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Multifunctional nanoparticle developments in cancer diagnosis and treatment

Sepideh Parvanian [a,*], Seyed Mojtaba Mostafavi [b], Meysam Aghashiri [a]

[a] ACTOVERCO Biopharmaceutical Company, Alborz, Karaj, Iran
[b] CinnaGen Medical Biotechnology Research Center, Alborz University of Medical Sciences, Karaj, Iran

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ABSTRACT

Nanotechnology, although still in the early stages, has the potential to revolutionize the early diagnosis, treatment, and monitoring of disease progression. Technological application of nanometer molecules in medicine with the aim of fighting and curing ailments is the globally definition of nanomedicine. The success of nanotechnology in the healthcare part is driven by the possibility to work at the same scale of several biological processes, cellular mechanisms, and organic molecules. With the growing understanding of methods to functionalize nanoparticles and the continued efforts of creative scientists to advance this technology, it is likely that functionalized nanoparticles will become an important tool in the above mentioned areas. This paper describes the role of multifunctional nanoparticle in diagnosis and treatment of cancer. Therefore, the aim of this review is to provide basic information on nanoparticles, describe previously developed methods to functionalize nanoparticles and discuss their potential applications in biomedical sciences and finally mention the therapeutic nanoparticle commercialization challenges.

Contents

1. Introduction

The number of new cases of cancer as one of the most deadly diseases in the world increases each year [1]. With regards to positive outcomes from early cancer diagnosis associated with a higher than 90% 5-year survival rate [2,3] cancer therapy and detection technologies is an emerging field. This can provide rapid and sensitive detection of cancer-related molecules, molecular changes detection even in a small percentage of cells and also potential to generate novel and highly effective therapeutic agents [4–7]. Furthermore, there is a strong probability that cancer nanotechnology could also open up opportunities for personalized cancer diagnosis and treatment approaches by means of multifunctional nanoparticles in four main area: detection of cancer disease-specific biomarkers, imaging of tumors and their metastases, the functional delivery of therapeutic agents to target cells, and real-time monitoring of treatment in progression. The purpose of this review article is to summarize the results of use of multifunctional nanoparticles in the cancer diagnosis, treatments and therapy and introduce the different types of therapeutic nanoparticles. Thus, the first part will emphasize the key properties of therapeutic multifunctional nanoparticles and how these properties affect the efficiency and specificity of nanoparticles as a complicated and useful system. Next, we will summarize current clinical uses of the therapeutic nanoparticles and new generation of therapeutic nanoparticles. Finally, we will discuss the challenges for commercialization of therapeutic nanoparticles.

1.1. Multifunctional nanoparticles

Multifunctional nanoparticle systems can integrate imaging, targeting and treatment modalities both on the surface and in the core

* Corresponding author.
E-mail address: sepidehparvanian@yahoo.com (S. Parvanian).

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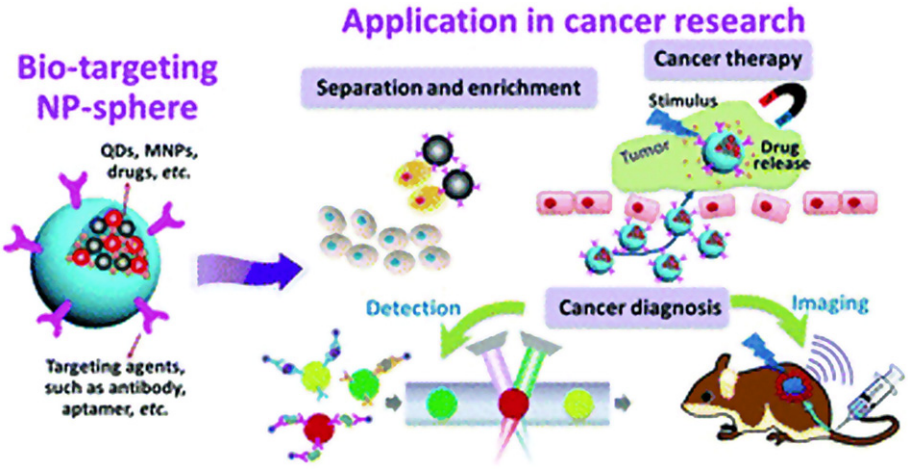

Fig. 1. Nanoparticle application in cancer diagnosis and therapy [76].

