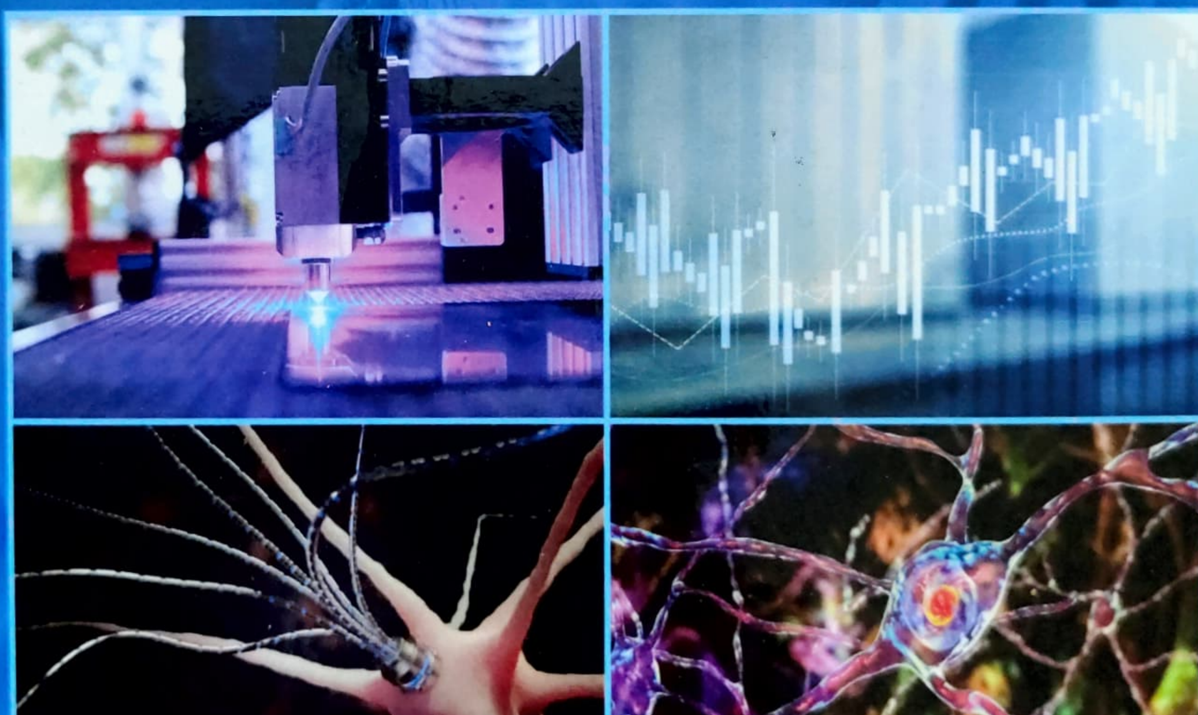
Nanobiomaterials
Research Trends and Applications

Thandapani Gomathi,
P.N. Sudha, *and* Sabu Thomas (*eds.*)



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Preface

In several fields of nanoscience, there is an ongoing interchange of ideas between the biological and physical sciences. Nanotechnology creates nanosized materials for use in biology and other fields by using biomimetic or bio-inspired processes. In this approach, nanoscale materials act as the "building blocks" for the creation of the "bridge," which is how nanobiotechnology bridges the gap between nano and bio. ***Nanobiomaterials: Research Trends and Applications*** cover a wide range of topics that can be used to illustrate the precious value of biopolymers in prospective applications in several disciplines, including drug delivery, tissue engineering, agriculture, electrochemical field, biosolar cells and wastewater treatment applications. As a contemporary collection, this book examines the extremely beneficial biodegradable and biocompatible materials. It will give an overview of various successful uses of nanobiomaterials. These nanobiomaterials are suitable for a variety of industrial applications since they can be employed directly or chemically altered to take advantage of their various chemical sites.

This book examines innovative methods for creating nanobiomaterials, characterisation of nanobiomaterials and its application for better agricultural practises, protracted drought conditions, and recent developments in biomedicine. Anyone who is interested in nanobiotechnology and nanobiomaterials can benefit from it.

