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# DEVELPOPMENT AND EVALUATION OF HERBOSOME SUSPENSION

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## ABSTRACT

Herbosome is a novel emerging technique in herbal drug technology that removes the limitations of the traditional drug delivery systems and enhances the bioavailability of herbal extracts. Herbosome structures contain the active ingredients of the herb bounded to phospholipids. Herbal plants are being used in the treatment of Diabetes mellitus in the traditional system of medicine. *Urtica dioica* (UD) known as stinging nettle is a medicinal herb and shown proven role of an anti-diabetic agent. In the present study extraction of *Urtica dioica* was done by maceration technique using ethanol (70%). Formulation of herbosome suspension was done by solvent evaporation technique. Herbosme suspension thus formed was evaluated for visualization, particle size, surface tension activity, stability, pH. Herbosome suspension appeared irregular spheres shape when seen through optical microscope and SEM. Particle size and charge determination of all formulation showed size in microns range and possess good stability. FTIR analysis and interpretation of all formulation reveals formation of complex and presence of hydrogen bonding, Short term stability studies on the most satisfactory formulation F5 was done as per ICH guideline showed no or little change in particle size, surface tension, and chemical integrity of suspension before and after stability studies. These findings suggest that herbosome suspension of *Urtica dioica* (100 mg/kg) shows better antidiabetic activity in comparisons to the powdered marketed formulations of *Urtica dioica*.

Keywords*: Urtica dioica*, phosphatidylcholine, antidiabetic, herbosome .FTIR

## 1. Introduction

Development of novel drug delivery system from natural resources is very much necessary because of the beneficial role of herbal drug in the management of varied diseases. The bioavailability of lipophilic drugs when administered orally as solid dosage forms is low. There are usually several factors responsible for this, but a particularly widespread problem is poor absorption due to slow and/or incomplete drug dissolution in the lumen of the gastro-intestinal

tract. In this case, improved bioavailability can be achieved by the use of delivery systems, which can enhance the rate and/or the extent of drug solubilizing into aqueous intestinal fluids.[1]

"Herbosomes" are the combined form of herbal product in combination with the phospholipids having better absorption and utilization profiles in our body and subsequently produce better therapeutic efficacy than the conventional herbal extracts or individual molecule, which can minimize the short coming of conventional herbal therapy.[2] The term "herbo" means plant, while "some" means cell-like. It is also mentioned as phytosome, planterosome. This is a new patented technology, where standardized plant extracts or water soluble phytoconstituents are complexed with phospholipids to produce lipid compatible molecular complexes, there by greatly increasing absorption and bioavailability Phospholipids play a major role in drug delivery technology. There are numerous advantages of phospholipids in addition to solubilizing property while considering them for a carrier system.[3]

Plant remedies have become increasingly popular and are often preferred to synthetically derived pharmaceuticals. It is therefore of interest to determine their active components and to elucidate their molecular mechanisms of action. The plant study for antidiabetic activity is *Urtica dioica* (UD), known as stinging nettle, available in many South Asian countries. The blood glucose lowering effect of *Urtica dioica* (Stinging Nettle) has already been noted in old writings such as those of Avicenna. [4]

*Urtica dioica* is a herbaceous plant with dark green leaves, inconspicuous flowers and abundant stinging hair. Recently, there are also been other investigators who indicated the hypoglycemic effect of *Urtica dioica*. In the present study we show that leaf extracts from stinging nettle, which are used in the treatment of diabetes mellitus. Diabetes is a metabolic disorder in which the blood glucose level increases, which is caused by decreased secretion of insulin or reduced sensitivity of insulin receptor.[5]

## 2. MATERIALS AND METHODS

### 2.1. PLANT MATERIAL

*Urtica dioica* plant was collected from eastern area of Nepal, identified and authenticated by botanical garden and herbarium GKVK Campus University of Agricultural Sciences, Bengaluru. The leaves were separated, dried at room temperature and were grounded into powder.Phosphatidyl choline (PC), stearic acid, dichloromethane were used in formulation of herbosome. Alloxan was used to induce diabetes in S.D rats

### 2.2. PREPARATION OF PLANT EXTRACT

The extraction was prepared using maceration method. The 100 gm powder was macerated for 72 hours at room temperature using 70% ethanol and 30% water. The filtrate was evaporated at 60˚C temperature and the extract powder (11.75%) of leaf powder) the dried sample (was stored at 2-8°C in a freezer. The dried extract was utilized for formulation preparation.[6]

