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Nanoscale Drugs Carriers in Chronic Diseases Treatment: Applications

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Abstract--- *Nanomedicines address traditional therapy shortcomings, as shown by many preclinical and clinical studies that indicate site-specific drug delivery, decreased side effects, and better treatment result. Developing appropriate and the biocompatible drug delivery vehicles is a prerequisite effectively achieved through the use of simple and functional liposomes, hydrogels, nanoparticles, and dendrimers, micelles, and mesoporous particulates. Nanomedicine plays a key role for applications like the delivery and diagnosis of drugs in the medical field. Over the last decade, the need to build multiple systems that may distribute the pharmaceutical agent accurately and directly to the target site has expanded. Across medical fields such as cardiology, oncology, and immunology these programs have a major impact. However, it still needs a large number of extensive clinical trials to make sure the short-and long-term effects of the nanomedicines in humans. Smart drug delivery systems with the stimuli response, such as temperature, pH, illumination, electrical, ultrasound, and magnetic fields were developed in this regard. Several nanoparticles, including silver NPs, gold NPs, magnetic NPs, quantum dots, and mesoporous silica NPs, have been studied as nanocarriers for drug targeting.*

Keywords--- *Cancer Therapy, Cardiovascular Diseases, Diabetes, Nanomedicine, Stimuli Responsive, Targeted Drug Delivery*

I. INTRODUCTION

Targeted drug delivery could be linked to an increased concentration of the active pharmaceutical drugs at a particular body site, compared to the rest of the body. For most pharmaceutical agents, their ability to target particularly damaged sites relies on the aggregation of active pharmaceutical drugs to interact with the biological tracts. Commonly, blood flow is similarly proportioned to the distribution of the pharmaceutical drug released by the intended drug delivery system (DIDS)[1]. One major concern is that the drug carrier must resolve certain biological obstacles which can cause severe side effects in order to reach the target site. The concentration of drug at the desired site is ideal to be higher, and to decrease significantly in non-target sites in order to prevent unwanted side effects[2].

Targeted DIDSs arrive with such benefits, retaining the amount of medications in a favorable range which is not harmful In fact, side effects are reduced as similar location is reached by DDSs, resulting in patient compliance due to the smaller amount of medication produced. Pharmaceutical drugs can either be encapsulated, or connected to a polymer or a lipid to achieve drug safety and greater efficiency[2], [3]. Targeted delivery of drugs is also necessary for a prolonged period of time to a specific injured body site. There are few criteria that need to be considered in order to achieve targeted DDSs: the properties of the drug, the side effects that the drug may induce, the way the drug is

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introduced into the body, limited leakage throughout delivery etc[1].

Ideal optimized DIDSs must be both in vivo and in vitro stable in non-immunogenic, non-toxic, physical and chemical terms. The cars must be biodegradable from the body or at least easily removed. The planning method should also be simple, easy to reproduce, and cost effective. Pharmacokinetic, pharmacodynamic and pharmaceutic factors support opting to distribute controlled medicines over conventional drug delivery. The medicinal factors are the drug's toxicity and also its poor solubility[4]. The explanations for the pharmacokinetics are based on the delivery panel and the short half-life. The last explanation, as mentioned above, is that conventional medicines are poor in specificity. Smart DDISs need to fulfill a variety of criteria, such as supporting the solubility and safety of pharmaceutical drugs, reducing the amount of the medication required, and decreasing side effects. The carrier for the drug must be biocompatible and should not cause immune system responses[1], [3], [4]. The main property of smart DIDSs is the capability to deliver the pharmaceutical drug over an extended period of time to the desired location. For this, drug carrier should have its surface modified so it can bind itself to the cells of interest and deliver its charge by means of the stimuli provided. Either external stimuli such as electrical and magnetic field, temperature and ultrasound, or internal stimuli can be provided by environmental systems like temperature, pH, etc. Encapsulation of iron, silica, or magnetic nanoparticles into smart polymers increases the complexes' advantages[3].

