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CANCER DIAGNOSTICS, IMAGING AND TREATMENT BY NANOSCALE STRUCTURES TARGETING

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Recent research focused on finding new strategies in cancer therapy that did not have significant side effects and was more effective than traditional modules including the surgical intervention, radiation and chemotherapeutics. In this regard the nanoscale structures provide useful approaches for cancer treatment. So, the nanoparticle systems improve the efficiency of therapeutic drugs reducing their side effects. Although many studies reported the development of novel cancer cell therapies for future, the clinical success is lacking understand the effects of nanoparticle type, size and dose with their usage areas. Thus, this review was aimed to illustrate the usage of nanoparticles in cancer diagnostic, imaging and treatment.

Key words: cancer diagnostic, imaging and treatment, nanoparticles.

Cancer continues to be one of the world's most devastating diseases with more than 10 million new cases each year [1]. The number of people diagnosed with malignancy is expected to rise to 22 million annually in the next 2 decades.

The information about various types of nanoparticles (NPs) used in cancer treatment, diagnosis and imaging was given under the title of various types of NPs used in the field of cancer treatment. After that, this review was focused on the active and passive targeting importance for the cancer apoptosis. In addition, the impact of Contemporary Advancements in active targeting nanoformulations were explained. In the last part, development and importance of different types of NPs in cancer diagnosis and imaging was discussed. Significance of this review is presentation in the field of cancer to date nanoparticles; a review with a holistic approach to their use in vaccines, drugs, diagnosis and imaging will be of great importance. Nanoparticles are very diverse and their efficacy and advantages vary according to the fields of medicine, vaccine and imaging. Which type of nanoparticles that we are going to choose for our future studies could be seen in the reviews of our previous studies. Therefore, we aimed to present a work that we think it can be as useful as possible from the active, passive targeting of cancer to the varieties used in medicine and vaccines.

There is lack of understanding concerning the effects of the nanoparticle types, working in the future without confirming its reported function. This review will be useful for better comprehension of molecular basis of nanoparticles and the advent of new diagnostic technologies can help to improve the treatment of various cancers.

Various types of nanoparticles used in the field of cancer treatment

Treatment modalities, including immunotherapy, photo thermal, photodynamic, gene and hormone therapy display promising cancer eradicating potential in preclinical studies. However, surgery, radiation and chemotherapy continue to be the first treatment option for cancers and the next major strategy for cancer treatment is highly non-specific in targeting the drugs to the cancer cells causing undesirable side-effects to the healthy tissues

[2–4]. Unfortunately, there are no alternative for cancer treatments other than surgical removal of the cancer site, radiotherapy and chemotherapy. In addition, chemotherapy and radiotherapy have thousands of side effects that kill both cancer cells and healthy cells. Therefore, we see that cellular therapies, which we believe will be more effective for cancer treatment, have started to be developed. In developing cellular therapies, nanocarriers that can be produced up to cellular dimensions have been of great importance. There are possible risks in these systems. For instance, NPs can be phagocytosed as an enemy in the body by being exposed to attacks of immune cells and may cause failure of such cancer treatment intervention. In addition, NPs can produce molecular responses such as deleterious, allergic and toxic effects in cancer cells, thereby causing greater sensitivity to cancer progression [5]. For this reason, choosing the most accurate NPs for the cancer disease will prevent patients from complications and can provide more effective therapy. During the last decades, an abundance of NPs have been developed and a real hype has been created around their potential application as diagnostic and therapeutic agents. For example, although iron oxide NPs have been suggested as potential diagnostic agents, they have not been fully preferred for clinical purposes. Therefore, pre-clinical studies on many experimental animals are ongoing [6]. This is primarily due to the ability of NPs to be biologically suitable for the body. There are some problems related to biological degradation of NPs, expulsion from the body and the possibility of toxic effects. Further studies are needed to eliminate these drawbacks of Iron oxide NPs.

Molecular imaging, when used in conjunction with said nanosystems, may make cancer diagnosis and treatment more effective. Multidisciplinary studies can be combined to provide more effective diagnosis and treatment, and these disciplines can often be made possible by collaborating with researchers in different fields such as cell biology, biochemistry, engineering, health and medicine. Recent advances in NPs technology have enabled the fabrication of NPs classes with unique sizes, shapes and materials, which in turn has facilitated major advancements in the field of nanomedicine. The promising proposition of multifunctional NPs for cancer diagnostics and therapeutics has inspired the development of the approach for improved cancer therapy. The nature of NPs is closely related with the various materials that used for their synthesis, such as metals (gold and silver), ceramics (hydroxyapatite), lipids (cholesterol and non-toxic phospholipids) and polymers [alginate, chitosan, poly(ethylene glycol (PEG)] [7].

