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Biomedical Applications of Nanomaterials-Updated until 2022

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Abstract

In this mini-review, authors have systematically updated the various biomedical applications of nanomaterials in concise and more effective manner for the better understanding of upcoming researchers in the field to further explore the research. The data is updated until January 2022.

Keywords: Nanomaterials; Biomedical applications; Drug delivery; Antimicrobial; Anti-cancer

Introduction

The present and future era is of nano science and technology related to multidisciplinary applications like medical, mechanical, space, chemical and tools pertaining to the needs of day to day life [1-5]. In the present mini-review, we focus on mainly the biomedical applications of nanomaterials in a systematic and comprehensive way. Exploiting physical or optical properties of nanoparticles, new functional therapeutic agents can be utilized for effective drug delivery, medical diagnosis and developing newl medical devices, etc [6-9]. Nanoparticles either from nature or synthesized in the laboratory have enormous scope in various biomedical applications, as summarized below.

Biomedical Applications

Anti-Cancer

Cancer is one of the deadliest diseases defined by uncontrollable abnormal cell growth. Till date, there is no effective cure for effective diagnosis and treatments of cancer in the later stages of recognition and continues to be a big challenge for the scientists. Feng and Yong et al [10]. utilized mesoporous silica nanomaterials (MSNs) as multifunctional delivery platforms for therapeutic agents and their significance in next generation cancer therapy. MSNs were chosen because of optical transparency, size and shape tenability and more loading of drug possibility (Figure 1). Pravin and co-workers [11] reviewed usage of cyanine nanoprobes as imaging/phototherapeutic agents in tumor treatment. Silk (inspired) biopolymers have been utilized as interesting natural eco-friendly agents for effective drug delivery due to possessing excellent mechanical properties and biocompatibility. Sieb et al. [12] covered the use of Bombyx mori and recombinant silks as an anticancer nanomedicine. Zhao and others [13] reviewed functionalized mesoporous SiO_2 nanoparticles (fMSNs) for bio-related applications because of having several advantages such as larger pore volume and good biocompatibility. Gold nanoparticles were used in a variety of cancers studies particularly, due to possessing anti-angiogenic properties [14]. Das and co-workers also outlined the use of magnetic gold nanoparticles in multi dimensional imaging and therapy of cancer [15]. They covered clinical translation of nanomaterial-mediated tumor radiosensitization, too. Upconversion nanoparticles (UCNPs) are being used more for tumor diagnosis apart from multimodal tumor imaging [16]. 2D Bi_2S_3 nanosheets were applied into tumor therapy. The resulting nanosheets exhibit high photothermal conversion efficiency due to their strong broad absorbance in the near-infrared (NIR) region and serve as a nanotheranostic agent in drug delivery and cancer combination therapy [17]. Liang and Liu et al. [18] summarized the latest research advances in the development of various emerging nanomedicine approaches for cancer metastasis treatment.

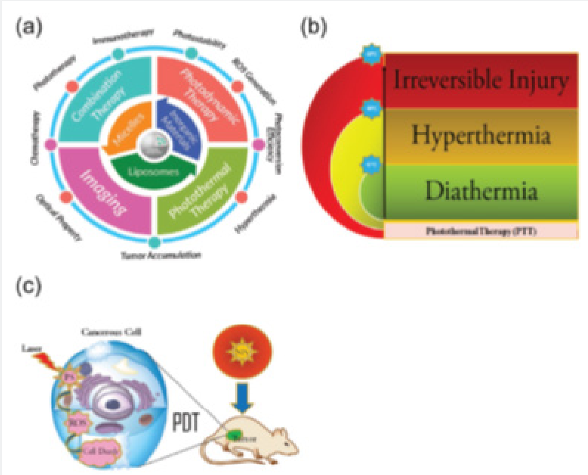

Figure 1: Nanoparticles exhibiting anti-tumor properties.