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Nanobiomaterials in Cancer Therapeutics

Noel Vinay Thomas,[1] *Nithya R.*[2,*] and *Nirubama K.*[3]

1. Introduction

In olden days, cancer was a deadly disease and due to ineffective treatments, there was no way out than cruel death. Today also, cancer is a dreadful disease in accordance with its advanced phases. The difference between the former and the present day spread is that it was a rare phenomenon in olden days and widespread nowadays. However, the disease remains the same and the treatment has become improved. The conceptions in finding drugs from natural resources which do not adversely affect health rather than taking recourse to chemical methods are essentially needed today. Resorting to nanobiotechnology is one such idea of preparing drugs from nature.

Nanobiotechnology can be explained as "nanotechnology applied to biological systems". Nanotechnlogy is a conglomeration of several aspects of science, i.e., physics, chemistry, biology, clinical science and technology. In the field of medicine, it is potentially active to overcome the shortcomings of traditional drug delivery system by reducing side effects and improving efficiency. Nanotechnology is efficiently helpful in cancer therapeutics with its potential for diagnosis, for imaging and for drug delivery (Lungu et al. 2019).

Nanobiotechnology involves the engineering of new materials at a nano scale level for various biological usages. As such, nanobiomaterials form a bridge between biology and nanotechnolgy. As already defined by many authors, nano materials are those whose length measures between 1 and 100 nm. At these standards, they sustain clear optical, mechanical and electrical properties (Avti et al. 2011) which at length cater to the needs of cancer therapeutics.

1.1 Key Properties of Nanobiomaterials

Several nanobiomaterials are in vogue, namely metallic, ceramic, organic, inorganic, carbon based, polymer nanobiomaterials and nanocomposites. Their key properties are their size, shape and surface features. These aspects assume significant part in targeted drug delivery.

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In order to gain a prolonged period of drug suspension, nanoparticles of small size are preferable for circulating through the blood stream (Ankamwar 2012). When designed in proper manner, the polymeric nanoparticles ranging from 20–100 nm act efficiently *in vivo* owing to their sustained journey in blood stream. As regards shape, it decides the cell absorption and targeted delivery of drug. Nanoparticles of spherical shape enter into the cells faster than cylindrical ones (Elsabahy and Wooley 2012). The surface of functionalized nanomaterials decide whether they are hydrophobic or hydrophilic, lipophobic or lipophilic, and also the range of the molecular interaction (Ankamwar 2012). The rough surface area of nanoparticles helps promote biomedical applications, drug release in particular (Lin and Gu 2014).

2. Types and Applications of Nanobiomaterials in Cancer Therapy

Numerous studies on cancer theraupeutics have been conducted by nanomaterials because they overcome the biological barriers, such as enzymatic degradation or non-specific delivery during circulation and improved intracellular penetration. The usage of biodegradable polymers can be targeted to a precise location which would make the drug much more effective and less harmful (Sinha et al. 2006). This present chapter will try to provide a broad understanding about different types of bionanomaterials towards cancer therapeutic applications.

2.1 *Chitosan Nanomaterials*

To be successfully used in cancer treatment, the materials used should be inert, biodegradable, biocompatible and should be free of impurities. Chitosan, a biodegradable biopolymer, mainly consists of β-(1→4)-linked 2-amino-2-deoxy-β-D-glucopyranose (GlcN) units. It is due to these amino groups that the pH alters significantly, which in turn alters its property, thereby influencing biomedical applications of chitosan (Kumirska et al. 2011).

The drug release study of chitosan encapsulated piperlongumine (PL) (PL–CSNPs) which was prepared *via* ionic gelation method revealed the sustainable release of PL from the CSNPs and are pH-dependent. The PL–CSNPs showed efficient cytotoxicity against human gastric carcinoma (Venkatesan et al. 2016). Magnetic nanoparticles are noteworthy as a therapeutic agent for cancer treatment. Chitosan oligosaccharide-stabilized ferrimagnetic iron oxide nanocubes (Chito-FIONs) with 30-nm-sized FIONs was developed as an effective heat nanomediator for cancer hyperthermia. The results showed excellent antitumor efficacy (Bae et al. 2012). The antitumor nanovaccines consisting of self-assembled chitosan (CS) nanoparticles and two-component mucin1 (MUC1) glycopeptide antigens prepared by physically mixing showed that it is a useful and safe adjuvant system for MUC1 glycopeptide based cancer vaccines (Chena et al. 2017).

