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Nanobiotechnology in health sciences: Current applications and future perspectives

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ABSTRACT

Nanobiotechnology is the discipline in which nanoscale tools are developed and applied to study biological sciences. It has evolved as increasingly significant frontier of various key areas especially healthcare in both diagnostic and therapeutic applications. Nanobiotechnology presents immense potential for evolving biological science thereby facilitating healthcare services all over the world. Several innovative nanodevices and nanoparticles are likely to be applied in near future having beneficial impact on human health. Nanotechnology in health sciences is still practically at initial stages. Execution of nanotechnology in life sciences means that the devices and mechanisms are designed efficient enough that have ability to interact with cellular/sub-cellular level with maximum efficiency and specificity. Therefore, high degree of therapeutic efficiency can possibly be attained with minimum or no side effects, by tissue/cell specific targeted interventions and/or therapy. More random trials and detailed researches are required to apply nanobiotechnology to humane models with success. This is an in-depth review of applications of nanobiotechnology i.e. diagnostic and therapeutic, with limitations, principles, challenges and future prospects of nanotechnology in health science are discussed.

1. Introduction

Nanotechnology is an innovative scientific field which includes material and the specific equipment capable of manipulating physico-chemical characteristics of that material at molecular level. Biotechnology is the use of techniques and biological knowledge to manipulate genetic, molecular and cellular functioning to develop useful services and products in a range of different areas from health to agricultural sciences (Stewart, 2016; Gartland and Gartland, 2018). Nanobiotechnology is considered as a novel combination of nanotechnology and biotechnology by which conventional microtechnology can be merged to a molecular approach in real. Using this technology, molecular or even atomic grade machines can be manufactured by incorporating or mimicking biological phenomena, or by synthesizing tiny tools to modulate diverse properties of living system at molecular level (Thirumavalavan et al., 2016). Nanobiotechnology therefore, may, facilitate many ways of life sciences by incorporating front-line applications of nanotechnology and information technology into recent biological issues. This is a leading technology with the potential of removing obvious boundaries between physics, chemistry and biology to some extent, and improve our recent understanding and ideas. Therefore, many new directions and challenges may arise in research and diagnostics by the wide use of nanobiotechnology with the passage of time.

1.1. Nanobiotechnology at a glance

Nanotechnology and biotechnology are the most promising technologies of 21st century. Biotechnology deals with physiological and other metabolic processes of living organisms including microbial species. Meanwhile, nanotechnology deals with the applications and development of materials whose least functional unit lies within 1–100 nm (Thomas et al., 2017). Combination of these emerging technologies, i.e. nanobiotechnology can play an amazing role in implementing and developing many useful tools to study biological systems. Current research has shown that microorganisms, plant extracts, and fungi can produce nanoparticles through biological pathways (Shafiq et al., 2016; Verma et al., 2019). They have exceptional properties that are unlike from large molecules of same element. Their electronic, optical and chemical properties are different from those observed in bulk compounds (Roy et al., 2015) than unpackaged or loose material due to their greater surface area/volume ratio.

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Nanotechnology is very vast, ranging from conventional device's extensions to a very unique physical approaches including molecular self-assembly, by the development of new materials with nanoscale dimensions to investigate the possibility of direct control of materials at atomic level. This idea involves the applications of this scientific field as diverse as organic chemistry, surface sciences, molecular biology, microfabrication and semiconductor physics.

2. Advantages of nanobiotechnology

Different anatomical and pathophysiological variations of inflamed/diseased tissues can possibly trigger the great scope for the development of various targeted nanostructured products. This construction is advantageous in many ways including: 1. drug targeting that can be achieved by distinct physiological or pathological parameters of diseased tissues (Hughes, 2017); 2. Normal drug wastage can be reduced using nanoproducts that can accumulate the dose at target area (Guo et al., 2018); 3. Vascular permeability enhancement in tumors coupled with impaired lymphatic drainage leads to the improvement of nanosystem in inflamed tissues, improving retention and transmission (Fenaroli et al., 2018; Chen and Zhao, 2018); 4. Nanosystems are capable of selective localization of tumor/inflamed tissues (Elmeshad et al., 2014); 5. Nanoparticles can cross blood-brain barrier, hence prove to be an amazing drug-carriers to transport/deliver to the brain (Saraiva et al., 2016; Yang et al., 2015; Van Tellingen et al., 2015); 6. Drug loaded nanoparticles alter tissue/cell-specific transport and can be used as targeted drug delivery which increase the drug efficacy by reducing potential toxic effects (Sahoo et al., 2017; Hua et al., 2015); 7. Nanodiamonds can act as fluorescent biomarkers for the detection of diseases e.g. Alzheimer's disease (Morales-Zavala et al., 2018).

3. Applications of nanobiotechnology in health sciences

Applications of nanobiotechnology in health sciences include targeted drug delivery, disease diagnostics, molecular imaging, nano pharmaceuticals, nanoarrays and cell/gene therapy are being studied. Several novel nano-structures are also being investigated using different *in vitro* and *in vivo* strategies (Kannegulla et al., 2018; Mousa et al., 2017; Shen and Zhu, 2016). Advanced applications of nanobiotechnology to living system will definitely transform the basis of prevention, disease diagnostics and treatment in the future. A detailed discussion of these applications is given below:

3.1. Diagnostic applications

Existing diagnostic techniques for wide range of diseases depends upon the visible signs/symptoms, before healthcare specialist can identify that the particular individual suffers from specific type of disease. Several electrochemical and enzymatic biosensors have been designed for disease diagnostic purposes especially in biomedical (Malhotra and Chaubey, 2003) and agricultural industry (Verma, 2017a; Verma, 2017b). Consequently, those symptoms have become visible, treatment may lack effectiveness as it could be. Therefore, the earlier the detection of disease, the improved the chance for a cure is. The most favorable way is the diagnosis and cure before the symptoms even manifests the patients. Nucleic acid (DNA and RNA) diagnostics will perform a crucial role in treatment of specific disease, as it will permit the diagnosis of diseased cells/pathogens at premature stage, the effective treatment would be more feasible. Recent technologies, e.g. polymerase chain reaction (PCR) leads towards this sort of devices, but nanobiotechnology is growing the formerly applicable options, that definitely will lead towards improved economy and far better efficiency.

