Vol 5|Issue 3| 2015 |238-242.

International Journal
of
Pharmacy Review & Research
www.ijprr.com

e-ISSN: 2248 – 9207
Print ISSN: 2248 – 9193

NANOPARTICLES AS APPROACHING TARGET FOR CANCER THERAPY AND THEIR PROMISES & PRECINCTS

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ABSTRACT

The present review provides an idea about the importance of application of nanoparticles in treating cancer and also shows the promises that a targeted nanoparticle can do and the limitations of these nanoparticles based on the so far applications in the medical field and the contribution that has to be done to improve the new formulation methods or new type of targeted nanoparticles like multifunctional targeted nanoparticles.

Key words: Nanoparticle, Cancer therapy, Multifunctional targeted nanoparticles.

INTRODUCTION

This review provides an idea about the nanoparticles as potential targeting agents for cancer therapy. The present focus is on the nanoparticles which makes them as an excellent candidate for their use in the medical field. Nano particles for anti-cancer drug delivery had reached the first clinical trial in mid1980's and the first Nano particle that has entered the market was doxorubicin encapsulated along with liposome in the year 1995.

Though nanotechnology is not a new concept it has gained the significant importance in recent years regarding the treatment of many dreadful diseases like "cancer". The drug delivery systems that were developed by using this technology are named with the prefix "nano" that means "one-billionth" of a meter [1].

This nanotechnology deals with the production of designed very small/ultra particles that are called as nano particles size range starts from 1nm-100nm that has a great extended use in pharmaceutical, chemical, agricultural and medical fields [2]. Due to the unique and novel properties of nanoparticles they were further divided in to two types based on their diameter and size like fine particles and ultra fine particles. Size ranges from 100-250nm and 1-100nm respectively [3, 4].

As the nanoparticles holds the most significant promises in the health sector they holds the interest of scientific research in the present era which presents the emerging trends of nanoparticles in drug delivery systems that can treat cancer [5,6].

The uncontrolled growth and spread of abnormal cells is characterized as the disease cancer. The common available conventional therapies for treating cancer are chemo therapy, radiation, surgery, and hormone therapies that has several limitations. To overcome the limitations caused by the conventional therapies nanoparticles are considered as the prospective agents for cancer therapy [7].

Delivering the therapeutic amalgam to the target site is a foremost problem in treatment of cancer. The conventional application of drugs has limited effectiveness, poor biodistribution, and lack of selectivity. Those limitations and drawbacks can be triumph over by controlled drug delivery. In controlled drug delivery systems (DDS) the drug is transported to the site of action, by which the undesirable side effects are minimized. In addition, controlled drug delivery system stops the rapid drug degradation, that improves the drug concentration at the target site and this shows the most potential effect of drug at low doses only [8].

Characteristic features of nanoparticles

The characteristic features of nanoparticles that made them to stand unique among all the drug delivery systems are ability of detecting the cells that could be proned easily to cancer and plays a major role in carrying and can transports the energy and oxygen to cells, and promotes the revitalization (growth of new skin cells). The most exclusive property of nanoparticles is that they can

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change their shape which is more helpful in detecting the malignant tumors in breast cancer cases and destroys the cancer cells without causing any harm to the rest of the normal cells of the body [9].

Cell-specific targeting nature of nanoparticles can be achieved by attaching drugs to individually designed carriers. Recent development in nanotechnology has shown that nanoparticles (size ranging from 1-100 nanometers) are impending as drug carriers. Due to their smaller size, the nanostructures have show evidence of unique physicochemical and biological properties that make them as a complimentary material for biomedical application [10]. Nano carriers that have been tested so far the drug delivery are Liposomes, solid lipids nanoparticles, dendrimers, polymers, silicon or carbon materials, and magnetic nanoparticles.

Methods of preparing nanoparticles

The synthesis of nanoparticles was based on the physic chemical characteristic features of the selected loading drug and the polymer that is going to be used in the synthesis of nanoparticles [11-13].

The following are the some of the generally used preparation methods for nanoparticles:

- Emulsion solvent evaporation method
- Double emulsion and evaporation method
- Salting out method
- Emulsion diffusion method
- Solvent displacement / Precipitation method.

