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NANOTECHNOLOGY IN CANCER TREATMENT

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Abstract: **Nanotechnology is rapidly developing subdivision of technology that affects on many fields. Medicine is also affected from nanotechnology; since, in cancer treatment nanotechnologically modified methods can be used. One of the developing usage fields of nanotechnology is cancer treatment. Nanotechnology can assist to have better diagnosis with less harmful substances as optical nanoparticles and ICG molecules, to provide efficient drug delivery to tumor cells with liposomes and functionalized micelles. Nanotechnology can be also used in molecular imaging with tomography and photoacoustic imaging of tumors and therapy of cancer as photothermal and radiotherapy. Finally, nanotechnology is still developing science can be defined as next generation techniques for cancer disease; at the same time it comes with many advantages to treat cancer patients.**

Keywords: **Nanotechnology; Cancer treatment; Imaging.**

1. INTRODUCTION

Technology is one of key words of in people's lives. In the near future, a subdivision of technology which is nanotechnology will have an important role. Bio-products, tools, devices, materials are influenced from consequences of research and developments on nanotechnology. With nanotechnology; more useful devices, better drugs for diseases, more appropriate materials for construction will be developed. Nanotechnology will also affect medicine and other life sciences. The numbers of research in cancer treatment with nanotechnologically modified drugs are increasing day to day and have had some good results on this issue. Nanotechnological improvements can be used for cancer patients; because nanotechnology can be used for better cancer diagnosis, more efficient drug delivery to tumor cells, and molecular targeted cancer therapy. First of all, nanotechnology can be used for better cancer diagnosis. One of the main usage fields of optical nanoparticles is to allow better cancer detection. To start with, classical methods that are used in diagnosis have limitations. Classified methods such as X-rays, tomography or mammography require using mutagenic agents on cells that cause cancer, too. Sadoqi et al. [1] express that using harmful substances and X-rays in cancer diagnosis are also related to the causes of cancer. To eliminate these concerns, optical nanoparticles in diagnosis is possible technique that can be used. This technique works with special dyes to interact with tumor cells and optical nanoparticles can be detected. According to Sadoqi et al. [1], preparing a nanoparticulate drug system which has to ability to be photo excited to produce singlet oxygen for detection and therapy is better than classical systems. Such interaction shows that, the detection of cancer with optical nanoparticles is new and developing subject, but it has considerable benefits for diagnosis. In addition to optical nanoparticles, ICG (Indocyonine Green) can also be used in cancer diagnosis. The binding properties of ICG make possible technique in tumor detection. ICG molecules can interact with plasma proteins such as albumin, lipoproteins and globulins; since this allows ICG to have around the bloodstream. Sadoqi et al. [1] state that because of amphiphilic property of ICG molecules give ability to interact with lipophilic and hydrophilic molecules. ICG molecules are also fluorescent molecules that with these characteristics of ICG are used for detection of tumors. From these properties, tumors and tumor-free areas can be detected in cancer diagnosis. It is a convenient way in diagnosis; thus very small tumors can be seen with fluorescence signals. Sadoqi et al. [1], also indicate that the ICG dose of 400 µg kg-1 body weight was used to conduct in preliminary investigations into human breast tumors. To have better detection of tumor

cells, the sensitivity of diagnosis techniques must be considered, and nanoscale solutions in diagnosis are very sensitive and have shown to be less harmful to patients. Secondly, nanotechnology can be used for more efficient drug delivery system to tumors. One of the significant missions of passive liposomal drug delivery is to cancer cells. Liposome molecules are easily diffused into the cells; since their structures and cell membrane structure can interact very well while drug uptake process. The EPR (Enhanced Permeation and Retention) effect is the concept that liposomes remain the bloodstream for a long time and are collected passively from tumor cells. Via the EPR effect, concomitant in toxicity problems of therapy are relatively solved as lower and repeated dose of liposomal drugs. Sengupta and Sasisekhanan [2] state that using EPR effect allows up to 10 times the amount of drug to be delivered to the tumor than the free drug method. Passive liposomal drug delivery is also observed in Reticular Endothelial System (RES) uptake. In this method PEG (Polyethylene Glycol) coated liposomes that enable the drug system to interact with hydrophilic molecules in cell membrane with high affinity. Moreover, these liposomal drugs with RES relatively break away immune recognition; so drugs are able to remain in bloodstream. Devalapally et al. [3] maintain that liposomes which altered with PEG are examined more systemic half life that is significant reduction in nonspecific HES uptake. Consequently, the benefit of passive liposomal drug delivery systems have more half life than free systems in circulation and deliver more amounts of drug to tumor cells. Besides passive liposomal drug delivery, targeting ligand to treat

