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Biomaterials Serving the Purpose of Drug Delivery in Human Body

Talukdar Raian Ferdous, Tahsin Solaiman*
Department of Biomedical Engineering, Khulna University of Engineering and Technology, Khulna, Bangladesh
Email: raianferdous1415020bme@gmail.com, tahsinsohan@gmail.com

ABSTRACT
Today is an era when we overcome all constrains concerning our health. Drug is a substance that when inhaled, injected, smoked, consumed, absorbed via a patch on the skin or dissolve under the tongue causes a temporary physiological change in the body. Total number of approved drugs is 3254. Delivering drugs on the body should be efficient enough. Different types of drug carriers are used for delivering these drugs into body. These carriers are more specialized in biocompatibility apart from other materials. Sometimes the carriers have good effective area coverage but it takes much time to affect and vice-versa**.** As a consequence several prolific researchers have been asked to contribute unique research findings and reviews that could stimulate continuing effort to look for or to understand new biomaterials with biocompatibility, desired residence time, larger area coverage. This text focuses on the recent and far attempts in drug delivery biomaterials that would allow people to have a clear view of materials role in health site. The discussion comprises of metal-organic frameworks, carbon materials, microporous mesoporous materials and Mechanoresponsive materials for drug delivery system.

Keywords: Metal Organic, Photopolymerized , Mesoporous, Carbon, Protein.

1. Introduction: In recent years progressive health care facilities have been aggrandized to increase the possibility of eradicating any health related problems. Different types of drugs are being used worldwide to prevent and cure diseases. Development of new drug molecule is expensive and timeconsuming [1]. The drugs are delivered to the body by several systems serving particular purpose. There are basically three types of novel drug delivery systems. They are (i) targeted drug delivery system (ii) controlled drug delivery system (iii) modulated drug delivery system. Each of them have distinguishable features with advantages and limitation. The field of drug delivery focuses on the development of technologies to deliver biomolecules to the site of the disease so as to maximize therapeutic benefits, minimize side effects and enhance patient compliance [2]. It depends on the system and its features how efficiently the drug is working. Many of the pharmacological properties of conventional drugs can be improved through the use of drug delivery systems (DDS), which include particulate carriers, composed primarily of lipids and/or polymers, and their associated therapeutics [3].Delivery of drugs to specific locations in the human body using materials-based systems has been approaching the forefront of biomedical research for the past few decades. The concept has arisen from our advancing knowledge of materials for example, biocompatible nanoparticles that encapsulate drugs and respond to environmental stimuli, biodegradable hydrogels with tunable drug-release profiles, and implanted depots that control the spatiotemporal presentation of a therapeutic and has been enabled by our increased understanding of disease and the biochemical pathways involved [4].Different materials hold the interest of being used in delivering drugs into the human body. We can mention mesoporous, microporous, mechanoresponsive, metal framework, protein based materials serving this cause. These limitations can be potentially overcome by designing carriers that perform multiple tasks including encapsulation and controlled release, minimization of immune-clearance, penetration of biological barriers and targeting the disease site [2].The objectives of this paper is to review the previous works and literatures of the materials that include the usages of drug delivery materials and helps providing necessary information about increasing effective area, shortening the duration to impact, alleviate the hazardous impact on human health as well as briefing the delivery systems of each type materials incorporated.Considerable literature was studied and gathered information on previous research and development of drug delivery materials. The most focused aspect of this paper is to accumulate these multiple works into a single sight so that the maximum benefits can be obtained at the time of selecting drug delivery materials simultaneously as all the available drug delivery materials are described.

2. Methodology and Materials: The key ingredient of any drug delivery system lies in the application of stable, attractive and biologically responsible materials. Materials having severe destructive impacts to the body internal affairs by releasing infectant, toxicity and depletion of natural resources are to be avoided. To check these destructive impacts precautionary steps are initiated during acquisition of drug delivery materials, their production and manufacturing processes and along with their transportation process. The manufacturing processes of these materials are to be conducted by taking some intensive cares. Selection of the materials depends on some factors (e.g. aesthetically preferable to

* Corresponding author. Tel.: +88-01748692078
E-mail addresses: raianferdous1415020bme@gmail.com

the habitants, cost effective and inserting to the living subject, surface area, volume etc.).