3.1.1. Detection: quantum dots

Several presently applied/conventional healthcare trials expose the incidence of a molecule/pathogenic organism or a microbe by the detection of precise antibody bound to targeted disease. Conventionally, inorganic/organic dyes are conjugated with the antibodies to visualize within the sample using imaging devices e.g. electron or fluorescent microscopy. Though, synthetic dyes usually reduce the practicality and specificity of diagnosis. Nanobiotechnology suggests a possible solution using nanocrystals (like "quantum dots") as represented in Fig. 1. Complex labelling of unknown molecules (proteins and different DNA fragments) and their subsequent recognition in a system offers an interesting alternative to visualize a single-color detection and binding event in planar.

Highly complex tags have been synthesized based on quantum dots (Bhatia et al., 2016; Yan et al., 2015). Quantum dots tagged molecules present various benefits over standard fluorophores (Mongin et al., 2016; Chan et al., 2002). Absorption spectra of quantum dots are very broad (e.g. inorganic colloidal semiconductor nanocrystals of a ZnS shell and a CdSe core). Spectra is extended from UV to a cut-off wavelength in the visible spectra. The position of wavelength is analyzed by the size of quantum dot (smaller the dot size, shorter will be the wavelength) and the core composition. Emission is restricted to narrow range (usually 20–40 nm) likewise placed at a wave nature of particle. Quantum dots can be excited using single wavelength to obtain different colors with negligible photobleaching. Color emission differentiation, spectral width and intensity can lead to thousands of different novel signatures.

3.1.2. Protein chips: microarrays

Proteins performance the central part in establishing both healthy and diseased person's phenotype and are functionally symptomatic. Therefore, proteomics is vital in diagnosis and pharmaceutics, because drugs are manufactured to alter signaling pathways. Small integrated protein components and chemical groups can be used to treat protein chips. That can intercalate with specific biochemical motif or special type of protein (Nagy et al., 2016). Optical detection of gold nanoparticles labeled on protein chip microarray by using particular molecular binding and surface plasmon resonance using rolling circle amplification (Zhang et al., 2018; Wu et al., 2015). Protein chips are usually manufactured by immobilization of proteins on a microslide using standard (Kung et al., 2009) or nonstandard contact (Moore et al., 2016).

Proteins are immobilized on solid surface e.g. N-hydroxyl succinimide (NHS) derivatized slides or epoxy- and aldehyde-derivatized glass attachment through nitrocellulose (Petralia et al., 2017; Kramer et al., 2004), amines (Gerdtsson et al., 2016) or gel-coated slides (Charles et al., 2004) for attachment through absorption/adsorption, diffusion or nickel coated slides for affinity attachment of His-tagged proteins. The function of surface is not only the physical support but also should also demonstrate highest biding and maintain native conformation of proteins. Surface is covered with another coating material to prevent protein denaturation and place the protein in appropriate direction to provide hydrophobic environment to promote binding reactions and to enhance accessibility of binding site.

NanoInk Inc. and Agilent Inc. both are operating in this regard. NanoInk Inc. is applying dip-pen nanolithography (DPN) to assemble nanoscale protein chips. Agilent Inc. applying inkjet non-contact technology for microarray chip production by printing whole cDNAs or oligos onto glass chips at nanoscale (Lee et al., 2002).

3.1.3. DNA target probe: nanotubes

Despite other detection methodologies including magnetic detection, calorimetric and optical detection will remain preferred by healthcare specialists. Nanosphere Inc. has advanced some techniques that permit healthcare community to recognize genetic makeup of biological samples optically. Short DNA segments labeled with gold nanoparticles form the basis of analyzing the existence of certain genetic sequence. If the sequence of interest present in the sample binds to cDNA nanocarrier and make a thick network of gold balls, target probes development technique efficiently enables the pathogen detection (Su et al., 2017).

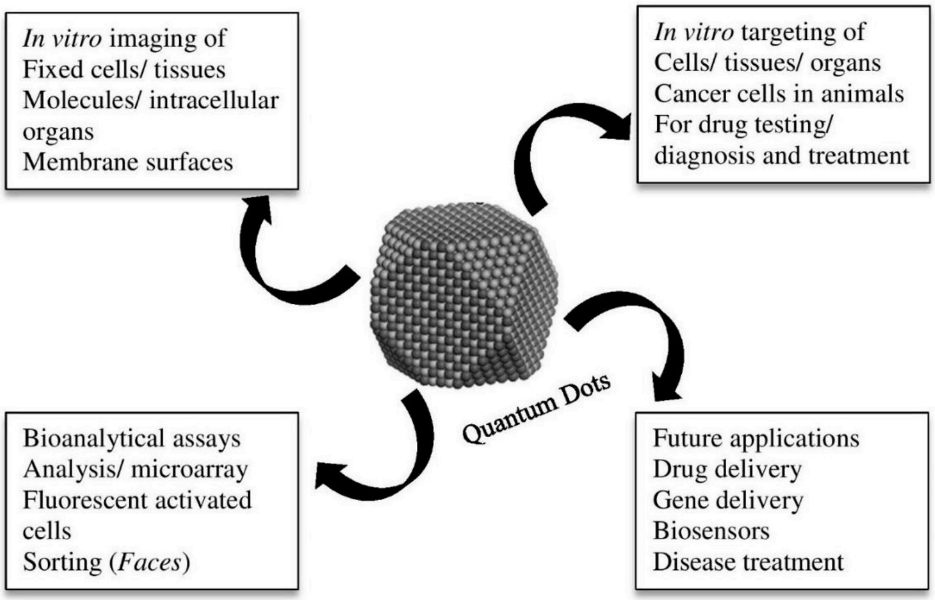

Fig. 1. Biomedical applications of quantum dots.

