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ТИБИЁТДА ПЛАЗМОН НАНОЗАРРАЧАЛАРИНИНГ ҚЎЛЛАНИЛИШИ

ПРИМЕНЕНИЕ ПЛАЗМОННЫХ НАНОЧАСТИЦ В МЕДИЦИНЕ

APPLICATIONS OF PLASMONIC NANOPARTICLES IN MEDICINE

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Tayanch so‘zlar: nanozarralar, metall nanozarralar, optikmateriallar, kompozitmateriallar, shakllarva o‘lchamlar, nanoo‘tkazgichlar, dori, fulleren, uglerod nanotrubkalar, kvant nuqtalar, tashxis, DNK, nanorobotlar.

Ключевые слова: плазмонные наночастицы, металлические наночастицы, оптические материалы, композитные материалы, формы и размеры, нанопроволока, лекарство, фуллерен, углеродные нанотрубки, квантовые точки, диагностика, ДНК, нанороботы, наномедицина.

Key words: plasmonicnanoparticles, metallic nanoparticles, optical materials, composite materials, shapes and sizes, nanowires, drug, fulleren, carbon nanotubes, quantum dots, diagnostics, DNA, nanorobots, nanomedicine.

Аннотация

Nanozarralar – turli xil materiallardan hosil bo‘ladigan, har xil shakl va strukturadagi 1-100 nm atrofidagi o‘lchamga ega zarralardir. Nanozarralar deyarli har qanday materialdan, jumladan: yarim o‘tkazgichlar, metallar va hattoki organik tabiatli strukturalardan ham tuzilgan bo‘lishi mumkin. Tibbiyotda istalgan materialdan tuzilgan nanozarralardan foydalanishda ularning dizay-nidagi uchta komponentdan foydalaniladi: 1) dori mahsulotlarini saqlab turish va boshqarishda – yadrodan, 2) zarrachani dorini yo‘naltirish nazarda tutilmagan organlardan himoya qilishda – qo-biqdan, 3) dori yoki boshqa vositalarning tana bo‘ylab uzoq masofalarni bosib o‘tishida – sirtni qoplovchi qatlamdan. Quyida biz nanotibbiyotda qo‘llanishi mumkin bo‘lgan turli xil nanozarra-chalarga misollar keltirib o‘tamiz. Ushbu qisqacha sharh yaqinda e’lon qilingan Letfullin&George hammuallifligidagi kitobda asoslangan[1].

Аннотация

Наночастицы – частицы, отличающиеся разнообразием форм и структурв диапазоне размеров от 1 до 100 нм. Наночастицы могут быть изготовлены практи-чески из любого материала, включая полупроводники, металлы и даже органические структуры. Плазмонные наночастицы, используемые в медицине, имеют три основных компонента в дизайне: (1) ядро, которое заполняется лекарственнымпрепаратом; (2) оболочка, которая защищает частицу от взаимодействия с имунной системой пациента, (3) и поверхностное покрытие ввиде агента распознания или лекарства, обеспечивающее более долгоеобращениенаночастиц в теле. Ниже мы приводим несколько примеров плазмонных наночатиц разных типов, которые могут быть полезны для наномедицинских процедур. Этот краткий обзор основан на недавно опубликованной книге Letfullin&George [1].

Abstract

Nanoparticles are particles made of different materials and come in variety of shapes andstructures in a size range 1 – 100 nm. Nanoparticles can be made from almost any material, including semiconductors, metals, and even structures that are organic in nature.Through, various processing techniques, nanoparticles can be multi-layered, or even hollow, allowing for avariety of uses. Plasmonic nanoparticles used in medicine have three distinct components in their design: (1) the core which is used to hold the drug, (2) theshell which protects the particle from being rejected by the immune system of the body, (3) and a surface covering of atargeting agent or drug to allow longer circulation in the body. Below we provide a fewexamples of plasmonicnanoparticles of different types, which can be practical for nanomedical procedures.This short review is based on a book recently published by Letfullin&George [1].