2.3 Formulation of herbosome suspension

Nine formulations of herbosomes were developed for *Urtica dioica* by solvent evaporation/ thin film hydration technique using phospholipid, dichloromethane, stearic acid and phosphate buffer. Phospholipid was used as vesicle forming component. Dichloromethane was used as organic solvent to dissolve phospholipid and extract and to form thin film of its mixture. Stearic acid was used to give charge to the vesicle for the stability and phosphate buffer solution was used as hydration medium[12.13]

2.4 PHYSIOCHEMICAL EVALUATION OF HERBOSOME SUSPENSION

Visualization-Visualization of herbosomes was achieved using by electron microscopic techniques and Scanning Electron Microscopy (SEM) used to assess shape and size.[14]

pH:pH of all nine formulation were measured by using pH meter.[15]

Surface Tension Activity Measurement: The surface tension activity of the drug in aqueous solution was measured by the ring method drop weight method with stalagmometer.[16]

Structure of vesicle by FTIR:The formation of the complex was confirmed by IR spectroscopy by comparing the spectrum of the complex with the spectrum of the individual components andtheir mechanical mixtures.[17,18]

2.5 STABILITY STUDIES

Optimized formulations (F- 5) was divided in to two sample sets and stored at 2-8°C in refrigerator and 30º C ± 2º C/65% RH ± 5% RH in thermo lab humidity chamber (GINKYA IM 3500 series) for 60 days. The optimized formulation stored in the sealed aluminum foil. The optimized formulation was analyzed after 30 and 60 days for particle size, FTIR analysis.[19]

## 3. RESULT AND DISCUSSION

Development of novel dosage forms like liposomes, polymeric nanoparticles, phytosomes have number of advantages in phytoformulation research including enhancement of solubility and bioavailability, protection from toxicity, enhancement of pharmacological activity, enhancement of stability, protection from physical and chemical degradation etc. Phospholipids can play a major role in development of novel phytopharmaceuticals because of their biocompatible nature with the phytochemicals. Several studies have indicated the beneficial role of phospholipids in enhancing the therapeutic efficacy of phytochemicals having poor oral absorption.[9]

3.1 EXTRACTIVE VALUE

The total yield was found to be 11.75% (11.75) g for 100 g of leaves and stem powder of *Urtica dioica.*

3.2 PREFORMULATION STUDY OF DRUG AND SELECTED LIPIDS.

The IR spectrum of the *Urtica dioica* extract, phosphatidylcholine, mixture of *Urtica dioica* and phosphatidylcholinewas recorded by FTIR spectrometer. During Fourier Transform Infrared Spectroscopy (FTIR) studies the intensity of the peak was modified but actually shift in the peak was negligible. So it can be concluded that the drug interaction between phytosomal excipient used in formulation and phytosomal complex was negligible as shown in Figure 1 and thus determining integrity and purity of the sample.