Diagnosis and Therapy

Magnetic nanoparticles to capture bacteria is the simple separation of bacteria from biological samples using magnets, as compiled by Pawar and others [19]. Inorganic nanoparticles (NPs), such as silica, gold and FexOy, were found to enhance resolution of image [20]. Polymeric nanocomposites were utilized for synergistic theranostics and associated imaging in the form of nanocarriers [21]. Polymers with long chain molecules are linked by covalent bonds and can be used to regulate the pharmacokinetics of drugs and/or imaging agents in the body, eg. polymeric micelles, polymeric/magnetic, polymeric/silica, polymeric/gold, polymeric quantum dots NPs. Drug-polymer conjugates are formed through the connection of various functional groups between the polymer and the drug or imaging agents, providing real-time observations on the localization and delivery efficiency of the conjugates. Several luminescent ions-based advanced nanocomposite materials (lanthanide, transition and main group metal ions) have been found several applications in broad areas, including diagnosis and therapy [22]. Multifunctional gold-based nanocomposites combine in several ways to fine tune the efficiency of the therapeutic and diagnostic treatment of cancer and other deadly diseases [23]. Iron oxide (Fe_3O_4), polydopamine (PDA) and their composites were used by Zhang and others for developing multifunctional nanodevices to perform non-invasive tumor diagnosis and therapy [24]. Owing to the collective effect of preassembled Fe_3O4 NPs, the superparamagnetism and photothermal performance of Fe_3O_4@PDA super particles (SPs) are greatly enhanced, thus producing nanodevices with improved magnetic resonance imaging (MRI)-guided photothermal efficiency. They showed that a facile approach for fabricating Fe_3O_4@PDA SPs with tunable Fe_3O_4 core size and PDA shell thickness using preassembled Fe_3O4 NPs as the core. Because of the optimized structures, the Fe_3O_4@PDA SPs exhibit enhanced superparamagnetism, molar extinction coefficient, and photothermal performance, which facilitate the subsequent applications in MR imaging and photothermal therapy.

Gaharwar et al. excellently composed the applications of nanoengineered biomaterials for effective wound healing and infection control [25]. Polymer-based nanotechnologies can be conveniently applied for the treatment and diagnosis of cardiovascular diseases (CVD therapy) and excellent review was compiled by Wang and co-workers [26]. Compared to conventional drug delivery systems, biodegradable polymeric nanocarriers can provide a number of advantages, including (1) extended drug half-life, (2) enhanced solubility of hydrophobic drugs, (3) decreased immunogenicity, (4) sustained drug release, (5) reduced side-effects and administration frequency, (6) increased drug uptake into cells/tissues, and (7) targeting functionality. Self-assembling amphiphilic polymers are ideal building blocks for nanocarriers. Over the last decades a number of polymer-based nanoparticle and nanocomposite drug delivery/diagnostic systems have been disclosed for treatment of CVD, with successes being reported in animal models. Compared with the conventional small organic molecular carriers or inorganic nanoparticles, polymers can maintain the stability and integrity of the incorporated substances for longer period of time and exhibit good biocompatibility and minimal unwanted side effects on other organs and/or tissues. In this regard, polypyrrole (PPy-obtained by cationic radical polymerization of pyrrole) based multifunctional nanoparticles have been extensively studied for the hyperthermia in cancer therapy due to their strong NIR (near infrared) light photothermal effect and superior biocompatibility [27]. PPy NPs has exhibited high photothermal conversion efficiency, photostability, and good biocompatibility, making it potentially become one of the excellent candidate agents for in vivo NIR photothermal cancer therapy.