Types of Nanoparticles Used in Medicine. Inorganic nanoparticles can be used to induce hyperthermia of cells [1,2]. The magnetic fields can be used to guide magnetic nanoparticles once injected into the body. A hyperthermia treatment is the placement of nanoparticles on tumor cells followed by an energizing of the particles via electromagnetic waves [3,4]. The nanoparticles effectively burn the tissue, and this can be used as either a method to kill tumor cells or as a means to increase the uptake of therapeutic drugs used in the treatment [5,6]. The examples of most commonly used inorganic particles are:metallic nanoparticles, nanowires, fullerenes, carbon nanotubes, silica shells, and quantum dots.

Metallic nanoparticles are mostly made of noble metals, like gold, silver and platinum, or metal oxides, like iron oxide, nickel oxide and cobalt oxide, and have a wide variety of applications in diagnostics and therapy [1].

Fullerene is the fourth allotrope of carbon, consisting of 60 carbon atoms forming a specific spherical shape, buckyball. Its unique properties, such as heat resistance and superconductivity, enable applications in high-temperature superconducting materials, high-power optical materials, high-performance catalyst, and high-strength composite materials [1].

Carbon nanotubes are arrangements of planar carbon lattices into cylinders of various chiralities, with sizes reaching several millimeters in length and only a few nanometers wide. In biology, the ability of nanotubes to get inside cell nuclei makes them invaluable in the diagnosis,imaging and treatment phases of cancer therapy. Carbon nanotube can be used to recognize target DNA sequences, as a drug delivery system, used in artificial heart valves, tooth roots,bones, blood vessels, artificial ligaments and tendons [1].

Silica-based nanoparticles(SiNPs) made of silicon dioxide have uniform morphology, adjustable pore volume, controllable diameter, modifiable surface potential, easy functionalization and synthesis [1].

Quantum dots are another example of inorganic nanoparticles that can be used for the purpose of increased imaging ability. The dots are small semiconductor crystals that can be fine-tuned to have very specific spectral bands, allowing differentiation between the location of the quantum dot(on the tumor cell) and the healthy tissue beside it, with a level of precision notpossible before. The labeling of multiple disease markers with quantum dot-based barcodes could pave the way towards more sensitive and accurate disease detection systems. Quantum dot-based probes may be used to study the heterogeneity of disease markers and link them to prognosis for improved diagnostic strategies [1].

Organic particles are used primarily for drug delivery or as a coating on inorganic particles to assure they are not rejected by the body's immune system [1]. The debate between using organic or inorganic particles isn't simply a matter of what works best, but also a matter of what hurts less – the toxicity level of nanoparticles vary widely and must be taken into consideration when determining what treatment diagnosis route to take. Examples of organic particles include *polymer-based nanostructures, dendritic nanoparticles, liposome nanoparticles, polymersome nanoparticles, lipid formulations, micelle nanoparticles, nanoemulsions, alginates, biological nanoparticles,* etc.

Polymer-based nanostructures are created from conjugating several functional units and soluble macromolecules or by co-polymer self-assembly. Many of these structures are loaded with therapeutic or imaging agents, which through diffusion or stimulation of local environment control the release [1]. Polymeric nanoparticles are a class of nanocarriers established for numerousdrug delivery applications. Polymeric cores are shielded by materials, such as polyethylene glycol(PEG), to guarantee the structure's stability. Targeting molecules can easily be added to the surface of polymer-based nanoparticles.

Dendrimer nanoparticles are a type of polymeric nanostructure. They can be synthesized as well-defined spherical structures over 1-10 nm in diameter. Multiple types of these can be created based on the core structure from the polymerization process. A single dendrimer is able to sense, image and perform therapeutic functions [1]. To achieve this, multiple function groups have to be coupled to the surface of a dendritic polymer.

