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Innovative Applications of Nanoparticles in Cancer Diagnosis and Treatment

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Abstract: *Numerous nanoparticles have been created and evaluated during the last few decades, sparking a great deal of interest in their possible applications as therapeutic and diagnostic tools. Iron oxide nanoparticles are the sole formulation of nanoparticles that has been used in clinical practice to date, despite the fact that they have been suggested as potential diagnostic tools. This is mostly because it is difficult to consistently produce monodispersed nanoparticles and get appropriate pharmacokinetic characteristics. Concerns exist over their possible toxicity, biodegradation, and remove as well. Currently, therapeutic applications account for the majority of nanoparticle formulations utilized in clinical settings. The goal of these therapeutic nanoparticles is to minimize accumulation in healthy tissues and organs while more effectively delivering (chemo-)therapeutic medicines to specific locations. The "enhanced permeability and retention" (EPR) effect forms a substantial part of their foundation. Furthermore, because nanoparticles can combine therapeutic and diagnostic properties in a single formulation, they exhibit significant promise for theranostic applications. They are extremely useful for customizing therapies based on nanomedicine because of this feature. In this study, we address the function of EPR in the development of nanotheranostic formulations, examine the application of therapeutic and diagnostic nanoparticles, and provide an overview of popular non-invasive imaging methods. We also look at the practical possibilities of image-guided drug administration and nanotheranostics for more individualized and effective (chemo-)therapeutic treatments.*

Keywords: Nanoparticles; Diagnostic agents; Pharmacokinetics; Drug delivery;(Chemo-) therapeutic interventions; Targeted drug delivery.

I. INTRODUCTION

Currently, one of the most important areas of medical research is in vivo molecular imaging. Early disease detection, precise disease staging, image-guided therapeutic interventions, and individualized treatment plans are all greatly aided by this quickly developing field. Moreover, it gives crucial information regarding the effectiveness of medicines, enabling clinicians to change treatment programs based on real- time data. Despite its potential, molecular imaging significantly relies on the employment of specific imaging probes that are designed to observe and characterize biological processes at the cellular and molecular level (1-5). These probes are vital resources for learning more about the pathophysiology of illnesses and how treatments affect those illnesses.

The development of nanotechnology, which has made it easier to create a variety of nanoparticle formulations for medicinal and diagnostic uses, has been one of the most revolutionary advances in recent years. The main purpose of diagnostic nanoparticles is to provide high-resolution imaging capabilities, which enable the visualization of illnesses and enhance our understanding of the fundamental (patho-

)physiological concepts that underlie a variety of diseases. By targeting particular biomarkers or illness- related cellular structures, these nanoparticles can be designed to improve disease progression detection and comprehension. The intrinsic properties of nanoparticles—such as their small size, surface area, and ability to be functionalized with targeting ligands—hold immense potential for integrating both diagnostic and therapeutic functions into a single nanoparticle formulation. This integration enables the development of theranostic nanoparticles, which combine both diagnostic and therapeutic capabilities within a single platform. Such theranostic nanoparticles have the unique ability

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to monitor the biodistribution and accumulation of therapeutic agents at target sites, visualize and quantify the release of drugs from nanoparticles, and longitudinally assess the therapeutic efficacy of treatment regimens.

In clinical settings, theranostic nanoparticles offer the ability to personalize treatment approaches. They enable the preselection of patients based on their molecular profiles, ensuring that only those who are most likely to benefit from a particular therapeutic approach are chosen. Furthermore, by providing continuous feedback on treatment efficacy, theranostic nanoparticles allow for real-time monitoring of therapeutic outcomes, enabling clinicians to adjust treatment strategies accordingly. This personalization of treatment holds great promise in the field of nanomedicine, as it can significantly improve the overall success rates of therapies, reduce unnecessary side effects, and optimize patient care (7-15).

This review article will delve into the current landscape of nanoparticle formulations used for both diagnostic and therapeutic applications, offering a detailed analysis of their functions and clinical relevance. Additionally, it will provide an overview of various non-invasive imaging modalities that can be used in conjunction with these nanoparticles to enhance disease diagnosis and treatment. The article will also explore the role of nanoparticles as molecular imaging probes and contrast agents, which can amplify the sensitivity and specificity of disease detection. Lastly, the review will address the potential for nanoparticles to play a transformative role in clinical practice, particularly in the context of facilitating personalized therapy interventions by improving treatment accuracy, efficacy, and safety.

