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REVIEW ON: NANOMEDICINE USED IN CANCER

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ABSTRACT

Nanomedicine offers a promising alternative approach for cancer treatment by enabling precise targeting at the molecular level. Due to their nanoscale size, nanomedicine can achieve site-specific drug delivery, enhancing bioavailability while minimizing systemic toxicity. This targeted approach also reduces the required drug dosages, thereby lowering treatment costs. Advances in nanotechnology have facilitated the design of diverse nanocarrier, including organic, lipid-based, inorganic, protein, and polymeric nanoparticles. These system support both active and passive targeting strategies, improving therapeutic efficiency compared to conventional chemotherapeutic agents. Notably, gold nano shells and other engineered nanostructure have demonstrated significant potential in enhancing drug stability, controlling releases rates, and promoting selective accumulation with in tumor tissues. Overall, nanomedicine represents a rapidly evolving field with the potential to revolution oncology by enabling safer, more effective, and personalized cancer therapies.

KEYWORDS: Nanomedicine; active targeting; passive targeting; nanomaterial; nano shells.

INTRODUCTION

The word “nano” has become extremely popular not only in the scientific community but also among the general public. The use of “nano” suggests objective way and subjective feeling of renewing existing things more innovative and/or opening up new possibilities.

Academia and industries have achieved remarkable progress through nanotechnology; in pharmaceutics and pharmacology, the generic property suggested by “nano”, innovation, have provoked significant anticipation in nanomedicine for cancer treatment.[1]

Looking back on the past 30 years, the overall clinical outcomes of cancer nanomedicine are, however, suboptimal, thus raising questions about reasons for their under performance and true prescriptions for better cancer nanomedicine.

In this short review, a concise summary of cancer nanomedicine from both retrospective and prospective views is provided. Herein, the prototypes of nanomedicine described are limited to intravenously administered therapeutic (not diagnostic) nanoparticles, such as polymer-drug conjugates (hereafter referred to as nanoconjugates), liposomes, polymeric micelles, and protein-based nanoparticles, because of the breadth of preclinical and clinical cases available to guide potential future directions.[3]

History of Nanomedicine

Nanomedicine is a young science. How nanotechnology can be of use to medicine, medical technology and pharmacology has only been researched since the 1990s.[6]

Nanotechnology itself has only existed for a few decades. After the invention of high resolution microscopy it evolved simultaneously in biology, physics and chemistry in the course of the 20th century and spawned new disciplines such as microelectronics, biochemistry and molecular biology.

For nanomedicine, nanobiotechnology knowledge which investigates the structure and function of cells as well as intra- and intercellular processes and cell communication is of prime importance. This research only became possible at the beginning of the 20th century when the door to the nano cosmos was burst open with the invention of innovative microscopes.

The mechanisms of maintaining and regulating metabolism, the role of enzymes and proteins and the functioning of the immune system were also researched and effective vaccines developed. The description and understanding of DNA and RNA in the 1950s and 1960s. led to the concept of genetic diseases and to the vision of cures at the molecular level tailor-made for patients.[5,6]