Polymersome nanoparticles are drug delivery carries having structural similarity to liposomes and made of synthetic polymer amphiphiles. When hydrated and extruded, they form polymer shell vesicles of about 100nm by self-assembly. The ratio of hydrophilicity/hydrophobicity can be used to regulate the morphology of the nanoparticle. These drug delivery systems have higher stability and higher fluidity on the sides/surface than liposomes [1].

Micelle nanoparticles are drug delivery carriers made up lipids. They are self-assembled into small nanoparticles having a hydrophobiccore(drug) within size range of 10 – 200nm [1].

Biological nanoparticles are unicellular microorganisms with different shapes and sizes. For example, a biological nanoparticle called "nanocell" consists of globular bacteria having no nucleus, which is impeccable, as it wouldn't lead to mutations. A nanocell can be filled by drugs and used as a drug delivery system [1].

Hybrid nanoparticles are nanocarries made up of the metallic and polymeric materials for the central core, which is coated with single or multiple layers of lipid to create a protective (surrounding) membrane. The hybrid nanoparticles are used as delivery systems with considerable high drug-carrying capacity, and the lipid layer on the surface of a nanoparticle is able to direct drug-releasing kinetics [1]. They are also able to serve as imaging agents.

Applications of Nanoparticles in Medicine. The application of nanotechnology to medicine promises to bring both incremental and breakthrough improvements [1-6]. Most incremental improvements are the result of miniaturizing current processes which nonetheless can have a huge impact. Lab-ona-chip technology, which has grown dramatically in the last two decades, now allows researchers to miniaturize multiple assays into a single small package. A single drop of blood can now be used to run multiple tests without the need for a fully stocked analytical laboratory, making the screening and diagnosis of diseases cheaper and easier, thus allowing doctors to make better decisions for the care of their patients. Breakthrough improvements create new avenues for prevention, diagnosis or treatment by capitalizing on properties or mechanisms unique to the nanoscale.

Nanomedicine is capable of treating any sites and organs of human body at the molecular level against (eventually) all diseases. Let us here briefly discuss a few current and potential applications of the nanoparticles in nanomedicine. Some of them are still in the research-and-development stage. This short review is based on a book recently published by Letfullin & George [1].

Drug Delivery. Nanoparticles (nanoshells, nanotubes) can delivery very strong drugs directly to a tumor site without causing any side effects to the body. Using the nanoparticles as drug delivery systems decreases the toxicity and side effects of chemotherapy, since drug dosage is limited. The drugs used in chemotherapy, or other cancer-killing drugs, are dissolved and either put into capsules, entrapped or attached to a matrix of nanoparticles.

Nanoparticle drug delivery systems come in many shapes and sizes. For example, researchers have found that mesoporous silica nanoparticles are very effective for controlled drug delivery. The nanopore openings of these nanoparticles can be easily controlled.

Three-dimensional DNA crystals can be used as molecular containers to build biochips, nanorobots, biosensors or drug delivery systems.

Polymersome nanoparticles are drug delivery carriers having structural similarity to liposomes and made of synthetic polymer amphiphiles. These drug delivery systems have higher stability and higher fluidity on the sides/surface than liposomes.

Lipid-based drug delivery systems include many different types. Such vehicles typically comprise a digestible lipid with (in the case of more complex self-emulsifying formulations) a blend of surfactants, co-surfactants and potentially co-solvents. The ability of a self-emulsifying drug delivery systems to be diluted is essential for its use as a drug delivery vehicle since, after administration, it will be diluted by intestinal media.

Micelle nanoparticles are drug delivery carriers made up of lipids. They are self-assembled into small nanoparticles having a hydrophobic core (drug) within the size range 10–200 nm.

Nanoparticles (especially gold nanospheres and gold nanorods) could be used themselves as drugs. They can be delivered to the tumor, selectively attach to the cancer cells, and then heated by radiation to cause ablation of cancer cells. This technology is called selective nanophotothermolysis of cancer cells, which we will discuss in more detail later.

