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NANOTHERMIC SYSTEMS FOR DIAGNOSIS AND TREATMENT

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Abstract **–** Nanotechnology is the science of controlling materials at the atomic and molecular levels. With the use of nanomaterials for diagnostic and therapeutic purposes, the field of molecular nanotechnology has emerged, enabling nanoelectronic biosensors and individual medical applications. One of the most important areas in nanomedicine is drug targeting. In drug targeting, different targeted nanocarriers are used. The aim of drug targeting is the transport, absorption dispersion of the active substance to the selective site. Undesirable effects may occur if the dose rate falls below a sufficient amount or exceeds the toxic level. Today, drug carrier nanosystems are used, reducing the dose of active ingredient to eliminate these unexpected situations, prolonging dosing frequency, purify toxic effects, distributes the active ingredient to the desired area. These carriers are materials which that carry a variety of drugs or imaging agents.

In this study, drug targeting and drug delivery systems will be discussed. For transporting drugs to specific or difficult-to-reach sites in the body, nanocarriers are targeted, with various agents or differences in structure. Drug delivery systems are divided into various classes as micelles, dendrimers, liposomes, nanoparticles and carbon nanotubes. There is a need to use an effective and suitable carrier system for effective entry into the cell.
Keywords *– Nanotechnology, nanocarrier, drug targeting, the active ingredient*

I. INTRODUCTION

Nanotechnology is the examination, production or manipulation of materials at the nanometer level [1-3]. It is a field that can include multiple disciplines and multiple researches. Nanotechnology by the US patent Office 'It is the name of research, production and processing controlled by nano-sized structures, and is a set of systems integrated into larger structures.' is expressed as. NASA (National Aeronautics and Space Administration) is control and fabrication of nano-sized structures to create larger structures and the acquisition of new properties with these structures is called nanotechnology [4]. In addition to these definitions, the US National Nanotechnology Unit Advisor Dr. Mihail C. Roco described nanotechnology as the control and restructuring of matter at a nano scale level between 1 atom and 100 molecular diameters (1-100 nm). Nanometer scale is one billionth of meter according to International System of Units (SI) [1].

Nanotechnology has numerous applications in different fields. Can be used in health and biomedical fields, drug delivery and therapeutics [5]. With the acceleration of studies in the field of nanotechnology nanotechnological materials and their use; increased in the field of biomedical and medical. The ability to study and design the material in a nano-scale has brought along a number of innovative ideas in the medical field. Among these, drug targeting and controlled drug delivery systems are the most widely used and studied topics. Drug targeting systems; the systems that allow a specific active substance to be transported to the targeted tissue or organ with special structures. They also have the advantage that the therapeutic functions can be easily integrated into the carriers. Controlled release systems; systems that release drugs to the environment in the region where the drug is directed, in the long term and within the effective value range. Today, these studies are continuing intensively and these studies are important in terms of effective dose administration of drugs. Development of new drug delivery systems and methods will be able to solve multiple problems in medicine and biomedical field [3].

Nanotechnology, which is used in all fields of science, has a wide range of applications in medicine. For example, by means of nanobiosensors, diseases can be detected and imaging or by means of nanorobots, disease detection and drug targeting can be performed easily. Nanotechnology is a branch which has a wide usage area and it develops depending on the developments in biotechnology and biomedical fields. The main reason for its development is the fact that structures such as proteins and DNA, which carry biological information or have various functions, are in nano-scale. Diagnosis, treatment, prevention of diseases and traumatic injuries, protection of human health and development of applications,

molecular knowledge of the body, the use of molecular devices are included in the scope of nanomedicine [6-7].

DRUG CARRIER NANOSYSTEMS

There are frequent and repeated dosages in classical drug applications. It is important here that the amount of dose used to condense the active agent administered to the diseased area or to a specified cell, tissue or organ. Undesirable effects may occur when the dose rate falls below a sufficient amount or increases above the toxic level. Today, in order to eliminate these unexpected situations, drug carrier nanosystems are used which reduce the dose of active substance, extend the dosing interval, purify side and toxic effects, and deliver the active substance to the target area [8,9]. Thanks to the researches, small size, biodegradable and low toxicity systems have been developed which can easily circulate in the vein. Structures having these properties are now called nanocarriers.