2.1 Mesoporous Materials: The mesoporous drug delivery system has contributed to turn the drug delivery system for its unique pore size, desired surface area, higher pore volume to carry out the drug. The drug incorporation is carried out by two ways. One is soaking of the matrix in a highly concentrated drug solution and another is subsequent drying [5]. The several structural and functional mesoporous-silica systems for sustained release of various drugs are being developed day by day. These systems include MCM-41 or M-41, MSU, SBA, HMA. MCM-41 as one of the importantly synthesized mesoporous materials, M41S [45], has been firstly employed as drug deliveryMatrix. The hexagonal structure of the wall of the cylindrical pores consists of a disordered network made up of siloxane bridges and free silanol groups acting as reacting nuclei against appropriate guest chemical. The M-41 has the slow rate of loading of the drug. The MSU mesoporous silica is another type of drug carrying system which is in under development. Tourne-Peteilh et al. [6]employed MSU to store pentapeptide. They found that pentapeptide could be encapsulated in the mesoporous silica and would be released instantly upon the solid washing with dimethylformamide (DMF). SBA-15 is another important mesoporous material which has a large, controlled pore size and highly ordered hexagonal topology [7].The SBA groups consist larger pore size of about 6mm than the M-41 considered more carrying capabilities of the bulky molecules. The subsumed amount of drug strongly depends on the amoxicillin concentration, solvent, pH, and amoxicillin concentration. It has the largest diameter. Hollow mesoporous spheres (HMS) are considered unique group of essential mesostructured materials, which exhibit much more advantages in mass diffusion and transportation compared with conventional hollow spheres of solid shells. They compared the drug loading with MCM-41 and found that the HMS exhibited much more storage
capacity than MCM-41 [8].This group has the highest loading wt% of the all.

2.2 Carbon Materials: One of the most recent strategies proposed to incorporate nanotechnology principles is through the application of carbon nanotubes (CNTs). It has the unique properties of biocompatibility in the drug delivery system and their indispensable role in the carrying of drug to the highly selective and sensitive area. It leads to the modulation of undesired effects and creating new conjugates with promising and developed pharmacological profiles. The CNTs are two of types single-walled (SWNTs) and the multi-walled (MWNTs), both has the optical absorption around 700-1000 nm which is in the range of NIR, having great opportunities in the therapeutic cancer treatment drug delivery. Differing from small drug molecules which are usually able to diffuse across cell membranes, biomacromolecules such as proteins, DNA, and RNA cannot penetrate the cell membrane by themselves, instead requiring delivery vehicles to help in their cellular entry. Proteins transported into cells via CNTs was achieved in a few early reports, where it was shown that proteins could either be conjugated or no covalently absorbed on CNTs for intracellular delivery [9-11]. Several other CNT-based photo-therapies is also reported. The photoacoustic effect of CNTs, showing great promise as a contrast agent for photoacoustic molecular imaging in vivo [12]. Carbon-nanotubes are preferable drug carriers for the purpose of cancer drug delivery and therapeutic treatment as well as imaging of tumors.