The advantages of nanoparticles, as such, is that they “can improve the stability of drugs and control their targeted delivery, allowing for a constant and uniform concentration at the site of a tumor and facilitating drug extravasation into the tumor system, thus reducing side effects”.

Metallic nanoparticles have a wide variety of applications in diagnostics and therapy. They are used as contrast agents for imaging modalities like MRI, CT, PET and optical imaging. They are also used in the therapy of cancer. Two therapies, nanophotothermolysis and nanophotohyperthermia, both utilize molecular-targeting to deliver nanoparticles to the localized area, and then use the unique light-absorption properties of the metallic nanoparticles to generate heat in the targeted region to ablate the tumor.

Silica-based nanoparticles have been successfully used for drug delivery because of unique mesopores and nanochannels which allow for a high payload of the drug and easy stimulated release. The silica-coated gold nanoparticles are ideal for imaging.

Carbon nanotubes have the ability to penetrate inside cell nuclei, making them invaluable in the diagnosis, imaging and treatment phases of cancer therapy. These nanotubes can be used to recognize target DNA sequences, as a drug delivery system, in artificial heart valves, tooth roots, bones, blood vessels, artificial ligaments, tendons, and so on.

Organic particles are used primarily for drug delivery or as a coating on inorganic particles to assure they are not rejected by the body’s immune system. Examples of organic particles include polymerbased nanostructures, dendritic nanoparticles, liposome nanoparticles, polymersome nanoparticles, lipid formulations, micelle nanoparticles, nanoemulsions, alginates, and biological nanoparticles.

Polymer-based nanostructures are a class of nanocarriers established for numerous drug delivery applications. Polymeric cores are shielded by materials such as polyethylene glycol to guarantee the structure’s stability. Targeting molecules can easily be added to the surfaces of polymer-based nanoparticles.

Nanovalves can open and close to release and trap drugs in response to pH factor changes. Thus, by plugging the pores of the mesoporous silica nanoparticles filled with a strong drug by nanovalves, a drug can then be released by changing the pH level. Researchers have found that a pH factor of normal cells differs from tumor cells. This can be used for selective delivery of drugs to abnormal cells only.

Improved imaging. The metal nanoparticles have the property of plasmon-resonance scattering at the visible and near-IR spectra of radiation, which we will study later in this book. By attaching these particles to the cancer cells or DNA, they become visible, providing much earlier diagnostics at the single cellular and molecular levels. The metallic

nanoparticles (gold nanoshels, nanospheres and nanorods; iron, cobalt and nickel oxides) are used as the contrast agents in CT and MRI scans and optical imaging techniques.

Hybrid nanoparticles are made up of metallic and polymeric materials for the central core, which is coated with single or multiple layers of lipid to create a protective (surrounding) membrane. These nanoparticles are able to serve as imaging agents.

Quantum dots are small semiconductor crystals that can be fine-tuned to have very specific spectral bands. The labeling of multiple disease markers with quantum dot-based barcodes could pave the way towards more sensitive and accurate disease detection systems. Quantum dot-based probes may be used to study the heterogeneity of disease markers and link them to prognosis for improved diagnostic strategies.

Gene therapy.Nanorobots can be used to repair different mutations of DNA. Delicate surgeries. A major application of nanomedicine would be in surgery. Cell repair machines can be used to perform genetic surgery.

Aging. The aging process involving cell damage could be repaired by nanorobots from the inside out.

Diagnosis and treatment of diabetes.Nanomachines are capable of controlling and monitoring glucose levels in diabetic patients.

Treatment of kidneys. Medical nanomachines could be designed for destroying kidney stones.

