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Biotechnology and Nanotechnology Drug Delivery: A Review

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Abstract: Nanobiotechnology is a blend of biotechnology and nanotechnology. Nanotechnology, as a field, has been tapped into in recent years, in search of alternatives to overcome challenges associated with drug delivery. Various techniques have been put together in order to fabricate nanoparticles with improved therapeutic efficacy enhanced drug stability, specific targeting of the cells and controlled release inside the cell. This review tends to look at the concepts involved in nanobiotechnology, the application of nanobiotechnology in nanomedicine, diagnosis, cancer treatment and drug delivery approaches.

Key words: Nanobiotechnolgy, drug delivery, targeting, nanomedicine.

1. Introduction

Biotechnology is the use of biological processes, organisms, or systems to manufacture products intended to improve the quality of human life. Nanotechnology on the other hand, is a branch of engineering that deals with the design and manufacture of extremely small electronic circuits and mechanical devices built at the molecular level of matter. Nanomaterials have been simply defined as materials having particles or constituents with external dimension in the nanoscale between 1 to 100 nm [1].

A greater number of biological systems found on earth are at the nanoscale level. By incorporating all the biological principles, a scientist can get in-lab results using chemistry, physics, nanotechnology and engineering principles for the production and characterization of nanoscale biological molecules and devices using biological systems. Using these facts, a new technology came into existence known as "nanobiotechnology" [2].

Nanobiotechnology is therefore the integration of biotechnology and nanotechnology. It has a blend of molecular biology approaches with classical microtechnology. Biotechnology makes use of the knowledge and techniques of biology to manipulate genetic, molecular and cellular processes to build products and services and it's used in various fields ranging from agriculture to medicine and other areas [3, 4].

Recently, there is a current rise in the exposure of living things in the ecosystem to nanomaterials and there is a prediction for continued increase [1]. Consequently, it has resulted to the fusion of biotechnology and nanotechnology to improve the quality of human life through drug delivery.

2. Nanobiotechnology

It is anticipated that, within a short time, the most significant application of clinical nanotechnology will be in pharmaceutical development [5]. Drug delivery research is now advancing from the micro to the

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nanosize scale. The applications associated with the technology of nanoparticles (NPs) as drugs or constituents of drugs are novel approaches for controlled release, targeted delivery and enhancement of bioavailability [6, 7]. Polymer capsules formulated at the nanoscale give benefits of degradation, release of drug with control pattern and high uptake at the targeted site [8].

Scientists all over the world are now stirred up towards formulating new polymers, refining existing ones and evaluating specific polymer – drug combinations. For example, nanocapsules have been manufactured from the monomers or by means of simple nanodeposition of a performed polymer [9].

Currently, nanocapsules have been produced from liposomes and albumin. Nanomaterials are formulated in a very unique way to make contact with molecules, interact and detect any change at the molecular level through diagnostic and therapeutic agent transportation [5, 10].

Nanoscale materials and devices can be fabricated using either “bottom-up” or “top-down” fabrication approaches. In bottom up methods, nanomaterials or structures are fabricated from buildup of atoms or molecules in a controlled manner that is regulated by thermodynamic means like self-assembly [11]. On the other hand, advances in microtechnologies can be used to fabricate nanoscale structures and devices. These techniques, which are collectively called top-down nanofabrication technologies, include photolithography, nanomolding, dip-pen lithography and nanofluids [12, 13].

3. Nanomedicine

The concept of nanomedicine was born out of the idea that tiny nanorobots and related machines could be designed, manufactured and introduced into the human body to carry out cellular repairs at the molecular level. Recent researches serve as a pointer to nanomedicine bringing enormous benefits to the practice of medicine.

Nanomedicine is described as the applications associated with nanotechnology for diagnosis, monitoring, control and treatment of physiological or pathological conditions by the National Institute of Health in 2002 [14]. Nanomedicine stretches to other areas such as nanomachines, biological mimetic, nanofibres, polymeric nanobiomaterials, diagnostic laboratory and as sensors [15]. The major applications in nanomedicine are rational drug delivery, pharmaceutical targeting, diagnostic agents and therapeutic methods.

