Nanotechnology-An Overview

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Abstract: Nanotechnology provides a wide technological platform for varying range of potential applications. Nanotechnology is the design, characterization, synthesis and application of materials, structures, devices and systems by controlling shape and size at nanometer scale, 1-100nm. Nanotechnology is being employed in the pharmaceutical field to improve drug solubility, bioavailability and delivery to various sites of action. To overcome the limitations in cellular uptake of highly active molecules, the use of nano carriers is the focus of modern drug delivery. Strategies like Nanosponges for enhancing solubility of poorly water soluble drugs, Nanocantilevers for detection of biomarkers of cancer, Quantum dots for medical imaging, Dendrimers for photodynamic therapy and gene transfection, Solid lipid nanoparticles as cosmeceuticals are employed. Nanodevices like respirocytes and microbivore are used for temporary replacement for natural blood cells in case of emergencies. In this review, therapeutic applications of various nano-structured materials have been discussed.

Keywords: Nanotechnology, Nanostructure materials, Nanodevices, Biomarkers.

INTRODUCTION

Nanotechnology is the design, characterization, synthesis and application of materials, structures, devices and systems by controlling shape and size at nanometer scale, 1- 100nm [1].

Nanotechnology in terms of pharmaceutical sciences is majorly categorized into two types namely, Nanostructured materials and Nanodevices [1]. Raw materials undergo reduction by some process to yield nanostructured materials. Based on their shape and functionality these materials are differentiated into following types, namely Quantum dots, Carbon nanotubes, Dendrimers and Fullerenes. Nanodevices are miniature devices in the nanoscale, which include Respirocytes and Microbiviores.

History of Nanotechnology

The design of nanotechnology has been laid by Richard Feynman**,** a physicist at California Institute of Technology. He defined nanotechnology as miniaturization of materials achieved by manipulating and controlling things at small scale.

Method of Synthesis

Nanostructured materials are synthesized by two basic approaches: Bottom –up approach and Top-down approach [2].

Bottom-Up Approach

The growth of nanostructures is achieved by assembling of atoms or molecules which are referred to as building blocks. Self assembling of building blocks are obtained by controlled chemical reactions to yield nanostructures like nanotubes and quantum dots. Probes are used to physically manipulate atoms or molecules to produce nanostructures. Self assembling of atoms or molecules can be achieved by templating and non- templating. The process of templating involves formation of nanostructures by interaction with biomolecules that are under the influence of a specific sequence, pattern or spatial constraint. Such a process is referred to as Templating. In case of Non-Templating, nanostructures are formed from atoms or molecules with external influence.

Top-Down Approach

Top down approach is achieved by adopting techniques like etching or breaking where bulk materials are reduced to form nanostructures. Bulk machining, surface machining and mold machining are employed for reducing bulk materials.

Nanotechnology Areas and Applications

Nanotechnology, being an interdisciplinary field, has three main extensively overlapping areas: Nanoelectronics, Nanomaterials and Nanobiotechnology which find applications in materials, electronics, environment, metrology, energy, security, robotics, healthcare, information technology, pharmaceuticals, manufacturing, agriculture, construction, transport, and food processing and storage.

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Nanotechnology in Drug Delivery

Fabrication of polymeric nanostructures at sub micron scale and nanoscale offer multiple advantages. The approach of nanotechnology in drug delivery is designed to overcome the challenges like poor bioavailability, *in vivo* stability, poor dissolution rate, plasma fluctuations of drugs as observed in other drug delivery mechanisms. The uptake of nanostructures was found to be 15-250 times greater than that of micro particles in 1- 10μm range [3]. Through the manipulation of the characteristics of polymers, release of drug from nanostructures can be controlled to achieve the desired therapeutic concentration for the desired duration. For targeted delivery, nanostructures are conjugated with targeted moieties by a linker. The linkage may be achieved by incorporation of amino acids, lipids, peptides or small chains as spacer molecules. The selection of linkage molecule depends on the site of action. In case of chemotherapy where the incidence of systemic effects is high, in such conditions drug targeting plays a crucial role. Therefore nanostructures in drug delivery system are designed so that it can target only the malignant tumors while shielding the healthy cells from uniform distribution of chemotherapeutics in the body and their harmful effects [4]. The use of nanostructures such as polymeric nanoparticles is a non-invasive approach of penetrating the blood brain barrier for management of neurodegenerative disorders, cerebro vascular and inflammatory diseases.

DENDRIMERS

Dendrimers are highly branched three dimensional structures [5] with 2-10nm in diameter [6]. Each dendrimer is built from a starting atom i.e., Nitrogen to which carbon and other elements are added repeatedly that extend out towards periphery. Repetition of this process is continued until close densely packed structures are attained. The building of dendrimer chain is continued upto a certain critical stage. After which the growth of dendrimer is halted because of lack of space. This phenomenon is referred to as Star burst effect. For example, After 10^{th} generation star burst effect is observed in PAMAM dendrimers.