The combination of anti-cancer drugs and different types of agents with NPs in the treatment of cancer has many advantages:

1. Enhancing the stability of hydrophobic drugs, making them suitable for application. In other words, it increases the water solubility of drugs. Especially in imaging and drug therapies developed with these nanoscales, only cancer cells can be targeted and adverse effects such as systemic chemotherapy, hair loss, immunosuppression, muscle weakness, etc. can be completely eliminated.

2. Reducing toxicity by using biocompatible nanomaterials. In both conditions it results in a therapeutic index increase, the limit between doses causing therapeutic efficacy (e.g. cancer cell apoptosis) exhibits high differential uptake efficiency in the target cells over normal cells.

3. Developing pharmacokinetics and bio distribution which increase drug efficiency on the tumor and enhance absorption of the drugs into a selected tissue (for example, solid tumor) [8].

4. One of the most important advantages of the NPs is the fact that they are able to treat cancer which is caused by cell organelle disorder. For example, effective targeting of mitochondria and nucleus has emerged as an alternative strategy in cancer chemotherapy agent which is Dual drug conjugated NP [9].

Nevertheless, before the plethora of nanodevices currently under investigation become proper for clinical usage, they have to pass the rigorous tests set forth by regulatory agencies such as Food and Drug Administration (FDA) and European Medicines Agency (EMEA) [10–12]. To date, at least 12 polymer–drug conjugates have entered Phase I and II clinical trials and we need to find more treatment model for cancer cell targeted therapy. Various biocompatible (NPs)-based drug-delivery systems such as liposomes, dendrimers, micelles, silica, quantum dots, and magnetic, gold, and carbon nanotubes have already been reported for targeted cancer treatment.

Silver Nanoparticles (AgNPs)

Therapeutic applications of silver nanoparticles (AgNPs) agents in the diagnosis and probing of many cancer diseases are noteworthy [13]. AgNPs cause apoptosis in

cancer cells as they produce reactive oxygen species (ROS) that cause oxidative stress and DNA damage that cause mitochondrial damage within the cell. Cellular penetration of AgNPs usually occurs through endocytosis [14]. In another study, it was found that AgNPs for cell morphology may affect the function of other factors. These effects include the ability to adsorb cytosolic proteins and regulate gene expression and proinflammatory cytokines, for example, microarray analysis showed that human lung epithelial cell line A549 affects cellular transcriptome analysis upon exposure to AGNPs. According to the results of the microarray study, it was found that AgNPs affect the regulation of more than 1000 genes [15]. AgNPs can induce autophagy by allowing the accumulation of autophagolysis in human ovarian cancer cells and autophagy can have a dual cell bodies. The use of autophagy inhibitors or autophagy protein 5 (ATG5) with small-mix RNAs (siRNA) in combination with AgNPs causes the death of cells in cancer cells [16]. As a result, AgNPs can induce cell death including ROS generation, leakage of lactate dehydrogenase, increasing of apoptosis and autophagy genes, cause endoplasmic reticulum stress and mitochondrial damage, activation of caspases pathways and DNA damage so that AgNPs can be used as nanoparticle that is significant to deliver drugs for cancer treatment. In addition, AgNPs has significant importance to modulate ABC transporter activity for chemotherapy in multidrug resistant cancer [17].

Gold nanoparticles

Gold nanoparticles (AuNPs) are ideal for drug targeting and also for imaging-based detection of cancer diseases at an early stage. AuNPs were first produced in 1857 by Faraday and exhibit favorable physical properties and tailored surface functionalization, providing a potential for developing cancer theranostics and they are solid balls of gold and are made by the reduction of chloroauric acid, and their diameter varies from 5 to 100 nm. They are biocompatible and less toxicity and display the relatively low rate of clearance from circulation. AuNPs was demonstrated [18] where AuNPs were conjugated with an antibody against the epidermal growth factor receptor (EGFR, it is known to overexpress on many cancers). PEGylation of AuNPs effectively downregulate this uptake by macrophages and monocytes [19]. AuNPs conjugated with carbohydrates and proteins have been utilized in novel approaches toward the development of vaccines such as Glyco-conjugated AuNPs (1–5 nm) capped with carbohydrate-based antigens that are present in cancer cells [20, 21]. Targeting mitochondria with conjugated Au- cationic NPs maltotriose-modified poly(propylene imine) (PPI) dendrimers effects on apoptosis induction in the human breast cancer cell line [22]. Doxorubicin (DOX) loaded oligonucleotides attached to (AuNPs) as a drug delivery system is useful for cancer chemotherapy [23]. Micro RNA (miR)-375 loaded AuNP exhibits high cellular uptake and preserves miR-375's activities to suppress cellular proliferation, migration/invasion, and colony formation, and to induce apoptosis in hepatocellular carcinoma cells [24].

