallic, and nanocomposite materials. To emphasize the ever growing, changing landscape of new materials being developed for orthopedic applications, the first article in this series reports on the use of carbon nanotubes (CNTs) in bone tissue engineering applications. CNTs are known to be one of the toughest materials today and, simultaneously, they appear to possess optimal cell adhesion properties for orthopedic applications. The advent of CNTs in bone tissue engineering, in the form of nanocomposites with metallic and ceramic materials, would be a welcome signal for the next generation of orthopedic biomaterials. These materials are both bioactive (osteoinductive and osteoconductive) and mechanically tough. Similarly, another article in this section emphasizes the use of silk-based matrices for bone tissue engineering applications. Natural silk is composed of the biopolymeric protein, fibroin, and is a well-known biomaterial for use in many soft tissue engineering applications as a soft sponge. The authors of this article demonstrate that electrospun nanofibers of silk are far more osteoinductive than those of sponges obtained from conventional freeze-drying methods. The authors emphasize that nanoscale biomaterials have an edge over microscale equivalents in terms of strength and bioactivity. The last three articles in this section deal with metallic glass-based biomaterials. Metallic glasses are considered to be fairly new in the field of material science. Of course, they are ceramics, but are not fragile. Their unique properties like mechanical–chemical rigidity, bioactivity, nanoscalability, and coatability place them in a privileged position in the crowded field of biomaterials. The third and fourth papers studied metallic-based glasses and advocate that cheaper prosthetics could be made out of metallic glasses if a mere thin-film coating of the former is layered over steel implants. The fifth paper proves that these metallic glasses (such as TiO_2) in nano-confirmation have superior bone cell-promoting properties.

Category 2

Novel materials for wound healing and nerve applications

Normal wound healing is a biological restorative response that comprises sequential phases of hemostasis, inflammation, proliferation, and tissue remodeling. For successful wound healing, it requires the stimulation of interaction between cells, extracellular matrix production, and growth factor secretion through all phases of healing. To evaluate the wound-healing effect, emerging technologies center on the use of engineered scaffolds that can perform all the functions of native skin, like re-epithelialization and granulation tissue proliferation, and can reestablish functional extracellular matrix during healing. An ideal wound dressing should be biocompatible, can retain a moist environment (due to the proactive role oxygen plays in wound healing), protects against dust and bacteria, and is permeable to gases to improve healing. Various natural polymers derived from engineered skin substitutes in the form of 2D films, 3D gels and sponges, and electrospun mats of collagen, chitosan, fibrin, elastin, gelatin, fibroin, alginate, cellulose, and hyaluronic acid are known. A range of synthetic polymers are used and are also commercially available or are being developed. Due to a lack of biological signals for cell attachment and proliferation, synthetic polymers illustrate limited clinical success. Currently, no specific engineered skin substitute can fully achieve all the functions of intact human skin.

A series of chitosan–gelatin hydrogel/nanofibrin ternary composite bandages (CGFBs) for the treatment of burns has been investigated and is described in this section. The prepared CFGBs are macroporous, biocompatible, and biodegradable, showing wound-healing efficacy and skin-tissue regeneration in rats. Similarly, alginate hydrogel/nZnO composite bandages have been evaluated for wound-healing potential. The composite bandages showed excellent antibacterial activity against a number of tested microbes. Additionally, it was demonstrated that such bandages have a controlled degradation profile with a fast blood-clotting ability. The developed composite bandage was shown to be nontoxic to human dermal fibroblast cells, indicating its wound-healing potential.

