DRUG DISCOVERY

Formulation and evaluation of curcumin loaded ethosomes as novel drug delivery system

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ABSTRACT

Curcumin having an excellent safety profile including anti-inflammatory, antioxidant, anti-cancer and antimicrobial activity. Curcumin will help in the management of oxidative and inflammatory conditions, metabolic syndrome, arthritis, anxiety and hyperlipidemia etc. With all these advantages it will also show some poor oral bioavailability and limit the usage of oral dosage form. Curcumin loaded Ethosomes are prepared to overcome the problem of bioavailability and permeation. It can be prepared by two methods hot method and cold method. The Curcumin loaded ethosomes are successfully prepared and the maximum amount of drug release was found to be 72% in cold method while 42% in hot method in which cold method giving more amount of drug release as compared with hot method. Ethosomes are the vesicular drug delivery system which consists of various advantages to the conventional Dosage form. These are the non-invasive dosage form which will enable the drug to reach the deeper layer to the skin with the lesser side effects which will cause increase with their application. These are soft, vesicular delivery which enhances the action of active drug. The size ranges about 10 nanometers to micrometre. These are convenient for the usage with lesser harm. Ethosomes are the modified form of liposome that consists of high content of ethanol.

Keywords: Curcumin, Ethanol, Propylene glycol, Buffer

1. INTRODUCTION

Curcumin having an active constituent of turmeric and it is obtained from rhizome, family zingiberaceae. Curcumin has antioxidants, anti-inflammatory function. But Curcumin has poor oral bioavailability. Curcumin loaded Ethosomes are prepared which will enhance the transdermal penetration of drug to the skin which will overcome the problem of poor permeability effect (Cevc et al., 1997). Skin is an extensive and best route for systemic and topical administration the stratum corneum, outermost layer of the skin which is acting as a barrier to the most of the drug which is causing limitation for medication which are taken topically (Paolino et al., 2005). Ethosomes are the non-invasive drug delivery carrier that enables drug to reach deeper skin layer. These are the transdermal drug delivery system which will show a promising result with comparison to oral drug delivery system. The barrier stratum corneum will only make entry of the lipophilic drug having 500 daltons. So, to improve the

DISCOVERY SCIENTIFIC SOCIETY

penetration of drug into the skin various vesicular drug delivery system are invested like liposome, niosomes and ethosomes which will enhance permeation of drug through the stratum corneum. This permeation enhancer will increase the penetration of drug into the skin (Dayan and Touitou, 2000). Ethosomes are promising medication delivery as a lipid carrier. Many researchers have developed a lipid elastic vascular drug delivery system in order to penetrate deeply through the skin it consists of mainly phospholipid, ethanol, bile salts and surfactant which is used in the preparation of the ethosomes (Lodzki et al., 2003).

Ethosomes

Ethosomes are the vesicular drug delivery system which consists of phospholipid, Ethanol 30-40% and propylene glycol. These are soft and malleable vesicle which causes deeper penetration to skin layer. It consists of high level of ethanol content. This ethanol content will help to soften the skin and make the drug to penetrate (Godin and Touitou, 2004).

Composition of ethosomes

It consists of the number of phospholipids like phosphatidylcholine, glycerol and other propylene glycol. It consists of 30 to 40% of ethanol content which will help to deliver the drug very efficiently across the membrane (Elsayed et al., 2006).

Mechanism of action

The drug absorption probably occurs in following two phases first ethanol effect and second is ethosomes effect

Ethanol effect

It is act as a penetration enhancer through the skin. Ethanol penetrates into the intracellular and increase fluidity of membrane lipid and decrease density of lipids of multilayer of cell membrane.

Ethosomes effect

This will increase cell membrane lipid fluidity which will cause by the ethanol. Later increased the skin permeability which permeates the drug inside deep skin layer (Paolino et al., 2005)

Necessity of ethosomes

Ethosomes are in size ranges about 30 nanometers to micrometer. These are smaller than the liposomes. The size of the ethosome is reduced due to the high content of alcohol. Liposome and Ethosomes are different as it having high content of ethanol which will improve and increase the skin permeation (Touitou et al., 2000).

Advantages

Ethosomes will incorporate the larger molecules like peptide and protein molecule. It consists of non-toxic raw material. It will increase the drug absorption through the skin. The Ethosomes will be used in the various preparations of pharmaceutics and cosmetics. Ethosomes have high patience compliance. Due to its non-invasive property, it can be used in the marketed formulation. These are used in the several industries including pharmaceuticals, biotechnology, cosmetics, nutraceuticals etc (Touitou et al., 2001; Jain et al., 2004).