Polymeric particles

Synthetic polymers are polylactic acid (PLA), poly(lactic-co-glycolic acid (PLGA), polycaprolactone (PCL), PEG, and poly(vinyl alcohol (PVA) are composed of commonly used natural polymers. Chemotherapeutic drugs (Trastuzumab, Pentuzumab, Paclitaxel, DOX, 5-Fluorouracil and Dexamethasone, etc.) become more effective when they are encapsulated with polymeric NPs.

NPs synthesized from PLGA, a synthetic polymer, are widely studied for anticancer drugs [26, 27]. PLGA has several advantages over cell-targeted therapies compared to other delivery systems:

1) It has been approved by the FDA for drug delivery in humans [28, 29].

2) Biodegradable.

3) Has sustained release activity, ranging from days to weeks under physiological conditions.

4) Provides long-term stability of charged bioactive molecules.

5) Shows ability to capture hydrophobic and hydrophilic drugs.

6) Has comprehensive functionalization options.

PEG is a water-soluble, biocompatible polymer commonly used for coating a wide variety of drugs to improve encapsulation efficiency. Especially in Human Epidermal Receptor 2 (HER2)-related breast cancer, mir-21 is effective in tumor immunity of Antisense Oligonucleotides (ASO) [30]. It has been demonstrated in the animal model that the antitumor effect is quite high even though MiR-21 was used previously only with targeting ligand by PLGA-PEG encapsulation of ASO [26, 31–33]. A biodegradable poly (D, L-lactide-co-glycolide) -block-poly (ethylene glycol) (PLGA-b-PEG-COOH) copolymer will be

synthesized. The most important factor in PEG expression is the prevention of immune system agents [34]. The strong buffering capacity of cationic polymers could effectively help themselves to escape from endo/lysosome as a result of "proton sponge" effect. For instance, 25 kDa polyethylenimine is well known of its excellent transfection activity *in vitro* largely due to its strong buffering capacity and these NPs is very useful for cancer immunotherapy for vaccinations [35–38].

Superparamagnetic iron oxide (SPIO) nanoparticle

Chemotherapeutic agents have been associated with SPIO-based nanocarriers through different strategies (e.g., conjugation via cleavable linker and π-π stacking with polymer layers) for delivery to tumors. Dual paclitaxel (PTX)/superparamagnetic iron oxide (SPIO)-loaded PLGA-based NPs have a potential role in tumor growth [39] in passive targeting.

"*iRGD*" peptide affects the uptake of iron oxide during labeling of panc1 cells for this reason an appropriate "*iRGD*" peptide concentration enhances the uptake of intracellular iron tumor cell proliferation in active targeting [40]. Trastuzumab is conjugated to SPIO NPs which labor as magnetic resonance imaging (MRI) contrast agents to detect HER2-positive tumors [41, 42].

Carbon nanotubes (CNTs)

Carbon NanoTubes (CNTs) are carbon allotropes with a cylindrical nanostructure which have gained intensive interest during the past 20 years because of their unique mechanical properties in addition to very interesting values in electrical and thermal conductivity and also the possibility of their surface to functionalize with a wide group or biochemical species paving the way for numerous therapeutic and drug delivery applications [43, 44]. They are able to penetrate easily through the cellular membrane and have low immunogenicity with significant uptake of delivered small interfering RNA (siRNA) and a working gene silencing effect in the tumor tissue [45]. Many of them have high general toxicity and additional drawbacks, like limited solubility and a poor non-selective biodistribution [46].