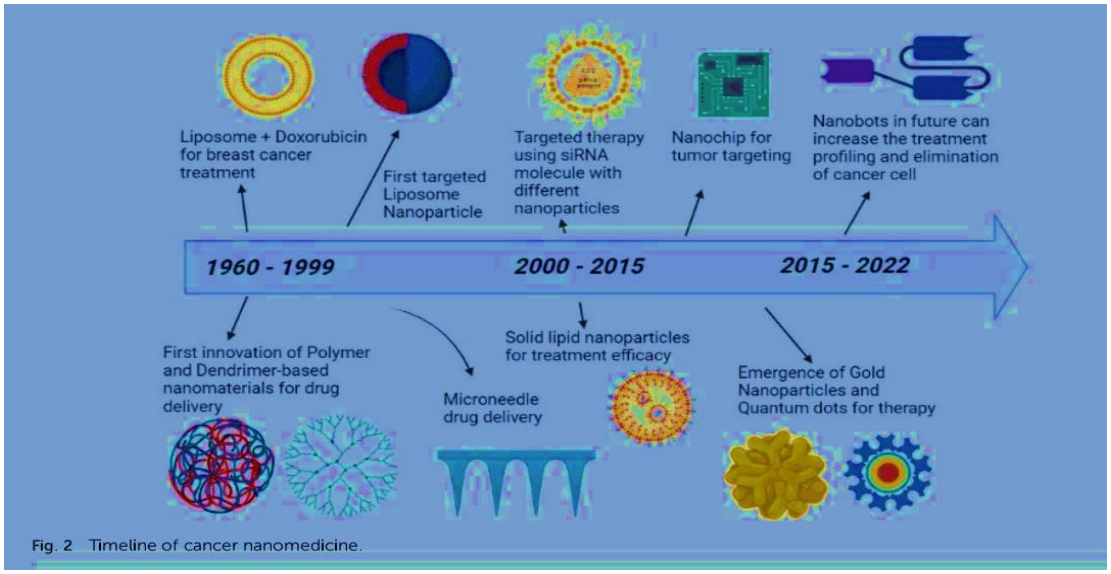

Figure: treatment of cancer.

Possible Uses of Nanomedicine

The possible uses of nanotechnology in medicine are based on three pillars.

1. nanomaterials and nano instruments which can be used as biosensors, as aids in treatment and as transporters of active substances,
2. knowledge of molecular medicine in the fields of genetics, proteomics and synthetically produced or modified microorganisms.
3. nanotechnologies which can be used for rapid diagnosis and for therapy, for repair of genetic material for cell surgery.
4. Improve wound dressing and coating of implants to prevent infection.
5. Nano based treatment increases survival by minimizing damage to normal cell and overcoming drug resistance in tumours.[2]

What is cancer

Cancer is a group of diseases characterized by the uncontrolled growth and division of abnormal cells, which can invade nearby tissues and spread to distant parts of the body through metastasis.

Cancer is currently among one of the leading causes of deaths worldwide, with 1,688,780 new cases and 600,920 cancer deaths projected for 2017. Over the next 20 years, the number of new cases is projected to increase by about 70%.[1]

Current treatments may include chemotherapy, radiation, and surgery, but the effects of these procedures may damage not only the tumour tissue but also normal tissue.

Even in the absence of injury or development, cancer cells can maintain growth signals and continue proliferation. Normal regulators of cell growth and apoptosis Cancer cells can also migrate to new sites and form new, secondary tumours.[2]

Nanoparticles

In nanomedicine, nanoparticles are engineered at the nanoscale to act as sophisticated tools for disease diagnosis, treatment, and prevention.

The development of better and safer medications, tissue-focused activities, and personalised nanomedicine.[3]

Types of Nanoparticle (nanomedicine)

1. Protein‑drug conjugated nanoparticles
2. Liposomal nanoparticles
3. Polymeric nanoparticles
4. Other nanoparticle platform

1. Protein‑drug conjugated nanoparticles

Protein-drug conjugated nanoparticles consist of proteins directly conjugated to drug molecules. The link between the protein and the drug is typically biodegradable upon arrival in the cell. This can lead to premature release of the drug, as the biodegradable linker is readily destroyed by proteases and redox altering agents found in blood.

Recent platforms, such as protein-drug conjugated systems with linkers that stay in place until the nanoparticles reach the target site, have overcome this barrier. This system allows more precise and controllable delivery of the cytotoxic drug molecules, lessening the toxic effects of the treatment on the body.[4]

Protein drug conjugated nanoparticles are typically very small (10 nm), allowing the nanoparticle to have a long half life in vivo and thus facilitating its delivery to the target tumour site.[4]

More recently, antibody proteins have been added to protein-drug conjugated nanoparticles, improving their targeting ability. An inherent issue with protein-based nanoparticles is that the structural sensitivity of some drugs makes them difficult to attach to a protein base. Therefore, certain drugs may not be suitable for this nanoparticle delivery system.[7]

2. Liposomal Nanoparticles

Liposome-based nanoparticles are spherical nanoparticles created via the use of lipid bilayers. These nanoparticles are created immediately when an amphiphilic lipid is added to water or other hydrophilic liquids, yielding spheres roughly between 50 and 500 nm. This procedure allows for the encapsulation of hydrophilic drug molecules by simply dissolving the drug in the liquid used for formation of the nanoparticles.[10]