cancer with modified liposome method is being developed. One of the concepts in targeted drug delivery is covalent binding of ligands. This approach depends on using thioether bonds to couple ligands onto the surface of liposomes. The thioesther bonds are established with reaction between thiol functions and maleimide groups, those thioesther bonds which are also combined with crosslinking agents make covalently bound ligand system. To develop effective antitumor agent and less toxic drug systems is possible to couple monoclonal antibodies and liposomes. Nobs et al. [4] state that sterically stabilized liposomes can be modified with immunoliposome technology to deliver compounds in vesicles which provide staying longer in bloodstream and efficiently find targets. The other concept in targeted drug delivery is noncovalent binding of ligands. To prepare these drug systems, ligands are mixed with phospholipids. The main advantage of the noncovalent binding of ligand is this method does not require strong reagents. However, there are some noticeable concerns observed in this method. One of the problems is antibody orientation and attachments of liposome surface. The liposomal ligand and carrier interaction is relatively lower and difficult to control. According to Nobs et al. [4], the rate of ligand to carrier attachments is weaker which around 40% is and liposomes are usually observed in aggregate form. The targeted liposomal drug delivery is a convenient way to deliver drugs with antibody – liposome carrier systems to tumor cells. Aside from liposomal drug delivery systems, micelles drug delivery to cancer cells with nanotechnology is being developed. Micelle is described as aggregate form of molecules that generates colloidal shape. The functionalized micelles systems can be used for targeted drug delivery to cancer cells. One of the methods in micelles systems is micelles with small organic molecules as targeting ligands. Micelles are functionalized with glycosyl-phosphatidylinositol that binds folic acid in high levels to inhibit cell proliferation activity. Folic acid acts as a carcinogenic agent that affects on breast, lung and ovarian cells. Sutton et al. [5] prove that tumors permit up to 300 times higher level of expression of folic acid receptor systems than normal tissue. Due to this property, micelles system can be used for targeted drug delivery. Another method for targeted drug systems is micelles functionalized with peptide ligands. The polypeptide property of ligands helps developing cancer-targeted drug system, as cRGD (cyclic arginine, glycine, aspartic acid) amino acids take part in integrin structure. Integrin proteins with cRGD ligands and copolymer micelles are conjugated to form drug systems. Sutton et al. [5] point out that the 5% rate of cRGD on surface results more cell uptake; since cRGD attachments reach a level of 76% as measured by flow cytometry. Micelles are also functionalized with carbohydrate ligands to deliver drug systems. ASGPR (Asialoglycoprotein Receptor) is a kind of lectin receptors onto surface of liver cells. Functionalized lectin ligands interact with carbohydrate molecules from mannose and galactose monosaccharides as targets. Micelles modified ASGPR are observed more cell uptake and tumor cytotoxicity than free ASGPR ligand systems. Sutton et al. [5] also indicate that modified ASGPR methods have ability to affect efficiently on liver cells; hence it is proper way to treat liver diseases with targeted micelles drugs. The last commonly developing method is micelles functionalized with monoclonal antibodies as targeting ligands. Tumor targeting ligands are combined with pluronic micelles and monoclonal antibodies. Monoclonal antibodies are specific to only one type of antigens in these methods, cancer cell receptors are recognized from anti-cancer monoclonal antibodies. Sutton et al. [5] declare that the binding affinity of ligands is quite specific as Kd ~ 0,1nM; therefore, this method is observed a good binding range to antigens of cancer cells. From all these conditions, it can be considered that micelles drug systems are highly specific drug delivery methods that can be used in tumors via targeted ligand recognition. Thirdly, nanotechnology can be used for