Chen and Wu et al. synthesized tantalum carbide (Ta_4C_3) MXene-based composite nano sheets for multiple imaging guided photothermal tumor ablation [28]. Hou and other co-workers synthesized monodispersed Au-Fe_2C Janus nanoparticles (JNPs) for precision therapy based on imaging-guided photothermal therapy (PTT) [29]. Smart multifunctional modified mesoporous silica nanoparticles (MSNs) have a great potential ahead and can

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be the answer to cure of several deadly diseases [30]. Enhanced optical/plasmonic and magnetic properties offered by bimetallic nanoparticles and their corresponding impact on both diagnostic and therapeutic applications was nicely highlighted by Lee and others [31]. Li and et al. synthesized multilayered coating single nanoparticles (Fe_3O_4@PDA@Shiff base ligand) [PDA= polydopamine] for utilization as bacterial cellular fluorescent marker therapeutic purpose [32]. Benefiting from the excellent luminous and antibacterial properties, high luminous efficiencies and physiological stability, long-term imaging, good circulation ability, along with rapid response time were also achieved, all of which were crucially significant for its utilization as intracellular fluorescent bioimaging and therapeutic agents.

Anti-microbial

Zhnag and co-workers prepared MoS_2-Polydopamine (PDA)-Ag nanocomposites which exhibited high catalytic activity towards 4-nitrophenol reduction and great antibacterial activity compared with that of pure MoS_2 and MoS2-PDA [33]. To the best of their knowledge, this was the first report for the preparation of MoS_2 supported AgNPs through PDA thin films as ad-layers with the help of microwave irradiation. Nobel-metal silver nanocomposites decorated with polymeric grapheme carbon nitride (g-C_3N_4) were synthesized using a neat and clean methodology and found to be potent against various bacterial strains such as *E. coli, S. aureus* and *P. aeruginosa* [34]. Plasmonic photocatalyst nanomaterials (TiO_2 in combination with noble metal nanostructures) possessing surface enhanced Raman scattering (SERS) could be useful in ultra-detection of bio- molecules and exhibit antibacterial activities [35]. Synthesis of robust biofilm made up of chitosan (CS), zinc oxide (ZnO) nanoparticles and alginate (Alg) plays antimicrobial role for the abdominal wound healing and biomedical fields [36]. Al Ehsani et al demonstrated that TiO_2/ZnO nanoparticles supported in 4 ^{0}A zeolite were shown to possess moderate activity as antimicrobial agents [37] (Figure 2). One-pot biosynthesized Fe_3O_4, ZnO and MgO NPs with novel shape resulted in remarkable antimicrobial property as demonstrated by Karimi and co-workers [38-39]. Tungsten oxide nanodots (WO3-x) exhibited considerable potential in antibacterial applications, while also being biocompatible at macro level [40]. Natarajan and others synthesized magnesium oxide nanoparticles (MgONPs) using the marine brown algae Sargassum wighitii as the reducing and capping agent and analyzed that they have potent antibacterial activity and antifungal activities against human pathogens [41]. Padawala and Murthy synthesized ZnO NPs in a greener approach using Annona squamosa (AS) leaf extract (AS-ZnO NPs) and exploited them as having potential of antibiotic activity and anticancer activity in a biocompatible perspective [42]. A new nanocomposite, Fe_3O_4-TSPED-Tryptophan (FTT), for the adsorption of Congo Red (CR) dye and it's antibacterial properties were discussed by Sahoo and co-workers [43]. Stannic et al. compiled antimicrobial activity of metal oxide nanoparticles (MO-NPs) [44]. Gao et al. discovered that vitamin B_2 (VB2)-IONzymes could be a promising reagent in the treatment of mouth ulcer because of their intrinsic anti-inflammation and antibacterial potential [45]. Neogi et al. [46] synthesized CuO-NiO-ZnO mixed metal oxide (MMO) nanoparticles which possessed potent antibacterial activity [46].

Figure 2: Potential of antimicrobial nanomaterials in combating infections in different parts of the human body.