Each dendrimer consists of three basic components, namely (i) An initiator core (ii) Interior layers (generations) composed of repeating units that radically attached to the initiator core. (iii) Exterior end group (terminal functionality) attached to the outer most interior generation. The figure is illustrated in Figures **1** and **2**.

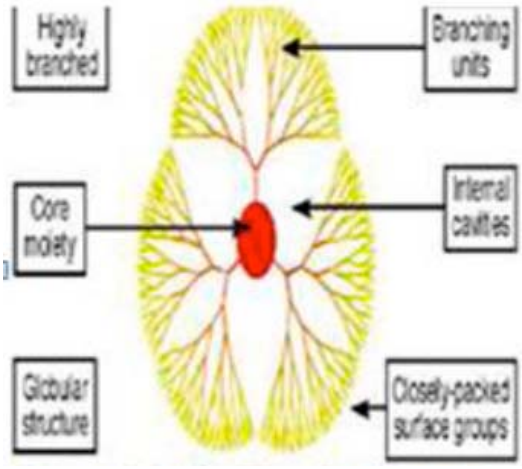

Figure 1: The Dendritic structure.

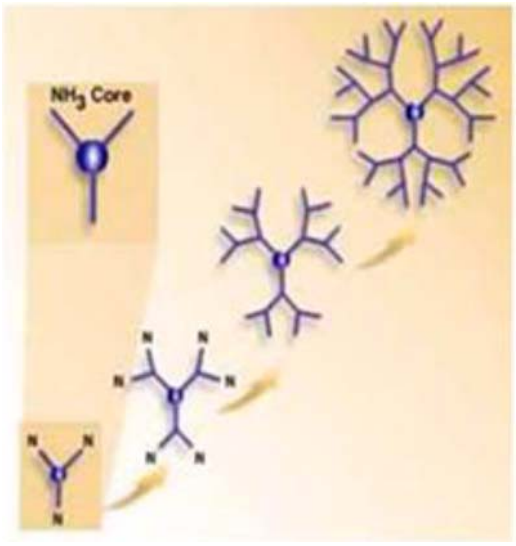

Figure 2: Dendrimer structure.

Types of Dendrimers

Based on availability of surface functional groups dendrimers are of following types: [7] Poly (amido-amide) dendrimers (PAMAM), Poly (amidoamine-organo silicon) dendrimers (PAMAMOS), Poly propylene imine (PPI) dendrimers, Multiple antigen peptide dendrimers and chiral dendrimers.

Properties of Dendrimers

Well defined three dimensional structure

The availability of many functional surface groups and

Low polydispersity index.

Mechanism of Action

Dendrimers acts as potential drug carriers. The terminal functional groups of dendrimer interact with

the drug moiety *via* weak electrostatic bonds or through covalent bond (can be used as prodrugs) [8].

Applications

To protect or deliver drugs to specific sites in the body and to achieve control drug release, Dendrimers are widely used as coating agents.

Dendrimers as nano carriers offer the potential to enhance the bioavailability of drugs that are poorly soluble and substrates for efflux transporters. E.g. Propranolol, conjugated to surface modified G3PAMAM dendrimers, the solubility of Propranolol increased by over two times of magnitude.

Dendrimers in Gene Therapy [9]

PPI/PAMAM Dendrimers acts as vectors in gene therapy. A transfection agent called Superfect -TM consisting of activated PPI dendrimeric agent enhances the transfection of DNA by endocytosis and efficiently transport DNA into cell nucleus than liposomes .This might be attributed to its well defined structure and low PKa of amines (3.9).The low PKa permit the dendrimer to buffer the pH change in endosomal compartments. The figure is shown below (Figure **3** Dendrimers in Gene transfection).

Dendrimer Based Products [10]

A) VIVAGELTM (Starpharma): In clinical phase II trials, it's a topical vaginal microbicide, prevents infection by HIV

B) Stratus® CS Acute Care TM (Dade Behring) - for cardiac diagnostic testing [10].

C) Superfect-TM (Qiagen) - gene transfection agent.

SOLID LIPID NANOPARTICLES

The SLN's are colloidal carriers ranging in size between 50-1000nm [11]. They are majorly composed of physiological lipids. The lipids are dispersed in an aqueous system with the help of an emulsifier.

Examples of lipids are Triglycerides (Tri-stearin), Partial glycerides (Imwitor), Fatty acids (Stearic acid, Palmitic acid) and emulsifying agents like Pluronics F68, F127.