I.I. Smart Drug Delivery Systems (DDS) -Drug Carriers

Microspheres and nanoparticles are the most-used targeted drug delivery carriers. Nanoparticles have dimensions ranging from 0.1 to 0.5μm, apart from microspheres having a size range of 30 to 20.0μm. Based on physicochemical properties of the drug, it can be encapsulated in nucleus of nanoparticles, or attached to its surface providing protection of the drug against unfavorable environmental properties[5]. In the pharmaceutical field nanoparticles have been used for more than 10 years to decrease side effects and harmful effects of drugs. Many researches indicate that nanoparticles used to deliver targeted drugs may enhance damage to organs. Proteins, polymers or peptides must be bound to the drug carrier surface for assembly of functionalized nanosized carriers[2]. Many functional elements may also be encapsulated into the nanosized containers, such as magnetic nanoparticles trapped in polymer shells. Surface attachment could be achieved either through noncovalent procedures, or through chemical mechanism[6]. Controlled DDSs can consist of nanoparticles, hydrogels, or multifunctional nanostructures, nanotubes of the carbon, and the radioactive microspheres. Furthermore, multifunctional nanoparticles are used to target tumors, destroy and attack cancer cells. Regardless of active or passive targeting, longevity in the blood flow is an essential property of the nanosized particles[4], [6]. Another way to do this is to maintain the drug in the blood flow for an extended period of time before it reaches the target site. For this the most commonly used approach is the chemical modification of drug carriers with the different synthetic polymers[5]. For instance, the use of hydrophilic polymers has attained promising results against different solutes.

I.II. Nanotechnology Applications In Drug Delivery and Targeting

Nanotechnology is prevalent in about every field of the industry. Although the word “nanotechnology” can be defined in various ways, it primarily refers to the measurements that need to be within the range of 0.1–1.00nm[7]. At first, nanotechnology focused only on developing the current therapeutic methods, but lately, thanks to nanoscale technologies, which had a significant contribution, it came up with new ones. There have recently been experiments attempting to create scaffolds to induce bones, skin, or body organs to expand. In the near future, nanomedicine aims to provide study and practice instruments and tools that could revolutionize the existing way of thinking (diagnostic and preventive) and taking action (applied treatments) in medical field, particularly in the sphere of influence of chronic degenerative diseases[1], [7]. Nanomedicine provides innovative and new solutions to solve the health problems, with a positive impact on society via contributions made to improve the quality of life and longevity and to reduce health care costs.

Nanotechnology offers four major areas of interest: guided pharmaceuticals transporting medicines to the desired location; tissue engineering capable of forming new tissues; molecular imaging capable of detecting specific diseases by sophisticated imaging; and biosensors and diagnostics capable of detecting dysfunctions in the body, and also developing diagnostic tools for laboratory work[3], [4]. Nanomedicine is an area that requires knowledge from many different disciplines, is an area of ongoing development and change, and expected to contribute to enhancing drug delivery, science discovery acceleration technologies, diagnostic or imaging methods. Nanomedicine uses approaches other than traditional methods, focused on destroying only the diseased cells rather than both healthy and diseased as in the case for chemotherapy[2].

I.II.I. Targeted Drug Delivery for the Cancer Therapy

Targeted drug delivery could be used to treat many diseases but is mostly used to cure cancerous tumors. Provision of controlled release systems which provide drugs that target only tumor sites is beneficial. Use of nanomaterials in this aspect is a successful and exciting field. Development of truly targeted DIDSs will require a better understanding of multiple factors, blood distribution regulation, dynamic tumor spatial elements, temporal and spatial heterogeneity[8]. Nanotechnology was due to the major advances in targeted drug delivery which culminated in the creation of a nanosized drug delivery platform with much advancement in cancer therapy.

Cancer is a globally leading cause of death, along with cardiovascular diseases. Cancer is an irregular and unregulated growth and cell proliferation that leads to the formation of tumors. Tumors are classified into two major categories: benign and malignant, based on their mode of development. The former grow locally, primarily at the site of emergence, while the others may disperse among other tissues or body parts[8], [9]. Cancer happens when an alteration in DINA is caused by diet or environmental factors. Persons who are constantly exposed to Ultraviolet rays or to various chemical compounds, food, polluted air, or nicotine are predisposed to changes in DINA[9]. When the tumor grows it is gradually isolating itself from the blood vessels, resulting in loss of oxygen and nutrients. Such compounds are essential to the survival and production of tumor cells. The tumor sends a signal to activate angiogenesis that will cause cancer cells to grow faster. The strain applied to the surrounding tissue will facilitate the growth of tumors[3], [5], [6].

Curing cancer is extremely difficult and even if the patients are treated properly using modern medical procedures, the result is usually not a good one. Surgery may be used to eliminate tumor sections but it does not help if the tumor is already distributed. In addition to surgery there are other common cancer treatment methods, like radiation or chemotherapy therapy[1], [7], [9]. The goal of chemotherapy is primarily to kill primary tumors, regardless of the fact

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that metastatic disease causes cancer deaths. Targeted DIDSs, due to their beneficial effects, constitute a very enticing and innovative strategy used more and more often in the medical field. It is defined as an approach that leads the particular drug delivered to the targeted area, without influencing the normal cells. The carriers used for these procedures need to have special characteristics in order to obtain positive results: they should have the proper size to penetrate the intended tissues and cells by blood circulation to carry the drugs[8].