Liposomes

Liposomes are broadly used as drug delivery systems and several liposomal nanomedicines have been approved for clinical applications. Liposome-based combination chemotherapy contributes a novel avenue in

	Particle type	Composition/Structure	Properties	Applications
	Polymer	e.g., PLGA, glycerol, chitosan, DNA; monomers, copolymers, hydrogels	Some biodegradable	Drug delivery; passive release (diffusion), controlled release (triggered)
	Dendrimer	PAMAM, etc.	Low polydispersity, cargo, biocompatible	Drug delivery
	Lipid	Liposomes, micelles	Can carry hydrophobic cargo, biocompatible, typically 50–500 nm	Drug delivery
	Quantum dots	CdSe, CuInSe, CdTe, etc.	Broad excitation, no photobleaching, tunable emission, typically 5–100 nm	Optical imaging
	Gold	Spheres, rods, or shells	Biocompatibility, typically 5–100 nm	Hyperthermia therapy, drug delivery
	Silica	Spheres, shells, mesoporous	Biocompatibility	Contrast agents, drug delivery (encapsulation)
	Magnetic	Iron oxide or cobalt-based; spheres, aggregates in dextran or silica	Superparamagnetic, ferromagnetic (small remanence to minimize aggregation), superferromagnetic (~10 nm), paramagnetic	Contrast agents (MRI), hyperthermia therapy
	Carbon-based	Carbon nanotubes, buckyballs, graphene	Biocompatible	Drug delivery

Fig. 1. **NPs types and their application areas for cancer imaging and treatment [25]**

drug delivery research and has increasingly become a significant approach in clinical cancer treatment. Liposomes are grouped into two types:

1) unilamellar vesicles and
2) multilamellar vesicles.

For the treatment of multidrug resistance (MDR)/cancer immunotherapy, mixtures of siRNA/plasmid DNA and hydrophobic drug can be used with Liposomes [47].

Paclitaxel and Rapamycin (with anti-tumor and immunosuppressant properties and an inhibitor of mTOR protein kinase) are encapsulated with PEG-Liposome in breast cancer — Liposomes released in slow and sustained fashion ↑ Cell line cytotoxicity ↑ *In vivo* therapeutic effects. The system controlled the tumor growth [48].

Folate receptor, a membrane-associated folate binding protein, is overexpressed in over 90% of ovarian cancer and other epithelial types of cancer [49, 50]. Xu et al. developed a FR targeted co-delivery formulation by folate-DOX/Bmi1 siRNA liposome (FA-DOX/siRNA-L), demonstrated a great tumor targeting effect and prevented tumor growth *in vitro* and *in vivo* experiments [51, 52].

A thermosensitive magnetic liposomal delivery system is effective co-delivery of gene silencing short hairpin RNA (shRNA) vector and antitumor drug (DOX) into gastric cancer [53]. Liposomal system with an antimicrobial peptide and co-delivery of antagomir-10b could trigger cell death in the meantime besides hindering of T cells migration [54].

Polimeric Micelles

Polymeric micelles used due to their ability to load therapeutics, deliver the cargo to the site of action, improve the pharmacokinetic of the loaded drug and reduce off-target cytotoxicity. They are also developed with improved drug loading capabilities by modulating hydrophobicity and hydrophilicity of the micelle forming block co-polymers and also cancer targeted by surface modifying with tumor-homing ligands. Their classroom contains in Polymeric micelles of therapeutic applications in cancer treatment.