Drug transport systems is divided into various classes micelles, dendrimers, liposomes, nanoparticles and carbon nanotubes. Nanoparticles can be of various shapes and sizes due to different methods and materials used in their production. They cause the nanoparticles to have different properties [11].

Micelles are macromolecular structures consisting of a spherical core and an outer shell. Amphiphilic, consists of a single polymer chain and these chains are called 'unimer'. Amphiphilic diblock (hydrophilic polymer-hydrophobic polymer) and triblock (hydrophilic polymer-hydrophobic polymer-hydrophilic polymer) co-polymers and graft polymers are used. In micelles composed of diblock polymers, the core is hydrophobic and the shell is hydrophilic. Hydrophilic, hydrophobic active substances can be loaded into the core [12-13]. Targeting can be achieved when ligands specifically designed to micelles are bound. They can protect the active substance from inactivation in biological environment. Within the diseased area, they can remain in the body for long enough to allow the active substance to be collected. The nanometer size of the micelles allows them to accumulate in areas with weak vascularization [8,14]. Although micelles are small in size, they have high drug loading capacity. Surface modification of micelles and remain in the circular system for a long time is a very important drug carrier systems [8,15].

Dendrimers are cellular macromolecules synthesized by center-to-surface growth of repeating monomers. Dendrimers consist of 3 parts. These are nuclei, branches and reactive functional groups. They are active macromolecular structures with high active substance loading capacities, easily synthesized, stable, functionalizable, controllable in size and active targeting. When the dendritic structures made with flexible bonds are examined, it is seen that the maximum density is displayed in the center and the density decreases towards the periphery. Dendrimer consisting of apolar nucleus and polar crust is called single molecule micelle. Dendrimers are composed of repetitive structures (monomers), such as polymers, but are synthesized by organic synthesis methods. Dendrimers are mostly used in targeting, drug delivery systems, and drug loading efficiency is high. Dendrimers are preferred in drug delivery system applications due to their co-surface groups, excellent encapsulation capability and highly controllable chemistry [3,16].

Liposomes, one of the colloidal delivery systems, are single or intertwined spherical vesicles with a diameter of about 0.02-3.5 micrometers. These materials are synthesized from non-toxic phospholipid and cholesterol structures. Liposomes are spontaneous spherical, closed colloidal, double-layer lipid layers. They are most commonly used for drug release and targeting in gene therapy. They are more likely to be used in gene therapy because; liposomes can easily pass through the cell wall due to their structure [3,11,17]. The first made liposomes were recognized and taken up by macrophages because they had unmodified phospholipid surfaces. This caused them to be cleared quickly from circulation. This feature inhibited the delivery of liposomal drugs to tumors. Nowadays, liposomal drugs that are being tried to be developed are capable of avoiding macrophage recognition. Surface modified liposomes generally have hydrophilic carbohydrates or polymers attached to the liposome surface. This surface modification solves the problem of rapid clearing of the circulation, giving liposomes a markedly increased half-life in the blood [11,18,19].

Solid lipid nanoparticles are lipid-based nanostructures. They consist of a matrix that is solid at body and room temperature. Developed as an alternative to liposome and polymeric nanoparticles. Solid lipid nanoparticles are nanocarrier systems that can transport gene and drug derivatives safely and effectively. Their dimensions range from 50-1000 nm. According to other carrier systems; There are many advantages easily participate in the structure of lipophilic and hydrophilic drugs, have improved physical stability, provide controlled drug and gene release, biocompatibility, site-specific drug activity, protect the encapsulated active substances from external influences and chemical degradation. Control and targeting of active substance release are the major advantages. It is used as an important nanocarrier because of these advantages [8,20].