This technology represented promising effects in *in situ* detection of prostate cancer using photothermal therapy response (Lu et al., 2010), breast cancer cells (Beqa et al., 2011), anthrax detection (Kim et al., 2015) giving much improved sensitivity than currently available test methods (Kim et al., 2013).

Carbon nanotubes (CNTs) have potential for enhanced sensitivity in identification of DNA hybridization. Sorgenfrei et al. (2011) described detection of DNA hybridization at molecular level using field-effect transistor nanotube. The ssDNA probe was covalently attached to a carbon nanotube. Two-level fluctuations were measured in the carbon nanotube in the presence of targeted cDNA. They described the non-Arrhenius behavior in the kinetics, similar to DNA hybridization using fluorescence correlation spectroscopy. Carbon nanotubes can be used to single molecule dynamics at very short timescale e.g. microseconds. Fig. 2 representing schematic illustration of nanotubes and nanoparticles using for the diagnosis of cancer.

3.1.4. *Molecular imaging: chromophores and quantum dots*

Molecular imaging technology is used for the quantification of *in vivo* physiological changes, using labeled probes with the ability to detect noninvasively. Nanoimaging has advanced rapidly in past few decades as a part of nanotechnology. Intercellular imaging has become possible in modern era using target molecules labeled with synthetic chromophores or quantum dots. Such fluorescent protein that enables to visualize by direct examination of intracellular signaling using optical molecular techniques i.e. correlation imaging or confocal fluorescence microscopy (Minchin and Martin, 2010). Struggles are being made by nanotechnologists to develop nanomaterial that may be useful to study biological processes associated with human disease to monitor modifications by giving specific treatment. The versatility of molecular imaging modalities has been significantly improved by the development of several innovative nanoparticles e.g. quantum dots (Fig. 1). Imaging probes may be useful in the study of biological functioning e.g. ion-channel activity, enzyme activity, gene expression or protein-protein interaction. Nanoparticles that bind with specific receptors with high affinity could prove to be helpful in monitoring receptor density in real time.

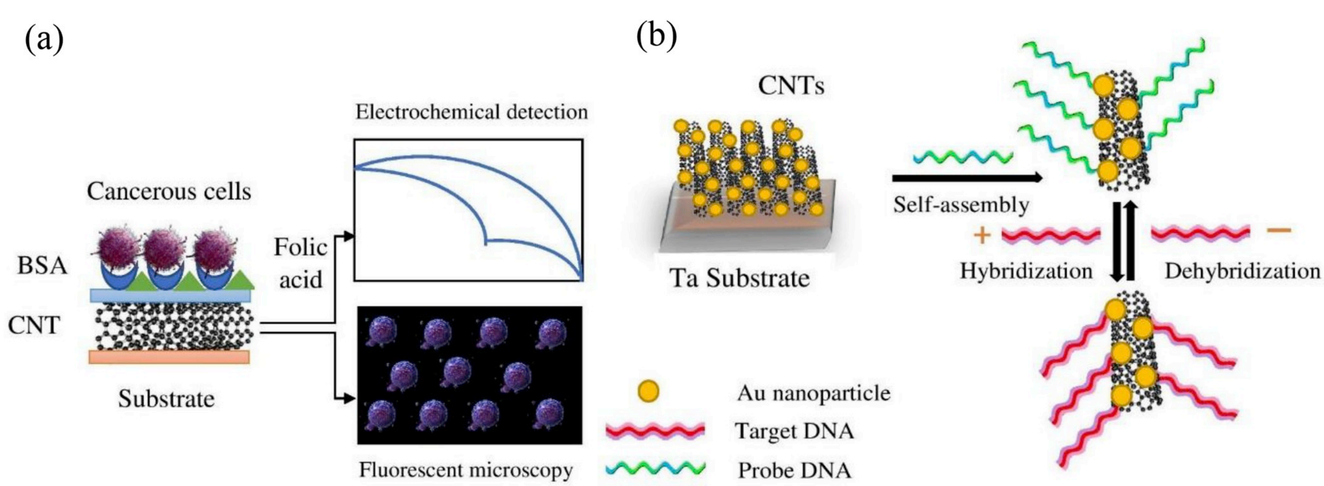

Fig. 2. Electronic and electrochemical carbon nanotubes for the detection of cancerous cells (**a**) Representation of cytosensing technique for improved electrochemical detection using CNTs; (**b**) Schematic illustration of DNA biosensor for the diagnosis of cancer using Au-nanoparticles immobilized on CNTs. Adapted from Tilmaciu and Morris (2015), distributed under Creative Commons Attribution License (CC-BY).

3.1.5. Sparse cell detection

Sparse cells are different from other nearby located cells in typical physiological circumstances e.g. HIV-infected T-cells, cancer cells, lymphocytes and fetal cells. These are significant in diagnosis of numerous genetic disorders. Still it is so difficult to recognize and separate these sparse cells. Hence, in this regards, nanobiotechnology offers novel opportunities for improvement in this field. Researchers successfully established nanotechnologies able to categorize healthy tissues and blood from sparse cells. Nanobiotechnology presents the novel characteristics of sparse cells demonstrated variances in surface charges, deformation and affinity of particular ligand and/or receptor e. g. by implanting electrodes into microchannels, the precise separation can be performed, on the basis of surface charges. Sparse cells can also be categorized by using precise nanopores of biocompatible surfaces.