3.1 Application of Nanomedicine in Diagnosis

Modern medicine functions by targeting the biological cell and recognizing the site of human disease. Initially, diagnosis was made based on the concept of cell theory but progress has been made to atomic and molecular level studies. With the emergence of nanometer domain of cell, the various techniques previously used to study molecules and atoms such as nuclear magnetic resonance, x-ray diffraction and spectroscopy were expanded to nanometer- sized structures and other macromolecules [5]. For example, nanotubes have been employed in the diagnosis of lung cancer by analysis of the compounds found in the breath obtained from the patients using the nanotubes, nanowires obtained mainly from silicon compounds are used in detecting cancer also. There are other unique nanomaterials used in more precise diagnosis such as nanobots and biosensors, etc [16].

3.2 Application of Nanomedicine in Treatment

The purpose of nanomedicine is to deliver and target the pharmaceuticals, diagnostics and therapeutic agents. These involve the authentic targets identification (cells and receptors) associated with precise clinical conditions. Next is the choice of most suitable nanocarriers of the target sites to obtain the required responses and at the same time, reducing the NANOPARTICLES side effects. Most commonly, macrophages, dendritic cells, cancerous cells and endothelial cells are the key targets [14].

3.2.1 Application of Nanomedicine in Cancer Treatment

In a four year study conducted on the mouse model in advanced breast cancer metastasis in the eye's anterior chamber, it was found that the new nanoparticle not only killed tumor cells in the eye but also extended the survival of the experimental mice bearing 4T1 tumors, a cell line that is extremely difficult to kill [15].

Nanoparticles have been discovered as a tool to kill off tumors using heat. Gold is a popular material for nanoparticles used therapeutically, as it is well tolerated and does not usually trigger any undesirable reactions. Plasmonic particles (a kind of nanoparticles), in particular, is found to heat up when they absorb near-infrared light. This enables them to kill tumor tissues [17].

4. Nanobiotechnology for Drug Delivery

Nanoscale materials can be used as drug delivery vehicles to develop highly selective and effective therapeutic and diagnostic modalities. Nanoparticles are comparatively more beneficial than microparticles. For instance, nanoscale particles can travel through the blood stream without sedimentation or blockage of the microvasculature. Small nanoparticles can circulate in the body and penetrate tissues such as tumors. Nanoparticles can also be taken up by the cells through endocytosis. Nanoparticles have been used to deliver drugs to target sites for cancer therapeutics [18] or deliver imaging agents for cancer diagnostics [19].

Targeted nanoparticles usually consist of the drug, the encapsulating material and the surface coating. The encapsulating material could be made from biodegradable polymers, dendrimers or liposomes. Controlled release of drugs (such as small molecules, DNA or RNA or proteins)from the encapsulating material is determined by the release of the encapsulated drugs through the surface or bulk erosion, diffusion or triggered by environmental factors such as changes in pH, light, temperature or by the presence of analytes such as glucose [20].

4.1 Metal Nanoparticles

Various researches in the development of nanotechnology over the past few years have been centred on the study of metal nanoparticles for their antimicrobial effects [21]. The reduced size of metal nanoparticles facilitates the interaction between metal nanoparticles and cellular membrane of the microorganism [22, 23]. Immobilization of metal nanoparticles with antimicrobial agents offers many applications in medical devices, food industry and in water treatment. Also, metal nanoparticles can make conjugates with polymer and can be used for anticancer, antitumor and antimicrobial activities [24]. Nanoparticles obtained from metals and their compounds are mostly used in the treatment of infectious diseases. Examples of such metals used include: gold, silver and copper which are the most common ones. They have vast applications which include actions on: fungal, viral, bacterial and protozoal infections in addition to their drug delivery and diagnostic functions [25].

4.2 Polymer Nanoparticles

Controlled-release biodegradable nanoparticles can be made from a wide variety of polymers including poly (lactic acid), PLA, poly (lactic co-glycolic acid), PLGA, poly (glycolic acid), PGA and polyanhydride. PGA, PLA and their co-polymer PLGA are common biocompatible polymers that are used for making nanoparticles. Nanoparticles made up of polymers having an average size < 100 nm is formulated from both synthetic and natural polymers. The reduced size of nanoparticles used for drug delivery is very essential for systemic circulation. Natural polymers such as carbohydrates and proteins have not been broadly evaluated for drug delivery because of the purity differences and mostly needed cross-linking that might denature the encapsulated drugs. Hence, synthetic polymer nanoparticles gained substantially more attention [5].

5. Polymer Nanoparticles as Drug Delivery System

5.1 Nanofibres

These are fibres with diameters of less than 1,000 nm. Medical applications include special materials for wound dressing and surgical textiles, materials used in implants, tissue engineering and artificial organ components. Nanofibres made of carbon also hold promise for medical imaging and precise scientific measurement tool.