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Drug delivery

Assunta et al. [47] reviewed recently developments in the field of polymeric, ceramic nanocomposite hydrogels exclusively meant for biomedical applications as mentioned in Figure 3. In addition, Memic and co-workers, discussed on the use of nanocomposite hydrogels within the framework of biomedical and pharmaceutical perspective [48]. Several multifunctional composite materials based on Ln3+ had been designed for controlled drug delivery and multimodal bioimaging [49]. Saad et al. reviewed summarizing the most important applications of nanotechnology in drug delivery systems [50]. Polymeric nanoparticles and nanocapsules, involving non-toxic biodegradable polymers, liposomes, solid lipid nanoparticles, and inorganic-organic nanomaterials, are among the most used carriers for drugs for a broad spectrum of targeted diseases [51]. Swihart and others compiled the topic of nanobiophotonics for NIR activation of photodynamic therapy (PDT) applicable in drug delivery systems [52]. Bansal et al. outlined the utility of solid lipid nanoparticles (SLNs) as nanocarriers developed as substitute to colloidal drug delivery systems, etc. [53].

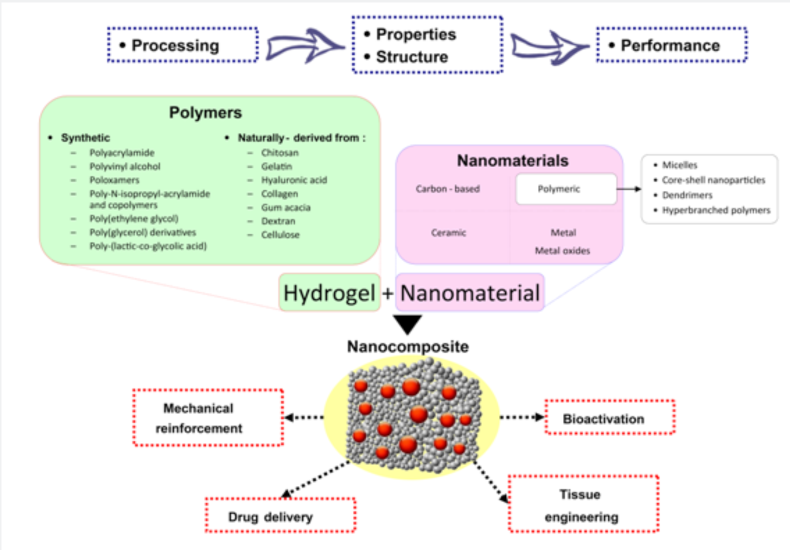

Figure 3: Nanoparticles in drug delivery system.

Biotechnology

Table 1: Nanobiomaterials used in hard tissue engineering.

S.No	Material	Applications
1	Hydroxyapatite	Artificial bone
		Bone regeneration therapy
		Dental tissue regeneration
2	Metal nano particles	Tissue and cartilage regeneration therapy
		Dental tissue regeneration
3	Carbon nanostructures	
	3.1- Nanotube	Nanocomposite in regeneration, nanoscale sensors
	3.2- Nanofiber	Cartilage regeneration therapy
	3.3- Graphite	Joint replacement therapy
4	Nanocomposite films	Fiber strengthening in regenerative therapy
5	Porous scaffolds	Bone reformation and bone implants
		Tooth regeneration
6	Nanohybrid membrane	Bone regeneration therapy
		Periodontal regeneration
		Endodontic regeneration

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Keles and Lin et al. focused on applications of non-viral gene delivery systems, including those based on lipids, polymers, graphene, and other inorganic nanoparticles for effective gene therapy [54]. Overview of recent nanotechnologies and their potential applications in cell and organ transplantation was well discussed by Ennio and Mauro group [55] (Table 1). Nanofiber-based hydrogels (NFHGs) possess super hydrophilicity, good biocompatibility, enhanced mechanical strength, and excellent structural tunability. Li and Ding outlined the use of these NFHGs especially in the field of tissue engineering, drug delivery [56]. Jaafari and Ramezani et al. reviewed the applications of nanomaterials for targeted delivery of biomolecules for bone tissue regeneration [57]. Martino and co-workers highlighted recent delivery approaches based on the natural interaction between growth factor and the extracellular matrix (ECM) [58]. Kallio and their group summarized the applications of nanocellulose/nanocarbon composites in the electrical stimulation of damaged tissues (e.g., cardiac, neural), neural and bone tissue engineering, engineering of blood vessels [59].

