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Solid Lipid nanoparticles as a novel carrier for effective treatment of cancer

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Abstract

Cancer is a class of disorders characterized by abnormal growth of cells that multiply in an uncontrolled way and a major drawback of anticancer drugs is their lack of selectivity for tumor tissue, which causes severe side effects and results in low cure rates. Thus, it is very hard to target the abnormal cells by the conventional method.

The development of engineered nanoparticles with substantial biomedical significance has portrayed new opportunities and challenges for pharmacology and therapeutics. Nanoparticles and their use in drug delivery is a far more effective antitumor strategy than conventional chemotherapy, which is typically limited by the toxicity of drugs to normal tissues, short circulation half-life in plasma, limited aqueous solubility, and non-selectivity restricting therapeutic efficacy.

Solid lipid nanoparticles (SLN) have been proposed as alternative drug carriers. Solid Lipid Nanoparticles consists of a solid lipid matrix, where the drug is normally incorporated, with an average diameter below 1 μm. SLN as colloidal drug carrier combines the advantage of polymeric nanoparticles, fat emulsions and liposome; due to various advantages, including feasibility of incorporation of lipophilic and hydrophilic drugs, improved physical stability, low cost, ease of scale-up, and manufacturing. SLNs are prepared by various advanced techniques. The site specific and sustained release effect of drug can better achieved by using SLNs.

This review provides a thorough update on the development in SLN optimization toward chemotherapy improvement. Nanoparticles have been used extensively for applications in drug discovery, drug delivery, and diagnostics and for many others in medical field. We looked at the usefulness of solid lipid nanoparticles as a tool for cancer therapy.

Keywords: *Cancer, Chemotherapy, Multi drug Resiatance, Drug Delivery System, Nanotechnology, Solid lipid nanoparticles.*

1. Introduction

Cancer is one of the leading causes of death worldwide, second only to heart diseases. Chemotherapy is considered an important treatment modality in cancer and will probably remain so for considerable time. The efficiency of conventional anticancer drugs is hampered by the following limitations: i) drug resistance at the tumour level due to physiological obstacles ii) drug resistance at the cellular level and iii) non-specific distribution, biotransformation and rapid clearance of anticancer drugs in the body (Tiwari and Upadhyay, 2014). Therefore, significant efforts have been made to develop novel targeted delivery systems that can provide higher specificity to cancer cells with no/minimal effect on normal cells (Tiwari and Upadhyay, 2014).

Currently, nanotechnology is developing into a rapidly growing field with applications in health and drug therapy. Nanotechnology has great potential to make an important role in prevention of cancer, its detection, imaging, diagnosis and treatment. Nanoparticles are solid colloidal particles ranging in size from 1 to 1000 nm and composed of macromolecular materials and high surface area (Pragati et al., 2009). The nano-size distribution effect is due to some physical and chemical properties (Yassin et al., 2013). Various types of nano drug delivery systems are nanoparticles, dendrimers, nanotubes, micelles and liposomes. Nanotechnology-based combinational drug delivery systems increase the bioavailability by enhancing permeability, retention and reaching the cancers tissues target site (Kadian, 2018). It helps to conquer the systemic toxicity towards normal tissue and adverse effects which result from conventional cancer therapeutic agents (Parhi et al., 2012).

2. Solid lipid nanoparticles

Solid lipid nanoparticles were defined as oil in water emulsion for parenteral nutrition, but the liquid lipid (oil) of the emulsion has been replaced by a solid lipid *i.e.* yielding solid lipid nanoparticles are solid at room temperature and also at body temperature with mean diameter approximately between 50 and 1000nm. Therefore, the mobility of encapsulated drugs is reduced, which is an essential characteristic for controlled drug release. The drug can either be directly incorporated during polymerization or by adsorption onto preformed nanoparticles (Tiwari et al., 2012). SLNs are a drug delivery system consisting of a drug carrier which helps in increasing bioavailability and reducing erratic absorption.