Due to its unique size dependent properties SLN's offer a new drug delivery that can used for drug targeting at secondary and tertiary level. Therefore the ability to incorporate drug into nanocarriers provides SLN's for site specific and controlled drug delivery [12].

Method of Preparation

SLN's are prepared by employing various methods like High speed homogenization, Hot homogenization, Cold homogenization and Solvent emulsification/ evaporation.

Hot Homogenization

This technique is performed by maintaining at a temperature above the melting point of lipid. In this method drug is initially dispersed in a lipid melt. This mixture is then transferred into an aqueous phase to obtain O/W emulsion. The resultant emulsion is subjected to high shear homogenization by employing Silverson–type homogenizer. In general, 3-5 homogenization cycles at 500-1500 bar pressure is sufficient. On further increase of homogenization cycles, it may lead to particle coalescence because of increased particle size. The reason for coalescence

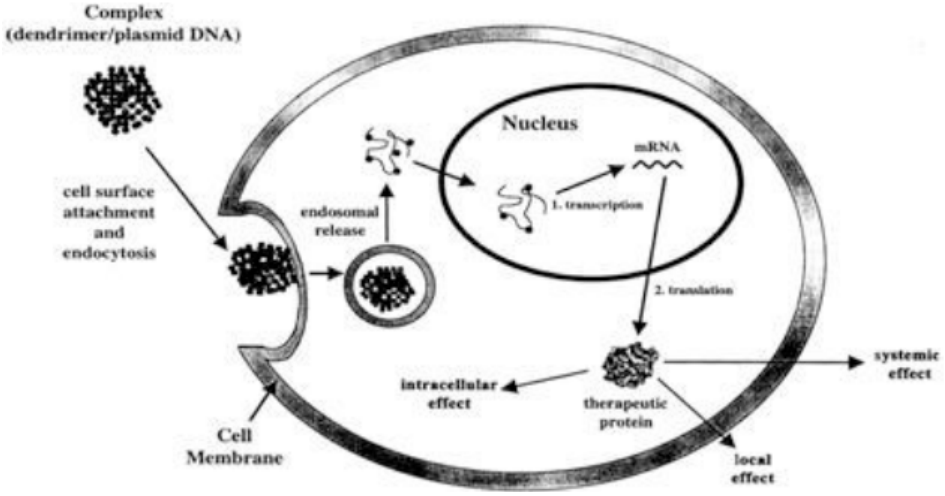

Figure 3: Dendrimers in Gene Transfection.

might be attributed due to high kinetic energy of particles [13].

Cold Homogenization

The process of cold homogenization bears similarity with milling of suspension at elevated pressure. Initially the drug is dispersed in the lipid matrix. Then the drug loaded lipid melt is cooled rapidly to achieve uniform drug distribution in the lipid matrix. By employing ball/ mortar milling the obtained lipid matrix is pulverized to attain desired size. The so formed particles are dispersed in chilled emulsifier solution. The resultant dispersion is then undergone through high homogenization at or below room temperature [14].

Advantage: This method is useful for incorporation of thermo labile drugs.

Solvent Evaporation

This method is useful incorporation of lipophilic drugs. For production of nanoparticle dispersion by solvent evaporation method, the drug and polymer are dissolved in a water immiscible O/W emulsion. The emulsion was stirred until complete evaporation of solvent has occurred. Upon evaporation of the solvent nanoparticle dispersion is formed by precipitation of polymer loaded nanoparticle into the aqueous medium.

Applications

SLN's for Topical Use

Epidermal targeting is better achieved by Podophyllotoxin-SLN [15] due to its increased penetration into stratum corneum in comparision with conventional formulations.

Preparation of Glyceryl behenate, vitamin A-loaded Nanoparticles provided improved sustained release characteristics.

SLN's as Cosmeceuticals

The SLN's have been applied in the preparation of sunscreens and as active carrier agent for molecular sunscreens and UV blockers [16]. Better localization has been achieved for vitamin A in upper layers of skin with glyceryl behenate SLN"s compared to conventional formulations.

Nanosponges

Nanosponges are spherical shaped three dimensional structures consisting of hyper cross linked (mostly beta- Cyclodextrin) with an average diameter of 500nm. Nanosponges occur both in crystalline and amorphous state. They possess excellent swelling properties (about 30 folds in water). Because of its small size they circulate around the body until they encounter the specific target site and stick to the cell the drug in a controlled manner and begin to release the drug in a controlled manner.

Properties of Nanosponges

Insoluble in water and organic solvents

Solid and porous in nature

Remain stable at high temperatures upto 300°C.

Nanosponges interact with lipophilic and hydrophilic drug moiety by complexation. The commonly used cross linking agents are diisocianates, diaryl carbonates and carbonyl diimidazoles, carboxylic acid dianhydrides and 2,2-(bis (acryl amido)acetic acid) [17]. Nanosponges can be administered through oral, topical and pulmonary routes.