1. Pluronics®
2. PEG-PLA
3. PEG-PCL
4. PEG-Lipid
5. PEG-PLGA

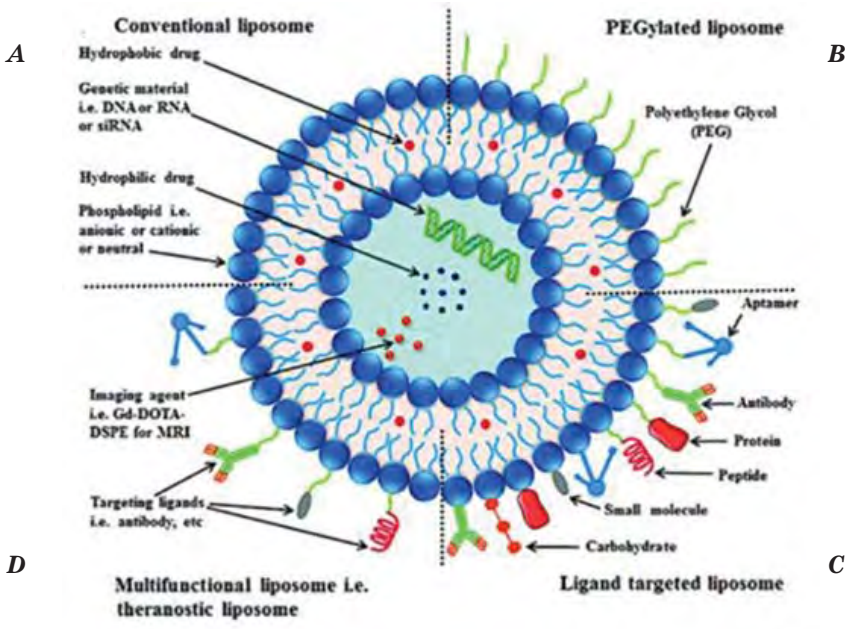

Fig. 2. **Illustration of the versatile functions of liposomes:**
A — Conventional liposomes are composed of two layers of phospholipids and when administered intravenously and remain in the circulatory system for a short time. Also they are widely used for the maintenance of hydrophilic drugs that did not pass through the cell membrane;
B — When protected with PEG, they have the ability to be protected from immune cell attacks and stay longer in circulation;
C — When liposomes are used for active targeting with small molecules such as aptamer, peptide, ligand and protein, they show very high effect on cancer cells;
D — Especially in the diagnosis and treatment of solid tumors they have teranostic effects. They are also often preferred for imaging (such as MRI) [55]

6. PEG-poly(amino acids)
7. Stimuli-sensitive polymeric micelles
8. Endogenous stimuli-sensitive polymeric micelles
9. pH-sensitive polymeric micelles
10. Reduction sensitive polymeric micelles
11. Thermo-sensitive polymeric micelles
12. Exogenous stimuli-sensitive polymeric micelles
13. Light-sensitive polymeric micelles
14. Magnetic field-sensitive polymeric micelles
15. Ultra-sound sensitive polymeric micelles
16. Margination of micro/nanoparticles: Requirement for optimum drug delivery.

Other hydrophilic block forming polymers include chitosan, poly(N-vinyl pyrrolidone) (PVP), and poly(Nisopropylacrylamide) (pNIPAAm). There are various polymer blocks used to form micellar core, including the class of polyethers such as poly(propylene oxide) (PPO), various polyesters such as PLA, PCL, PLGA, poly(β-aminoesters), polyamino acids such as poly(L-histidine) (pHis), poly(L-aspartic acid) (pAsp) and lipids such as dio leoyl(phosphatidylethanolamine) (DOPE), distearoyl (phosphatidylethanolamine) (DSPE). The assembly of block co-polymers, in which PPO attached to PEG as A-B-A triblock co-polymers (PEO-PPO-PEO) is known as Pluronics [56].

Protein Nanoparticles

Protein NPs are also used including water-soluble proteins (e.g., bovine and human serum albumin) and insoluble proteins (e.g., zein and gliadin). So far, most of proteins NPs of article are focused on the preparation and characterization of nanoparticles derived from gelatin, albumin, gliadin, legumin, Methoxy-PEG-polylactide, PEG-asparaginase and two milk proteins that have been investigated for drug delivery applications are Beta-lactoglobulin (BLG) and casein [57, 58]. To promote drug targeting ability, protein nanoparticles have been chemically modified to incorporate targeting ligands that recognize specific cells and tissues. Such modification allows targeting of albumin nanoparticles to breast cancer cells, which overexpress HER2 [59]. Gliadin NPs used as a bioactive delivery system for oral vaccines administration to aid the sustained release delivery of anticancer drugs as well as colon cancer-targeted cyclophosphamide drug therapy and effective for apoptosis of breast cancer cells [60]. Cisplatin-loaded casein is a milk protein nanoparticles demonstrated their ability to penetrate cell membranes, target tumors, and inhibit tumor growth in hepatic tumor [61].

Cancer Treatment with Active and Passive Targeting

Active Targeting Strategies

NPs are used for active targeting [71] to cancer cells including antibody and antigen, peptide, protein, aptamer and ligand fragment based targeting in figure 3 [64]. HER2 is overexpressed in approximately 25–30% of invasive breast cancer but is less expressed by normal adult tissues. Targeted treatment with humanized Trastuzumab (Monoclonal Antibody) targeting the HER2 receptor has become the mainstay of HER2 positive breast cancer. The significant effect of Trastuzumab-conjugated nanoparticles to specifically target HER2 positive cancer cells has been