Carbon nanotubes are cylindrical structures formed by the rolling of carbon layers. It is expressed as a tubular, well-arranged and flat carbon network. They are suitable for chemical modifications. Therefore, they are preferred as nanomaterials in many fields such as electronics, biosensor design, drug development and biomolecule carrier [8-21]. They are used to detect antigen by means of DNA and protein sensors and to increase antibody response. Carbon nanotubes have hollow tubular structures. It is chemically and mechanically stable and is not cytotoxic. The diameters of the nanotubes were 2-100 nm. and its dimensions are 5550 nm. Carbon nanotubes also have features such as large surface

areas, binding of desired functional groups to or into the surface of the nanotube and releasing directly to the target cell. All these properties lead to the efficient use of carbon nanotubes in drug delivery systems [8,22].

The successful results of nanotechnological applications and numerous studies of nanotechnology in this area have improved the drug delivery systems considerably and brought innovation to effective drug delivery procedures. Nanocarriers are being used in the diagnosis and treatment of many diseases. These studies, called nanomedicine, have led to the development of high precision, tissue-targeting nanoparticles that provide early detection. Nanoparticle structures have the opportunity to show biotactivity when robot and artificial intelligence technology is used in the tissue thanks to the application of desired surface modifications. This ensures that the nanoparticles are targeted not only to a specific region but to a particular vein or environment [8,10].

DRUG TARGETING

Drug targeting is two divided into passive and active targeting.

In passive targeting, it is ensured that particles are delivered to the targeted regions by means of passive factors or natural physiological processes. There are some important criteria in passive targeting. These are the surface properties of the nanoparticle, particle size, active substance loading capacity and active substance release. Drug release can be controlled depending on the size of the particles. When the small molecule drug molecules are close to the surface, the release is fast. In larger particles, the release is slow as the nucleus retains more drug molecules in their structure. They are coated with hydrophilic polymers to increase drug transport success. The release of the active substance from the nanospheres occurs by matrix diffusion or matrix erosion. Release is controlled by diffusion if nanoparticles are polymer coated [23].

Active targeting is the result of orientation of specific cells, tissues or organs and various modifications of the active substance structure. Active targeting is performed according to the characteristics of the target region. In the targeting of nanoparticles, chemical (pH, reactive oxygen species, proteases) and physical (heat, magnetic field, ultrasound) factors or strategies such as cell specific binding and targeting are utilized. Functionalization of particle surfaces in various ways; It provides active targeting ability, decreases the side effect by increasing the regional cytotoxic effect of drugs, multiple drug resistance is overcome. Factors affecting active targeting; ligand density, particle size and shape, surface and ligand charge. The specific targeting of chemical and physical quantities to cells takes place depending on the targeting of nanoparticles. Excessive concentration of ligands can have detrimental effects on cell binding. Due to the high curvature of spherical nanoparticles, problems may occur in ligand structures. The surface hydrophobicity of the nanoparticles affects the interaction with the cells. The minimum possible coating, circulation time and distribution in the diseased area are maximized. When targeting the surface receptors, the uptake of nanocarriers from the cell increases and the diseased cell is targeted and destroyed. Activation-dependent targeting by ligand-mediated targeting and stimulation (internal stimulation; pH-mediated targeting, enzyme-mediated targeting) occurs [8,24].

II. RESULTS

Nanocarrier systems are able to deliver less soluble active ingredients to the body due to their reduced side effects and modifiable properties. It has been found that nanotransmitters can be targeted by means of various effects, agents, or properties that can be altered in their structures for transporting drugs to specific or difficult sites in the body.

The nanocarrier systems may be targeted by external or internal stimulation by alterations in the region to be targeted in the body or by agents conjugated to the nanocarriers. Nanocarriers are actively targeted by passive or external magnetic methods, temperature, ultrasound or IR (infrared) laser by conjugating various agents to their structures by means of pH, temperature and enzymatic changes in the diseased areas. With surface modifications, drug delivery systems; Increased blood circulation stability, prolonged blood circulation stay, changing biodistribution profiles, gaining or increasing targeting abilities, sensitivity to stimuli such as pH or heat have been improved.

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