3. Solid Lipid Nanoparticles Provide the Following Advantages

- Control and target drug release of active drug over a long time period.
- Improves the stability of pharmaceuticals
- Small Size and less toxic
- High and enhanced drug content when compared to other carriers
- Feasibility of carrying both lipophilic and hydrophilic drugs
- Water based technology
- Easy to scale-up and sterilize
- Good biocompatibility
- Avoidance of organic solvents
- Incorporation of drug can reduce distinct side effects of drugs.
- SLNs particularly those in the range of 120-200 nm are not taken up readily by the cells of the reticulo-endothelial system and thus bypass liver and spleen filtration (Mukherjee et al., 2009).

4. Methods of SLN preparation

SLNs are made up of solid lipid, emulsifier and water/solvent. The two phases (lipid and aqueous) should be thoroughly mixed to form one homogenous phase (emulsion) with droplet size in the nano range. Then, the particles are allowed to solidify by cooling or solvent evaporation based on the employed method of preparation. According to the drug solubility, the type of emulsion is determined and accordingly, the emulsifier(s) were chosen. Many types of lipids were used including triglycerides, partial glycerides, fatty acids, steroids and waxes. Various emulsifiers and their combinations have been used to stabilize the lipid dispersion. Combination of emulsifiers might prevent particle agglomeration more efficiently.

There are different methods of SLNs preparation (Ekambaram et al., 2011):

- High pressure homogenization
    1. Hot homogenization
    2. Cold homogenization
- Ultrasonication or high speed homogenization
    1. Probe sonication
    2. Bath sonication
- Micro emulsion based method
- SLN preparation by using super critical fluid
- SLN prepared by solvent emulsification/evaporation
- Double emulsion method
- Spray drying method

5. Role of Solid lipid nanoparticles (SLN) in cancer chemotherapy

The cytotoxicity of many chemotherapeutic agents was compared when loaded in SLN with their conventional therapeutic forms and their in-vitro and in-vivo efficacy have been evaluated. The first in-vivo studies of SLN containing anti cancer compound was carried out by Yang et al. in 1999, they have used a chemically reactive compound Camptothecin which known for its carcinogenic property (Yang et al., 1999). In one study, the cytotoxicity of SLN formulations carrying cholesteryl butyrate, doxorubicin (Dox) or paclitaxel (PTX) were evaluated on the human colorectal cancer cell line HT-28 (Serpe et al., 2004). Methotrexate- loaded SLNs, prepared by coacervation, showed an increased cytotoxicity towards MCF-7 and Mat B-III cell lines compared with free drug (Battaglia et al., 2011). An in vitro study was conducted to determine the effect of solid lipid nanoparticle on the human breast cancer cell lines (MCF-7 and MDA-MB231) (Abbasalipourkabir et al., 2011).

Outcomes of these studies have been shown to improve the efficacy of chemotherapeutic drugs, simultaneously reduction in side effects associated with them. Improved stability of drugs, encapsulation of chemotherapeutic agents of diversified physicochemical properties, enhanced drug efficacy, improved pharmacokinetics and less

in-vitro toxicity are the important features of SLN which make them a suitable carrier for delivering chemotherapeutic drugs. Several obstacles frequently encountered with anticancer compounds, such as normal tissue toxicity, poor specificity and stability and a high incidence of drug resistant tumor cells, are at least partially overcome by delivering them using SLN. The rapid removal of colloidal particles by the macrophages of the RES is a major obstacle to targeting tissues elsewhere in the body, such as bone marrow and solid tumors. The ability of SLN to inhibit the Pgp as a main multidrug resistance in cancer therapy was investigated (Kang et al., 2010).

6. Conclusion

The conventional anticancer strategies of chemotherapy and radiotherapy are highly effective at killing cancer cells, but they lack target specificity and can also kill healthy noncancerous cells, resulting in unwanted side effects, such as nausea and vomiting. Cancer treatment is extremely complicated, thus to overcome the problems with conventional therapy nanotechnology is opening prospective future in pharmaceutics. Nanoparticle is novel approach for drug delivery which we can achieve better therapeutic action, better bioavailability and reduce toxicity.

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