II. LITERATURE REVIEW

Nanoparticles for imaging the MPS

Numerous nanoparticle formulations have been designed and evaluated over the last years, including e.g. liposomes, polymers, micelles, proteins, antibodies, gold nanoparticles, ultrasmall superparamagnetic iron oxide nanoparticles, and nanotubes, which possess intrinsic properties that influence their biodistribution, elimination, and target site accumulation The majority of these nanoparticles are used for therapeutic purposes (6,16,50,51). Currently, several therapeutic nanoparticles are applied in clinical practice. Doxil (PEGylated, doxorubicin-loaded liposomes, Janssen, Horsham, PA), Abraxane (paclitaxel-containing albumin nanoparticles, Celgene, Summit, NJ), and AmBisome (liposomal amphotericin B, Gilead, Foster City, CA) are some prominent examples of clinically approved therapeutic nanoparticles; many other nanomedicine formulations are currently being tested in preclinical and clinical trials (52-54). In contrast to the therapeutic application of nanoparticles, diagnostic applications are still lagging behind (6,8). Although nanoparticles are frequently proposed as diagnostic agents, there is still only one nanoparticle formulation, namely iron oxide nanoparticles, that was used in clinical practice (ferucarbotran, Resovist, Bayer Schering Pharma, Germany). However, even ferucarbotran was recently taken off the market. Instead, ferumoxytol (Feraheme, AMAG Pharmaceuticals Inc., USA), which is an FDA approved therapeutic iron oxide nanoparticle formulation for treating anemia, is now used offlabel by many radiologists (55). Despite enormous progress in the synthesis of novel diagnostic nanoparticle formulations, there are several limiting factors that impede the clinical translation of diagnostic nanoparticles. The major difference between nanodiagnostics and nanotherapeutics is their intended pharmacological behavior. While nanotherapeutics should possess pharmacological activity, nanodiagnostics should not generate (patho-) physiological effects. Furthermore, nanotherapeutics should be characterized by a long blood circulation time, as their main purpose is to achieve a selective accumulation of drugs in tissues characterized by enhanced permeability and retention (EPR), such as tumors. In this regard, therapeutic nanoparticle formulations are advantageous over standard low- molecular-weight drugs, as their renal excretion is reduced, causing prolonged circulation times and decreased volume of distribution. This leads to less accumulation in healthy tissue and thus less side effects, and improves the ability of drug molecules to accumulate at the pathological site, and thereby increase their therapeutic efficacy (6,8-11). For nanodiagnostics, short circulation times and fast biodegradation and elimination without pharmacological and toxicological activity are preferred. In addition, with respect to their application as molecular imaging probes, diagnostic nanoparticles should possess a good and efficient delivery to the target site and should exhibit highly specific binding and internalization capabilities. Their non-specific accumulation in healthy tissue should be low and short. Furthermore, a high sensitivity of the imaging method to detect the molecularly targeted diagnostic nanoparticles is

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required (the intrinsic properties of nanoparticles often do not correspond with the pharmacokinetic and pharmacodynamic demands. If not taken up by the mononuclear phagocyte system (MPS) (formerly known as RES), due to their size, ranging from a few nanometers to 1000 nm, the biodistribution tends to be restricted to the compartment in which they were administered. For diagnostic agents targeting extravascular structures, it is essential that they rapidly extravasate out of blood vessels and penetrate and distribute within the interstitial space. The unbound fraction also has to leave these compartments rapidly in order to keep the unspecific background signal low. However, although nanoparticles accumulate in the interstitial space, their penetration into the tissue is slow and their intratumoral distribution is significantly smaller than for low-molecular-weight diagnostics (6,8,11). It should be noted, that for therapeutic nanoparticles, it is often sufficient that the nanoparticles reach the interstitial space and here release their drug load, while tumor cell-targeted diagnostic probes need to pass the entire interstitial space to ultimately reach and bind to the tumor cell. Those demands for diagnostic nanoparticle formulations are often not adequately addressed (6).