Hydrophobic and amphiphilic drugs can be encapsulated by direct addition to the lipid solution before formation of the nanoparticles, leading to a layer of drug molecules between the lipid bilayer. Common lab methods used to create liposomal nanoparticles include sonication, extrusion, reverse phase evaporation, and solvent injection.

the liposomal nanoparticle can either fuse with the cell membrane or lyse once combined with harsh environments inside the cell, releasing the drug inside the cell. Hydrophobic and amphiphilic drug molecules can be kept inside of the liposomal nanoparticle via the creation of a polymeric encasement around the lipid bilayer. Depending on the polymer used, the ability of the nanoparticle to easily fuse with the target cell.[10]

3. Polymeric nanoparticles

Polymeric nanoparticles are comprised of synthetic polymers, allowing customization of many key properties, such as molecular weight, biodegradability, and hydrophobicity.

The synthesis of polymeric nanoparticles has also been well studied. A variety of methods have been designed to efficiently encapsulate drug molecules. Some examples of these methods include nanoprecipitation, electrospray, and emulsification.

Polymeric nanoparticles are typically composed of dense matrices with well known degradation curves, making the drug release of these nanoparticles easier to manipulate in comparison to many other nanoparticle drug delivery systems.[13]

Issues using polymeric nanoparticles include limited shape and wide size distribution. Polymeric nanoparticles are typically spherical, while a wide variety of different sizes may be generated during synthesis. New techniques are currently being investigated to resolve these issues. The most recent approach is **particle replication in nonwetting templates (PRINT).** PRINT allows for the creation of uniform polymeric nanoparticles, allowing the customization of properties such as shape and size.[12]

4. Other nanoparticle Platforms

• One well-characterized example of inorganic, metallic nanoparticles is gold. Gold has been widely used for both detection and direct cancer therapy with and without drug loading. The strong optical absorbance of gold allows it to be used for detection, while its photothermal properties make it suitable as an anticancer therapy. for example, on the tumours to heat the gold nanoparticles when they are near the tumour site can increase effective drug loading while minimizing non specific toxicity.[9]

• Carbon nanotubes have also been analyzed for cancer treatment. These structures can bind to materials and enter cells via endocytosis. **Single walled carbon nanotubes (SWCNTs)** form highly stable suspensions in physiological buffers, making them suitable for use in biological environments. Carbon nanotubes can also be used to image cancer growth via resonance-enhanced Raman signatures.[10]

• A third type of nanoparticle with cancer treatment potential are silver nanoparticles. While the exact mechanism of action of silver nanoparticles in cancer remains unclear, silver reacts with the acidic environment that is often found in cancer cells to create reactive oxygen species.[19]

• Although there are multiple types of nanoparticles that can be created for cancer treatment, many of the treatments currently undergoing clinical trials are of the same nano platforms mainly liposomal and to a lesser extent polymeric nanoparticles.[18]

How nanomedicine target cancer

1) Passive targeting

Most nanocarrier-based cancer cures are passively targeted first-generation nanomedicines. First generation nanomedicine drugs rely primarily on manipulating the pharmacokinetics and biodistribution by regulating physicochemical properties.[5]

Examples of first-generation drugs based on inactive targeting are pegylated liposomal doxorubicin and nab-paclitaxel. Cancers' pathophysiological features and their surroundings have been used for inactive targeting, particularly where the accumulation of nanomedicine in cancer cells is further promoted by the EPR effect.

Therefore, through diffusion and convection, nanomedicine treatments from passive targeting into neoplasms can occur without the attachment of a particular substance to the nanocarrier surface. Nevertheless, it has been widely accepted that EPR effect-based passive targeting is insufficient to control cytotoxic drug side effects, and there are greater benefits using directed delivery.[4,5]

2) Active targeting

In active targeting, a high-affinity substance attaches to the nanocarrier surface. The ligand selectively binds to the target cell receptor.

A wide ligand range, such as carbohydrates and folic acid, or macromolecules, such as amides, proteins, oligonucleotides, and aptamers, has been utilized for this purpose, which includes small particles of substances. The preferred ligand binds to a targeted cell while minimizing binding to healthy cells.[4]

Mechanism of targeting by nanodrug vehicles

A very important criterion for the selection of a nanomedicine formulation for cancer therapy would be its efficiency in targeting the cancer tissue in a specific manner and having minimal side effects on the normal tissue.