Category 3

Novel nano antibacterial applications and calcium phosphate-based anti-toxicity studies

Thanks to the discovery of antibiotics in the early 20th century, we survived many microbial infections. However, in the 21st century, infections have grown alarming again. Pathogenic microbes are evolving faster than science itself and are becoming resistant to the latest generation of antibiotics. In fact, our approach to killing bacteria has not steered away from developing new pharmaceutical agents similar to the discovery of penicillin. The discovery of a newer generation of antibiotics is based on imparting certain superficial molecular changes on existing antibiotic molecules in order to make them more effective. Microbiologists, however, correctly predicted that microbes may evolve to resist antibiotics. Recent findings have highlighted that, indeed, multidrug-resistant bacteria have emerged which we do not know how to kill using traditional medicine. What could be the solution, then? Scientists are trying to find a probable solution to this problem using nanotechnology. This section highlights some nanomaterials which have promising antimicrobial properties without using antibiotics. The first article focuses on the in situ deposition of silver nanoparticles on titanium implant surfaces to protect it from immediate as well as late-phase postoperative infection. Apart from that, nano-hydroxyapatite is considered to be highly osteoinductive and has been used profusely as bone fillers in numerous orthopedic surgeries. Loading any microbicidal drug in such a bioactive nano-delivery system may reduce the chance of postoperative infection significantly; this is the idea undertaken by the authors of the second paper. In order to make the process economical, they used egg shells as a raw material for the synthesis of nano-hydroxyapatite.

There are certain plant extracts which have high antimicrobial properties. However, as they are water insoluble, their usage has been restricted in medicine. The subsequent two articles in this section discuss the development of stable nanoemulsions of microbicidal oils derived from eucalyptus and neem plants. Stable nanoemulsions of plant-extracted microbicidal oils are highly homogenous in water and, in the future, could be used as injectable antibiotics in humans. Concurrently, it is a well-known fact that microbes cannot only infect us but also can spoil our food and even clothes. The next paper highlights the synthesis of nano-silver-impregnated fabrics to protect our clothes from bacterial colonization, which usually gives out a bad odor and subsequently damages our clothes.

Category 4

Novel calcium phosphate-based nanobiomaterials

There is an increasing risk of bone injury due to road accidents, bone cysts, tumors, and bone-related pathological conditions which drives active research for the development of more effective biomaterials for bone regeneration. Bioceramics have been used for a long time for skeletal repair and reconstruction. Although bioceramics are not new to bone tissue engineering, their bioactivity and osteoconductive properties make them a preferred choice in numerous dental and orthopedic applications. During recent years, biomaterials scientists have made an effort to improve bioceramics for promoting prolonged tissue responses to biomaterials after implantation. In this section, two articles provide an overview of the development of advanced bioceramics for bone regeneration. Specifically, Nachiappan et al pay special attention to the development of a hydroxyapatite–magnetite composite for both cancer therapy and bone healing after tumor resection. The bioactivity of a composite of HaP and TiCN developed on steel using magnetron sputtering has been discussed in detail by Anusha et al. In addition to this, the bioactivity of a nanocomposite film consisting of Hap and Polycaprolactone loaded with ciprofloxacin is also reported in this section. In the second part, the relatively less explored bioglass–wollastonite is studied in its nanocrystalline form, and the influence of its needle-like morphology on bioactivity is reported.

Category 5

Nanoparticle drug-delivery studies

The advent and use of chemical and biological therapeutic agents and drugs against specific causative factors have significantly improved the prognosis of numerous conditions, thus improving and extending the quality of life. Despite the extraordinary success achieved by the use of these agents, concerns still remain regarding a lack of intended efficacy at the site of disease and undesirable side effects of drugs in other parts of the body. It was believed and proved beyond any reservation that site- or targeted-intervention and administration of drugs would both improve therapeutic efficiency by increasing bioavailability at the site of the disease, reducing unwanted systemic drug toxicity. However, direct local administration of drugs to certain inaccessible regions of the body poses a challenge. In recent years, we have witnessed an increase in the engineering and development of drug-delivery systems for the targeted delivery and also for controlled release of drugs.