Nanoparticles for imaging tumor vascularization and angiogenesis

The use of nanoparticles in monitoring tumor vascularization and angiogenesis—two important markers of tumor aggressiveness and malignancy—is growing. While targeted nanoparticles bind to activated endothelial cells and enable the evaluation of tumor vascular changes and treatment effects during therapies such as anti-angiogenic treatments and radiotherapy, non-targeted nanoparticles aid in determining the enhanced permeability and retention (EPR) effect.

The use of imaging agents based on nanoparticles to track tumor angiogenesis and treatment outcomes is highlighted in a number of publications. For example, when employed for ultrasound imaging, microbubbles that were targeted to the integrins VEGFR2 and αvβ3 demonstrated specific binding to the blood arteries of angiogenic tumors. The monitoring of anti-angiogenic therapy in human colon cancer xenografts was made possible by these microbubbles. Similar to this, MR imaging using paramagnetic liposomes coated with RGD peptides revealed clear tumor accumulation patterns, especially in the tumor rims. Another study employed MRI to distinguish between tumors with high and low αvβ3 integrin expression using USPIO nanoparticles coupled with RGD peptides.

By evaluating polymeric drug carriers modified with RGD- and NGR-based peptides using optical imaging, a theranostic strategy was shown. Active targeting boosted tumor accumulation, but it also resulted in higher liver uptake and shorter blood half-lives.

Last but not least, patients with malignant melanoma underwent PET and optical imaging using hybrid silica nanoparticles (C dots) functionalized with RGD peptides in a first-in-human clinical trial. Nanoparticles show potential for clinical translation in cancer diagnosis and treatment monitoring because they provide a flexible method for visualizing tumor angiogenesis and assessing anti-angiogenic medicines.

Nanoparticles for imaging EPR and targeted drug delivery

As mentioned earlier, most nanoparticle formulations are based on the Enhanced Permeability and Retention (EPR) effect and are made for tumor medication targeting. Because solid tumors usually have abnormally leaking blood arteries, nanoparticles, which can be anywhere from a few tens to hundreds of nanometers in size, can enter the tumor from the bloodstream. Abnormal angiogenesis and the overproduction of vascular permeability-enhancing substances like VEGF are the causes of the enhanced permeability of the tumor vasculature. An incomplete endothelium layer with strongly fenestrated (porous) walls—often with fenestrations greater than 300 nm—is the result of an imbalance between the formation of new blood vessels and their maturity. The absence of functional lymphatic drainage in solid tumors contributes to the EPR effect in addition to the increased permeability of tumor blood vessels. This limits the evacuation of nanoparticles from the tumor site and is caused by aberrant lymphangiogenesis and lymphatic artery compression. Consequently, nanoparticles stay in the tumor tissue for a long time. Here are a few instances of targeted medicine delivery using nanoparticles.

pHPMA-copolymers were used as a medication delivery mechanism in a study by Lammers et al. Gemcitabine and doxorubicin were used to functionalize these copolymers for therapeutic applications, and gadolinium and 131I for imaging. Using γ-scintigraphy and MRI, the biodistribution of these copolymers was assessed. According to the study, longer circulation durations and increased tumor accumulation were observed with bigger copolymers. These findings showed that HPMA-copolymers can be used as flexible, multipurpose drug carriers that enhance low-molecular-weight drug delivery and increase anticancer activity.

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86Re-labeled Doxil (PEGylated liposomal doxorubicin) was administered to naked rats with head and neck squamous cell cancer (HNSCC) in a different study by Soundararajan et al. SPECT-CT and γ- scintigraphy were used to track tumor accumulation, and the results indicated that 186Re-Doxil had significant tumor uptake, low liver accumulation, and long blood retention. The effectiveness of 186Re- Doxil in conjunction with radiofrequency ablation therapy was assessed in a follow-up research. The combination showed improved tumor growth inhibition, increased drug accumulation at the tumor site, and enhanced treatment efficiency. In a different investigation, Koukourakis et al. visualized and measured EPR-mediated passive medication targeting to tumors in sarcoma patients using radiolabeled stealth liposomal doxorubicin. By guaranteeing targeted drug accumulation, these results demonstrate the potential of image-guided nanoparticles for efficient drug delivery to tumors, enhancing therapeutic results.

Tuning the properties of diagnostic and therapeutic nanoparticles

The key characteristics of nanoparticle formulations include their size and charge, core and surface properties, shape and flexibility, as well as multivalency and controlled synthesis. These properties directly influence the nanoparticle's distribution, targeting potential, and toxicity in the body. Additionally, they have a significant impact on the drug loading capacity, release, and stability of the nanoparticles.

