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A REVIEW-NANOPARTICULATE ANTICANCER TARGETED DRUG DELIVERY SYSTEM

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ABSTRACT

Nanoparticles have critical advantage in the treatment of cancer and the inherent leaky vasculature present serving cancerous tissues. The strategy for targeting the tumor vasculature can allow targeted delivery to a wide range of tumor types. Hence considering the importance of treating cancer, an attempt will be made to target and deliver an anti-cancer drug to these cancerous cells so as to minimize adverse effects, dose and also dosing frequency. This is achieved by formulating anticancer drugs in the form of nanoparticles. The importance and necessity of nano based formulation was discussed with the help of giving present situation in cancer world, their study based review on the basis of scientific data and patent across different countries. The present review gives an idea about formulation development for specific tumour targeting of cells causing cervical cancer, their method of preparation and characterization study.

KEY-WORD: Lipid Nanosphere, Formulation Optimization, Characterization.

INTRODUCTION

The present scenario for cancer population has been getting worse day by day and there are 25% of population death in United States due to cause of cancer. Cancer not only affects and targets the surface also can affect any part of the body. So many types and their adverse effects exists with the cause of cancer thats why it is a leading cause of death worldwide. Estimated survey suggests that 12 millions of population has death reason of cancer. Nearly

70% of all cancer deaths are occurring from low and middle income countries and it will continue to rise as per projection hence it is much need to treat and formulate nano medicines to target cancerous cells in its early stage to avoid more number of future deaths. Treatment of cancer includes chemotherapy, radiation therapy, gene therapy, photodynamic therapy, biologic therapy, surgical removal of tumor cells, etc. Chemotherapy is the most convenient and non-expensive when compared to other modes of treatment. Varieties of anticancer drugs are available in the market and some of them are under clinical trials. The main problem with anti-cancer drugs is that they not only affect the cancerous cells but also affect the normal cells. These happen due to non-specific targeting to cancerous cells and hence other normal cells get affected. Recently, drug targeting especially targeting of drugs by nanoparticles have been getting much attention by the researchers for treating cancer. Tremendous opportunities exist for using nanoparticles as controlled drug delivery systems for cancer treatment. Natural and synthetic polymers including albumin, fibrinogen, alginate, chitosan, and collagen have been used for the fabrication of nanoparticles. [1-3]

Nanotechnology has capability and effectiveness for changing the way cancer is diagnosed, imaged and treated. There is a lot of research going on to design novel nano formulations capable of detecting cancer in its early stage, targeting the tumour site within the body and delivering anticancer drugs specifically to malignant cells. Nanoparticulate formulations smaller than 50 nanometers can easily enter most cells, while those smaller than 20 nanometers can transit out of blood vessels. They are already proving that they can deliver therapeutic agents to target cells, or even within specific organelles. Despite their small size, nanoparticles are capable of holding tens of thousands of small molecules, such as a contrast agent or drug. The major areas in which Nanoparticulate formulations are developed in cancer are for developing nano medicines to deliver cancer prevention agents and designing multicomponent anticancer vaccines. Also designing targeted contrast agents that improve the resolution of cancer to a single cell and to create the therapeutic devices that can control the release of cancer fighting drugs and optimally deliver medications. [4]

Advantages of Nanoparticulate Drug Delivery System

- Nano particulate systems involve low cost for development of formulation as compared with that for discovery of new molecule.
- Nano medicines with low drug concentration will also target effectively on affected sites. This will minimize the drug use and reduce the effective cost of drug which would give financial relief to the patients.

- Nano particulate Delivery systems increase commercial opportunity by distinguishing a drug from competitive threats and.
- Novel drug delivery with implementation of nano technology methods can be effective and easily available as that of generic composition formulations. It will also releases branded formulation from generic competition.

DRUG DELIVERY SYSTEM

Nanoparticulate DDS (Drug Delivery System) is very effective for providing opportunity to improve both the pharmacokinetic and therapeutic properties of drugs which are given parenterally. It is challenging to develop formulation with anticancer drug. There are much research effort has been spent in the development of new drugs to improve clinical outcomes with minimal toxicity. Its applications in cancer therapy are already confirmed, with several formulations of anticancer drugs in clinical use. Apart from improving the pharmacokinetic and therapeutic profile, DDS can also provide some attractive options to the drugs that have poor physicochemical properties.