Method of Preparation

Nanosponges can be prepared by Solvent method and Emulsification solvent diffusion method.

Solvent Method

In this method, initially polymer is dissolved in a partially water immiscible solvent. Then this was added to excess of crosslinking agent. The obtained solution is refluxed for 48 hrs at a temperature of 10^{o}C and it is allowed to cool at room temperature. The resultant solution is washed with double distilled water and the product is filtered. The obtained nanospheres are purified by employing Soxhlet extraction with ethanol [18].

Emulsion Solvent Diffusion Method

In this method hydrophobic polymer is dissolved in a volatile organic solvent. Then the organic phase was transferred into an aqueous solution containing colloidal stabilizer. The so formed O/W emulsion was kept for stirring at 1000rpm for 2hrs.After that the dispersion is filtered and dried in an oven at 40^{o}Cfor 24 hrs [19].

Applications

By virtue of their biocompatibility and versatility, nanosponges can act as multifunctional carriers, i.e., to enhance solubility, protect fragile molecules and to achieve sustained release profile.

Solubility Enhancement

The porous nature of nanosponges allows effectively incorporate water insoluble drugs by complexation. These complexes can be used to increase the dissolution rate, solubility and stability of drugs, to mask unpleasant taste.

E.g. Solubility of Itraconazole was found to be 1ng/ml but when formulated as nanosponges the aqueous solubility of Itraconazole showed an improvement to about 27 folds.

Nanosponges based Cyclodextrin can strongly bind organic molecules and remove them from water even at lower concentrations [21].

Drugs Formulated as Nanosponges [22]

Paclitaxel, Camptothecin: In the treatment of Cancer.

Resveratrol: In the treatment of Cardiovascular diseases.

Dexamethsone: In the treatment of Brain tumors.

NANOCANTILEVERS

Nanocantilevers resemble diving spring board like in structure with dimensions of 100nm long and 20 nm wide and 1nm thick. These nanocantilevers are physical sensors made of silicon wafers which respond to surface stress changes that occur due to chemical/biological process. Each sensing device possess three characteristic features, they include (i) response time, (ii) selectivity, and (iii) sensitivity [23]. Cantilever sensors are fabricated with very small force constant (of less than 0.1N/m), they can measure minute variations in stress changes with high sensitivity. Because of its ability to measure minute surface stress variation that occur due to the adsorption (or specific surface –receptor interaction) of molecules [24] they could be used as detectors. The figure is illustrated in Figure **4** (Cantilevers as biomarkers).

Mechanism of Cantilever Deflection

Cantilevers reveal the presence of toxic substances based on vibrations at different frequencies. Adsorption of molecules on a surface results in a decrease in surface free energy. If the adsorption of molecules on a surface is restricted mostly to one side by making the opposite surface inert. A differential surface stress is generated between the two surfaces of a cantilever beam when contaminants stick on them at one side, which manifests as a deflection.

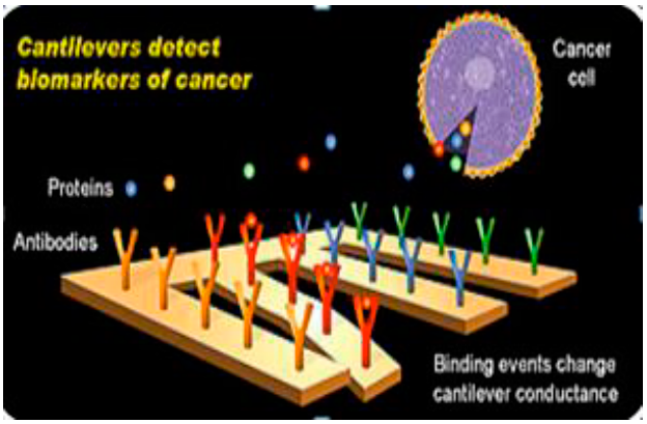

Figure 4: Cantilevers as Biomarkers.

In comparision with various detectors nanocantilevers offer high sensitivity that enables it to diagnose and provide an early warning if a pathogen is present.

QUANTUM DOTS

Quantum dots are tiny inorganic semiconductor particles of 1-10nm size range. These can be made to fluorescence brightly in different colours depending on their size. They are generally composed of atoms from groups II and IV elements (E.g. CdSe and CdTe) of groups III and V (E.g. InP and InAs)of periodic table.

Mode of Action

Quantum dots act by binding with target materials. On binding to target, based on the size, quantum dots emit light and glow at different colours [25].

Properties of Quantum Dots

Size tunable light emission, improved signal brightness, resistant against photo bleaching and simultaneous excitation of multiple fluorescent colours are the unique optical and electrical properties of Quantum dots. The figure for CdSe Quantum dot is illustrated in Figure **4**.