2.3 Mechanoresponsive Materials: To date, different physical and chemical based stimulus drug delivery systems had been found. Among those the emerging mechanical force-based stimulus is up to date and has a vast research area which offers a suitable and robust controlled drug delivery systems. Mechanical activated delivery systems comprise three delivery systems compression, tension, shear though the process is still under developing. Compressive delivery systems require substrates which withstand compressive loading and respond to it (Elastomers). In example, Yang et al. describe another example of cyclical compressive release demonstrating controlled release of bovine serum albumin (BSA) from porous matrices [13]. Lee et al. report one of the earliest hydrogel compressive systems, composed of calcium cross linked alginate, as a device to stimulate neovascularization through the delivery of physically entrapped vascular endothelial growth factor (VEGF) [14,15]. Tension responsive drug delivery is another method. The method uses tension to activate and control the rate of drug flow. Tension property is used because it is the dynamic nature of the human body. While most hydrogels are capable of compressive loading, hydrogels often yield at low tensile strains (i.e., <50% strain, [16]). From a highly stretchable interpenetrating alginate polyacrylamide hydrogel, first developed by Sun et al. [17], Zhang et al. release horseradish peroxidase and Candida antarctica lipase B by stretching [18]. The shear-responsive system has the potential to use in the cardiovascular system where narrowing blood-vessel increases the shear stress. This system includes liposome deformation, particle aggregation and dispersion, supramolecular disassembly.

2.4 Metal Organic Frameworks as Material: Great effort is being applied devoted to the development of methods to control drug release to satisfy the ever-growing demand for prolonged and better control of drug administration [19].Two methods are introduced. The first one titled “organic route” which uses either biocompatible dendritic macromolecules or polymers [20]and the second one is “inorganic route” in which the hosts are inorganic porous solids such as zeolites and mesoporous silicate materials. In case of organic route a wide range of drugs can be encapsulated but controlled

release is difficult. On the contrary for inorganic route release is performed by grafting organic molecules one pore walls but implies a decrease in drug loading capacity [21,22]. A third way: the "hybrid" route a combination of high and regular porosity with the presence of organic groups within the framework may cumulate the advantages to achieve both a high drug loading and a controlled release [19]. But microporous is a restriction here that has been observed. To overcome this major problem, researchers developed a method that combines targeted chemistry and structural computer predictions to obtain mesoporous hybrids with large pores. This approach leads to the characterization of two new cubic (Fd3m) zeotypic metal carboxylates, denoted MIL-100 and MIL-101 (MIL=Materials of Institut Lavoisier) and built up from trimers of metal octahedra and di- or tricarboxylic acids [23]. The drug content of MIL-101 is four times larger than in MCM-41 and the delivery rate tends to be slower, thus taking 6 days for MIL-101 relative to 2 days for MCM-41 [19].Thus, MIL-101 is allowed a higher dosage of drug and a longer controlled delivery, which is supposed advantages for larger pharmacological molecules.

2.5 Chiral Nanoporous Metal-Organic Frameworks with High Porosity as Material: For drug delivery, chiral nanoporous metal- organic framework (MOF) with high porosity has been synthesized based on nontoxic zinc and achiral hexadentate ligand. The high drug loading and slow release of the loaded drug of the material is desired function for many drug delivery. Sometimes there is a complete delivery time of about one week being used as a material for adsorption and delivery of anticancer 5- fluorouracil. The delivery of bioactive gas molecules such as NO from MOFs as an antithrombosis and vasodilation agent, Gd III -based nanoscale MOFs being used as magnetic resonance imaging (MRI) contrast agents, [24] and lanthanide-based MOFs being efficient multimodal cellular probes materials [25]. 5-FU containing methanol solution is helpful for different spectroscopy.

2.6 Photopolymerized Hydrogel Material: Matrices of hydrophobic polymers such as ethylene-vinyl acetate copolymers is used for sustained release of proteins, polysaccharides, oligonucleotides [26] but it is difficult to homogenously disperse hydrophilic materials within a hydrophobic copolymer matrix resulting in unpredictable release profiles. However there is a need of hydrophilic polymer which have potential to be used for sustained release. A hydrogel material is developed which may be suitable for delivery of proteins, peptides, oligonucleotides [27]. The hydrogel is generally formed by photopolymerization of an aqueous solution of a macromolecular precursor. The precursor is consisted of a central polyethylene glycol (PEG) chain with oligomeric blocks of a hydrolysable a-hydroxy acid, or other degradable moiety on each side. The hydrogel materials have also been used to prevent thrombosis and vessel narrowing following vascular injury [28]. The synthesis of hydrogels appropriate for a wide variety of drug delivery options is allowed byThis versatile design of precursor. A small drug would require a low molecular weight PEG in the precursor to achieve release mediated by hydrogel degradation. It is possible to control the release of macromolecular drugs from these photopolymerized hydrogels through the design of the precursor. Drug which is released from this type of hydrogel has been maintained for as long as 2 months in vitro [27]. Numerous variations on the acrylated PEG-co-α-hydroxy acid format can be synthesized, thus allowing one to essentially tailor the hydrogel to the requirements of a specific drug delivery application.