Basic laboratory research will be the foundational component of nano based research formulation. This will provide help for institution and opportunities to significantly expand the interactive, peer-reviewed, funded research base. Also useful for the institution to build a stable, competitive research base that is interactive between the basic, clinical, and prevention and control sciences, and that will position the institution to have an impact on reducing the incidence and mortality of cancer through research.

The surface of nanoparticles can be decorated with various molecules in order to avoid being recognized by the immune system, enabling them to reach their target more efficiently. Nanoparticles may be designed to overcome physiological barriers like the blood brain barrier and dermal tight junctions. Due to the leaky constitution of neovasculature in malignant tumors, nanoparticles may penetrate the lesion. Nanoparticles may carry drugs and be designed to release their contents at a site of disease. Nanoparticles may consist of an inorganic core of super paramagnetic materials coated with polymer such as dextran. These particles are used as contrast agents in magnetic resonance imaging for diagnostic applications and therapy monitoring. More specific tissue targeting (“functionalizing”) can be achieved by the conjugation of the nanoparticle with a ligand e.g. monoclonal antibodies. [14]

Nanoparticles for Cervical Cancer Treatment

Chemotherapy is essential for the treatment of a variety of cancers. Although the use of modern anticancer drugs has improved the clinical outcome for patients with a wide range of cancers, the same could not be said for neuroblastoma, which is the most common solid tumor in childhood. This is because this tumor often presents with only few symptoms in the early clinical stages. Furthermore, patients often become refractory to available drugs very quickly. Thus, there is an urgent need for newer agents to develop and to improve the overall survival of these patients. The most useful and common rationale for the use of chemotherapy is to control the growth of tumour cell population by cell-kill mechanism. Possible mechanisms of tumor killing include induction of apoptosis, the mitochondria-mediated apoptotic pathway, and production of reactive oxygen species. It has been estimated that approximately one third of potent anticancer drugs are hydrophobic. A drug administered by either oral or parenteral route is distributed to all the tissues without any selectivity to tumours. This leads to toxic effects of anticancer drugs on rapidly proliferating cells and also on normal cells. Recent research will mainly focus on the delivery of anticancer drugs at the target site (active targeting), thus maximizing the therapeutic efficacy of the drug and reducing its side effects. To achieve active targeting, drug carriers are derivatives with ligands that bind to specific receptors expressed on target tumour cells. The major goal to develop Nanoparticulate drug delivery system against cancer cells. Main formulation approach using Lipid Nanosphere (LN) can be used to achieve targeted delivery of anticancer drugs by suitably modifying the size, charge and specific ligands on the surface attached with tumour-specific ligands to achieve active targeting of drugs to the tumour site. The LN developed can be attached with folate or monoclonal antibody ligands to mediate the targeting process.

- Development of high anticancer drug containing LN using conventional manufacturing methods.
- Developing new ‘LN’ technology based therapy using nanotechnology.
- Maintain the therapeutic drug concentration in the blood for a prolonged period of time.
- Improve bioavailability.
- Improve the efficacy of the drug.
- Reduce the dose related side effects.
- Targeting the drug to the tumor.
- Physicochemical properties of drug.

- Analytical method development for drug moiety.
- Cell line study of drug for cervical cancer treatment.
- Dose and administration.
- Potential of new formulation development of drug.

FORMULATION APPROACHES

Optimization of Process Variables: General Processes in the Preparation of Lipid Nanospheres

The LN will be prepared by High shear homogenization, during homogenization, the fracture of drug particles is brought about by cavitations, high shear forces and the collision of the particles against each other, breaking the microcrystals into nanocrystals. The implosion forces are sufficiently high to break down the drug microparticles into nanoparticles. Additionally, the collision of the particles at high speed helps to achieve nano-sizing of the drug.