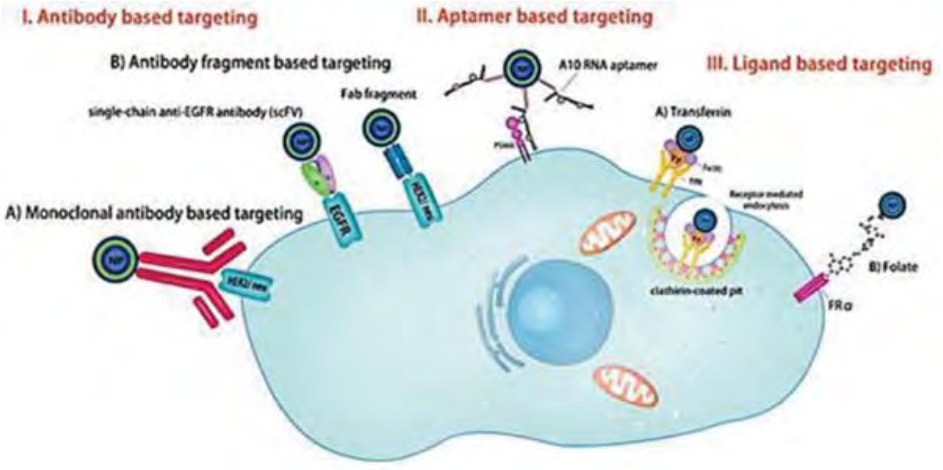

Fig. 3. **Illustration of active targeting components in cancer cells [62]**

proved *in vitro* using different cell lines and *in vivo* [62]. The ZHER2 antibody protein molecule consisting of 58 amino acids and 3 domains is designed as a high affinity linker to HER2 receptors. ZHER2 binds to the HER2 receptor, a domain point different from the point at which the therapeutic antibodies of Trastuzumab and Pertuzumab bind [63]. For this reason ZHER2 protein is highly used for diagnosis (imaging) and treatment of cancer diseases [64, 65]. Cetuximab has been targeted specifically and efficiently AuNPs in Epidermal Growth Factor Receptor (EGFR)-positive pancreatic and colorectal carcinoma cell lines [66].

Passive targeting facilitates the efficient localization of NPs in tumor interstitium but cannot further promote their uptake by cancer cells [71]. Uptake can be achieved by actively targeting NPs to receptors or other surface membrane proteins overexpressed on target cells. The addition of targeting ligands allows the delivery of drug-encapsulated NPs to uniquely identifiable cells or even subcellular sites, thereby reducing the unwanted systemic exposure of cytotoxic drug. Specific interactions between the ligands on the surface of nanocarriers and receptors expressed on the tumor cells may facilitate NPs internalization by triggering receptor-mediated endocytosis. Furthermore, active targeting of nanocarriers with small molecule therapeutic cargo has shown the potential to suppress multidrug resistance (MDR) via bypassing of P-glycoprotein-mediated drug efflux [67, 68]. As a result, although passive targeting facilitates the effective localization of NPs in the tumor interstitium, it cannot over-stimulate cellular uptake by cancer cells, such as active targeting.

NPs are functionalized with different biological molecules, peptides, antibody, and protein ligands for targeted drug delivery and also contain non-coding RNA, viral [69] and bacteria's DNA [38] or RNA for cancer immunization and cell death progress. Natural plant-based drugs that can be used in the field of pharmacology have also been found to be more effective when used with NPs such as Prosopis Cineraria. It is a leaf located in India, which can be used as NP-plant-based drug system for cancer treatment [70]. Ligands for active targeting in drug delivery approach on its great affinity to somatostatin receptors (SSTRs), which is overexpressed in several cancer cells such as core-shell type liposome co-encapsulating VEGF-targeted siRNA (siVEGF) is very effective drug system for VEGF based cancer types. SPIO NPs are accumulate in cancer through passive targeting by the EPR effect and with active targeting to help of targeting by ligands.