The common and general factors that were affecting these methods were the rate of stirring, temperature, viscosity of the phases (either oil/water or both), the concentrations of dispersing and stabilizing agents added.

Characterization methods of nanoparticles

The general characterization methods of nanoparticles that were used to estimate the characters of nanoparticles are

- Particle size
- Dynamic light scattering(DLS)
- Scanning electron microscopy (SEM)
- Transmission electron microscopy (TEM)
- Atomic force microscopy (AFM)
- Surface charge
- Surface hydrophobicity
- Drug release

These were the some of the important characterizing tools of nanoparticles by which the characteristic features of nanoparticles are determined [14, 15].

Nanoparticles for targeted drug delivery

A key area in treating cancer is drug delivery system. That is used to deliver the drug to the specific site where it is needed. The Drug targeting systems should be able to control the fate of a drug entering the body. Present drug delivery technologies are far away from the design of the so called “magic bullet”, that was proposed at the beginning of the 20th century by Paul Ehrlich, in which the drug is exactly under fire to the exact site of action. Nanotechnology offers another confronts to come to conventional methods of drug delivery systems to distribute the drug in the right place at the right time**.** Nanotechnology is estimated to bring a deep-seated change in development in the next few years and will have a gigantic blow on Life Sciences, including drug delivery, diagnostics, nutriceuticals and the production of biomaterials [16].

Therefore, the most considerable aspects of nanoparticles drug delivery are:

- The exact targeting of the tissue of choice with nanoparticles (appropriate size and fictionalizations with antibodies-or by means of selective binding-that provides enhanced drug delivery and reduced nonspecific toxicity); and
- The timed release of the drug (to prevent nonspecific cell toxicity, and must remain encapsulated until the particle binds to the target) [17].

Promises of targeted Nanoparticles for cancer therapy

Using of nanoparticles to deliver the chemotherapeutic agent in cancer therapy offer many advantages to improve the drug delivery and to beat many problems associated with conventional therapy [18-20]. For eg: if nanoparticles are delivered by either passive or active targeting they have been shown the enhanced intracellular concentration of drugs in cancer (tumor) cells while toxicity is avoided in normal cells. In addition to this the targeted nanoparticles are designed as either pH-sensitive / temperature-sensitive carriers. The pH-sensitive nanoparticles are capable of releasing drugs in the more acidic environment of cancer cells. The temperature-sensitive nanoparticles are capable of releasing drugs with changes in temperature locally in the tumor region provided by sources such as magnetic fields, ultrasound waves, and so on where the combined therapies like chemotherapy or hyperthermia can be applied. The targeting of nanoparticles to tumors via cancer-specific moieties has been shown to have the effects of composition, size, and molecular mass of nanoparticles on their effectiveness. Targeted nanoparticles can be further tailored to trim down toxicity [21].

Limitations of targeted nanoparticles for cancer therapy

Although targeted nanoparticles have developed as a strategy to overcome the lack of specificity of conventional therapy, there are also potential risks and challenges associated with this novel strategy. For example, some cancer cells may develop drug resistance over the course of drug treatment, thereby depiction of drugs released from the targeted nanoparticles to be unpromising. Similar to other newest technologies, targeted nanoparticles for cancer therapy also visage many challenges. One of the challenges of targeted nanoparticles is that, change in the stability, solubility, and pharmacokinetic properties of the carried drugs. But still, these aspects are not broadly investigated. Factors like aggregation, shelf life, leakage, and toxicity of materials

used to prepare nanoparticles are the other boundaries for their use. Some materials that are used to prepare nanoparticles such aspoly (lactic-co-glycolic acid**)** (PLGA) have low toxicity, but it degrades quickly and don't circulate in tissues for a long period enough for sustained drug delivery. On the further hand over other materials such as carbon nanotubes and quantum dots are long-lasting and can stick with in the body for weeks, months, or even years, making them potentially noxious and limiting their use for repetitive treatments [22]. New materials to make targeted nanoparticles such as silicon/silica (solid, porous, and hollow silicon nanoparticles) have been developed; though, their use for drug delivery to cancer patients has taken off at a snail's pace due to the prospective health risks coupled with introducing new materials in the human body. Besides mounting new materials and selecting suitable materials for apiece of specific treatment, further factors need to be optimally chosen to propose better targeted nanoparticle [23-25]. The common factors like particles size, shape, sedimentation, drug encapsulation efficacy, desired drug release profiles, distribution in the body, Circulation, and cost plays the major role in treatment, and most of these nanoparticles may last part up in the liver and spleen, thus the use of targeted nanoparticles is impractical and futile [26,27].