Bio sensors

Biosensors are devices that provide a measurable signal by analyzing the interaction between bio element and analyte. They play a vital role in pharmacy, food industries, clinical analysis, drug development, forensics, environmental monitoring, food safety analysis, monitoring of progression and treatment of diseases. Carbon nanotubes (CNTs) have enormous applications in the field of biosensors due to their unique intrinsic and potentially tunable properties [60]. Two-dimensional (2D) layered nanomaterials possessing more versatility, greater flexibility and better functionality with a wide range of potential applications such as electrochemical biosensing, optical biosensing and bioimaging [61] (Figure 4). Polyaniline (PANI) and its derivatives have been found as conducting polymers in vast applications such as gas vapor sensors and biosensors [62] because of their inexpensive reactants, green approach, excellent conductivity and strong bimolecular interactions. As the material science-based technologies are advancing day by day, the fabrication of materials could result in fine tuning the mechanical and processing properties of polymers with unique electrical characteristics of metals. PANI nanomaterials have been extensively explored and used in biosensors to detect DNA, proteins, and molecules. PANI nanofibers due to their large surface area are considered to be far better candidates for use in biosensors compared to the conventional dense films PANI nanofibers and nanocomposites due to their electroactivity at neutral pH and incorporation of biological materials are promising for use in biosensors to obtain synergistic effects. PANI-based electrochemical biosensors have been used for realtime monitoring of glucose levels in vivo. PANI provides a biocompatible environment for immobilization of other enzymes, including cholesterol oxidase, lactate oxidase, lactate dehydrogenase for quantification of cholesterol, hydrogen peroxide/lactate, and lactate, respectively.

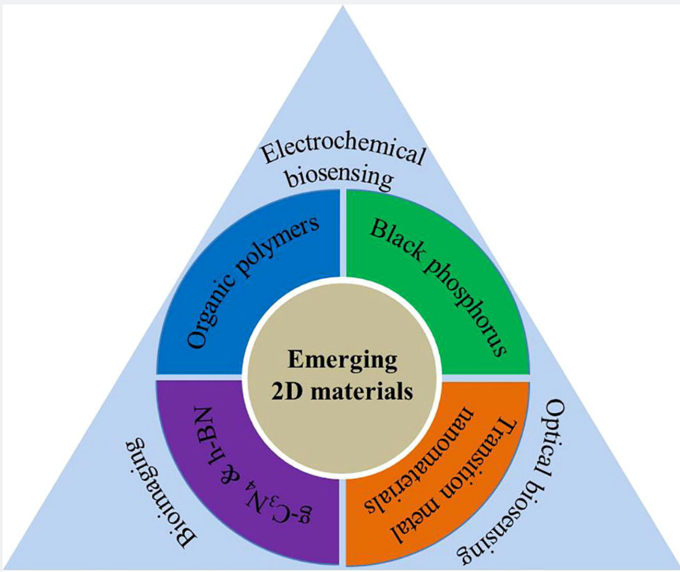

Figure 4: Nanomaterials as biosensors.

Food packaging

Dash and Rusu group have very recently reviewed the applications of inorganic nanoparticles in food packaging [63]. In the present fast technological world, packaging of food materials plays vital role in terms of maintaining freshness and durability for longer periods of time. Decontamination and antimicrobial properties of food package materials that consist of nano fillers

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such as Ag, AU, ZnO, SiO_2, CuO, TiO_2 NPs in the polymer matrix of polysaccharides, protein, chitosan, cellulose, polyethylene or polylactic acid based substrates, would assist to overcome deficiencies in packaging materials by improving mechanical strength and thermal stability. The hybrid polymeric metal nanocomposites increase antimicrobial properties primarily due to their large surface area to volume ratio.

Conclusion

In nutshell, we tried to compile various applications of nanomaterials in the field of biomedicine and the topic was categorized mainly based on their functions into anti-tumor, diagnosis and therapy, anti-microbial, drug delivery, biotechnology, biosensors and food packaging industry. We firmly believe this mini-review will be a valuable addition to the researchers both from the biomedical field and nanotechnology.

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