In addition, selective delivery of drugs has gained more and more attention and it has been shown to be an excellent alternative for treating disease, particularly for cancer therapy. Even though multiple cancer treatments, like chemotherapy or surgical intervention, have been established, none can treat cancer; thus the mortality rates correlated with this disease remain high. Chemotherapy is one radiation-based process. All cell types, regular and impaired, suffer from this technique[2], [6], [9]. Targeted DDSs were produced so as to kill only cancerous cells. Smart DIDSs can encapsulate and release specific anticancer drugs, such as doxorubicin, under stimulating conditions. Under well-established conditions, light, temperature levels, ultrasound, electric, pH conditions, and magnetic fields engage directly in drug production. This means it will affect only dysfunctional cells. Nanocarriers require proper size to penetrate target tissues and get positive results. There are many types of nanoparticles which are used for these applications with effectiveness[8]. Magnetic waves, silver, gold, or quantum dots (QID) are ideal for the distribution and tracking of drugs because of their unique properties[7]. An improved response is given by combining those particle types with polymers.

I.II.II. Targeted Drug Delivery for Cardiovascular Diseases

Cardiovascular diseases are conditions which affect the functioning of the heart. Physiological characteristics of the cardiovascular system should be considered for the achievement of controlled release mechanisms for cardiovascular diseases. Cardiovascular drug therapy is distinct from other schemes because of the heart system's anatomy and physiology. MII is the leading cause of congestive heart failure (CIHF), and is one of the world's major causes of death[10]. The MI is caused by a coronary artery obstruction that leads to cell death. Ischemia induces myocardial necrosis, which is the restriction of coronary blood. All of these variables mean that a certain area is affected.

The innovative management methods are very critical to full recovery treatments for ischemic heart disease treatment. Work on the interactions between toxin and the targeted cells contribute to molecular pharmaceutical growth. It is important to understand the basics of various cardiac disorders, their etiology, clinical symptoms, pathological manifestation and preferred therapy and transportation operators for a regulated delivery system; heart-appropriate target drug must be chosen and the properties of successful targeting of these carriers must be monitored to improve the safety of the loaded drug[9], [10].

Cardiovascular diseases typically occur because of blood perfusion restriction. If neoangiogenesis occurs in the vicinity of the ischemic site, this induces oxygen and nutrient delivery, leading to a reduced cell death. Targeted delivery of drugs to the endothelium has been commonly researched. Carriers of heart targets play an important role in preventing pharmaceutical drugs from weakening in the blood flow[8].

Intracoronary or intravenous (IIV) injection of small molecules is the most commonly used delivery system for MII care since it is a minimally invasive process. Nonetheless, this form of procedure comes with the drawback of frequent

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long-term dosing to maximize the concentration in the infarction region contributing to severe side effects. Specially designed surgical instruments could be used to inject therapeutic drugs directly into the myocardium to achieve delivery of pharmaceuticals to targeted site. This method also shows a significant drawback: local injection allows the drug to be taken over very rapidly in the blood flow, thus altering the pharmaceutical drugs and being unable to reach localized delivery[10].

Bioengineering has developed, evolved and established new nano-sized tools to overcome the problems. Pharmaceutical modified nanoparticles have acquired considerable interest as they are DIDSs capable of detecting and separating early stages of the diseases. Liposomes were also studied for the drug delivery and diagnosis as therapeutically nanosized vehicles[7], [9]. It was concluded that the liposomes are the most commonly used nanosized carriers because they have a range of size 50–10.00 nm and therefore can encapsulate many prescription medicines. In fact, they possess acceptable properties as drug carriers, like biodegradability, biocompatibility and decreased degrees of toxicity (Table 1)[1].

Table 1: Cardiovascular applications of nanoparticles

Cardiovascular Applications	Types of Nanoparticles
MRI	Gold nanoparticles, nanoK, superparamagnetic iron oxide nanoparticles, liposomes
Positron emission tomography	Fe_3O_4 nanoparticles
Atherosclerosis	Magnetic-fluorescent nanoparticles, liposomes
Cardiac arrhythmias	Superparamagnetic iron oxide nanoparticles
Aortic stenosis	Magnetic-fluorescent nanoparticles

Several applications in nanotechnology are currently under investigation for the purpose of treating mechanical stents with a special interest in atherosclerosis, which contains nanosized constituents. This kind of stents provided new solutions to the distribution of medications. The main challenge is to facilitate revascularization of blocked arteries[2], [4]. Several companies have created drug-eluting stents which were able to deliver narcotics, such as Paclitaxel.