Currently, the surgical meshes used to repair the protective membrane that covers the brain and spinal cord are made of thick and stiff material, which is difficult to work with. But lead nanofibre mesh is thinner, more flexible and more likely to integrate with the body's own tissue [26].

5.2 Polymersomes

In recent times, researchers are focused on the use of polymeric vesicles for drug delivery system. These are made up of hydrophilic-hydrophobic diblock copolymers [27]. A research carried out in 2003 proved that the blood circulation time of polymersomes increased with the increase of the thickness of the lipid bilayers *in vivo* [28]. Another research proved that polymeric lipid bilayers properties with respect to lipid bilayers are completely different and can be used for modifying the carrier properties [29].

5.3 Liposomes

Living cells use lipid bilayers to control and regulate molecules within and outside the cells. Evaluation of liposomes that have the ability to mimic natural cell functions, specifically those lipids that are engaged in the transport of different chemicals, ultimately led to their utilization as a drug delivery system [22, 23].

The main advantage offered by liposomes is their biocompatibility. Hence, liposomes constitute a major focal point for drug delivery. Liposomes are also capable of transporting a vast variety of active drugs such as lipophilic, amphiphilic or hydrophobic. This implies that the amphiphilic nature of phospholipids gather together in water to form a bilayer phase and enclose an aqueous centre. This centre serves for the entrapment of hydrophilic drugs while the hydrophobic drugs are entrapped in bilayers of the phospholipids [30]. However, the disadvantage of using liposome drug delivery system is the fast clearance of the drug from circulation through the reticuloendothelial system. But this can be reduced by introducing 'PEGylated stealth®' liposomes, which shunt the absorption of protein and results in active transport through PEG surface [31, 32].

5.4 Worm-like Micelles

Worm micelles are a new group of cylindrical supermolecular dye/drug carriers [33]. Nanoparticles produced from worm micelles are very stable and appear similar to the phages (filamentous) which have been used *in vivo*, with high rates of success for phage display targeting ligands for tumors [34]. Just like phages that transport nucleic acids, micelles can transport drugs of lipophilic nature.

5.5 Polymeric Micelles

Polymeric micelles are obtained from the co-polymers composed of hydrophilic and hydrophobic parts. The hydrophobic region of the micelles makes up the inner core while the hydrophilic region makes up the outer shell [35]. Polymeric micelles can serve as a tool for drug delivery by two different mechanisms: either the drug is physically encapsulated in the central core, that is, hydrophobic drugs or by chemically linking to the hydrophobic block before the micelles formation [36].

6. Non-nanotechnology Drug Delivery

Besides polymeric nanoparticles, other types of nanomaterials have been used for medical purposes. These include polymer quantum dots, nanoparticles with novel electroluminescent properties and magnetic resonance imaging (MRI) contrast agents been used to image cancer cells. Others are carbon nanotubes, nanowires and nanoshells used for therapeutic and diagnostic applications [37]. The various materials have their unique physical, chemical and biological properties which are based on the size of the nanoscale and structure of the materials.

6.1 Top-down Nanofabrication and Microfabrication in Drug Delivery

Top-down nanofabrication and microfabrication approaches based on integrated circuit processing may be used to fabricate controlled- release drug delivery devices. Using photolithographic and integrated circuit processing methods, silicon- based microchips have been made that can release single or multiple chemicals on demand using electrical stimuli [38].

Microfabrication techniques have also been used to develop transdermal drug delivery approaches based on microneedles [39]. The microfabricated needles are much smaller than hypodermic needles and may be used to deliver drugs in a painless and efficient manner.

Bottom- up and top-down approaches have merged to optimize drug delivery vehicles. For instance, microfabricated approaches have been used to develop microfluidic devices that mimic the body's vasculature and can be used to test and optimize the interaction of targeted nanoparticles with cells that line the cancer blood vessels [40].

6.2 Bottom-up Approach

This involves the use of fluid particles to make up nanoparticles. This process may involve physical means, which may be one of the methods of spraying, laser use, condensation, etc [41].

7. Conclusions

Nanobiotechnology is a field that holds great promises in medical research and pharmaceutics particularly in drug delivery. It provides a platform for innovative nanodevices and nanosystem, which would ultimately avail us the opportunity to design and produce targeted delivery system of most efficient drugs. However, certain barriers need to be overcome in order to push this field into clinically viable therapies.