The use of microvesicles and exosomes as biomarker in patient care had been restricted due to their small size (30 nm–1 μm) and wide sample production for separation and detection. The use of nanobiotechnology to isolate and detect microvesicles and exosomes in biomedical samples and the applications of nanotechnology to monitor cancer diagnosis has been increased. Sparse autoencoder have been used for efficient detection of nuclei on histopathological high-resolution image for detection of breast cancer (Xu et al., 2016). Different nanobiotechnology centers have been established worldwide, using this technology for the development of powerful diagnostic tools for humane disease management.

3.2. Therapeutic applications

Nanobiotechnology can facilitate novel designs of drugs (referred to as nanomedicines) with minimum side effects. In past few decades, the number of nanoparticle-based drugs has been increased rapidly as commercially available therapeutic products. According to survey conducted by European Science and Technology Observatory (2006), nanoparticle-based therapeutics has now been developing by more than 150 companies worldwide (Wagner, 2012).

3.2.1. Nanocarriers mediated drug delivery

Main hurdle in many disease treatments is the transport of therapeutic drug to the target site. Lack of selectivity, limited effectiveness and poor biodistribution are the ways by which conventional applications of few drugs are characterized by drug delivery control, these drawbacks and limitations can be overcome. Drug transportation to the site of action via controlled drug delivery system (DDS), thus, its unwanted effects on vital tissues can be reduced (Cui et al., 2009). Drug delivering system protects drug from clearance or rapid degradation and increases concentration of drug in target tissues (Nevozhay et al., 2007; Chamundeeswari et al., 2019). This modified form of therapy has gained importance specifically when there is inconsistency between drug concentration and its therapeutic effects. By attaching specific drug to independently designed carrier, cell specific targeting may be achieved. Theranostics is another important term used to describe targeted diagnosis with focus on patient's care. Several theranostics have been developed and applied for *in vivo* applications. Senapati et al. (2018) developed doxorubicin-Ce6 conjugated nanoparticles (Fig. 3). Results were highly significant as described in Fig. 3(B) the black areas represent tumor tissues and Fig. 3(C) shows the ex-vivo imaging from xenografted mice.

By nanosized drug encapsulation (e.g. nanoshells, hollow capsules and organic dendrimers), controlled drug release can be so precise than ever before. Encapsulations are performed to transport therapeutic payload (gene therapy, chemo- and/or radiation therapy) and also for imaging applications (Kesharwani and Iyer, 2015). Several drugs, which can not be administered orally because of poor availability, will now have become possible to use with the aid of nanobiotechnology (Ramalingam and Ko, 2016; Yao et al., 2015). Nanosized formulations provide protection to agents vulnerable to denaturation/degradation in the presence of high pH and increased half-life of drug by increasing retention through bioadhesion (Griffin et al., 2016). Another important application of nanobiotechnology is the antigens delivery for vaccinations (Dolen et al., 2016; Zaric et al., 2015). Recent studies about development of encapsulations and suitable clinical trials have presented that nanoparticles and microparticles have immune enhancing capacities (Benne et al., 2016).

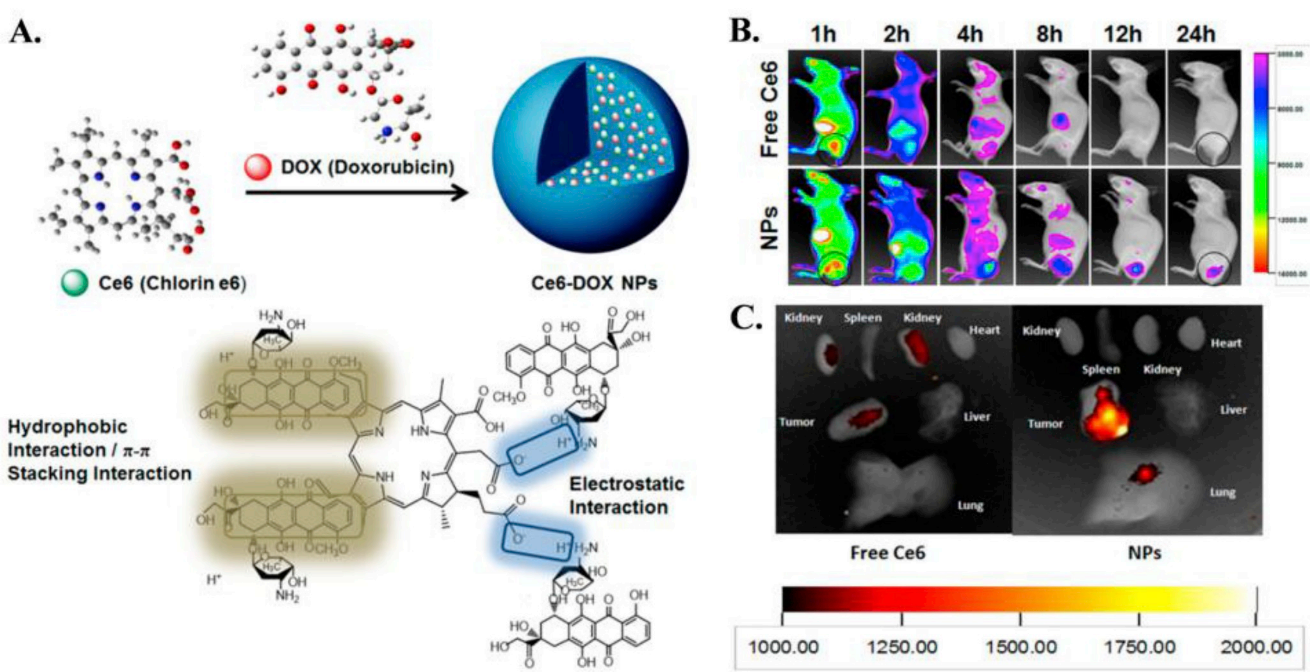

Fig. 3. Nanoparticles with co-assembled drug molecules and photosensitizer for better imaging of tumor cells. (A) Co-assembly of doxorubicin and chlorine e6 molecules onto the nanoparticle; (B) *in vivo* bioimaging of doxorubicin/Ce6 nanoparticles; (C) *Ex-vivo* imaging of tumor cells from xenografted mice. Adapted from Senapati et al. (2018); Article distributed under creative-common (CC-BY).

