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Design and *In Vitro* Characterization of *Mimosa pudica* Loaded Transfersomes

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Abstract: *Mimosa pudica* herb is widely found in western ghat. The anticancer potential especially against breast cancer is proved by many scientific investigators. However, poor skin permeability of active constituents limits the therapeutic use of this herbal active. Transfersomes are modified liposomes with improved skin permeation ability. Thus, extract loaded transfersomes were formulated to improve skin permeation of extract. The transfersomes are phospholipid based vesicles with edge activators. The edge activators increase skin permeation of transfersomes. The extract loaded transfersomes were fabricated using thin film hydration and assessed for vesicle size, microscopic imaging and thermal behavior. The transfersomes showed acceptable vesicle size and zeta potential. Thus, formulated transfersomes could be promising alternative for skin permeation enhancement of herbal active.

Keywords: Transfersomes, *Mimosa pudica*, Breast cancer, Phospholipid vesicles

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Introduction

Plant extract or isolated therapeutically active phytoconstituents have long been used worldwide for treatment of various diseases as well as accepted by physicians and patients because of their fewer side effects. Therapeutic efficacy of herbs is widely reported and extensively explored in the literature by ancient Indians (Kaur and Saraf, 2011). Plant derived

phytoactives based drug delivery systems are becoming more popular in the modern world for treating various diseases with lesser toxic impressions and better therapeutic potential. Modern herbal medicines are developed on the basis of traditional ayurvedic knowledge. Nearly, 50% of modern herbal medicines are developed using isolated active phyto-constituents from

various parts of herbs. In addition to this, most of the novel therapeutic molecules discovered nowadays are developed using plant based lead molecules. However, therapeutic effects of some herb based products are limited due to various constraints like limited solubility as well as stability in gastrointestinal tract (GIT), poor absorption across GIT linings, considerable first pass metabolism and limited oral bioavailability. These issues are well documented in the scientific literatures. In order to tackle limitations associated with conventional herb based products various scientific experts have utilized nanotechnology based approaches (Gupta *et al.*, 2021).

The transdermal route of administration has aroused great interest in pharmaceutical research, as it eliminates many of the problems associated with the oral route of administration (Coma-cros *et al.*, 2018). Several strategies have been used recently to increase transdermal bioactive transmission. These include electrophoresis, iontophoresis, chemical permeability enhancers, microneedles, sonophoresis, as well as vesicular systems like liposomes, niosomes, ethosomes and transfersomes. These strategies include promising transitions. A new patented vesicular systems successfully utilized to improve skin permeation of drugs is transfersomes. Transfersomes are elastic supramolecular lipid bundles containing phospholipid bilayer modified with edge activator. In simpler term these are newly modified liposomes consist of phospholipid bilayer modified with edge activator (single chain surfactant molecules) (Gupta *et al.*, 2021).

Transfersomes are preferred to deliver transdermal drugs as vesicle phospholipids (Chaudhary *et al.*, 2013; Sarwa *et al.*, 2014). The phospholipid membrane of transfersomes is more flexible than standard liposomes which confer its suitability for transdermal drug delivery. The highly flexible membrane properties of transfersomes potentiate its permeation across stratum corneum. These are capable to undergo self-deformation and reformations while its

transport across pore. Edge activators in phospholipid bilayer of transfersomes generates transepidermal osmotic gradient which potentiate its squeezing across layers of skin. The use of transfersomes for effective topical delivery of herbal extracts is recently investigated by various researchers. There have been multiple previous attempts to encapsulate various bioactives in transfersomes (Avadhani *et al.*, 2017; Sundralingam *et al.*, 2020).

Thus, present study was initiated with aim to formulate *Mimosa pudica* extract loaded transfersomes and characterization of drug loaded transfersomes.

Materials and Methods

Materials:

Mimosa pudica leaves powder was purchased locally. Lipoid S-100 was gifted by Lipoid (Germany). Tween 20 were purchased from S.D. Fine Chemicals Ltd. (Mumbai, India). All other reagents, solvents and chemicals were analytical grade and purchased locally.

Preparation of *Mimosa pudica* extract loaded transfersomes:

Mimosa pudica loaded transfersomes were fabricated using thin film hydration technique (Jyothi *et al.*, 2021). Briefly Lipoid S-100 and Tween 80 were dissolved in chloroform. The resulting organic solvent mixture was then subjected to rotary evaporator at 58°C, to form a thin film of phospholipid. The dry phospholipid film was then hydrated with aqueous solution of *Mimosa pudica* leaves powder. The concentration of extract in the formulation was 0.1% w/w. The hydrated film was subjected to heat-cool cycle by heating in water bath up to 58 °C and cooling to room temperature with vortexing.

Evaluation of *Mimosa pudica* extract loaded transfersomes:

Particle size distribution:

The photon correlation spectroscopy principle (Zetasizer Nano ZS, Malvern, UK) was utilized for assessment of particle size of designed

transfersomes (Rai and Pandey, 2017). Transfersomal dispersion was diluted with double distilled water and subjected to particle size assessment at 24 °C.