References

[1] Jackson, T. C., Patani, B. O., and Israel, M. B. 2017. "Nanomaterials and Cell Interactions: A Review." *Journal of Biomaterials and Nanotechnology* 8 (4): 220-228.

[2] Roco, M. C. 2003. "Nanotechnology: Convergence with Modern Biology and Medicine." *Curr Opin Biotechnol* 14 (3): 337-46.

[3] Ernest, H., Shetty, R., 2005. "Impact of Nanotechnology on Biomedical Sciences: Review of Current Concepts on Convergence of Nanotechnology with Biology." *J Nanotechnology* Online 1: 1-14.

[4] Sahoo, S., Parveen, S., Panda, J. 2007. "The Present and the Future of Nanotechnology in Human Health Care." 3 (1): 20-31.

[5] Khan, I., Khan M., Umar, M. N., Oh, D. H. 2015. "Nanobiotechnology and Its applications in Drug Delivery System: A Review." *Journal of the Institution of Engineering and Technology* 9 (6): 396-400.

[6] Brigger, I., Dubernet, C., Couvreur, P. 2002. "Nanoparticles in Cancer Therapy and Diagnosis." *Adv Drug Deliv Rev* 54 (5): 631-51.

[7] Crommelin, D. J., Storm, G., Jiskoot, W., Stenekes, R., Mastrobattista, E., Hennink, W. E. 2003. "Nanotechnological Approaches for the Delivery of Macromolecules." *J Control Release* 87 (1-3): 81-88.

[8] Na, K., Bae, Y. 2002. "Self-assembled Hydrogel Nanoparticles Response to Tumor Extracellular pH from Pullulan Derivative/Sulfonamide Conjugate: Characterization, Aggregation and Adriamycin Release *in Vitro*." *Pharm Res* 19 (5): 681-8.

[9] Couvreur, P., Barratt, G., Fattal, E., Legrand, P., Vauthier C. 2002. "Nanocapsule Technology: A Review." *Crit Rev Ther Drug Carrier Syst* 19 (2): 99-134.

[10] Xia, Y., Xiong, Y., Lim. B., Skrabalak, S. E. 2009. "Shape-controlled Synthesis of Metal Nanocrystals: Simple Chemistry Meets Complex Physics?" *Angew Chem Int Ed Engl* 48 (1): 60-103.

[11] Ferrari, M. 2005. “Cancer Nanotechnology: Opportunities and Challenges.” *Nat Rev Cancer* 5 (3): 161-171.

[12] Peppas, N. A. 2004. “Intelligent Therapeutics: Biomimetic Systems and Nanotechnology in Drug Delivery.” *Advanced Drug Delivery Reviews* 56 (11): 1529-1531.

[13] Sahoo, S. K., and Labhasetwar, V. 2003. “Nanotech Approaches to Drug Delivery and Imaging.” *Drug Discov Today* 8 (24): 1112-20.

[14] Moghimi, S. M., Hunter, A. C., Murray, J. C. 2005. “Nanomedicine: Current Status and Future Prospects.” *FASEB J* 19 (3): 311-30.

[15] Rolland, J. P., Maynor, B. W., Euliss, L. E., Exner, A. E., Denison, G. M., Desimone, J. M. 2005. “Direct Fabrication and Harvesting of Monodisperse, Shape-Specific Nanobiomaterials.” *J Am Chem Soc* 127 (28): 10096-100.

[16] Jackson, T. C., Patani, B. O., Ekpa, D. E. 2017. “Nanotechnology in Diagnosis: A Review.” *Advances in Nanoparticles* 6 (3): 93-102.

[17] Zurich, E. T. H. 2014. “Hot Nanoparticles for Cancer Treatment.” *Science Daily* http://www. Sciencedaily.com/releases/2014/03/140324111331.htm.

[18] Gerf, R. et al. 1994. “Biodegradable Long-Circulating Polymeric Naonspheres.” *Science* 263 (5153): 1600-3.

[19] Lemarchand, C. et al. 2004. “Polysaccharide-Decorated Nanoparticles.” *Eur J Pharm Biopharm* 58 (2): 327-341.

[20] Langer, R., and Tirrell, D. A. 2004. “Designing Materials for Biology and Medicine.” *Nature* 428 (6982): 487-92.