Synthesis of Quantum Dots

Quantum dots comprises of three component system which consists of precursors [26,27], organic surfactants and solvents.

Surfactants: makes Quantum dots water soluble and prevent aggregation.

Precursors and solvents: Organo metallic precursors like Se compounds are dissolved in suitable solvent.

End point: Colour change from colourless to yellow.

Advantages of Quantum Dots

Quantum dots are much resistant to degradation and the other imaging probes.

Fluorescence lasts for longer periods when compared to conventional dyes.

Applications

In biomolecular and medical imaging.

CARBON NANOTUBES

Carbon nanotubes are fullerene shaped structures which consists of graphene cylinders closed at either end with caps containing pentagonal rings. Carbon nanotubes are cylindrical molecules formed by rolling single layer or multiple layer of grapheme sheets into cylindrical and capping each end with half of a fullerene molecule. As they have needle shape, they are capable of penetrating into the cellular membrane and pass into cellular components without causing damage [28]. They conjugate with variety of therapeutics and biomolecules as they posses high surface area.

Types of Carbon Nanotubes [29]

Based on their structure, they can be classified into single walled (0.4-3nm), double walled (1-3nm) and multiwalled (2-100nm)carbon nanotubes. The figure is illustrated in Figure **5**.

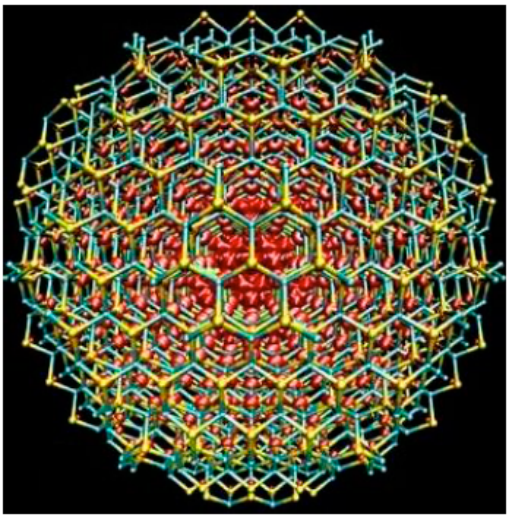

Figure 5: CdSe nanoparticle (QD) structure.

Production of Carbon Nanotubes

Arc Discharge Method

Arc is generated by applying a current of 40-100 A in helium with pressure of 100-700 torr at the electrode. The constant distance between electrodes leads to production of electric discharge which is collected in the inner wall of the chamber. By using Cesium oxide, the product is extracted and washed off with 1N con.HCl and dried at 100˚C to remove the impurities, fullerenes and catalyst.

Catalyst Chemical Vaporization Method

Fixed Bed reactor is used for the synthesis of SWCNT. H_2 and CH_4 are used as catalysts.1gm of catalyst is placed in centre of reactor and carrier gas allows the methane and hydrogen to flow through FBD at 1000° C with a time of 10min. Once the reaction is completed the catalysts are removed by using con.HCl.

Mechanism of Cellular Uptake

Because of its needle shape, it penetrates into the cell membrane without causing cell damage. Cellular uptake is based on the surface chemistry and size.CNT coated with polymers and surfactants are phagocytized through endocytosis [30].

Applications [31,32]

In Photo thermal therapy of cancer and lymph targeting.

MICROBIVORES

These are mechanical phagocytes designed by Robert S.Freitas Jr.It is a micro machine with numerous oblate spheroidal nano, mechanical devices having dimensions of 3.4microns in length and 2micron in width and consists of 610 billion structural atoms and 150 billion water molecules [34].

The invading pathogens stick to the surface of the microbivore at specific reversible binding sites. Then the device stimulates the nanorobotic manipulators to direct the pathogens into an ingestion port. The targeted microbes are then passed to a digestion chamber and released into the blood stream after they have broken down by the enzymes. The figure is illustrated in Figure **6**.

RESPIROCYTES

Respirocytes are nanomachines measuring about 200nm [35]. They function as artificial RBC which performs gaseous exchange [36].

Components of Respirocytes

Molecular rotors: pump gases in and out of storage chambers and collect glucose for energy.