The identification of novel anticancer substances derived from natural sources is of great interest. Using breast cancer cell line (MCF 7) to test the anticancer extract's ability to inhibit the proliferation of cancer cells, Indigofera intricata crude alcoholic extract and chitosan were combined, and the findings were encouraging (Shahiwala et al. 2019). Curcumin was successfully encapsulated in chitosan-gum arabic nanoparticles via an emulsification solvent diffusion method with 136 nm size, which showed superior anti-colorectal cancer activity (Udompornmongkol and Chiang 2015). The evaluation of chitosan loaded nanoparticle of *Allivum sativum* by using ionic gelation method was prepared and the *in vitro* release of the drug was found to be the highest, i.e., up to 90.65% and was more stable. Hence, it can be used to treat cancer (Gupta et al. 2019).

Because of their stability, low toxicity, and straightforward and gentle manufacturing processes, silk fibroin-modified chitosan nanoparticles are excellent candidates for chemotherapeutic drug delivery in the treatment of cancer (Yang et al. 2015). Peripheral blood mononuclear cells (PBMC) were used to create a cancer-associated fibroblast (CAF) cell line, which was then subjected to an in vitro treatment with 100 μg/mL of chitosan nanoparticle. The results indicated that Ch-Np could be used as a delivery system for targeting cancer cells for the treatment of esophageal cancer (Potdar and Shetti 2016).

2.2 Alginate Nanomaterials

Natural biopolymer alginate is a linear copolymer made up of blocks of (1,4)-linked d- and l-mannuronate residues. The blocks are made up of alternating M and G residues (GMGMGM), followed by consecutive G residues (GGGGGG), and then consecutive M residues (MMMMMM). It allows efficient cell penetration into matrix and cell encapsulation. It is used as anticancer drug because of its biocompatiblity, nontoxicity, and biodegradability.

Inverse-micelle process was used to prepare calcium-crosslinked alginate matrix with 90 nm size. These nanoalginate (NALG) carriers were assessed by a doxorubicin (DOX) formulation (NALG-DOX) and examined their potency on breast cancer cells (4T1-luc2-GFP) (Rosch et al. 2018). The alginate-conjugated folic acid nanoparticles (AF NPs) were encapsulated with 5-aminolevulinic acid (5ALA) through a water-in-oil (W/O) emulsion method and was accurately delivered to cancer cells without any degradation (Lee and Lee 2020).

The side effects of an oral chemotherapeutic drug Exemestane (EXE) was reduced by loading with alginate nanoparticles by gelation method. *In vitro* drug release studies showed that ALG-NPs loaded EXE was used to treat breast cancer effectively (Jayapal and Dhanaraj 2017).

Curcumin, polyphenolic compound of turmeric, has excellent biomedical applications. But, its poor solubility, short half-life and low bioavailability make its application limited in cancer therapy. Hence, to overcome these drawbacks, curcumin is loaded with biopolymer. Curcumin loaded magnetic alginate/chitosan nanoparticles were fabricated and tested the cytotoxicity of loaded curcumin to Human Caucasian Breast Adenocarcinoma cells (MDA-MB-231) (Song et al. 2018). Curcumin diglutaric acid (CG), a prodrug of curcumin, was loaded with chitosan/alginate nanoparticles and revealed better anticancer activity against Caco-2, human hepatocellular carcinoma (HepG2) and human breast cancer (MDA-MB-231) cells (Sorasitthiyanukarn et al. 2018).

2.3 Carbon Nanomaterials

Carbon nanomaterials like graphene, carbon nanotubes, carbon quantum dots, and carbon nanospheres are highly used in biomedical applications because of their high surface to volume ratio, unique size and excellent mechanical and electrical properties. Carbon nanotubes are hydrophobic and hence they cannot be used as such. The surface modification or functionalization of CNTs allows them to disperse into aqueous solutions which makes them most advantageous in biomedical applications (Shao et al. 2013).

Supramolecular π–π stacking to load doxorubicin (DOX) onto branched polyethylene glycol (PEG) functionalized SWNTs for *in vivo* drug delivery applications was carried out by Zhuang Liu et al. (2009) and found that the new drug formulation SWNT–DOX revealed an enhanced therapeutic efficacy with less toxicity compared with free DOX. Zhang et al. (2011) studied doxorubicin-loaded PEGylated nanographene oxide (NGO-PEG-DOX) to facilitate combined chemotherapy and photothermal therapy in one system both *in vivo* and *in vitro*. This combined treatment resulted in higher therapeutic efficacy with less toxicity than DOX alone.