Low temperature manufacturing is preferred. The addition of viscosity enhancers is advantageous in certain cases as increasing the viscosity increases the powder density within the dispersion zone (homogenization gap). The high pressure homogenizer can be operated at pressures varying from 100 to 2000 bars. A number of homogenization cycles usually 3, 5 or 10 cycles can be carried out to obtain the nanosized drug. However, the drug should be pre-milled to get the particle size below 25 µm in order to prevent blocking of the homogenization gap.

i) Effect of Homogenization Time on Particle Size
ii) Effect of Ultrasonication Time on Particle Size

Formulation Optimization

In a series of experiments, the optimum formulation composition will be evaluated with respect to type and concentration of primary emulsifier, co-emulsifier and stabilizer in the formulations.

i) Primary Emulsifier Type and Concentration

Various emulsifiers and their combination (Pluronic F 68, F 127) have been used to stabilize the lipid dispersion. The combination of emulsifiers might prevent particle agglomeration more efficiently. E.g (polysorbate 20, polysorbate 60, soy phosphatidylcholine, and sodium taurodeoxycholate)

ii) Co-emulsifier Type and Concentration

Butanol and Sodium monooctylphosphate are co-emulsifiers used for preparation of Lipid nanoparticles.

iii) Stabilizer Concentration

The type and amount of stabilizer has a pronounced effect on the physical stability and in vivo behaviour. Stabilizers that have been used so far are poloxomers, polysorbate, cellulosics, povidones, and lecithins. Lecithin is the stabilizer of choice.

FIGURE PRESENTING PIE-DIAGRAMS OF NANO-BASED PUBLICATION

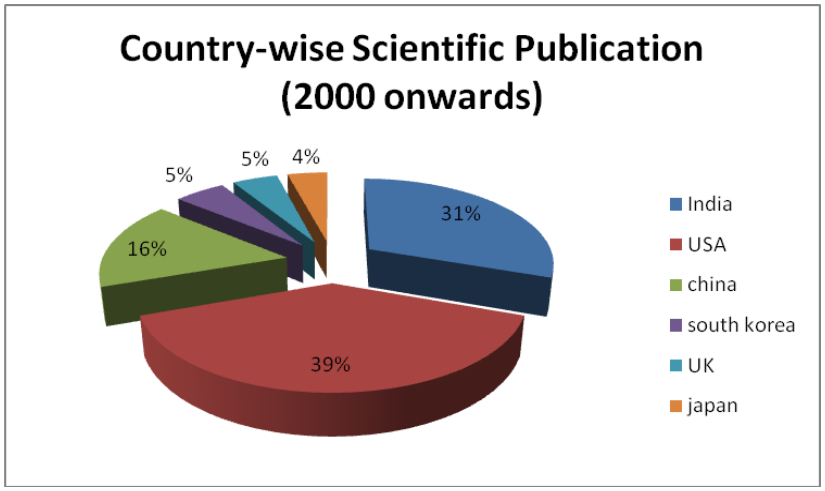

Fig. 1 Nanobased scientific publicaions.

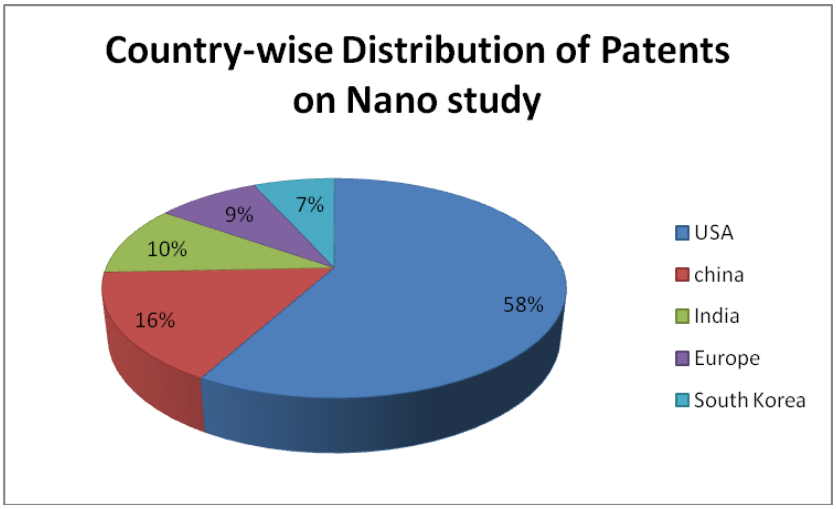

Fig 2: Patent distribution on Nano study.

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