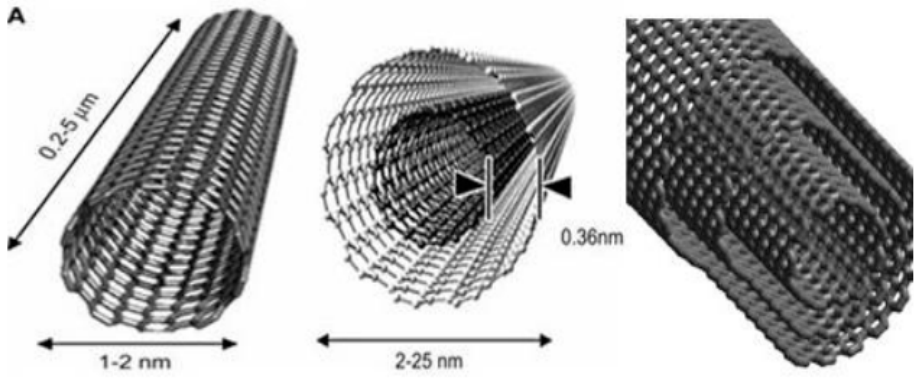

Figure 6: Types of Carbon Nanotubes.

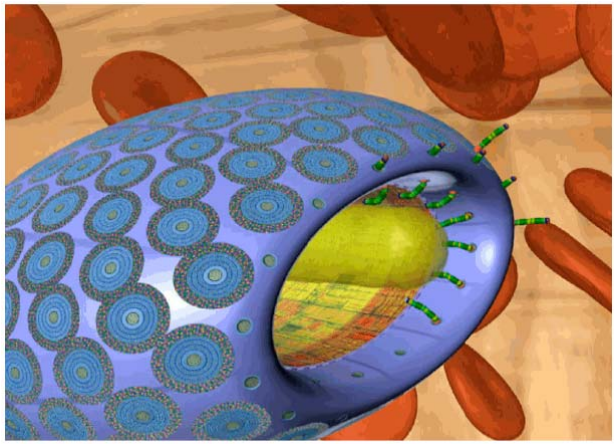

Figure 7: Microbivore.

Water ballast chambers: control buoyancy.

Sensors: determine concentration of O2 and Co_2. And determine pressure within gas storage tank.

Computer: interpret input from sensor and monitors the gas flow.

The figure is illustrated in Figure **8** (Construction of Respirocyte cell structure).

Working of a Respirocytes

Respirocytes exchange gasses *via* molecular sorting rotors [37]. The rotors have specially shaped tips to catch particular types of molecules. Gas molecules are stored tightly in tanks. Each respirocyte has three types of rotors. One gathers oxygen at the lungs or in production before introduction to the body and releases it while traveling through the body. Another captures carbon dioxide while in the bloodstream and releases it at the lungs. The third takes in glucose from the bloodstream, which is burned in a reaction similar to cellular respiration in order to power the respirocyte.

Respirocytes can provide a temporary replacement for natural blood cells in the case of an emergency. If an individual has lost access to a natural oxygen supply due to drowning, choking, or any other form of

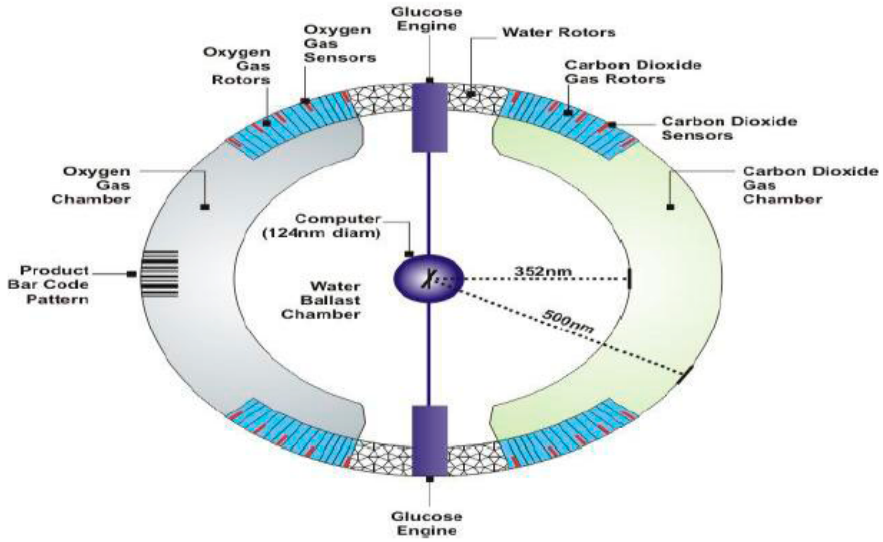

Figure 8: Construction of Respirocyte cell.

asphyxia [38, 39], respirocytes can release oxygen throughout the bloodstream until the danger has been removed.

Respirocytes can also be used for other problems with gasses in the bloodstream. Another useful application is in deep sea diving. If a diver dives too quickly, one often suffers from the "bends", a problem caused by dissolved nitrogen bubbles in the bloodstream [40]. Respirocytes could be designed to capture nitrogen molecules during dives.