The movement of single functional Qdots in tumors of mice from a capillary vessel to cancer cells was observed by Hiroshi Tada et al. (2007) and the *in vivo* processes of delivery were successfully analyzed. Indium phosphide (core)-zinc sulphide (shell) quantum dots (InP/ZnS QDs) were created and discovered to be highly effective and non-toxic optical probes for imaging live pancreatic cancer cells (Yong et al. 2009).

2.4 Hydroxyapatite Nanoparticles

Hydroxyapatite nanoparticles (HANP) are known to be biocompatible and non-immunogenic and are accumulated in bone tissues. The magnetic hydroxyapatite nanoparticles were prepared by adding Fe^{2+} by co-precipitation method. Then this magnetic-HAP powder (mHAP) or pure HAP powder (HAP) was mixed with phosphate buffer solution (PBS) and injected around the tumor cells of a mouse and the results revealed good biocompatibility and less toxicity (Hou et al. 2009).

Mesoporous hydroxyapatite nanoparticles containing significant quantities of chemotherapeutic drug vincristine was found to be a potential nanocarrier for bone cancer treatment (Maia et al. 2018). Mesoporous silica/hydroxyapatite (MSNs/HAP) hybrid carrier loaded with anticancer drug doxorubicin (DOX) (DOX@MSNs/HAP) fabricated. Oligo HA (oHA) and hyaluronan (HA) were coated onto the nanoparticles (HA-DOX@MSNs/HAP, oHA-DOX@MSNs/HAP). oHA-DOX@MSNs/HAP showed much higher efficiency cellular uptake and drug release in tumor regions, which proved that the anticancer effect of oHA-DOX@MSNs/HAP is better than HA-DOX@MSNs/HAP (Kang et al. 2019).

HAP nanoparticle (nHAP) possessed the ability for inhibiting cancer cell growth *in vitro* for 3 days and *in vivo*. *In vitro* studies revealed that the proliferation of human cancer cells was inhibited by more than 65% and *in vivo* injection of nHAP about 50% (Han et al. 2014). HAP nanoparticles were used to treat human breast cancer cells (MCF-7) in culture at different doses, and the results showed that HAP both slows cell growth and promotes apoptosis (Meena et al. 2012).

2.5 Gold Nanoparticles

GNPs exhibit unique properties like large surface area, penetrating deep into the biological tissues, the ability to bind amine and thiol groups and allows surface modification which makes them suitable for biomedical applications. The colloidal gold also exhibits plasmon surface resonance (LPSR), which means that it can absorb light at specific wavelengths, which makes them suitable for hyperthermic cancer treatments (Vines et al. 2019).

Gold nanoparticles (GNPs) can be used in radiation as well as chemotherapy together. GNP-mediated chemoradiation has the potential to improve cancer care treatment (Yang et al. 2018). The detection of oral epithelium alive cancer cells *in vivo* and *in vitro* was demonstrated via surface plasmon resonance (SPR) scattering imaging or SPR absorption spectroscopy produced from antibody-conjugated gold nanoparticles (El-Sayed et al. 2005).

3. Future Perspectives and Conclusion

Nanotechnology is a fast-growing area of science. The size and shape of nanoparticles plays an important role in biomedical applications. Even though there are many *in vitro* studies on cancer therapy, *in vivo* studies have to be conducted to check the viability. Then, they will reach their full potential as common drug delivery methods for regular cancer chemotherapy. For example, though there are many studies on the toxicity of carbon nanotubes, uncertainty on CNT toxicity prevails. If this uncertainty is resolved, the CNT-based therapeutics can be possibly applied clinically.

One of the directions for the best results is the integration of therapies and diagnosis like phototherapy, photodynamic therapy (PDT), photoacoustic therapy, chemoradiation therapy, etc., along with conventional therapies. Good example is iron oxide coated hyaluronic acid as a biopolymeric material in cancer therapy. More attention should be paid to improve the basic theories of drug release from nanocarriers and to improve biocompatibility in future investigations.

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