One of the most thoroughly explored aspects of nanoparticle pharmacokinetics and biodistribution is the effect of particle size on its in vivo behavior. It is generally accepted that nanoparticles with sizes ranging from 10 to 100 nm are optimal for drug delivery systems. These formulations can effectively exploit the EPR effect in tumors while avoiding premature elimination by the spleen. Moreover, smaller particles tend to accumulate more easily and penetrate tissues better. Therefore, the size of nanoparticles, along with their surface composition, plays a critical role in ensuring effective accumulation at the target site. Additionally, the dispersion and size variation of nanoparticles are crucial for their in vivo behavior. Polydisperse nanoparticles tend to have varied retention times and biodistribution. Hence, controlled synthesis that produces nanoparticles with uniform size, shape, charge, and functional group density is essential for achieving consistent distribution. Only monodisperse nanoparticles can be expected to exhibit similar biological half-life, biodistribution, and target affinity.

Another important feature of nanoparticles is their multivalency. Nanoparticles possess a high surface area-to-volume ratio, allowing for significant loading capacity for various imaging probes, targeting ligands, and therapeutic agents. For instance, a carbon nanotube with the same volume as a large protein (100-150 kDa) offers a surface area 15 times larger than that of the protein, facilitating the attachment of numerous targeting ligands to the nanoparticle and enhancing target binding. Additionally, the shape of nanoparticles significantly affects their in vivo behavior and biological function, particularly their internalization into cells. For example, a study comparing PEGylated rod-shaped gold nanoparticles with PEGylated spherical nanoparticles showed that the gold nanorods were less taken up by the liver and macrophages, exhibited longer circulation times, and accumulated more in tumors than their spherical counterparts. The modification of nanoparticle surfaces and charge can either enhance or reduce their circulation times. Research has shown that polystyrene microparticles with primary amine groups on their surface underwent more phagocytosis compared to those with sulfate, hydroxyl, or carboxyl groups. As a result, it is well understood that positively charged nanoparticles tend to have a higher rate of nonspecific internalization and a shorter blood circulation time than neutral or negatively charged formulations.

There are several strategies for modifying nanoparticle surfaces to influence their in vivo behavior and alter their biodistribution. One common modification is the use of polyethylene glycol (PEG), which forms a hydrophilic layer on the nanoparticle surface, protecting it from immune system recognition and reducing uptake by macrophages in the mononuclear phagocyte system (MPS). This process, known as the "stealth effect," enhances the nanoparticle's circulation half-life and promotes accumulation at target tissues. Another popular surface coating is dextran, which is commonly used for nanoparticles such as SPIO (superparamagnetic iron oxide) and USPIO (ultra-small superparamagnetic iron oxide) for MRI imaging of the MPS.

In addition to surface modifications, nanoparticle formulations have been developed to respond to various intrinsic stimuli in the tumor microenvironment, such as low pH or overexpressed enzymes, as well as to externally applied stimuli like ultrasound, magnetic fields, hyperthermia, or light. These stimuli- responsive formulations trigger site-specific drug release. For example, temperature-sensitive liposomes containing both chemotherapeutic agents and MRI

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contrast agents enable the monitoring of drug release triggered by temperature changes by tracking changes in relaxation times. Many of these trigger- responsive MRI contrast agents exploit the chemical exchange saturation transfer (CEST) effect, a novel class of MR contrast agents. CEST agents are characterized by exchangeable protons (such as -NH, -OH) that resonate at distinct frequencies. When these protons are selectively saturated with an MR pulse, they exchange with protons in bulk water, causing a reduction in the water peak's signal intensity, which can be measured.

For instance, in a study by Langereis et al., a combined temperature-sensitive liposomal 1H CEST and 19F MR contrast agent system was evaluated as a carrier for MR-guided drug delivery alongside high- intensity focused ultrasound (HIFU)-induced hyperthermia. Both the CEST agent and 19F MR probe were loaded into the aqueous core of the liposomes. At temperatures below the liposome's bilayer melting point, the CEST effect allowed localization of the liposomes, while the 19F signal was suppressed. Upon heating above the liposomal bilayer melting point, the CEST and 19F probes were released from the liposome, and the 19F signal increased, allowing for real-time tracking of local drug release. These stimuli-sensitive nanoparticle formulations may offer valuable feedback on the effectiveness of temperature-triggered drug release, particularly when used in combination with treatments like radiofrequency ablation or MR-guided HIFU-induced hyperthermia.