3.2.2. Nanosized gene carriers

Gene therapy have provided effective treatment of several human diseases caused by defective genes e.g. cystic fibrosis, cancer, muscular degradation and Parkinson's disease (Loh et al., 2013; Kaplitt et al., 2007). Existing gene therapeutic systems are suffering from the complications of chance of mutant reversion to its native type and the formulation and processing of effective pharmaceutics. Possible immune attack from viral vector that is being used for gene delivery is also problematic (Pluvinage and Wyss-Coray, 2017). To overcome these issues, nanotechnology provides novel therapeutic techniques in human gene delivery i.e. nanocarrier-based non-viral gene therapy (Fig. 4).

Functional inorganic nanocarriers used for gene therapy (usually 50–500 nm in size) are emerged as versatile and robust nanoscaffold for effective gene therapy (Ghosh et al., 2008). Inorganic nanomaterials also deliver remarkable properties for practical applications, including thermal and chemical stability, facile functionalization and scalability synthesis. These properties are significant for sterilization, low toxicity (specifically for silica, gold and iron oxide nanoparticles), availability in a broad range of shapes and sizes. Therefore, introduction of nanosized gene carriers which are less immunogenic in place of viral vectors prove to be helpful in replacing or repairing impaired genes in human (Sahoo et al., 2017).

3.2.3. Liposomes

A liposome (80–300 nm in size) due to its lipid bilayer structure, can be used in drug and/or gene delivery because of having lipophilic nature and capability to pass cell membrane of target cells/tissues. They are spherical shaped vesicles consists of steroids (cholesterol) and phospholipids, or other surfactants and they form spontaneously when some lipids are spread in aqueous media where such liposomes can be synthesized, i.e., by sonication. Liposomes have been tested to enhance the solubility of drugs and to advance their pharmacokinetic characteristics, especially therapeutic index of chemotherapeutic representatives, reduction of harmful side effects, rapid metabolism and increase of *in vivo* and *in vitro* anticancer activity (Santos Giuberti et al., 2011).

Drug is fused in liposomes by the process of encapsulation. The release of certain drug from liposomes relies upon liposome composition, osmotic gradient, pH, and surrounding environment. Interactions of these liposomes with neighboring cells can be comprehended by: adsorption, lipid transfer, endocytosis, and fusion. There are many drug examples in liposomal formulations, for example, neurotransmitters (serotonin), anticancer drugs, antibiotics, anti-rheumatic drugs and anti-inflammatory. Nanocarriers can help in achieving target therapy. Several successful trials conducted by (Franze et al., 2018; Patil and Jadhav, 2015) reflects the prospective of this targeted therapy and the value of nanoscale medicines in molecular diagnostics.

3.2.4. Nanobased biopharmaceuticals

Nanobiotechnology can also be applied for the development of nanobased medicines to target diseases that cannot be targeted effectively using conventional pharmaceuticals (Pelaz et al., 2017). Industry traditionally focuses on the development of drugs for a defined universe of diseases. Approximately 70–80% of the candidates fail for drug development, and this negligence is often revealed late in the

