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A Review on Liposome Encapsulated Curcumin for Treatment of Arthritis

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ABSTRACT

The most common treatments for rheumatoid arthritis include nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, disease modifying antirheumatic drugs (DMARDs), and some biological agents. However, none of the treatments available is able to achieve the ultimate goal of treatment, that is, drug-free remission. However, to improve its clinically relevant parameters, nanoformulation of curcumin is emerging as a novel substitute for their superior therapeutic modality. It enhances its aqueous solubility and targeted delivery to the tissue of interest that prompts to enhance the bioavailability, better drug conveyance, and more expeditious treatment.

Keywords: Curcumin, Antirheumatic drugs, Liposome.

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1. INTRODUCTION :

With the passage of time, the curiosity to explore the medicinal benefits of natural habitat is being increased and has now become one of the prime areas of scientific research [1,2] *Curcuma longa* (*Linn.*) commonly kenned as turmeric, belongs to Zingiberaceae family and is widely utilized as an ingredient spice [3,4] The history of *Curcuma longa* (Linn.) dates back over antediluvian time of Ayurveda, commonly found in tropical, sub-tropical and Southeast regions are widely cultivated areas for use as an ingredient spice.

In previous work, we used the NF-B inhibitor Bay11-7082 to inhibit the maturation of DCs (6, 7). After application of NF-B inhibitors, DCs generated from bone marrow or peripheral blood precursors ex vivo expressed fewer CD40 and MHC class II molecules and only weakly stimulated proliferation and IFN- production by T cells [5,6] These DCs, when exposed to Ag and injected into mice, suppressed previously primed immune responses, including full-blown inflammatory arthritis, through the induction of Ag-specific regulatory CD4 T cells (Treg cells). Experiments in knockout mice showed that the RelB subunit of NF-B expressed by DCs controlled the outcome of Ag presentation to T cells and that Ag-specific Treg cells induced by RelBlow DCs produced IL-10 and induced tolerance when transferred from one animal to another[6]

Liposomes are small artificial vesicles of spherical shape that can be created from cholesterol and natural non-toxic phospholipids. Due to their size and hydrophobic and hydrophilic character(besides biocompatibility), liposomes are promising systems for drug delivery. Liposome properties differ considerably with lipid composition, surface charge, size, and the method of preparation. Furthermore, the choice of bilayer components determines the 'rigidity' or 'fluidity' and the charge of the bilayer. For instance, unsaturated phosphatidylcholine species from natural sources (egg or soybean phosphatidylcholine) give much more permeable and less stable bilayers, whereas the saturated phospholipids with long acyl chains (for example, dipalmitoylphos phatidylcholine) form a rigid, rather impermeable bilayer structure.

2. MECHANISM OF LIPOSOME FORMATION:

The basic part of liposome is formed by phospholipids, which are amphiphilic molecules (having a hydrophilic head and hydrophobic tail). The hydrophilic part is mainly phosphoric acid bound to a water soluble molecule, whereas, the hydrophobic part consists of two fatty acid chains with 10 – 24 carbon atoms and 0 – 6 double bonds in each chain[8].

3. COMPONENTS OF LIPOSOME STRUCTURE:

Liposomes are versatile in that the entire membrane of the liposome can be composed of either natural or man-made phospholipids. The properties of the liposomes can be changed entirely depending on the phospholipids used. The basic components of liposomes are phospholipids which are stabilised by cholesterol, with other stabilisers sometimes added to the mixture depending on the specific use of the

liposome. Many different types of lipids and lipid mixtures can be used or mixed-and-matched to obtain a certain type of liposome.[9]

4. LIPOSOMES PREPARATION PROCEDURES

4.1 Classical Technique:

There are four classical methods of liposome manufacture. The difference between the various methods is the way in which lipids are drying down from organic solvents and then redispersed in aqueous media.[10] These steps are performed individually or are mostly combined.

a. Hydration of a Thin Lipid Film:

This is the original method which was initially used for liposomes production.[11] A mixture of phospholipid and cholesterol were dispersed in organic solvent. Then, the organic solvent was removed by means of evaporation (using a Rotary Evaporator at reduced pressure).

b. Detergent Dialysis:

A pilot plant under the trade name of LIPOPREPR II-CIS is available from Diachema, AG, Switzerland. The production capacity at higher lipid concentration (80 mg/ml) is 30 ml liposomes/minute. But when lipid concentration is 10-20 mg/ml then up to many liters of liposomes can be produced. In USA, LIPOPREPR is marketed by Dianorm-Geraete.[12]

c. Microfluidization:

A method based on microfuidization/ microemulsification/homogenization was developed for the preparation of liposomes. MICROFLUIDIZERR is available from Microfudics Corporation, Massachusetts, USA. A plot plant based on this technology can product about 20 gallon/minute of liposomes in 50-200 nm size range. The encapsulation efficiency of up to 75% could be obtained.[13] Aqueous dispersions of liposomes often have tendency to aggregate or fuse and may he susceptible to hydrolysis and or oxidation.

d. Proliposomes:

In proliposomes, lipid and drug are coated onto a soluble carrier to form free-flowing granular material which on hydration forms an isotonic liposomal suspension. The proliposome approach may provide an opportunity for cost-effective large scale manufacturing of liposomes containing particularly lipophilic drugs.[16]

e. Lyophilization:

Freeze-drying (lyophilization) involves the removal of water from products in the frozen state at extremely low pressures. The process is generally used to dry products that are thermolabile and would be destroyed by heat-drying. The technique has a great potential as a method to solve long term stability problems with respect to liposomal stability. It is exposed that leakage of entrapped materials may take place during the process of freeze- drying and on reconstitution.[16]

5. DESIGNING LIPOSOMES TO ACHIEVE OPTIMIZED PROPERTIES:

Drug loading and control of the drug release rate It soon became clear that there were a number of problems associated with the in vivo use of the 1st generation liposomes, sometimes termed 'classical' or conventional liposomes. A very early observation was the difficulty in retaining some types of entrapped molecules in the liposome interior[17] Drug release was shown to be affected by exposure to serum proteins[18] Changing the content of the liposome bilayer, in particular by incorporation of cholesterol was shown to 'tighten' fluid bilayers and reduce the leakage of contents from liposomes. Switching [19] from a fluid phase phospholipid bilayer to a solid phase bilayer also reduced leakage as did incorporation of sphingomyelin into liposomes.

6. CONCLUSIONS:

Liposomes have been explored for various diseases ranging from cancer treatment to pain management. Advantages of using liposomal formulations include: (1) the properties of these liposomes like pharmacokinetics and pharmacodynamics are easily maneuverable, (2) improved bioavailability and (3) reduced toxicity. Different liposomal formulations are made for various applications such as temperature sensitive liposomes, cationic liposomes and liposomal vaccines. Collectively, these liposomal formulations have the ability to enhance or to overcome the limitations of conventional therapies. Furthermore, liposomes have shown great promise in their design to label them with molecular probes for imaging. Exploitation of liposomal characteristics to improve the target specificity and encapsulation can achieve significant therapeutic efficacy. Many liposomal formulations have successfully translated to clinical applications after extensive research on their efficacy and preclinical trials have demonstrated a greater impact on patients with various ailments, thereby improving the quality of life.

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