Theranostics and therapy individualization

The concept of theranostics incorporates two distinct approaches, which encompass all steps of a patient's healthcare management The "biomarker" or "companion diagnostics" approach offers the opportunity to assist treatment selection, response prediction, and treatment monitoring, while the "image guidance" approach allows planning, pre-operative guidance, and follow up of the therapeutic action, including e.g. local drug delivery. Companion diagnostics are diagnostic clinical tests on specific biomarkers or biological targets that aim to identify patients that are (more) likely to benefit from a specific treatment by elucidating the efficacy and/or safety of a specific drug for a targeted patient group. Furthermore, companion diagnostics can provide information about the target receptor density. Companion diagnostics can be categorized into two main groups, comprising assays that have been developed after a therapeutic drug has come to the market and assays that are developed in conjunction, as companion to a specific therapeutic agent. The co-development of companion diagnostics offers the potential to significantly alter the drug development process and commercialization of potential drug candidates by yielding safer drugs with enhanced therapeutic efficacy in a faster and more cost-efficient manner. An example of a companion diagnostic imaging agent is etarfolatide (Folcepri, Endocyte Inc., West Lafayette, IN). It consists of a small-molecule high-affinity ligand for the folate receptor linked to technetium-99m for SPECT imaging. Etarfolatide is used in platinum-resistant ovarian cancer or non-small cell lung cancer to stratify patients for treatment with the folate receptor-targeted chemotherapeutic drug vintafolide (Vynfinit, Endocyte Inc., West Lafayette, IN) (90). The combination of diagnostic and therapeutic properties into a single nano- or microparticle formulation for theranostic purposes holds significant potential for image-guided drug delivery and personalized therapies (Fig. 4) (91-93). Theranostic nanoparticles enable monitoring of their biodistribution and target site accumulation, the visualization and quantification of their local activation and sometimes even drug release, and the non-invasive and longitudinal assessment of their therapeutic efficacy (11-12,91,94-96). In this context, Lammers, Koczera et al. for instance investigated the potential of poly(n-butyl-cyanoacrylate) (PBCA)-based microbubbles, that contained USPIO nanoparticles in their shell to simultaneously induce and monitor blood-brain barrier permeation (97). Transcranial ultrasound-mediated microbubble destruction led to USPIO release and the permeation of the blood-brain barrier was subsequently visualized and quantified by MRI. Such theranostic strategies are considered to be useful for monitoring and assessing efficient and safe drug delivery across biological barriers. The application of theranostic nanoparticles may facilitate patient preselection based on noninvasive imaging, providing insights on drug delivery, drug release and drug efficacy, and predicting, which patients are likely to respond to nanomedicine treatments. In addition, preselected and nanomedicine-treated patients can be longitudinally monitored to visualize their responsiveness to the administered nanomedicine formualtion. Patients showing insufficient therapeutic response can be assigned to alternative therapies, to facilitate and refine individualized treatment interventions (8,11,90,98). Therefore, theranostic nanoparticles hold significant potential for enabling personalized medicine and patient

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individualization by optimizing treatment strategies and drug delivery, and by longitudinally monitoring therapy efficacy

III. CONCLUSION

Nanoparticle formulations have versatile applications and can serve both as diagnostic and therapeutic tools in cancer treatment. From a diagnostic standpoint, there is a growing demand for agents capable of accurately characterizing the enhanced permeability and retention (EPR) effect. Theranostic nanoparticles, which combine both therapeutic and diagnostic functions, can be used to visualize and assess the biodistribution and accumulation of nanoparticles at the target site, monitor drug release, track long-term drug efficacy, and predict potential treatment outcomes. This dual capability allows for the pre-selection of patients for the most appropriate (nano-)chemotherapeutic treatments, aligning with the principles of personalized medicine and improving patient-specific treatment approaches.