Disadvantages

Ethosomes formulation can't be economical. It will cause skin irritation. These are cost effective preparations. In the preparation of the ethosomes it may cause loss of product when it will transfer the solution from organic to the water media. It is having poor yield effect. For the preparation of Ethosomes drug delivery system it should have adequate molecular size (Bangham et al., 1965; Lopez-Pinto et al., 2005).

2. MATERIALS & METHODS

Method of preparation

There are 3 types of preparation of Ethosomes but mainly in the liberatory first two are mostly preferable (Jain et al., 2003).

Cold method

Hot method

Cold method

Required amount of soya lecithin and drug was taken. Then add few ml of ethanol which is kept on magnetic stirring. A small amount of propylene glycol was added and kept it for 30 degrees centigrade at 700 RPM for 20 minutes.

Another phase was prepared by taking distilled water in a beaker and aqueous phase was heated at 30 degrees centigrade then the aqueous phase was added to the organic phase. The above mixture was stirred for another 30 minute which leads to formation of Ethosomes.

Hot method

Required quantity of soya lecithin and water was mixed and heat it to 40 degrees centigrade and simultaneously ethanol and propylene glycol was also heated about 40 degrees centigrade.

Based on solubility characteristics of drug was mixed and with the ethanol mixture and both the mixture mixed and subjected to stirring for about 30 minutes at 700 RPM. This further leads to the formation of ethosomes (table 1).

Table 1 Composition of Curcumin ethosomal formulation

Ingredients	Quantity
Curcumin	100 mg
Soya lecithin	10 mg
Propylene glycol	2ml
Ethanol	4ml
Buffer	R.S

Characterization of Ethosomes

Visualization of ethosomes

The Ethosomes is visualized by using scanning electron microscope.

Vesicular size and Zeta potential

The vesicular size and Zeta potential will determine by computer-based system and the photoemission spectroscopy.

Surface tension activity

It can be determined by DUNUOY ring tensiometer it will measure the presence of drug concentration within the aqueous solution.

Penetration and permeation study

The permeation and penetration studies can be determined by CONFOCL laser scanning.

Vesicle stability

The Vesicular stability is determined by assessing the size and their structure vehicle overtime the mean size will measure by the DLS and their structure changes are observed through the TEM (Lodzki et al., 2003; Godin and Touitou, 2004; Elsayed et al., 2006; Touitou et al., 2000; Touitou et al., 2001; Jain et al., 2004; Bangham et al., 1965; Lopez-Pinto et al., 2005; Jain et al., 2003; Jain et al., 2005).

Evaluation test

Drug content

Take 10ml of suspension in 10ml volumetric flask and then make up to 10ml with methanol and shake it about 15 to 20 minutes then check the absorbance by using UV. The drug content was determined using formula practical drug content divided by theoretical drug content into 100.

Entrapment efficiency

50 mg Curcumin loaded ethosomes was taken and dissolved in 50ml of 7.4 pH phosphate buffer then kept for ultra centrifugation for about 45 minutes at 17,000 RPM speed then supernatant was taken and absorbance was determined by using UV.

Dissolution studies

The dissolution study was carried out by using Franz diffusion cell it consists of donor and receptor compartment a membrane was placed between the two compartments and sample was withdrawn at regular interval and analyzed by using UV spectroscopy.

Vesicle skin interaction study

For evaluating better skin permeability of ethosomal formulation TEM and laser scanning microscopy was employed. This will improve the comprehension of modification of structure and vesicular penetration.

6HPLC Assay

In this the amount of drugs, that will penetrate into the receptor compartment. The in vitro skin permeation test and MT-2 cells are measured by using HPLC assay with the methanol and distilled water (Godin and Touitou, 2004).

3. RESULTS AND DISCUSSION

Optical microscopy

The Ethosomes are obtained by cold and hot method which was observed under projection microscopy. It was found that the particles were showing multi lamellar structure (Figure 1, 2).