In spite of widespread research efforts to develop new targeted nanoparticles, only a few of them are in clinical use those are permitted by FDA. The major account for the slow development of effective targeted nanoparticles is due to the lack of familiarity about the distribution and location of targeted nanoparticles after either oral administration or injection. Most of the studies have not examined the targeting efficiency of nanoparticles real time *in vivo*, thus precise bio-distribution and subsequently therapeutic effects are not well-known. Consequently, detecting cancer (malignant) cells in the body and monitoring treatment effects on these cells in real time is another challenge looked-for to be triumph over to widen efficient targeted nanoparticles [28, 29].

Table 1. Types of nanoparticles with size range

Name of the Nanocarrier	Size range (nm)
Liposomes	80-300nm
Solid lipids nanoparticles	80-300nm
Dendrimers	01-10nm
Polymers	10-100nm
Carbon materials	01-05nm(diameter)
Magnetic nanoparticles	10-100nm

Fig 1. Normal cell

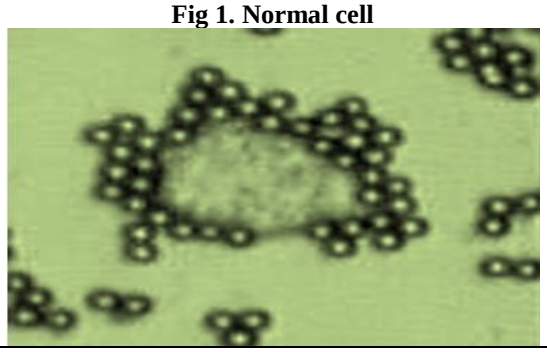


Fig 2. cancer cell

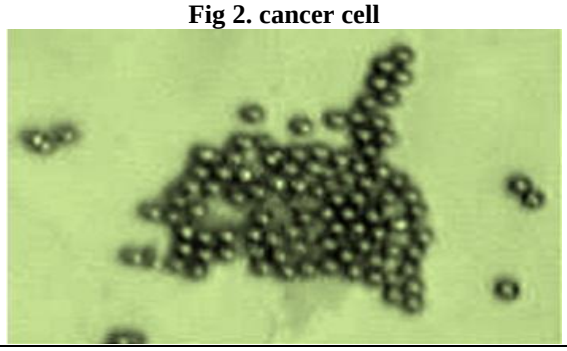
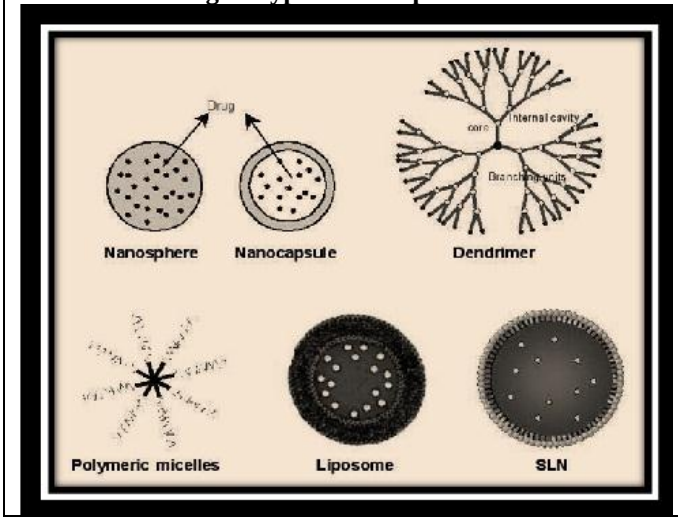
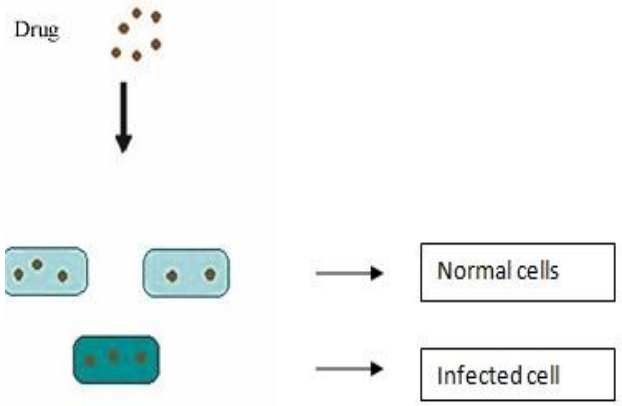


