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Review on Nanostructures in Bionanotechnology

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ABSTRACT

Nanotechnology is developing nanoproducts for improvement and advancement of healthcare and medical research. Applications and potential for nanotchnological developments are enormous but their safety and risk-benefit features are areas of concern for their long term usage. Main biomedical applications of nanotechnology in medicine are diagnostics techniques, drug delivery and implants including nanostructured materials. Researchers are showing a great interest in development of nanosensors and lab-on-a-chip technology for external use which are highly suitable and safe. In-vivo applications include anticancer nanodrugs, gene therapy and implantable devices like insulin pumps. The future of nanotechnology lies in the areas like synthesis of different nanostructures and their uses, therapeutic applications, biomimetic & biological nanostructures, devices& instruments for early detection and study of diseased molecules and nano-tissue engineering. Progress is made in the development of implantable sensors for monitoring and manipulating molecular processes. Due to the advancement of nanotechnology, biosensors are advancing at a very rapid rate for the detection and diagnosis of many biological problems. Various materials used for the synthesis of nanostructures are Pt, ZnO, TiO_2 etc. Biomedical nanotechnology is an emerging area of research and the research will continue till the technology is translated from research to potential clinical applications.

Keywords: Bio-nanotechnology, biomedical, biosensors, nanostructures.

1. INTRODUCTION

Over the past few years nanotechnology is advancing at a rapid rate and is among the fastest growing field of science and technology. The nanotechnology and engineering comes together to develop miniaturized and multifunctional biosensors. The developed biosensors can be used for comprehensive applications with enhanced sensitivity. Recently, for selecting the material for matrix, various nanostructures are finding the applications for biomolecules binding. ZnO has high exciton binding energy of about 60meV for near-UV and efficient excitonic blue emission, and is a wide band gap oxide semiconductor with band gap of about 3.37eV [1]. Its wide band gap makes it suitable for light emitting devices of shorter wavelength and being oxide semiconductor is attractive for wide range of sensors from simple gas sensors to biological sensors. Nanostructures are preferred for sensing applications due to their biocompatibility, abundance in nature and have characteristics properties including strong adsorption ability, high catalytic efficiency and high isoelectric point of about ~9.5 [2]. ZnO high isoelectric point helps in immobilization of low isoelectric point enzyme by electrostatic interactions and can also be used for developing enzymatic detection devices [3]. Nanomaterials can be used as a biomimic membrane material and to develop implantable biosensors because of its properties like high chemical stability, nontoxicity and high electron transfer capability, which help in biomolecules immobilization without electron mediator [4, 5]. Wang has described the importance of nanobelts and nanowires in the emerging field of nanotechnology [6], Zhou *et al.* reported nanowires as biocompatible and bio-safe [7] which makes them preferred option for applications in implantable biosensors. Singh and Solanki have shown the application of nanostructures in cholesterol biosensor [8, 9], Kang *et al.* have focused on gas sensors [10],Pearton and co-authors highlighted the importance of semiconductor materials in biological molecules sensing[11]. Enzymes and antibodies are used on the nanomaterials surface for detection of specific antigens in the biomedical field for diagnosis and detection of various problems. ZnO is a good choice for high performance transducers for bioelectronics devices as it is available as epitaxial layer and single crystal substrates. Nanomaterials are preferred for biosensors design due to their specificity for surfaces, good selectivity and high activity [12]. Different nanostructures are used in various biomedical applications but in this report, our main emphasis is on the biosensing applications.

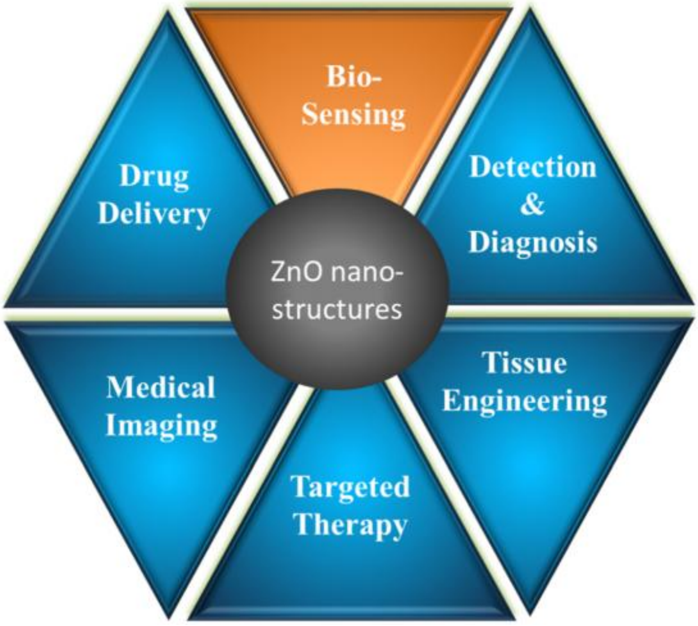

Fig. 1:Nanostructures used in various biomedical applications.