Zeta potential:

The zeta potential of formulated transfersomes was measured using Zetasizer Nano ZS, Malvern, UK) (Guo *et al.*, 2018). Transfersomal dispersion was diluted with double distilled water and filled in zeta potential cuvette. The resulting dispersion was subjected to particle size assessment at 24 °C.

Differential scanning calorimetry:

Differential scanning calorimetry was used to assess thermal behavior of extract, phospholipid and formulated transfersomes. The Perkin-Elmer DSC was used to assess thermal behavior of samples. Briefly, 10 mg of each sample was placed in sample pan separately and sealed. The samples were then heated in the range of 30°C to 200°C (heating rate: 10°C/min) using nitrogen purging (rate: 20 ml/min) to record DSC thermograms.

Assessment of surface morphology of formulated transfersomes:

Surface morphology of transfersomes was analyzed using scanning electron microscope. The samples were loaded on aluminium stub with carbon adhesive tape and on this about 1-1.5 min of sputtering had applied enough gold to conduct the SEM electrons to ground and prevent charging without noticeably altering the topography of sample. The samples were scanned separately at a voltage 20kV and the images were taken.

Results and Discussion

Preparation of Mimosa pudica extract loaded transfersomes:

Mimosa pudica is well known herbal treatment for management of breast cancers. The anticancer potential of herb has been proved by many scientific investigators. However, poor skin permeability of active constituents limits the therapeutic use of extract. Thus, extract loaded

transfersomes were formulated to improve skin permeation of extract. The extract loaded transfersomes were formulated using thin film hydration technique and evaluated for particle size, zeta potential, thermal behavior and surface morphology.

Evaluation of Mimosa pudica extract loaded transfersomes:

The formulated extract loaded transfersomes were evaluated with respect to following characteristics:

Particle size distribution:

The photon correlation spectroscopy principle (Zetasizer Nano ZS, Malvern, UK) was utilized for assessment of particle size of formulated transfersomes. The particle size distribution curve of transfersomes is illustrated in Figure 1. The transfersomes revealed average particle size of 366.8 nm.

Zeta potential:

The zeta potential of formulated transfersomes was measured using Zetasizer Nano ZS, Malvern, UK). The zeta potential of nanosystems indicates physical stability of nanocarrier based system. The high positive and negative value indicates better stabilization of nanocarrier through electrostatic repulsion. The zeta potential curve of transfersomes is illustrated in Figure 2. The zeta potential was found to be -24.2 mV. The negative value of zeta potential indicates good physical stability of transfersomes.

Differential scanning calorimetry:

Differential scanning calorimetry was used to assess thermal behavior of extract, phospholipid and formulated transfersomes. The DSC thermograms of *Mimosa pudica* extract, phospholipid and transfersomes is highlighted in Figure 3. The DSC thermograms of formulated transfersomes showed endotherms of both extract as well as phospholipid which indicates entrapment of active constituents of extract in transfersomal vesicles without any degradation.

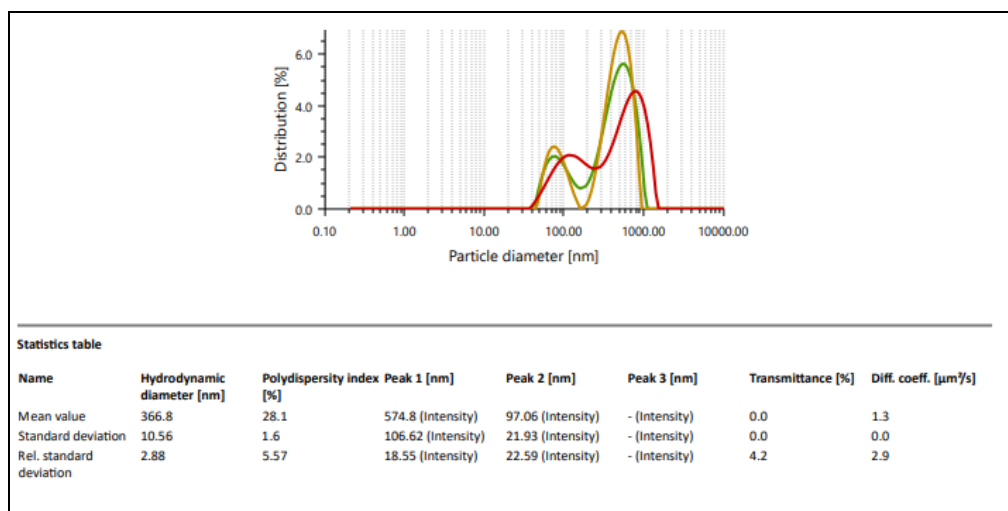


Fig. 1: Particle size distribution of formulated transfersomes.