Cleaning nanorobots. Artery-cleaning nanorobots could remove extra fat and bad proteins from the walls of blood vessels and arteries. The size of these nanomachines is very small. They can easily swim in blood vessels and penetrate into any organs, and even be placed inside the cells through the porous membrane. Artery-cleaning nanorobots can be used for prevention of a heart attack and can be applied in the treatment of atherosclerotic plaques. Medical nanomachines can help find atherosclerotic lesions in blood vessels and help in their removal.

Lung-cleaning nanorobots are inhaled, where nanorobots can collect foreign particles like fibers of asbestos and toxic particles from the lungs.

Teeth cleaning nanorobots may collect harmful bacteria in the mouth and can help to detect different oral diseases.

Improving brain capability. A nanostructured data storage system may store a nanocomputer and an amount of information equivalent to an entire library Thesenanochips/nanomemory then can be attached to brain cells to create an extra network of memory in the brain. Thus, in the future we may be able to browse our brain in searching information instead of browsing the Internet.

Superior implant materials. Creating new allows and discovering new nanomaterials can provide much stronger and lighter implant materials for dentistry and artificial body parts.

Artificial tissues and organs. Researchers hope to regenerate skin, bone and more sophisticated organs by means of nanotubes and nanomaterials. Nanorobots can be used as support devices for regeneration of skin, bone and injured organs.

Body surveillance.Nanorobots can be used to continuously monitoring vitals inside the human body. This can be an effective tool for cancer prevention. If any bacteria or cancer cells invade the body, they will be destroyed by the nanorobots patrolling the body, since the bacteria or mutated DNA do not match the blueprint recorded in the nanomachine.

Conclusions. In conclusion, nanomedicine is revolutionizing the way we treat the patients. We have discussed here only a few current and potential applications of nanomedicine recently published in the book by Letfullin & George [1]. Rapid detection and treatment at the cellular level are very important to many life threatening diseases. For cancer, early detection would cure the cancer and save lives instead of just extending the patient's life. As seen in this paper, nanodevices/nanoparticles will play a very large role in the future of medicine, taking part in many new advances in the fields of diagnostics and treatment of diseases.

Nanoparticles can provide very good solutions for some medical problems we face and improve currently used methods. Nanorobots and nanomachines as discussed here are the

new molecular technologies that have gradually developed over the years, creating robots or machines made up of parts that are at or close to the scale of nanometers.

These new technology fields have evolved through several developmental stages and are still under research and development. These small devices have opened a new world of discoveries and feasibilities in nanomedicine.

REFERENCES

1. Letfullin R.R., T.F. George. "Computational Nanomedicine and Nanotechnology: Lectures with Computer Practicums".– Switzerland: Springer, 2016.– 700 p.

2. Letfullin R.R., George T.F. "PlasmonicNanomaterials in Nanomedicine," in Springer Handbook of Nanomaterials, edited by R. Vajtai (Springer, 2013).– P. 1063-1097.

3. Letfullin R.R., George T.F. "New Dynamic Modes for Selective Laser Cancer Nanotherapy," in Computational Studies of New Materials II: From Ultrafast Processes and Nanostructures to Optoelectronics, Energy Storage and Nanomedicine, edited by T. F. George, D. Jelski, R. R. Letfullin and G. P. Zhang (World Scientific, Singapore, 2011).– P. 131-172.

4. Letfullin R.R., C.E. W. Rice*, George T.F., Murzagulova K. "Nanoparticle-Enhanced X-Ray Therapy of Cancer," International Journal of Theoretical Physics, Group Theory and Nonlinear Optics 17, 133-145 (2014).

5. Letfullin R.R., C.E.W. Rice*, George T. "Bone Cancer Therapy by Plasmonic Nanoparticles". Therapeutic Delivery 2, 1259-1273 (2011).

6. Letfullin R.R., Iversen C.B.* and George T.F. "Modeling nanophotothermal therapy: kinetics of thermal ablation of healthy and cancerous cell organelles and gold nanoparticles," Nanomedicine: Nanotechnology, Biology and Medicine 7, 137-145 (2011).