2. VARIOUSNANOSTRUCTURES

In fact, the specific properties of nanostructures and their applications depend on its morphology, size and structure. So, there are various reports available in literature for the growth of nanostructures with different morphology. Table 1 summarizes a few techniques generally used for growth of nanostructures.

Table: 1 Summary of various methods of synthesis of nanostructures and their morphologies

Synthesis Method	Morphologies	Synthesis Temperature	Reference
Hydrothermal	Nanorods, nanotubes, petal-like Nanostructures	70-180	13-15
Electrodeposition	Nano-spikes and Nano-pillars	70	16
Chemical bath deposition	Nanorods and nano-spines	80	17
Wet Chemical Route	Multidimensional	200	18
Chemical Solution Route	Dendrites like nanostructures	95	19
Aqueous solution Route	Needle and flower like	85	20

Although nanostructures are very promising for biomedical applications but the problems concerning nanostructures are about results reproducibility, size distribution and structural quality. It is clearly observed that the morphology, size and crystallinity of nanostructures vary to a great extent with different synthesis technique. Different nanocarriers for various applications are shown in Fig. 2.

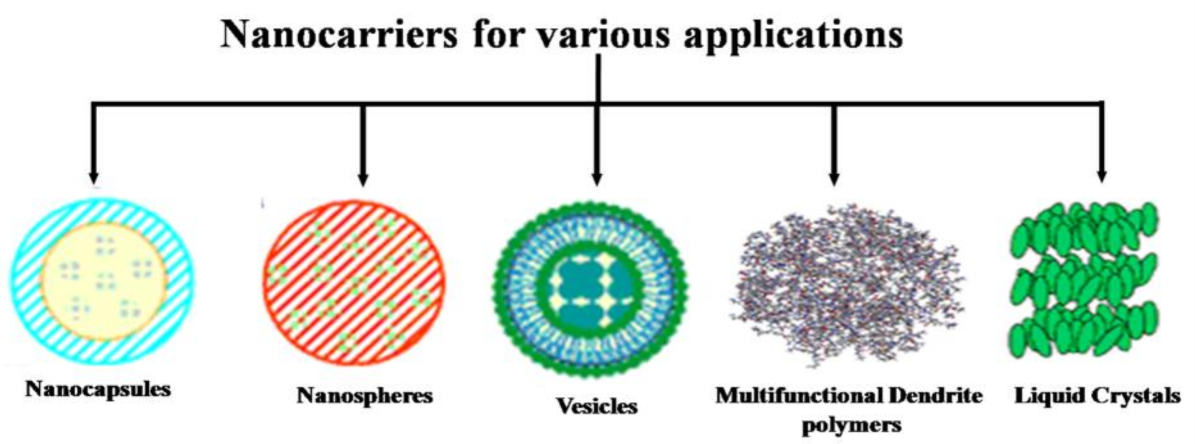

Fig. 2: Different nanocarriers for various biomedical applications.

3. NANOSTRUCTURES BASED BIOSENSORS

Nanomaterials based matrix is used for various biomolecules (such as antibodies, antigens, DNA, proteins like hemoglobin etc.) binding for the detection of different analyte. Recently, Ali *et al.* also demonstrated the wireless remote monitoring of glucose based on ZnO nanowires. Various nanostructures can act as future platforms for multi parameter health monitoring outside the hospital setup [21].

3.1 Electrochemical biosensors

Electrochemical biosensor senses a biochemical signal originating from bio-receptors. Electrochemical techniques have been the most widely usedform of transduction in biosensing applications. Most commonly used electrochemical techniques are differential pulse voltammetry (DPV), cyclic voltammetry (CV) and amperometrictechniques [22]. In electrochemical biosensors the electron transfer occurs by two ways: through redox mediator and by direct electron transfer, which has an advantage of absence of mediator. Recently, Zhao and coworkers prepared nanowires based electrochemical biosensor for L-lactic acid amperometric detection. They have used chemical vapor deposition (CVD) based nanowires for the sensing purpose. The sensitivity of the proposed electrochemical biosensor is of the order of 15.6 μA cm^{-2} mM^{-1} as nanostructuresprovide efficient electron transfer between the enzyme active sites and the electrode surface[23].Lei *et al.* have used nanotetrapods for L-lactic acid. Amperometric response measurements on nanotetrapod was utilized for L-lactic acid biosensor and the sensitivity is very high of the order of 28.0 μA cm^{-2} mM^{-1}[24].