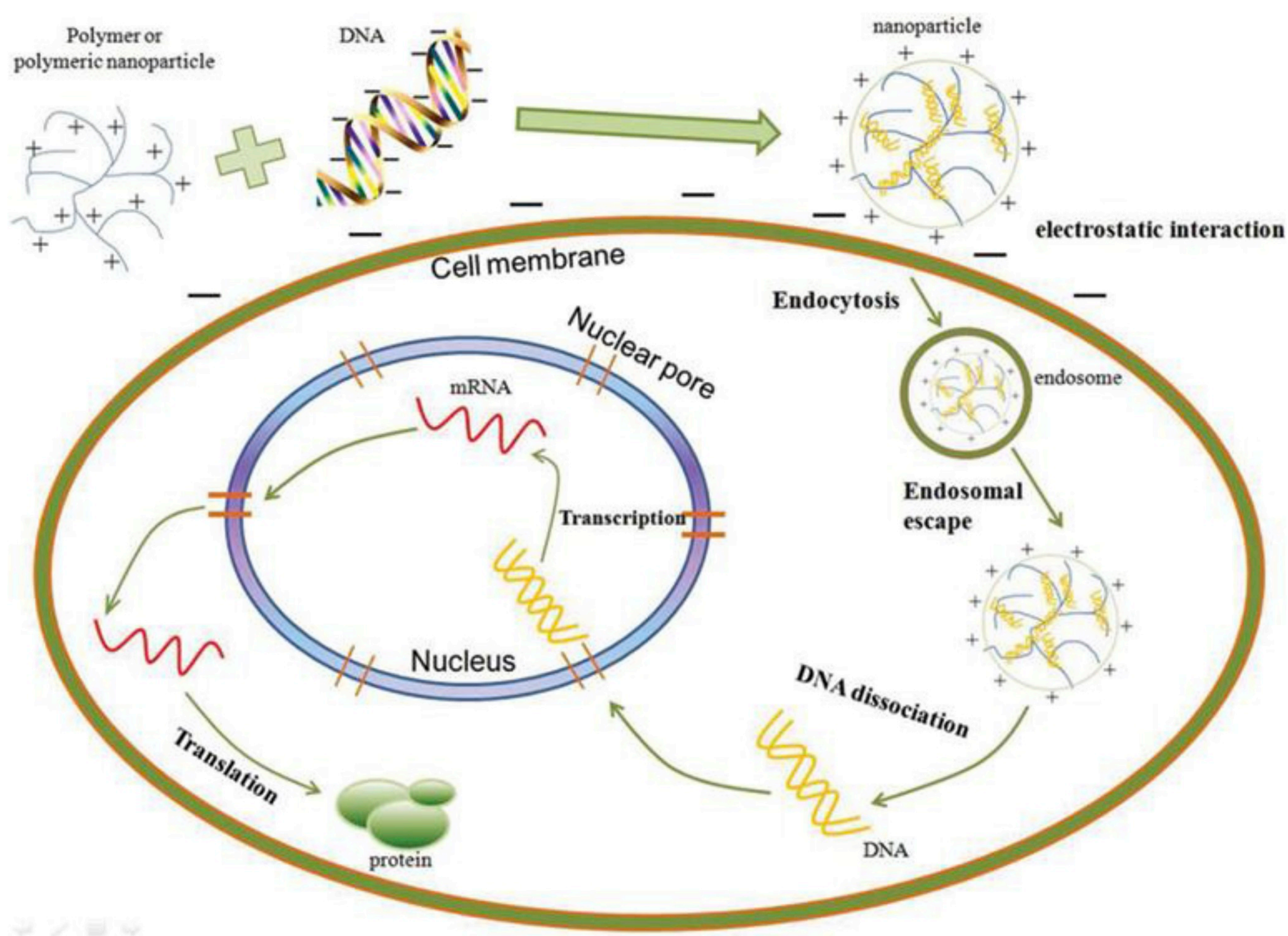

Fig. 4. Gene transport mechanism using polymer hydrogel or nano-structures. Adapted from Prabu and Ruckmani (2017). Distributed under creative-common (CC-BY) license.

development process, after the loss of millions of dollars in research and development investment. Nanoscale drugs development will be advantageous to pharmaceutical companies, which cannot spend hundreds of dollars on organic chemists to manufacture and analyze thousands of different compounds (Chen et al., 2016; Jiang et al., 2017).

Nanobiotechnology possesses the ability to physically manipulate the atoms and molecules on solid surfaces by adhering them to biomembranes and controlling when and where chemical reactions take place, in a fast process that involves few constituents (solutions and reagents). Advancement in nanomedicine will facilitate the highly specific drug development by reducing the discovery cost.

3.2.5. Nanoscale biomolecular engineering

The time and expense involved in classical biomolecular engineering have limited the availability of biologically active molecules. Nanoscale synthesis and assembly provides an incredible alternative to classical techniques. Nanoparticles can be applied for controlled synthesis of nanostructures and nanomaterials, immobilization, synthesis of hybrid biomaterial with improved biocompatibility. Development can be performed by the ability to carry out biological and chemical reactions using solid substrates, rather than performing classical solution-based processes. The use of solid matrix commonly means reduced wastage and far more precise biomolecular manipulation. Biomolecules are bound to solid matrix surface through molecular linkers. Immobilization of different types of biomolecules can be achieved e.g. bioactive peptides, enzymes and antibodies on solid surface e.g. nanocarriers (Verma et al., 2013a, 2013b) as represented in Fig. 5.

3.2.6. Nanosurfaces

In nature, multiple examples of complex interactions among surfaces and molecules can be found e.g. interaction between brain and the blood cells, pathogens to infection sites depend upon complex interactions among cells and surface characteristics. Nanofabrication can alter surface characteristics with nanoscale determinations, that can prove to be central part of hybrid biological system. Hybrid nanomaterial can be used as sensors, or implants and medical devices, or to screen drugs. Park et al. (2014) described the functionalization of PLGA (poly-lactic-*co*-glycolic acid) nanoparticles with few surface modifiers e.g. folate, a polymer [poly (carboxybetaine methacrylate)] and a peptide (Arg-Gly-Asp). Surface modified nanoparticles represented desired interactions with no residual bioactivity of dopamine and cytotoxicity.

3.2.7. Nanobiotechnology for dental therapy

Future of nanobiotechnology is very bright in the field of dentistry. Nanodentistry by the use of biotechnology (Ramakrishnaiah et al., 2018; Krishnan et al., 2016; Bhardwaj et al., 2014), nanomaterials (Besinis et al., 2015) and nanorobotics (Bhat et al., 2017) will ensure improved oral health. In current era millions of people suffering from poor dental health will benefit from such extraordinary innovation in the science of dental care. Moreover, nanodentistry in major teeth repair, may also develop. Nanorobotics in dental care can facilitate precise and selective occlusion within minutes and will lead to quick and permanent recovery. Natural tooth maintenance using nanodentistry could also prove remarkable milestone. Sapphire, ceramic, zirconia (covalently bonded artificial materials) may substitute dental enamel layer to enhance the durability and appearance of teeth (Hoffmann and Zafiropoulos, 2012;