Despite the availability of drug-delivery systems, concerns have arisen regarding the effect of these systems on the human body. Therefore, there is a need for the use of biomaterials and bioinert agents in the development of intelligent drug delivery systems. The age of nanotechnology has provided an array of choices for the development of smarter and safer drug-delivery systems. The desired characteristic features of drug-delivery systems achieved recently are in the predictability of the incorporation and release of the drug, stability in both shelf-life and after administration, no/minimal interaction with drug, and precision in homing to the delivery site, in addition to the safety profiles rendered by their biocompatibility and their ability to reduce toxicity of the drug by localizing its activity at the desired site and protecting early and non-site-specific metabolism of the therapeutic agent.

This section presents numerous original studies which address some of the key features of these drug-delivery systems such as their safety profile, efficient incorporation, and release of therapeutic agents by these systems. Detailed in vivo toxicity investigations including biochemical, hematological, and histopathological analyses on polyethylene glycol-modified hydroxyapatite and titanium dioxide nanoparticles used for targeted drug-delivery systems are reported in terms of favorable toxicity and biocompatibility profiles. In addition, this section also details the functionalization of silk fibers with silver nanocolloids, a potential suture system to curb localized bacterial infection. Finally, the use of liposomes as a drug-delivery system devoid of undesired interactions with the drug, favorable controlled release behavior, and acceptable stability of the therapeutic agent are presented. These reports add significant valuable information to the knowledge of drug-delivery systems developed to date.

Category 6
Nanomaterials

In addition to the implant material and their biocompatibility, the scope of this conference was also focused on new trends in therapeutics, the green synthesis of biomaterials, and diagnostics. Along this line, novel drug-delivery formulations, like buccal films for metformin delivery in diabetic patients and mucoadhesive microsphere systems for the sustained release of antihypertensive drugs, are quite interesting. A nanobiosensor matrix created using gold nanoparticles and hierarchically ordered, porous TiO_2 nanotubes has been recognized as a potential biosensor matrix for the detection of glutathione. Also, a noninvasive electrochemical nanobiosensor platform, designed for quantitative determination of the glucose with an integrated programmed drug-delivery system, represents an area of immense future research, particularly for asthma and rheumatoid arthritis cases. A novel route for the development of CdS nanoparticles using a one-step process with an agro-waste as a capping agent is reported. All of these efforts are highlighted in this section.

Category 7
Mechanical properties and surface engineering of biomaterials

Among the various biomaterials at our disposal today, the dramatic growth of the orthopedic implant market globally and the need for long-lasting implants have provoked great interest from material scientists to develop new biomaterials or surface-engineer existing materials. Following the mounting evidence of various adverse effects of debris and ions released from the wear of articulating surfaces, scientists have been challenged to develop a high-performance, long-lasting, safe, and reliable prosthetic material or material surface. In addition, failure of hip and knee replacements due to the high implant modulus (not matching that of surrounding bone) leading to stress shielding and accumulation of Ti particles in the nearby tissue remains a crucial issue in orthopedics. This has prompted researchers to develop new Ti-based alloys with a low modulus and subject them to various thermomechanical treatments to develop an appropriate microstructure which will possess optimum properties with regard to corrosion, wear, and mechanical behavior.

Papers presented in this section highlight the development of new Ti alloys and thermomechanical processing that will lead to enhanced wear and corrosion properties, the influence of using different media on the corrosion of Ti alloys, and the effect of ceramic coatings on reducing wear resistance of Ti alloys. Thermomechanical processing is considered to be an effective tool to improve the strength of Ti alloys, and an article on the behavior of warm rolling has highlighted the effect of fine grains on the enhancement of wear and corrosion when compared to hot-rolled alloys which generate micron grains on processing. Various ceramic coatings have proved to enhance the hardness, leading to a reduction in the wear of

Ti-based implants. The paper on plasma spraying of alumina and zirconia powders on Ti-6Al-4V alloy have clearly outlined the importance of processing parameters on the development of porous free hard coatings for biomedical applications. The studies on effects of thermomechanical processing of newly developed Ti-20.6Nb-13.6Zr-0.5V alloys clearly outline a structure–property correlation in this alloy and the effects of various microstructures on the mechanical properties and corrosion behavior in the simulated body solutions.

Disclosure

The authors declare no conflicts of interest in this work.