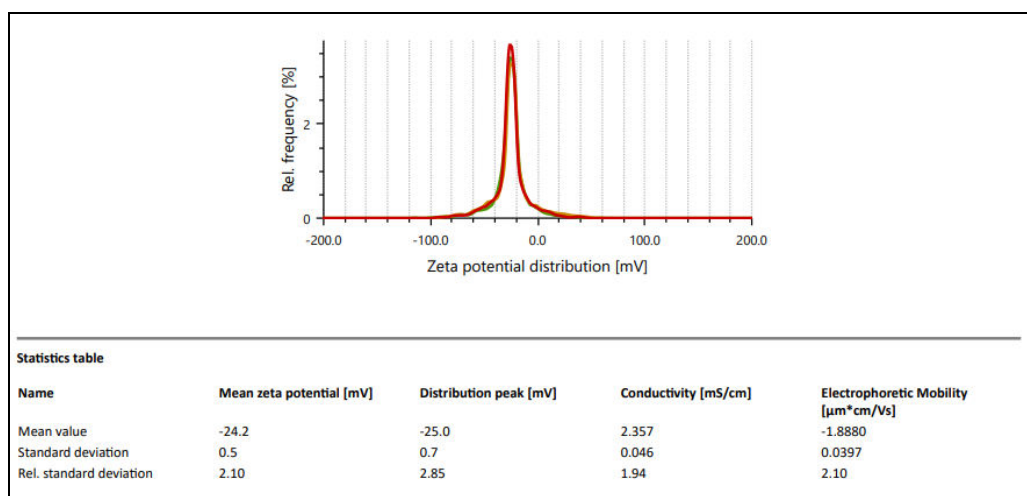


Fig. 2: Zeta potential curve of formulated transfersomes.

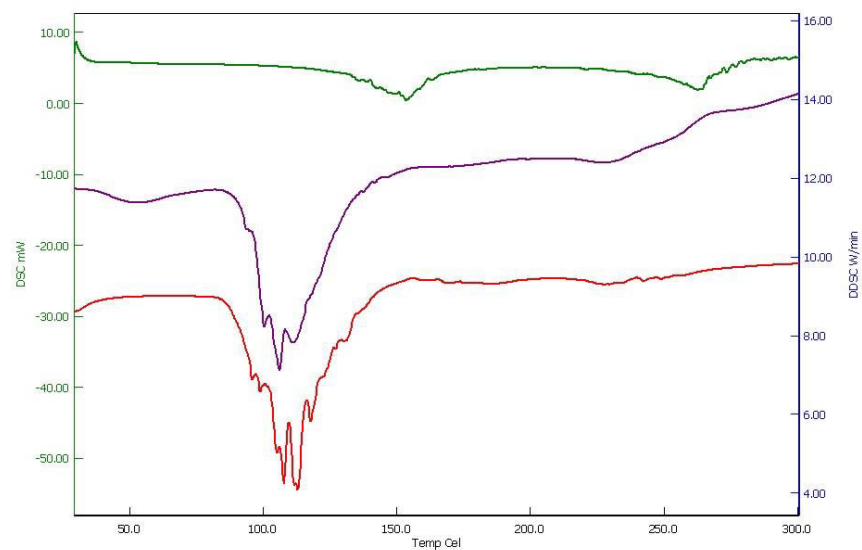


Fig. 3: DSC thermograms of extract, phospholipid and formulated transfersomes.

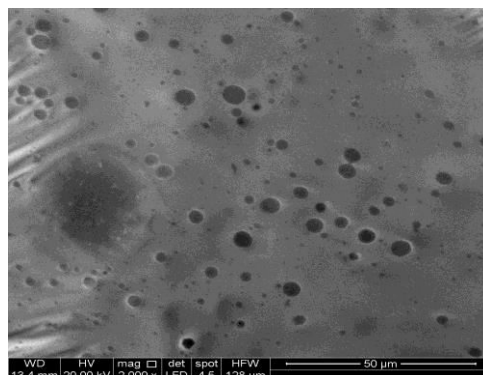


Fig. 4: SEM image of formulated transfersomes.

Assessment of surface morphology of formulated transfersomes:

Surface morphology of transfersomes was analyzed using scanning electron microscope. The SEM image of transfersomes is represented in Figure 4. The SEM image showed exactly spherical vesicles of transfersomes. The SEM imaging confirmed formation of extract loaded transfersomes in spherical shape.

Conclusion

The poor skin permeability of active constituents limits the therapeutic use of extract. Thus, extract loaded transfersomes were formulated to improve skin permeation of extract. The transfersomes are phospholipid based vesicles with edge activators. The edge activators increase skin permeation of transfersomes. The extract loaded transfersomes were fabricated using thin film hydration and assessed for vesicle size, microscopic imaging and thermal behavior. The vesicle size and zeta potential were found to be 366.8 nm and 24.2 mV. The DSC confirmed loading of extract in transfersomes without chemical degradation. Thus, formulated transfersomes could be promising alternative for skin permeation enhancement of herbal active.

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