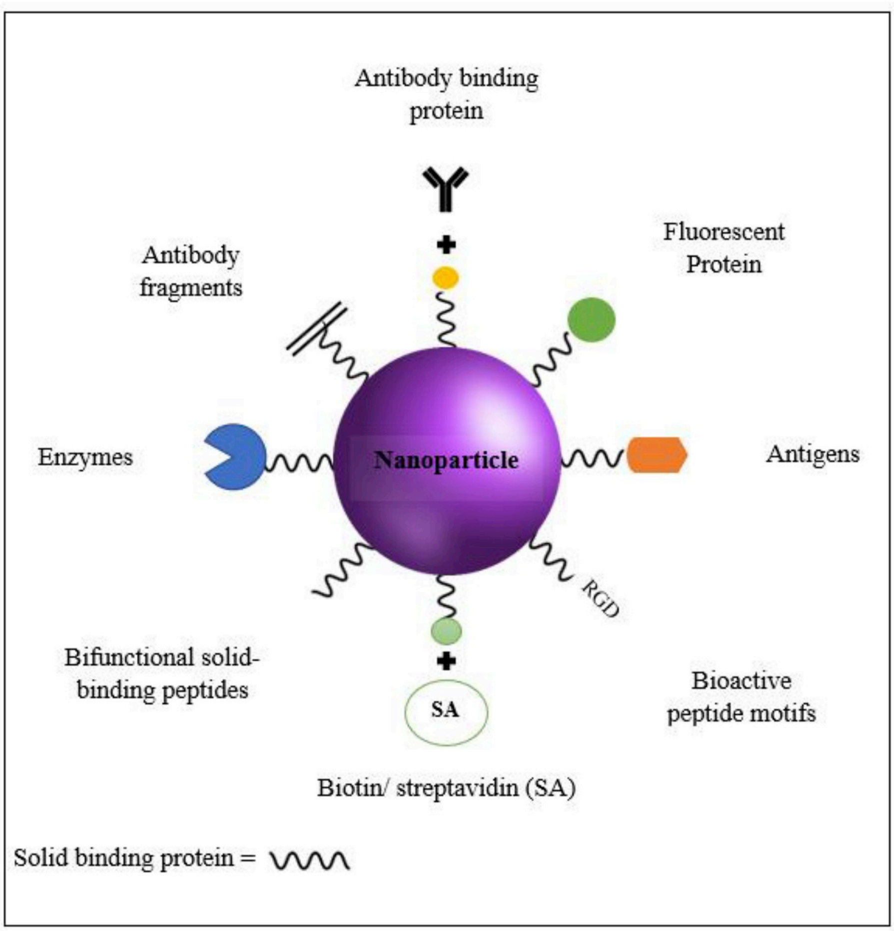

Fig. 5. Illustration representing the immobilization of various types of biomolecules e.g. antibodies, enzymes or bioactive peptides onto the surface of solid particles (nanoparticles) without compromising their function.

Osman et al., 2014).

3.2.8. Nanobiotechnology in orthopedic applications

Nanoparticles with the size ranging between 1-100 nm have role as efficient and novel constituent of bones, produced from nanoscale mineral and organic phases (Naskar et al., 2017; Zhang et al., 2016). Nanomaterials (nanotubes, nanopolymers, ceramic nanocomposites and carbon nanofibers may help in more effective mineral deposition containing high calcium constituent. Based on these observations and evidences, nanoscale materials possess exceptional place in R&D that may enhance the attachment of bone matters with implant by increasing bone cells interaction, this technology will definitely help in improving implant efficiency while considerably reducing the problems of patient compliance.

3.2.9. Nanobiotechnology in cardiac therapy

Nanobiotechnology is contributing promising applications in cardiovascular therapy to discover current frontiers in cardiovascular sciences at cellular level and treat CVDs more effectively. Nanotherapeutic tools can be applied in imaging, detection and tissue engineering (Lakshmanan and Maulik, 2018). Nano-sensors e.g. nanobarcodes, nanocrystals, and quantum dots are able to sense and monitor complex immune signaling as a result of cardiovascular inflammatory events (Anselmo et al., 2014). Nanobiotechnology can also help in diagnosis and define clinically important mechanisms concerned with cardiac complications. Moreover, it is important in designing nanomachines that can be incorporated in living system at molecular level. These nanostructured machines may alter many hypotheses and ideas in the treatment of critical CVDs. Nanotechnology could also possess excessive influence in tackling problems e.g. valvular clarification and unstable plaques. This nano approach could be a real breakthrough towards achieving sustained and localized cardiac therapy for the treatment of CVDs (Hughes, 2017).

3.2.10. Nanobiotechnology in immunotherapy

Nanobiotechnology is also contributing in cancer immunotherapy, including efficient transport of carrier molecules to tumor cells for intracellular uptake into lymphocytes and antigen presenting cells (Jang and Mok, 2016; Liu et al., 2018). For targeting tumor-draining lymph nodes, several polymeric and lipid nano-structures have been investigated (Yoon et al., 2018; Kim et al., 2018; Wang et al., 2018; Young et al., 2019). Non-specific uptake of therapeutic drugs can cause potential side effects in the living body. Nanobiotechnology provides as secure way to overcome this limitation by providing ligand-encapsulation on the surface of nanomaterials. Antibodies against epithelial, dendritic and CD40 cells were individually conjugated onto PLGA, which allowed targeted transport to dendritic cells (Cruz et al., 2014). These nano-structures have been shown to have immunomodulatory effect to tumor-draining lymph nodes after systemic inoculation and presented optimal characteristics for targeted delivery (Qian et al., 2016). Moreover, combination therapy using anticancer drugs in combination with immunomodulatory molecules have excellent synergistic anti-cancer effects (Heo et al., 2015; Zhao et al., 2017).

4. Future perspectives of nanobiotechnology

Up until now it has been proven that nanoparticles can attach to certain cells or tissues and provide images in their place and about the tissue structure as well as can launch their payloads into them by way of maximizing focused transport and minimizing systemic false results. Although scientists have made amazing *in vitro* demonstrations of micro- and nano-motors, great work towards *in vivo* programs is still in its initial stages. Nanobiotechnology is facing many challenges that are needed to be overcome, along with specific work in complex environments including real time *in vivo* imaging in deep tissues, reduction of undesired immunological reactions and toxicity, and subcellular delivery of medicine with managed dosage (Medina-Sanchez et al., 2018; Verma, 2018).