CONCLUSION

Pharmaceutical nanotechnology offers new tools, opportunities and scope which have a great impact on the diagnosis and the treatment of diseases. Nanoparticles are one of the novel drug delivery systems, which can be of potential use in controlling and targeting drug delivery. Judging by the current interest and previous successes, nanoparticulate drug delivery systems seems to be a viable and promising strategy for the biopharmaceutical industry.

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REFERENCES

[1] Gommersall L, Shergill IS, Ahmed HU, Hayne D, Arya M, Patel HRH, Hashizume M, Gill IS. Nanotechnology and Its Relevance to the Urologist. Journal of European Urology 2007; 52: 368-375. http://dx.doi.org/10.1016/j.eururo.2007.04.065

[2] Jain NK. Controlled and novel Drug Delivery, 1st edition 2001, CBS Publication; 292-301.

[3] Khar RK, Vyas SP. Nanoparticles in targeted and controlled drug delivery novel carrier systems. New Delhi: CBS publishers and distributors 2002; 331-385.

[4] Feng S, Chien S. Chemotherapeutic engineering: application and further development of chemical engineering principles for chemotherapy of cancer and other diseases. Chemical Engineering Science 2003; 58: 4087-4114. http://dx.doi.org/10.1016/S0009-2509(03)00234-3

[5] Cheng Y, Tongwen X. Dendrimers as Potential Drug Carriers. Part I. Solubilization of Non-Steroidal Anti-Inflammatory Drugs in the presence of Polyamidoamine Dendrimers. European Journal of Medicinal Chemistry 2005; 40: 1188-1192. http://dx.doi.org/10.1016/j.ejmech.2005.06.010

[6] Silva Jr, NP, Menacho FP, Chorilli M. Dendrimers as potential platform in nanotechnology-based drug delivery systems. Journal of Pharmacy 2012; 2(5): 23-30.

[7] Malik A, Chaudhary S, Garg G, Tomar A. Dendrimers: A Tool for Drug Delivery. Advances in Biological Research 2012; 6(4): 165-169.

[8] Ina M. Dendrimer: A Novel Drug Delivery System. Journal of Drug Delivery & Therapeutics 2011; 1(2): 70-74.

[9] Sonke S, Tomalia DA. Dendrimers in biomedical applications reflections on the Field. Advanced Drug Delivery Reviews 2005; 57: 2106-2129. http://dx.doi.org/10.1016/j.addr.2005.09.018

[10] Kumar P. Dendrimer: a novel polymer for drug delivery. JITPS 2010; 1(6): 252-269.

[11] Waghmare AS, Grampurohith ND, Gadhave MV, Gaikwad DD, Jadhav SL. Solid lipid Nanoparticles: A promising drug delivery system. International Research Journal of Pharmacy 2011 3(4): 2230-8407.

[12] Mukherjee S, Ray S, Thakur RS. Solid lipid nanoparticles: A modern formulation approach in drug delivery system. Indian Journal of Pharmaceutical Sciences 2009; 71: 349-358. http://dx.doi.org/10.4103/0250-474X.57282

[13] Mehnert W, Mader K. Solid lipid nanoparticles: Production, characterization, applications. Advanced Drug Delivery Review 2001; 47: 165-196. http://dx.doi.org/10.1016/S0169-409X(01)00105-3

[14] Ekambaram P, Abdul Hassan Sathali A, Priyanka K. Solid Lipid Nanoparticles: A Review. Sci Revs Chem Community 2012; 2(1): 80-102.

[15] Chen H, Chang X, Du D, Liu W, Liu J, Weng T, Yang Y, Xu, H, Yang X. Podophyllotoxin-loaded solid lipid nanoparticles for epidermal targeting. Journal of Control Release 2006; 110(2): 296-306. http://dx.doi.org/10.1016/j.jconrel.2005.09.052

[16] Waghmare AS, Grampurohith ND, Gadhave MV, Gaikwad DD, Jadhav SL. Solid lipid Nanoparticles: A promising drug delivery system. International Research Journal of Pharmacy 3(4): 2230-8407.

[17] Selvamuthukumar S, Anandam S, Kannan K, Manavalan R. Nanosponges: A Novel Class of Drug Delivery System-Review. Journal of Pharmacy and Pharmaceutical Sciences 2012; 15(1): 103-111.

[18] Shankar S, Linda P, Loredana S, Francesco T, Pradeep V, Dino A, Michele T, Gianpaolo Z, Roberta C. Cyclodextrin-based nanosponges encapsulating camptothecin: Physicochemical characterization stability and cytotoxicity. European Journal of Pharmacy and Biopharmaceutics 2010; 74: 193-201. http://dx.doi.org/10.1016/j.ejpb.2009.11.003

[19] Sharma R, Walker RB, Pathak K. Evaluation of Kinetics and Mechanism of Drug Release from Econazole nitrate Nanosponge Loaded Carbapol Hydrogel. Ind Journal of Pharmaceutical and Educational Research 2011; 45(1): 25-31.