[21] Morones, J. R., Elechiguerra, J. L., Camacho, A. et al. 2005. “The Bactericidal Effect of Silver Nanoparticles.” *Nanotechnology* 16 (10): 2346-53.

[22] Raveh, A., Zukerman, I., Shneck, R., Avni, R., Fried, I., 2007. “Thermal Stability of Nanostructural Superhard Coatings: A Review.” *Surf Coat Technol* 201 (13): 6136-6142.

[23] Parveen, S., Misra, R., Sahoo, S. K., 2012. “Nanoparticles: A Boon to Drug Delivery, Therapeutics, Diagnostics, and Imaging.” *Nanomedicine* 8 (2): 147-66.

[24] Govender, T., Stolnik, S., Garnett, M. C., Illum, L., Davis, S. S. 1999. “PLGA Nanoparticles Prepared by Nanoprecipitation: Drug Loading and Release Studies of a Water Soluble Drug.” *J Control Release* 57 (2): 171-85.

[25] Mordorski, B., and Friedman, A. 2017. “Metal Nanoparticles for Microbial Infection.” *Functionalized Nanomaterials for the Management of Microbial Infection* http://dx.doi.org/10.1016/B978-0-323-41625-2.00004-1.

[26] Paddock Catherine. Medical News Today published Friday 4, May, 2012.

[27] Discher, B. M., Won, Y-Y, Ege, D. S. et al. 1999. “Polymersomes: Tough Vesicles Made from Diblock Copolymers.” *Science* 284 (5417): 1143-6.

[28] Pata, V., Dan, N. 2003. “The Effect of Chain Length on Protein Solubilization in Polymer – Based Vesicle (polymersomes).” *Biophys J* 85 (4): 2111-8.

[29] Vinogradov, S. V., Bronich, T. K., Kabanov, A.V. 2002. “Nanosized Cationic Hydrogels for Drug Delivery: Preparation, Properties and Interactions with Cells.” *Adv Drug Deliv Rev* 54 (1): 135-47.

[30] Gabizon, A., Papahadjopoulos, D. 1988. “Liposome Formulations with Prolonged Circulation Time in the Blood and Enhanced Uptake by Tumors.” *Proc Natl Acad Sci* USA 85 (18): 6949-53.

[31] Papahadjopoulos, D., Gabizon, A., 1989. “Liposomes Designed to Avoid the Reticuloendothelial System.” *Prog Clin Biol Res* 343: 85-93.

[32] Lin, H-Y., Thomas, J. L., 2003. “PEG-lipids and Oligo (ethylene glycol) Surfactants Enhance the Ultrasonic Permeabilizability of Liposomes.” *Langmuir* 19 (4): 1098-1105.

[33] Dalhaimer, P., Engler, A. J., Parthasarathy, R., Discher, D. E. 2004. “Targeted Worm Micelles.” *Biomacromolecules* 5 (5): 1714-9.

[34] Gao, Z., Oh, K., Kim, C-K., 1998. “Preparation and Characterization of Sustained Release Microspheres of Chlorpromazine.” *J Microencapsul*e 15 (1): 75-83.

[35] Cammas–Marion, S., Okano, T., Kataoka, K. 1999. “Functional and Site-Specific Macromolecular Micelles as High Potential Drug Carriers.” *Colloids and Surfaces B: Biointerfaces* 16 (1-4): 207-215.

[36] Lavasanifer, A., Samuel, J., Kwon, G. S. 2002. “Poly(ethylene oxide)-block-poly(1-amino acid) Micelles For Drug Delivery.” *Adv Drug Deliv Rev* 54 (2): 169-90.

[37] Loo, C. et al. 2005. “Immuno Targeted Nanoshells for Integrated Cancer Imaging and Therapy.” *Nano Lett* 5 (4): 709-11.

[38] John T. Santini Jr, et al. 1999. “A Controlled-Release Microchip.” *Nature* 397 (6717): 335- 338.

[39] McAllister, D. V. et al. 2000 “Microfabricated Micro Needles for Gene and Drug Delivery.” *Annu Rev Biomed Eng* 2: 289-313.

[40] Farokhzad, O. C. et al. 2005. “Microfluidic System for Studying the Interaction of Nanoparticles and Microparticles with Cells.” *Anal Chem* 77 (17): 5453-9.

[41] Khan, I., Saeed, K., Khan, I. 2017. “Nanoparticles: Properties, Applications and Toxicities.” *Arabian Journal of Chemistry* 12 (7): 908-931.