Nanomedibots may additionally restore important tissues effected by injury or disorder, or destroy cancerous tissue, without the need of invasive surgery. Nanobiotechnology will also be useful for individual matching of prescribed drugs to individual people to maximize effectiveness and decrease chances of false results (Harikrishnan, 2018). It has presented promised techniques for the early detection of remodelling cell populations through *in vivo* imaging or *ex vivo* analysis. Moreover, it's going to allow the proper interaction of agents selected (based totally on accurate information on the tumor), then the targeting of these agents (while keeping off biological barriers) to the early cancer lesions to contain or remove them without collateral consequences on healthy tissue and real-time tracking of the medicinal outcomes (Vakili-Ghartavol et al., 2018).

Nanoparticles with anticancer effects, became critical to investigate nanoparticle cytotoxicity in most cancerous and/or normal cell lines. Typically using cancer cell lines and claiming that nanoparticle investigation has anticancer properties may be somehow confusing, as the nanoparticle can be cytotoxic to all cell types. *In vivo* trials are being taken by the scientists to verify the function of nanoparticles as observed during *in vitro* studies (Hill and Li, 2017). Researches also must be focused towards awareness related to formulation of nanobased early diagnosis to identify most of the cancer types. Nanomedicines related researches also needed to accelerate with *in vivo* trials, and FDA approval to allow clinicians to use those trials in the hospitals effectively as a preventive measure (Sebastian, 2017).

The delivery of healing stem cells for the simultaneous delivery of adjuvant capsules including TGF-b signalling inhibitors and receptor cytokines, that can increase their differentiation into a high therapeutic phenotype and replenish immune reconstitution. However, the excessive dosage and systemic delivery required, can cause toxicity issues due to their pleiotropic effects. A clinically relevant opportunity is to conjugate drug-loaded nanoparticles onto the cell surface, that could deliver low drug doses locally and follow the cell's migration patterns (Yang et al., 2019). For stem cells growth and reproduction in the internal environment, several elements can be covalently joined to nanofibers to prevent their degradation and might promote the expansion of stem cells consisting of human embryonic stem cells (Nur-E-Kamal et al., 2008).

There are various nanomaterials used for nanofabrication. However, their toxicities are not completely understood, particularly for those with repeated dosage. Similarly, future non-invasive delivery routes might be emphasised for ocular diseases in each segment (Weng et al., 2017). Cardiovascular diseases are considered as fundamental fitness risk all over the world. In reproductive biology, the availability of versatile transport carriers with massive loading capability and spontaneous internalization into target cells creates possibilities to explore and manage the first-class mechanisms underlying replica and early embryonic development for research purposes (Barkalina et al., 2014). Now, most of the researches are focussing on nanomaterial-mediated delivery in reproductive medicine are lying at experimental stages, and the use of "cell culture" systems or "animal models" of sickness.

Inside the target tissue, the idea of herbal nanoparticles for cancer drug delivery might also entice some potential research groups and create conspicuous consequences. Therefore, the use of "herbal remedy" inside the nan-companies will grow its capacity for the treatment of various chronic diseases and health therapeutics (Arulanandraj et al., 2018). The interpretation of scientific studies into remarkable products production remains a challenge, and the destiny of rising nanotherapeutics relies upon the potential studies results into fruitful industrial era for stake holders. In coming future, nanobiotechnology can result in important advances in the direction of personalized medication. The nanodiagnostics may be exploited for further progressed sensitivity and specificity of the diagnostics. Newer and greater unique nanoparticles may be diagnosed which can lead us to more specific disease prognosis and management.

5. Challenges for nanobiotechnology

Neither a single person nor an intellectual group can deliver the answer about challenges that nanobiotechnology brings. One of the major challenges is to build such efficient instruments to assess the exposure of nanomaterials with water and air. Human and animal exposure to nanomaterials contaminated air and water need to be monitored to prevent adverse outcomes. This fact becomes more adverse when we talk about nanomaterial contamination in edibles like food products. The next challenge would be the development of appropriate techniques to determine the nanomaterial toxicity in upcoming 10–15 years. Then again, *in vivo* studies including animal model for understanding the effect of these nanomaterials on environment and human health would be inevitable issue.

Another challenge would be the development of such system to analyze the specific impact of nanomaterials over entire life span of an individual and/or his environment. Finally, the biggest challenge would be commercialization of nanobiotechnology, including efficient scalability, patience, funding, innovation and scare resource etc. Several companies present immense potential in nanobiotechnology for improvement of current products and the development of new ones. Nanobiotechnology arises fundamental questions related to new guidelines. Authorities should evaluate possible hazards of nanomaterials and proper regulatory response for the advancement of this emerging technology.

6. Conclusion

Nanobiotechnology is the multidisciplinary science yet in its initial stages. It is carrying the science of about incomprehensibly small devices closer to reality. These advancements will at some stage be so vast that they possibly effect all the areas of science and technology. Nanobased biotechnology is offering wide range of applications in medicines. Innovations e.g. targeted drug/gene delivery systems are the basis of the beginning of something amazing. Several deadly diseases that don't have cure now, may can be efficiently cured by nanoscale devices in the future. Though the expectations are high and possible benefits are highly enlisted, the safety of nanomedibots/nanomedicines is not yet properly analyzed. Nanobiotechnological applications in medical diagnosis and therapy requires adequate assessment of safety and risk factors related to this technology. Scientists who were opposing nanotechnology in biological system also agree that nanobiotechnology should progress continuously because it is ensuring great benefits, but *in vivo* trials should perform to ensure the safety level. Possibly in future, nanomedicines would play an important role in tackling human diseases and to ensure normal human physiology. If nanotechnology continue to progress as such, soon it will be an inevitable part of day to day life and will also help in saving many lives.

Declaration of competing interest

Authors declared that they have no conflict of interest.

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