2.7 Protein Based Materials: Interests in protein-based biopolymers for drug delivery have been being increased in recent years. While comparing to synthetic polymers, they have advantages of being water-soluble, biocompatible, biodegradable and non-toxic [29]. Many fibrous protein materials such as keratin, collagen, elastin and silk have been widely used in drug-delivery related research[30]. Keratin could be derived from the outer layer of human skin and the epidermal appendages of animals such as feathers, hair, hooves, horns, nails, scales and wool [31]. At molecular level, keratin shows three different configurations: α–, β–, γ–Keratin. Collagen is a protein imperative to the structural integrity of tissues and cell growth in vertebrates and other organisms [32]. It can be processed into various forms suitable for drug delivery (such as hydrogels, microparticles and films) [33]. There are two categories to chemically crosslink collagen molecules: bi-functional and amide-type. By selecting and employing safe crosslinking modification methods to collagen, drug stability and retention times can be increased [30]. Similar to collagen, elastin is a protein within the extracellular matrices comprises different flexible tissues [34]. Elastin is a heavily crosslinked structure with beta-spiralsecondary structure, making up a major component in elastic fibers [34]. Various forms of thermoresponsive elastin, such as animal-derived soluble elastin, recombinant human tropoelastin (rhTE), and elastin-like polypeptides (ELPs), have been synthesized and utilized to engineer promising synthetic tissue scaffolds [35]. Silk is a protein of long historical use in biomedical applications, such as tissue and ligament repair, nerve regenerators, and artificial blood vessels [36]. Different silkworm silks have been used for drug-delivery applications including Bombyx mori, Tussah, and Eri silks [37]. Silk proteins can be prepared in various ways, such as films [38], 3D porous scaffolds [39], and micro and nanoparticles [40], with controlled degradation rates. They have a great contribution to biotechnical applications like drug delivery and tissue scaffolds. Resilin is an elastomeric protein which was first found existing in jumping insects' cuticles of many species [41]. Resilin exhibits high extensibility, low stiffness, efficient energy storage and extraordinary resilience, which enables some jumping insects to take jump many times' their body length. The resilin's

rubber-like elasticity possesses excellent biocompatibility and mechanical properties, which can be used for a broad range of biomedical applications such as drug delivery and tissue scaffolds [41,42][46]. Zein is a major plant-based storage protein rich in prolamine generally found in the endosperm of the corn kernel [43]. It has four classes, *α–, β–, γ–, δ*–zein, varies on molecular weights and modes of extraction [44]. All zein fractions have hydrophobic and hydrophilic domains but zein is frequently considered to be a hydrophobic protein as it has insolubility in water and solubility in ethanol, acetone, and acetylacetone. Zein shows to form aggregates and entrap solutes like drugs or amino acids which make it an excellent matrix material for sustained release [30].

3. Conclusion: In this paper we have discussed about drug delivery biomaterials that are used and may have the possibility of being developed efficiently for effective health standard. Implementation of these materials depends largely on the type of patient, conditions, symptoms, environment etc. Better drug delivery will result in better standard of life eradicating diseases. Manufacturer companies should adopt steps for researching these materials in order to develop a hybrid one which must be cost efficient at the perspective of Bangladesh. This will elevate the drug delivery system and people will be the most advanced technology's beneficiaries. This will contribute a lot in the advancement of health sector of Bangladesh.

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