I.II.III. Targeted Drug Delivery for Diabetes

Diabetes has become the fifth reason for death around the world, in the most recent decade, influencing just about 23.0 million individuals. The number is hoping to arrive at around 366 million by 20.30. It shows chronic condition, communicating a metabolic issue, which is described by not reasonable protein, fat, and carbohydrate metabolism[11]. Diabetes is partitioned into two significant classes: type .1 and type 2 diabetes. Type 1diabetes happens when the body can't deliver insulin any longer and it is connected with irregular ketosis and hyperglycemia[12]. Type .2 diabetes demonstrates to the most widely recognized sort that shows up when insulin isn't being utilized appropriately by cells. So as to acquire a superior control of type 2 diabetes, hypoglycemic substances was utilized for oral organization. There were likewise some different methodologies, which enrolled achievement, for example, gastric bypass or pancreas transplant[3], [4], [11].

Despite the fact that there are medications for diabetes, it despite everything can't be relieved on account of a few side effects that show up. Some of them are demonstrate by gastric aggravation or injection fear, however considerably more models exist. Higher levels of ROS and molecular oxygen provoke imbalance in ordinary oxidative metabolism and this will prompt a strangely higher level of glucose in blood. Therefore, oxidative stress is created and chronic entanglements showed up[9], [12]. The utilization of insulin for treatment displays some negative aspects and in the chronic treatment, it can develop fatty liver or brain atrophy. An issue in diabetes additionally represents to the way that injuries are healing gradually, yet it very well may be settled by utilizing nanoparticles. For instance, yttrium oxide nanoparticles may save cells experiencing oxidative stress. It is significant the molecule structure, however not its size[11], [12]. This particular metal oxide shows no harmfulness and it endures little changes under temperature and weight typical conditions. Recently, they have attracted more interest due to their advantages in terms of improved bioavailability, minimized side effects, and prevention of deterioration in the gastric environment. These systems are designed so that they can distribute the particular drug reliably and precisely to the target for a well-established time period in order to enhance monitoring and therapeutic impact over diabetes disease[3], [4], [9].

Insulin remains one of the best ways to balance the intermediate metabolism compromised in diabetes in over 30% - 40% of all cases. Such types of pumps might provide an enticing opportunity in the future to enhance sugar management, especially for people with type 2 diabetes[3], [7], [9]. Insulin delivery via a pump is a flexible and easy method. Researchers have developed a technique that is helpful in the diagnosis of diabetes for the delivery of drugs through the blood; the procedure uses a sponge-like polymer center that includes insulin. In the case of cancer treatment medication this approach could be used[8], [11]. In addition, medicines can be inserted from the national blood supply into the vascular system aimed at an organ. To reduce these impairments, regulated release of drugs was designed to meet the target and to seek to destroy damaged cells. Cardiovascular diseases are a worldwide leading cause of death. As DDSs, because of their ability to identify diseases in their infancy, nanoparticles loaded with drugs have been realized in the concern of overcoming medical problems[12]. Because of their unique properties and small sized sizes, magnetic nanoparticles and liposomes are the most common nanoparticles in cardiovascular applications.

II. CONCLUSIONS

In conclusion, nanotechnology is aimed at spreading its use to all medical fields. Drug delivery technologies form a large, significant area of pharmaceutical research and development. Medicine is focused on the use of medicines to prevent and treat diseases, but its effects apply to the distribution and release of medications. Nanoparticles have been designed to improve the delivery of drugs to treat cancer, to kill cancer cells. In the medical field, there has been a growing interest throughout guided DDSs because they can precisely release their charge onto preferred sites without damaging the healthy tissue. Physical-chemical properties of controlled drug release systems are very important for the treatment of a disease. There are certain criteria which should be taken into account in order to accomplish an optimal controlled drug delivery system: they must be non-toxic, non-immunogenic, and also biologically and chemically stable in body. Smart D DSs have a considerable advantage over traditional DDSs: the ability of responding to stimuli, whether external or internal. The medicines have been developed over the years to improve safety and extend life.

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Nanomedicine is a segment within health systems, whose production and implementation can lead to cost-efficient and cost-effective new solutions. Researchers have already obtained promising results in many application areas of nanomedicine, which give very important assumptions for further work on the applicability and usefulness of nanotechnology in medicine. Pharmaceutical sector and market demand are growing, and nanomedicine may play a key role in contributing to economic growth, with its great medicinal impact.

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