Fig 3. Types of nanoparticles



Conventional therapy Fig 4. Showing the conventional therapy showing the drug acting on both infected and normal cells



Targeted therapy

Fig 5. Showing the targeted therapy showing the drug acting only on infected cells

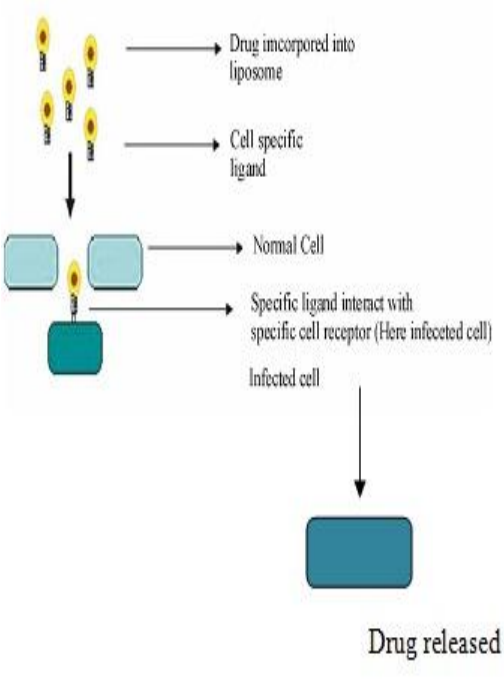
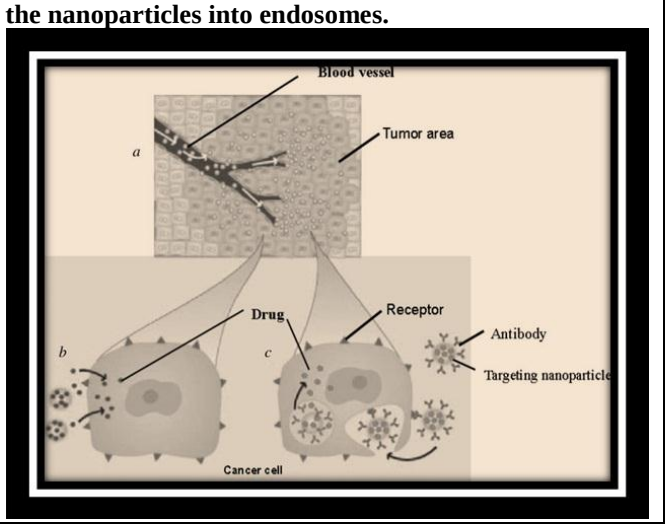


Fig 6 (a)Nanoparticles containing an anticancer drug in vascular endothelial cells and accumulate in tumor tissue, but not in normal tissue. (b) Drug is released from the nanoparticles in tumor cells and taken up into the cells. (c) Ligand-targeted nanoparticles containing anticancer drugs, or nucleic acid-based therapeutics such as plasmid DNA or antisense oligonucleotides, bind to cell surface receptors, which trigger internalization of the nanoparticles into endosomes.



CONCLUSION

However, the targeted nanoparticles have provided a successful platform for a better and more specific delivery of cancer therapeutics. With our care, desire, and hard work with the patient's benefits in mind to identify both risks and benefits of targeted nanoparticles for cancer therapy, multifunctional targeted nanoparticles can sooner or later be designed. The task and extent of targeted nanoparticles for drug delivery in cancer therapy is mounting, and the progress of successful multifunctional targeted nanoparticles will not be far-off in the prospect.

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