The various nano formulations used to deliver anticancer drugs to tumour sites use varying targeting mechanisms for this purpose.[21]

The mechanism of drug delivery and the advantages of nanocarriers will vary by carrier. Nanocarriers directly deliver therapeutic agents to the bloodstream and reach the targeted area.

They then induce DNA damage by reactive oxygen species (ROS) overproduction. This may finally lead to apoptosis and cell death.[4]

Two major types of targeting methods are used for nano based drug delivery: passive and active

- **In passive** method the properties of the tumour site are used to concentrate the nano-vehicles to the tumour site. The major factors used for this are Enhanced Permeability and Retention (EPR) and Tumour Micro Environment (TME) properties.

Unlike normal cells, tumour cells induce neovascularisation due to high proliferation and large pores in the vascular walls that favor passive targeting.40 Due to imperfect angiogenesis, particles can reach the tumour site and accumulate. Poor lymphatic drainage also increases particle retention resulting in EPR on tumours. Fig.no.1.

However, the high interstitialuid pressure inside the tumour microenvironment reduces the uptake and homogeneous distribution of nanoparticles.[4]

- **In Active** targeting also utilizes the properties of the tumour cells such as the cell surface receptors expressed by the cancer cells. However, the targeting is achieved by the use of various molecules hybridized along with the carrier to specifically target these.

Here, we look into the different modes of targeting used by the various nano-formulations and some of their advantages as well as disadvantages. Fig.no.2.

In general, passive targeting is based on the diffusion mechanism and it is affected by various factors such as size, shape, and surface properties. It is noted that high bioavailability and reduced renal clearance can be achieved with 40 to400 nm by increasing the circulation time.

Likewise, maintaining the particle size between 50 to 200 and with a rigid and spherical appearance improves the circulation time and also reduces kidney clearance.[5]

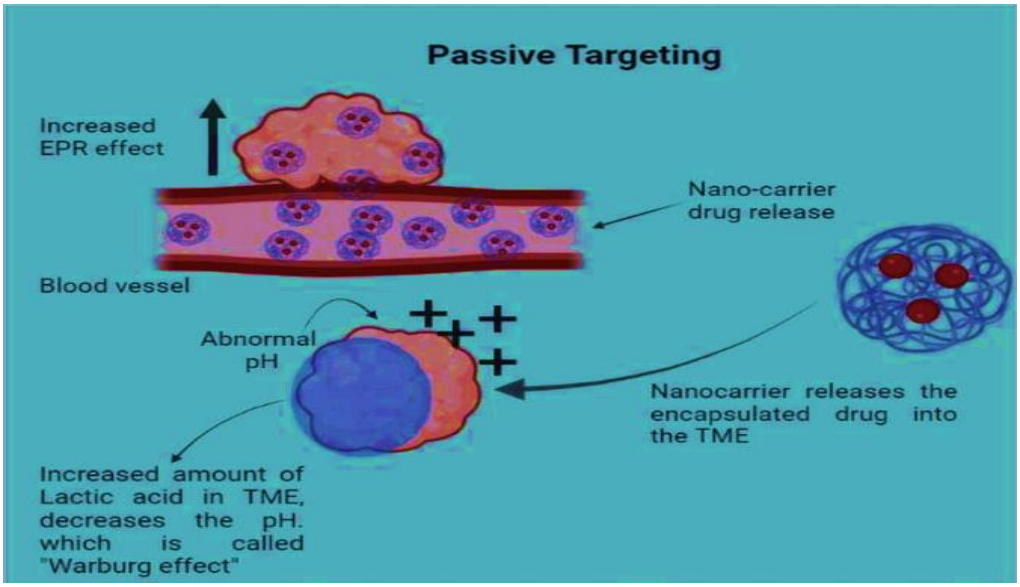

Fig. no. 1 Passive Targeting.