Moreover, nanoparticles can be utilized to study tumor angiogenesis, with very small nanoparticles (less than 5 nm) also serving as molecular diagnostics for targets outside the vasculature. However, while therapeutic nanoparticle formulations are typically designed for slow renal clearance and extended blood circulation times to enhance tumor accumulation and therapeutic effect, diagnostic nanoparticles require short circulation times to reduce nonspecific background and facilitate the development of clinically relevant imaging techniques. In this regard, the advantage of using nanoparticulate diagnostic agents over traditional low-molecular-weight drugs must always be carefully evaluated.

For further clinical translation of nanoparticle formulations for both diagnostic and therapeutic uses, particularly in oncology and personalized medicine, it is essential to address key regulatory challenges.

These include ensuring controlled nanoparticle synthesis, achieving consistency and reproducibility across batches, and scaling up production methods. Variations in nanoparticle size, charge, and shape from batch to batch can significantly affect blood circulation time, biodistribution, and elimination, making standardization a critical factor for success.

Ultimately, accelerating the clinical application of nanoparticles for diagnostic and therapeutic purposes, as well as advancing the development of clinically relevant nanodiagnostics, will require greater interdisciplinary collaboration and knowledge sharing among scientists across various fields.

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REFERENCES

[1]. Koukourakis MI, Koukouraki S, Giatromanolaki A, Kakolyris S, Georgoulias V, Velidaki A, et al. High intratumoral accumulation of stealth liposomal doxorubicin in sarcomas:rationale for combination with radiotherapy. Acta Oncol. 2000;39(2):207-11.

[2]. Brouwer OR, Buckle T, Vermeeren L, Klop WM, Balm AJ, van der Poel HG, et al. Comparing the hybrid fluorescent-radioactive tracer indocyanine green-99mTcnanocolloid with 99mTc-nanocolloid for sentinel node identification: a validation study using lymphoscintigraphy and SPECT/CT. J Nucl Med. 2012;53(7):1034-40.

[3]. Rubin GD. Computed tomography: revolutionizing the practice of medicine for 40 years.Radiology. 2014; 273(2 Suppl):S45-74.

[4]. Strijkers GJ, Mulder WJ, van Tilborg GA, Nicolay K. MRI contrast agents: current status and future perspectives. Anticancer Agents Med Chem 2007;7(3):291-305.

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[5]. Nystrom AM, Fadeel B. Safety assessment of nanomaterials: implications for nanomedicine. J Control Release. 2012;161(2):403-8.

[6]. Kircher MF, de la Zerda A, Jokerst JV, Zavaleta CL, Kempen PJ, Mittra E, et al. A brain tumor molecular imaging strategy using a new triple-modality MRI-photoacousticRaman nanoparticle. Nat Med. 2012;18(5):829-34.

[7]. Palmowski M, Huppert J, Ladewig G, Hauff P, Reinhardt M, Mueller MM, et al. Molecular profiling of angiogenesis with targeted ultrasound imaging: early assessment of antiangiogenic therapy effects. Mol Cancer Ther. 2008;7(1):101-9.

[8]. Mulder WJ, Strijkers GJ, Habets JW, Bleeker EJ, van der Schaft DW, Storm G, et al. MR molecular imaging and fluorescence microscopy for identification of activated tumor endothelium using a bimodal lipidic nanoparticle. FASEB J. 2005;19(14):2008-10.

[9]. Mulder WJ, van der Schaft DW, Hautvast PA, Strijkers GJ, Koning GA, Storm G, et al. Early in vivo assessment of angiostatic therapy efficacy by molecular MRI. FASEB J. 2007;21(2):378-83.

[10]. Kunjachan S, Pola R, Gremse F, Theek B, Ehling J, Moeckel D, et al. Passive versus active tumor targeting using RGD- and NGR-modified polymeric nanomedicines. Nano Lett. 2014;14(2):972-81.

[11]. Matsumura Y, Maeda H. A new concept for macromolecular therapeutics in cancer chemotherapy: mechanism of tumoritropic accumulation of proteins and the antitumor agent smancs. Cancer Res. 1986;46:6387-92.

[12]. Maeda H, Wu J, Sawa T, Matsumura Y, Hori K. Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review. J Control Release. 2000;65(1- 2):271-84.

[13]. Torchilin V. Tumor delivery of macromolecular drugs based on the EPR effect. Adv Drug Deliv Rev. 2011;63(3):131-5. 70. Nehoff H, Parayath NN, Domanovitch L, Taurin S,