better cancer imaging. One of the main usages of cancer imaging is tomography with contrast agents. Contrast agents have been known to do better diagnosis and imaging. Computer Tomography (CT) is a widespread diagnostic imaging method which measures, in its imaging process, the radio density of matter. Therefore CT has important effect on health. As it is explained by Nature Publishing Group, nanoparticle application for X-Ray CT imaging positron emission imaging probes combine both in a clinical setting and development of micro-CT and CT increased use of hybrid systems everywhere can have a significant impact on the environment due to health reasons and X-Ray tomography, single photon emission CT. Nonioinizing method that uses differential scattering and absorption of light waves for different tissue types is called Optical Coherence Tomography (OCT). Gold nanoparticles have important role for OCT method. Gold nanoparticles also can be used different sizes and shapes. Kannan and Katti [6] state that Younan Xia, Xingde Li and their job friends last OCT as a contrast agent using size 40 nm gol nanocages have reported the first results. As a result, tomography with contrast agents is useful than traditional methods. Not only tomography with contras agent but also Photoacoustic Tomography (PAT) can be used for better cancer imaging. Photoacoustic tomography is also called Optoacoustic Tomography (OAT). This method is based on the inherent light absorption contrast characteristics of biological tissues. Chamberlend et al. [7] indicate that the other names of photoacoustic tomography, optoacoustic tomography and thermoacoustic tomography, has high sensitivity, satisfactory imaging depth and good temporal and spatial result with noinvasive, nonionizing imaging modality in developing a hybrid. Using PAT without nanocages is not a good way because the photoacoustic signals are considerably lower when used blood only. On the other hand, nanocages are the key of photoacoustic tomography. With nanocages, studies are more open to solve. Yang et al. [8] stated that the blood was assimilated easily and the contrast between the vessels and brain tissues' background was improved. The improved contrast could allow more detailed vascular structures to be imaged at more depths. Finally, nanotechnology also can be used for better therapy. For example, Photothermal Therapy (PTT) is one of them. Photothermal therapy is using heat to control specific tumor. Tradition PTT uses radiation, along with dyes capable of absorbing radiation at the site of the tumor. Kannan and Katti [6] indicate that the temperature is increased to nearly 40°C by using hyperthermia in the chosen tumor to stimulate lipid transitions and also to cause mutation of RNA and DNA. Therefore tradition PTT used past time. Now photodynamic therapy is using more. Photodynamic Therapy (PDT) is a different method that uses a photosensitizer and a particular type of a light. A specific wavelength of light effect on a photosensitizer and it produce a form of oxygen which kills nearby cells. Huang et al. [9] indicate that alternative method of tumor therapy is in single kind of toxic oxygen and/or photochemical and photobiological processes, to form a series of cell destruction produced from other free-radical means: photodynamic therapy and photochemotherapy. PTT and PDT treatments have succeeded a lot of things but such methods are limited by photobleaching effects. Hence Plasmonic Photothermal Therapy (PPTT) is using most. Plasmonic photothermal therapy is a treatment which uses photon energy. Dickerson et al. [10] state that a spherical nanoparticle of various materials and show surface plasmon resonance in the viewable area, during the chance for therapy in vivo plasmonic photothermal visible wavelengths is limited by a high degree of absorption by the tissues. By using surface plasmon resonant absorption spectroscopy and light scattering imaging, cells are easily distinguished. In addition photothermal therapy, radiotherapy can be used for better therapy. Radiotherpy is another attractive approach to nanotechnology in nanomedicine. Gold has higher absorption than other using molecules and that doing important it for the radiotherapy. As mentioned by Kannan and Katti [6], for these tumor cells, cancer radioactivity with a higher concentration of the gold nanoparticles can be obtained directly from cells and cell fragments are of the interest for the treatment of diseases. Even lower concentration of gold nanoparticles is clear the blood faster than iodine. Therefore, gold nanoparticles have being used easily. Shang and Yang [11] state that 0.00 ml/g of +1.9mm or -1.9 mm nanoparticles are injected into the mice's tail vein, in the xenograft tumor, the gold nanoparticles can be observed in a short time. Hence gold nanoparticles can be used radiotherapy. Another important therapy is X-Ray therapy. X-Ray therapy use high-energy radiation to kill cancer cells and shrink tumors. Levy [12] explained that the nanoparticle used in NanoXray technology is an unreactive and unmoving matter which is measured at 50 nanometers in diameter (less than 1000 times than the diameter of a human hair). Therefore the gold nanoparticles can be used as X-Ray contrast agents with properties that overcome some significant limitations of iodine-based agents. In conclusion, nanotechnology prefers us to better medicine opportunities. It can be used better diagnosis, efficient drug delivery, better imaging and therapy of cancer. Classical methods are not enough to cure all of diseases, especially cancer treatment issue. With nanotechnology, it will possible to cure all diseases maybe it will cure in the beginning because of nanotechnology. As understanding of the importance of the nanotechnology, condition of life will be greater. Thus, nanotechnology has to be improved for the next generation.

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