3.2 Optical biosensors and FET's

The application areas of these sensors are in the field of cellular imaging, gene profiling, proteomics, environmental analysis and disease diagnosis. ZnO matrices are used for the detection of biomolecules using the principle of optical transduction and FET. Use of ZnO nanostructures for enhanced fluorescence detection was reported by Dorfman*et al.* for biomolecules like DNA and proteins [25]. The comparison between ZnO nanorods and Si nanorods fluorescence signal showed a stronger emission by ZnO nanostructures due to its inherent properties. Hagen and coworkers showed bio-functionalized zinc oxide field effect transistors for selective sensing of riboflavin. In aqueous solution riboflavin was detected to pM level by ZnO-FET using negative electrical current response [26].ZnO thin films showed weaker fluorescence as compared to ZnO nanorods. The enhanced fluorescence signal in ZnO nanorods is attributed to change in photonic mode density and decrease in self-quenching of fluorophores.

3.3 Piezoelectric biosensors

Great efforts are being made in exploring the possibilities of using the piezoelectric properties of nanostructures for biosensing. Piezoelectric biosensors are sensitive to mass loading [22]. In piezoelectric biosensors, when the alternating voltage is applied, piezoelectric crystal oscillates with the crystal faces vibrating in opposite direction giving rise to a resonant frequency response. Change in mass on crystal's surface modulates this frequency response which can be used for sensing. Reyes *et al.* reported that super-hydrophilic nanotip layer reduces the sample volume [27] and increases the device mass loading frequency shift significantly. Lu *et al.* have used micro membrane for piezoelectric biosensors applications. They calculated the stress of the membrane which can be used for stress monitoring[28]. Zhao *et al.* demonstrated a nanogenerator of SiO_2/ZnO nanowire for piezo-immunoglobulin-biosensing which is highly stable, self-powered/active biosensor. The piezoelectric output of the demonstrated nanogenerator can act as power source for the device as well as a sensing signal for the detection of IgG (immunoglobulin G)[29].

3.4 ZnO quantum dots (QDs) biosensors

QDs have been used as promising nanoparticles for highly sensitive detection of cancer biomarkers. ZnO QDs have fluorescent property and hence can be used as labels in assays quantifying biomarkers.For example, ZnO QDs in combination with peptides, nucleotides and antibodies can function as target cancer marker.The sensitivity of this type of detection for cancer biomarkers is very high because of electrochemical strip detection and amplification effect arising from ZnO QDs. A sandwiched-sensitive immunoassay is developed using ZnO QDs as fluorescent and electrochemical labels for detecting the carbohydrate antigen (CA19-9), which is a preferred label for pancreatic tumor [30]. The immunosensor developed is highly sensitivity, stable, and has good reproducibility. Wang and co-workers have reported that Quantum dot-functionalized porous ZnO nanosheets can be used for DNA detection. They have used the novel CdTe quantum dot (QD)-functionalized porous nanosheets via a covalent binding method with (3-aminopropyl) triethoxysilane as a linker. Using biotin-labeled DNA as capture probe, a model biosensor was proposed by immobilizing the probe on a nanosheet-modified electrode to recognize target DNA in the presence of an assistant DNA, which produced a"Y" junction structure to trigger a restriction endonuclease-aided target recycling. The 'signal on' strategy for photoelectrochemical detection of DNA showed a low detection limit down to the subfemtomole level and good specificity to single-base mismatched oligonucleotides [31].

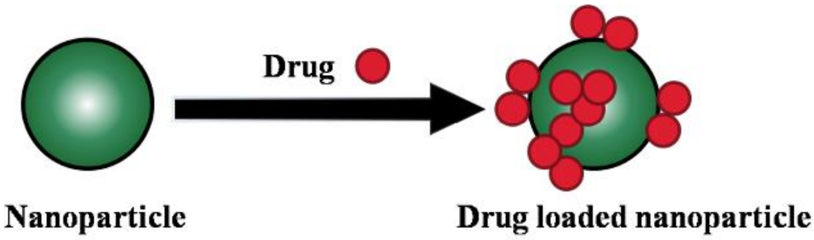

Fig. 3: Drug loaded nanoparticles.

4. CONCLUSION AND FUTURE PRESPECTIVES

Nanotechnology and nano-materials have had a great impact on biosensors for biodiagnostics and biodetection of various medical problems and have witnessed a lot of advancement over the past few decades. The size of nanomaterials is of the order of few nm (which is smaller than the size of human cells) and can interact with biomolecules on the surface as well as inside the cells. Now the researchers are focusing on combining different nano-platforms for performing therapies and in-vivo imaging simultaneously, for improving the efficiency of the treatment with accurate and non-invasive monitoring by multimodality imaging.Till now, no report is available which proves the use of some nanomaterials for in-vivo targeted imaging. This area of research needs more and more efforts for exploring the use of nanomaterials in this field. The detailed cytotoxicity and toxicological properties are yet to be elucidated for various nanostructures. The key question for researchers is not the toxicity of unadulterated nanomaterials but how to improve or modify the properties of the nanomaterials to reduce the toxicity and enhance biocompatibility so that it may be applied to the biological system and can be easily cleaned from the system. Also, great amount of efforts are needed for in-vivo toxicological studies of the nanomaterials for their long term uses in various captivating applications in medical science.

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