Passive Targetting Strategies

Although NPs refer to accumulate in the tumor cells due to the enhanced permeation and retention (EPR) effect, passive tumor targeting is dependent on the tumor vascularization and angiogenesis, and therefore lacks specificity and consistency. Both the tumor model type and conditions can seriously affect the passive targeting effectiveness [72–74]. General features of tumors include leaky blood vessels and

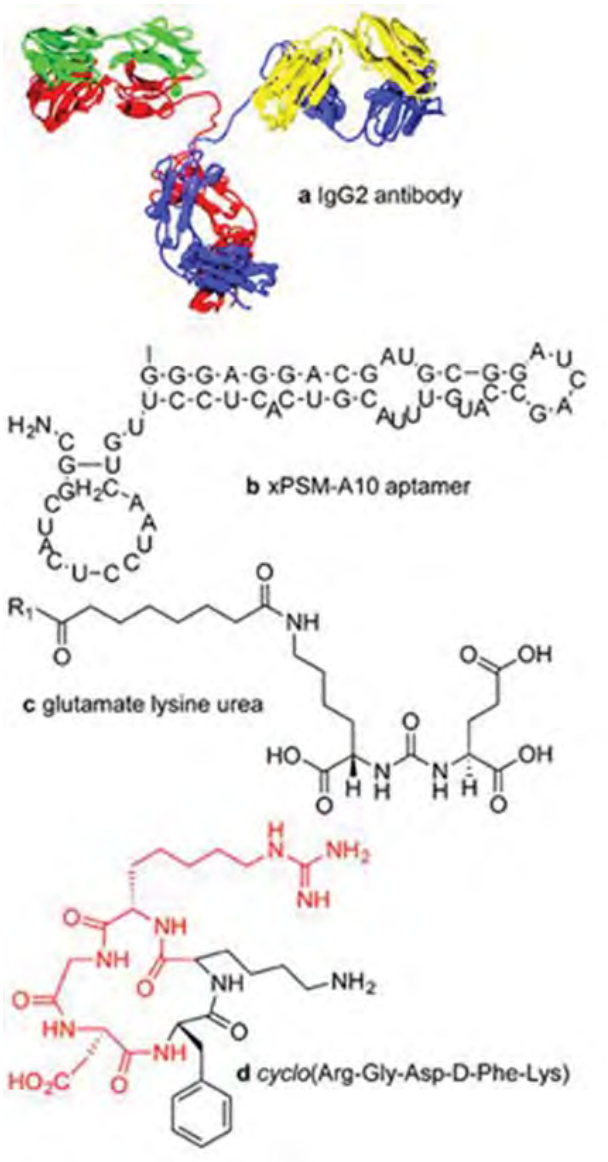

Fig. 4. **An example for Aptamer modeling to target cancer cells (generally receptors, ligands, etc.) [25]**

poor lymphatic drainage. Free drugs may be used nonspecically as a nanocarrier and can extravagate into the tumor tissues via the leaky vessels by the EPR effect. Sometimes, targeting cells within a tumor is not always feasible because some drugs cannot be used efficiently and the random nature of the approach makes it difficult to control the process which is lack of control may induce MDR.

Nanoparticle Imaging System

Imaging techniques used mostly in preclinical studies and clinical practice such as MRI, computed tomography (CT), ultrasound (US), optical imaging (OI), photoacoustic imaging (PAI), positron emission tomography (PET), and single-photon emission Computed tomography (SPECT).

Targeted NPs imaging agents provide a new technology for cancer imaging, which goes beyond anatomical characterization. It enables early detection of cancer as well as treatment monitoring at the molecular and cellular level. With the development of nanotechnology, magnetic NPs have been used in the MRI, adhering to target cells and drug release system [75, 76]. Tumor diagnosis and treatment can be obtained by the same NPs formulation and the disease can be monitored and fought by the synergistic effect of more than one therapy. The preparation and application of single multifunctional nano radiotracers based on iron oxides and enabling PET/MRI dual imaging can used for treatment and diagnosis for cancer [77]. New designed and realized a bimodal CT for SPECT and MRI with Superparamagnetic Iron Oxide NPs (SPION) privileged the magnetic properties to the CNT, while 99mTc granted the radioactive property.

Gold Nanoparticle Imaging

AuNPs are now used widely in bioimaging and phototherapy due to their tunable properties and highly sensitive optical and electronic properties of the surface plasmon resonance (SPR) [78]. AuNPs act as an active imaging probe for cancer detection facilitating whole-body scans. AuNPs can be easily functionalized with additional imaging agents by improving the AuNP-based imaging systems. That may allow the observation of tissues not only on its basic anatomic configuration but also on the molecular level for cancer diseases. For example, Au atoms using a one-step procedure for SPECT/CT imaging in an orthotropic mouse xenograft of triple-negative breast cancer (TNBC) and also PEGylation for favorable pharmacokinetics and d-Ala1-peptide T-amide (DAPTA) for targeting C–C chemokine receptor 5 (CCR5, a prognostic biomarker for breast cancer progression) [79, 80]. Multifunctional gold nanoprobe is designed for simultaneous miRNA-21 responsive fluorescence imaging and therapeutic monitoring of cancer. miRNAs provides a simple but powerful protocol with great potential in cancer imaging, therapy, and therapeutic monitoring [81].