[20] Swaminathan S, Vavia PR. Formulation of beta Cyclodextrin based nanosponges of Itraconazole. Journal of Inclu Phenom Macro Chem 2007; 57: 89-94. http://dx.doi.org/10.1007/s10847-006-9216-9

[21] Naga Silpa J, Nissankararao S, Bhimavarapu R, Lakshmi Sravanthi S, Vinusha K, Renuka K. Nanosponges: A versatile drug delivery system. International Journal of Pharmacy & Life Sciences -A Review 2013; 4(8): 0976-7126.

[22] Jilsha G, Viswanad V. International Journal of Pharmaceutical Sciences Review 2013; 19(2): 119-123.

[23] Nair PR, Alam MA. Performance limits of nanobiosensors. Applied Physics Letters 2006; 88 (23): 23-31. http://dx.doi.org/10.1063/1.2211310

[24] Lavrik NV, Sepaniak MJ, Datskos PG. Cantilever transducers as a platform for chemical and biological sensors, Review of Scientific Instruments 2004; 75: 2229-2253. http://dx.doi.org/10.1063/1.1763252

[25] Bakalova, Zhelev Z, Ohbc H. Quantum dots as photosensitizers. Journal of Nature and Biotechnology 2004; 22: 1360-1361. http://dx.doi.org/10.1038/nbt1104-1360

[26] Rathore KS, Lowalekar R, Nema RK. Quantum dots: A future drug delivery system. The Pharma Review 2006; 4: 30-32.

[27] Dey NS, Bhanoji Rao ME. Quantum Dot: Novel Carrier for Drug Delivery. International Journal of Research in Pharmaceutical and Biomedical Sciences 2011; 2(2): 448-458

[28] Kam NWS, Liu Z, Dai H. Functionalization of carbon nanotubes *via* cleavable disulfide bonds for efficient intracellular delivery of siRNA and potent gene silencing. Journal of the American Chemical Society 2005; 126 (36): 12492-12493. http://dx.doi.org/10.1021/ja053962k

[29] Zhang W, Zhang Z, Zhang Y. The application of carbon nanotubes in target drug delivery systems for cancer therapies. Nanoscale Research Letters 2011; 6: 555. http://dx.doi.org/10.1186/1556-276X-6-555

[30] Kam NWS, Jessop TC, Wender PA, Dai H. Nanotube molecular transporters: internalization of carbon nanotube-protein conjugates into mammalian cells. Journal of the American Chemical Society 2004; 126(22): 6850-6851. http://dx.doi.org/10.1021/ja0486059

[31] Elhissi AMA, Ahmed W, Israr Ul Hassan, Dhanak VR, D'Emanuele A. Carbon Nanotubes in Cancer Therapy and Drug Delivery. Journal of Drug Delivery 2012; 2012.

[32] Liu X, Tao H, Yang K, Zhang S, Lee S-T, Liu Z. Optimization of surface chemistry on single-walled carbon nanotubes for *in vivo* photo thermal ablation of tumors. Biomaterials 2011; 32(1): 144-151. http://dx.doi.org/10.1016/j.biomaterials.2010.08.096

[33] Yang D, Yang F, Hu J, Long J, Wang C, Fu D, Ni Q. Hydrophilic multiwalled carbon nanotubes decorated with magnetite nanoparticles asymphatic targeted drug delivery vehicles. Chem Commun 2009; 29: 4447-4449. http://dx.doi.org/10.1039/b908012k

[34] Mishra J, Dash AK, Kumar R. Nanotechnology Challenges; Nanomedicine: Nanorobots. International Research Journal of Pharmaceuticals 2012; 2(4): 112-119.

[35] Satyaveni M, Sai Sowjanya M, Sreenivasulu K, Sreekanth N, Baburao C. Respirocytes: Mechanical Artificial Red Blood Cells 2013; 4(4): 297-301.

[36] Drexler KE. Molecular engineering: an approach to the development of general capabilities for molecular manipulation. Proc Natl Acad Sci USA 1981; 78: 5275-5278.

[37] Merkle RC. The technical feasibility of cryonics. Med Hypoth 1992; 39: 6-16. http://dx.doi.org/10.1016/0306-9877(92)90133-W

[38] Spence RK. The status of bloodless surgery. Transfusion Med Rev 1991; 5: 274-286. http://dx.doi.org/10.1016/S0887-7963(91)70220-4

[39] Young son C, Nurse C, Yeger H, Cutz E. Oxygen sensing in airway chemoreceptors. Nature 1993: 363-155

[40] Pearson D, Shaw S. Life Extension: A Practical Scientific Approach. New York: Warner Books 1983.

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