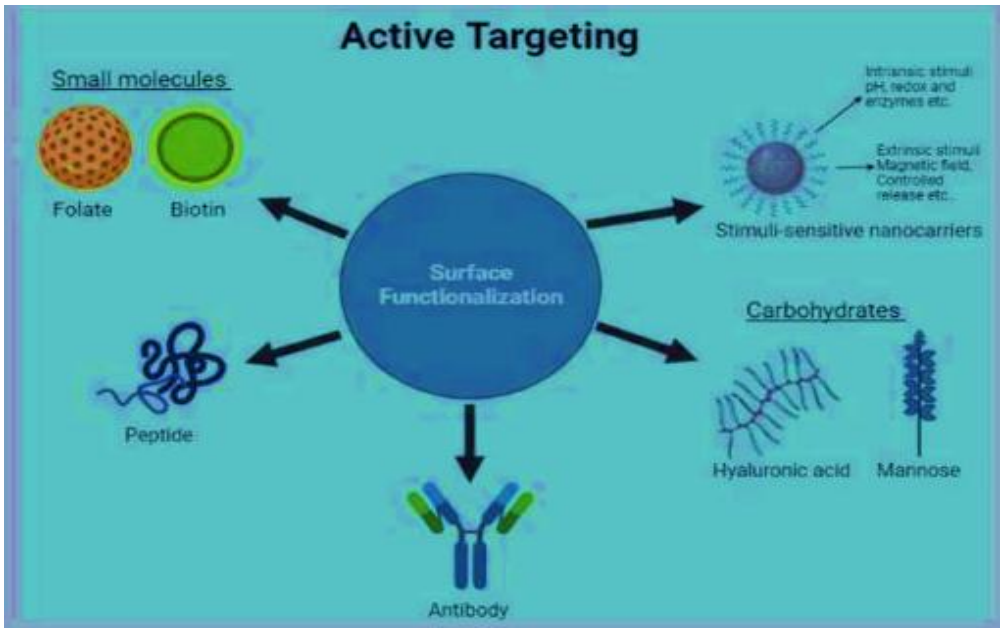

Fig. no. 2. Active Targeting.

Future Development of Nanomedicine

In the coming decade nanotechnology and nanobiotechnology applications will gain importance in medicine and medical technology. This trend is already clearly detectable at present: For the first half of this decade (2010-2014) the Web of Knowledge records the titles of 3,438 publications under the key word “nanomedicine”.[9]

Nanomedicine has the potential to significantly improve the quality of life of patients. Nevertheless, the new possibilities also involve risks and raise sociological and ethical questions which must be analyzed and debated.[9]

The nano therapy vision of the future is treatment of patients with individually tailor-made medicines (“personalized medicine”) at the molecular level as soon as the disease is in the development stage.

The preparation of nanodrugs and the various methods of targeted transport of active substances (drug delivery) will play a prominent role here. With these it could become possible to develop effective and well-tolerated treatments for hitherto incurable diseases.[20] Nanotechnologies provide methods by which biological information can be acquired easily, quickly and inexpensively and analyzed, and thus enormously increase the possibilities of preventive medicine.[21]

Future advancements in nanomedicine are expected to significantly improve cancer diagnosis and treatment by making therapies more targeted, effective, and less toxic. Smart nanoparticles are being developed for precise drug delivery directly to tumors, reducing damage to healthy tissues. Nano-diagnostics such as quantum dots and biosensors will enable early detection and real-time monitoring of cancer. nanoparticles combining imaging and therapy, along with nano-based immunotherapy and gene delivery systems, will lead to more personalized treatment approaches.

Overall, nanomedicine holds great promise for enhancing survival rates and transforming cancer care in the future.

CONCLUSION

Nanomedicine represents a transformative approach in cancer treatment, offering precise targeting of tumour cell with minimal impact on healthy tissues. The Reduces toxicity, and enable controlled and site-specific delivery. various nanoparticle system such as liposomes, polymeric nanoparticles, protein drug conjugates, and metallic nanoparticles have demonstrated potential for improve therapeutic outcome through both passive and active targeting mechanisms.

While nanomedicine hold great promise for, advancing personalized and cost effective cancer therapy, challenges remain in optimizing safety, scalability, and clinical translation. Continued research and innovation are essential to overcome these limitation and fully realize nanomedicine’s potential as a next generation solution for effective and less invasive cancer treatment.

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