Superparamagnetic iron oxide (SPIO) Imaging

Superparamagnetic iron oxide (SPIO) NPs were studied for the development of contrast agents in MRI for cancer diagnosis. First-generation of SPIO NPs had diagnostic capabilities only, whereas a new model of SPIO NPs has multifunctional characteristics for combined therapeutic and diagnostic applications for cancer. The magnetite (Fe_3O_4) and maghemite (Fe_2O_3) cores of SPIO NPs can be readily detected with MRI, thereby enabling real-time *in vivo* drug tracking. To provide colloidal stability of the magnetic core and better biocompatibility, SPIO NPs have been stabilized with polysaccharides (e.g., dextran and chitosan), PEG, polypyrrole (PPy), PLA, PLGA and their copolymers. Compared with other coating materials such as silica, polymer advantages with great biocompatibility and biodegradability to facilitate MRI-guided drug delivery, gene delivery, photo thermal therapy (PTT), photodynamic therapy 5 (PDT) or magnetic hyperthermia [82] growth through the EPR effect and available real-time *in vivo* drug tracking with MRI [83].

Discussion

Current cancer treatments include surgical intervention, radiation and chemotherapeutic agents. Side effects are an integral part of these treatment modules. So, recent studies focused on finding new strategies without any major side effects and were more effective instead of these modules. However, better comprehension of molecular basis of tumor and the advent of new diagnostic technologies (such as active and passive targeting models) and treatments can be decreased mortality rate in cancer patients. So the researchers continue to find strategies to improve the chances of survival and quality of cancerous patient's lives. NPs are used in the search for this new treatment method and can be preferred in imaging methods as well [84].

Nanoparticles and related biotechnologies provide needed augmented presentation for development of vaccine, treatments, diagnosis, imaging active and passive strategies for cancer and undoubtedly nanoparticle engineering. For this purpose an exciting ongoing and future studies and an increasing focus of clinical trials cancer treatments will remain.

Consequently, this review provides a brief manual for anyone in the field of nanotechnology for the diagnoses, treatment and vaccination of the cancer disease.

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ДІАГНОСТИКА, ВІЗУАЛІЗАЦІЯ ТА ЛІКУВАННЯ РАКУ З ВИКОРИСТАННЯМ НАНОРОЗМІРНИХ СТРУКТУР

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Сучасні дослідження спрямовані на пошук нових стратегій лікування раку, які не мають значних побічних ефектів і більш ефективні порівняно з традиційними методами, включаючи хірургічне втручання, променеву терапію і хіміотерапію.Застосування нанорозмірних структур уможливлює використання новітніх підходів для лікування раку. Системи наночастинок підвищують ефективність терапевтичних препаратів, знижуючи їхні побічні ефекти. Хоча в багатьох дослідженнях повідомляється про розробку нових методів лікування ракових клітин в майбутньому, клінічний успіх дає змоги зрозуміти вплив типу, розміру та дози ночастинок на зони їх застосування. Таким чином, в цьому огляді проілюстровано можливість використання наночастинок в діагностиці, візуалізації та лікуванні раку.

Ключові слова: діагностика раку, візуалізація та лікування, наночастинки.

ДИАГНОСТИКА, ВИЗУАЛИЗАЦИЯ И ЛЕЧЕНИЕ РАКА С ИСПОЛЬЗОВАНИЕМ НАНОРАЗМЕРНЫХ СТРУКТУР

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Современные исследования направлены на поиск новых стратегий лечения рака, не имеющих значительных побочных эффектов и более эффективных по сравнению с традиционными методами, включая хирургическое вмешательство, лучевую терапию и химиотерапию. Применение наноразмерных структур дает возможность использовать полезные подходы для лечения рака.Системы наночастиц повышают эффективность терапевтических препаратов, снижая их побочные эффекты. Хотя во многих исследованиях сообщается о разработке новых методов лечения раковых клеток в будущем, клинический успех не позволяет понять влияние типа, размера и дозы наночастиц на области их применения. Таким образом, в настоящем обзоре проиллюстрирована возможность использования наночастиц в диагностике, визуализации и лечении рака.

Ключевые слова: диагностика рака, визуализация и лечение, наночастицы.