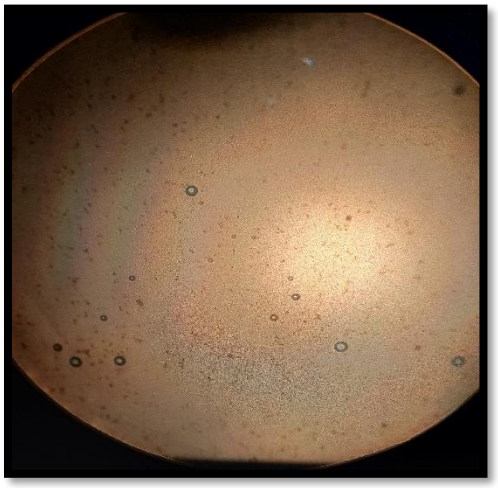

Figure 1 Structure of ethosomal formulation prepared by cold method

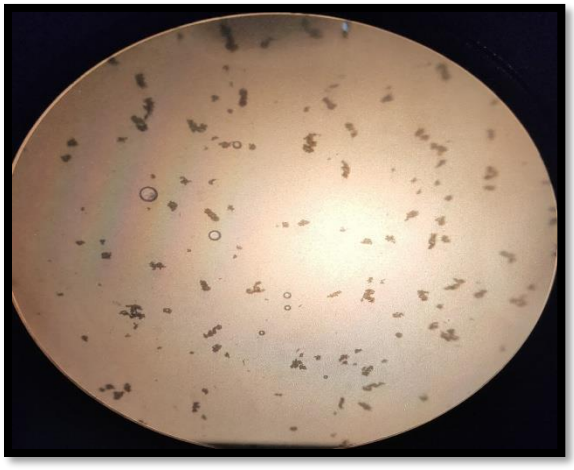

Figure 2 Structure of ethosomal formulation prepared by hot method

The drug content for cold method and hot was found to be 8.125 mg and 8.04 mg. The entrapment efficiency was obtained about 84.9% and 95%. The diffusion study was done by Franz diffusion cell by taking 7.4 phosphate buffer the amount of drug release

was found to be 72% at a time interval of 5 hours for cold method and by hot method the amount of drug release 42.6% at a time period of 3hours. The curcumin loaded ethosomes successfully prepared by cold method and hot method (Figure 3).

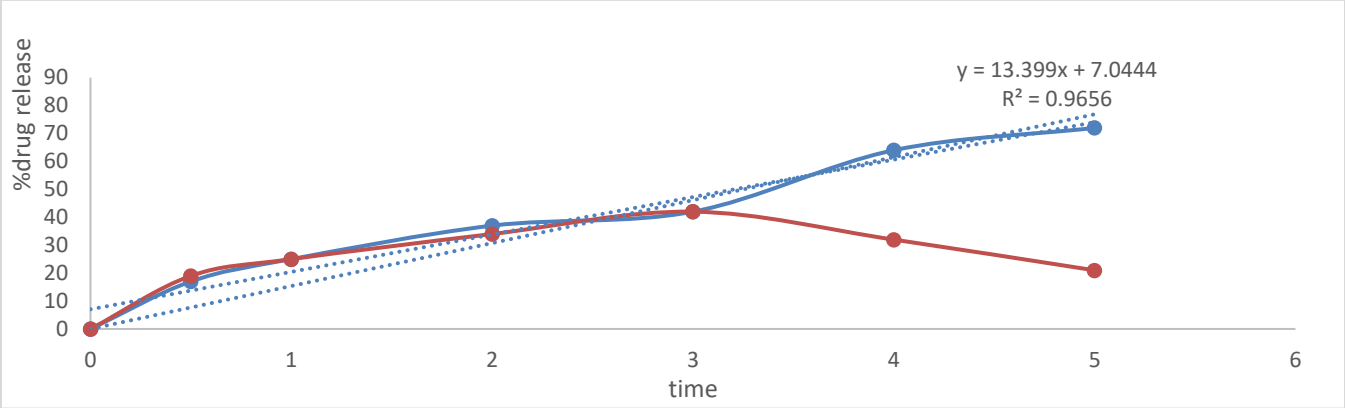

Figure 3 Dissolution data of Curcumin loaded ethosomal formulation prepared by cold method and hot method

4. CONCLUSION

The Curcumin loaded ethosomes were successfully prepared by hot and cold method. The maximum amount drug release was found to be 72% in a time period of five hours by cold method. It was estimated that the percentage of drug release was more observed in cold method as compare to hot method. By these two methods we can estimate maximum amount of drug release and their drug content. Curcumin loaded ethosomes will enhance permeation of drug and its solubility profile.

Informed consent

Not applicable.

Ethical approval

Not applicable.

Conflicts of interests

The authors declare that there are no conflicts of interests.

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The study has not received any external funding.

Data and materials availability

All data associated with this study are present in the paper.

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