to targeting tumor cells [8]. Multifunctional nanoparticles also use for simultaneous delivery of multiple treatment agents, to apply effective combinatorial therapeutic regimens against cancer [9]. Different factors contribute to multifunctional nanoparticle application resiliency, such as tumor location in the body, the inability of the treatment to reach the tumor cells, and the risk of damaging healthy cells (Fig. 1). Nanoparticles provide an opportunity to change the pharmacokinetic outline of drugs, reduce toxicity and enhance the therapeutic markers. This causes the development of "multifunctional" nanoparticles. For this reason, more capabilities like targeting and image contrast improvement are attached to the nanoparticles. On the other hand, additional functionality means additional synthetic steps and costs, more in vivo complex behavior and effects, and also greater regulatory impediments [10]. Advances in genomics and proteomics concepts have resulted in providing information about the molecular profiles and biomarkers of different cancers, in order to contribute in design of novel multifunctional NPs that can target tumor cells with more accuracy and specificity. As a result, commercialization of nanoparticle-based therapeutics is increasing considerably, with a rising in the number of available products on the market [4]. Nanomaterials that are used in medicine are including polymer carriers [hydrogels, polymersomes, dendrimers, and nanofibers] [11–23]; lipid-based vehicles [liposomes, solid lipid nanoparticles, and micelles] [24–26]; metallic nanoparticles [gold, silver, and titanium] [27–30]; carbon structures [nanotubes, nanohorns, nanodiamonds [NDs], and graphene] [31–41]; and inorganic particles [silica] [42–45].

Highlighting attributes such as adaptable surface chemistry, the ratio of nanoparticles surface area-to-volume and the ability to cofunctionalize nanoparticles, could competent nanomaterials for drug binding and high drug-loading capacities. Considerably, these features provide the possibilities for synthesis multimodal complexes for destroying cancer tumor cells enhancement, detection and elimination of cancer cells before they form tumors and highly sensitive imaging capabilities. One of the most important advantages of use of these nanoparticles is the possibility of reducing side effects as well as minimal damage to healthy tissue and organs compared with conventional cancer therapeutic drugs [46–47]. Some physicochemical features of available potentially potent therapeutic agents [both biopharmaceutical and small molecule drug related] such as large size, highly charged, too unstable metabolism and high insolubility, necessitate assistance of delivery vehicles to reach cancer target cells [48] [Table 1].

1.2. Cancer therapy and diagnosis

In spite of a huge number of researches about nanomedicine, unmet medical demands in cancer diagnosis and therapy remain substantial. Advanced multimodal imaging capabilities ensure diagnosis of disease in early stages, real-time monitoring and discernment of its response to the treatment regimen. David R J Snead and his colleagues provide statistical evidence to demonstrate that digital pathology has advantages over glass slid microscopy for the diagnosis of histopathology [49]. Recent studies have also examined how the innate features of different types of nanomaterials in combination with induce biological responses and signals can be used to get tumors constricted [50–51]. Nanomedicine, however, will have the greatest impact when administered in combination with traditional therapies, such as radiation and cell therapy. Recent studies in animals suggest that timed combination therapy in a research where a siRNA and a drug are released sequentially from liposomal nanoparticles could be the key to overcome chemoresistance [52]. In order to reduce cancer drug resistance, combination chemotherapy has long been applied as a primary cancer treatment regimen. Adapting multiple drugs with various molecular targets increase the genetic obstacles to frustrate mutated cancer cells, thereby delaying the cancer adaptation process. Furthermore, it has also been illustrated that multiple drugs targeting in the same cellular pathways could function synergistically in order to higher therapeutic efficacy and higher target selectivity [53].

The diagnosis and therapy approaches in some cancers, such as pancreatic and brain cancers, increase the use of nanoparticles potentially for some reasons including the position of the tumor nearing the

Table 1
Different types of nanodevices are used in clinical application.

Modality	Potential applications
Cantilevers	• High-throughput screening • Disease protein biomarker detection • DNA mutation detection [SNPs] • Gene expression detection
Carbon nanotubes	• DNA mutation detection • Disease protein biomarker detection
Dendrimers	• Image contrast agents
Nanocrystals	• Improved formulation for poorly soluble drugs
Nanoparticles	• Targeted drug delivery, permeation enhancers • MRI and ultrasound image contrast agents • Reports of apoptosis, angiogenesis, etc.
Nanoshells	• Tumor-specific imaging
Nanowires	• High-throughput screening • Disease protein biomarker detection • DNA mutation Detection [SNPs] • Gene expression detection
Quantum dots	• Optical detection of genes and proteins in animals and cell assays • Tumor and lymph node visualization