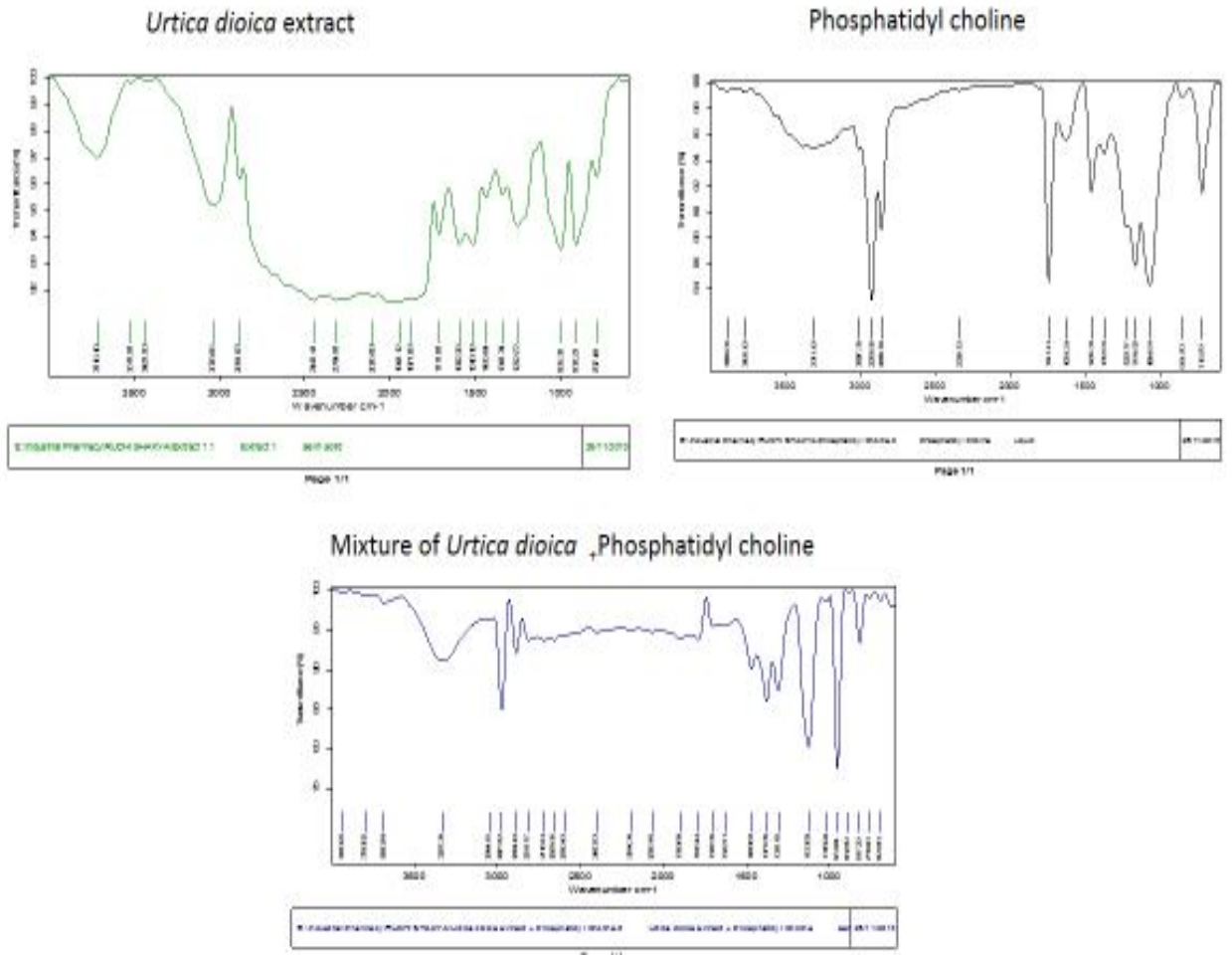


Fig1: Determining integrity and purity of the sample by FTIR.

### 3.3 PHYSICOCHEMICAL STUDY

#### Microscopic view of the complex

The microscopic view and SEM data indicated the presence of vesicles like structures consisting of PC and BE intercalated in the lipid layers. The surface morphology of the BPC at various magnifications depicted that the drug particles are associated with the phospholipid forming complexes with irregular size.

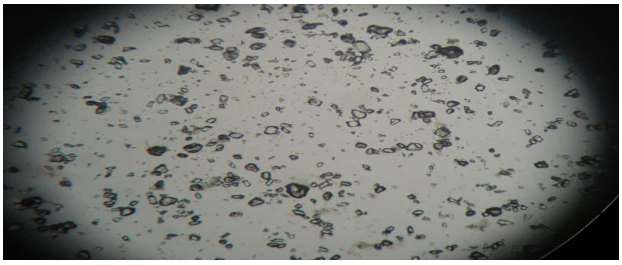

Fig 2: Vesicle size measurement

The particle sizesof all nine formulation of herbosome suspension were also measured by optical microscope using micrometric technique and their values formulation are shown in Table below.

3.4 pH

The pH of various formulations was found to be around 6.8 which is suitable for oral administration because the pH of the oral suspension is between 6.8-7

3.5 SURFACE TENSION ACTIVITY MEASUREMENT

Surface tension values of formulation were compared with that of water and found that the values obtained were less it is due to presence phosphatidylcholine which act as surfactant. Surface tension value indicates the nature of intermolecular forces or type of bonds

Table 1: Values of Surface Tension versus pH of the Formulations.

| S.No | Formulation No | Particle size in optical microscope | Surface tension | pH |
|---|---|---|---|---|
| 1 | F1 | 2.68 | 57.19 | 6.83 |
| 2 | F2 | 2.84 | 58.9 | 6.79 |
| 3 | F3 | 2.93 | 51.65 | 6.81 |
| 4 | F4 | 3.48 | 46.8 | 6.78 |
| 5 | F5 | 3.74 | 43.33 | 6.82 |
| 6 | F6 | 3.92 | 58.24 | 6.81 |
| 7 | F7 | 4.99 | 52 | 6.78 |
| 8 | F8 | 5.312 | 51.37 | 6.83 |
| 9 | F9 | 5.63 | 52.6 | 6.82 |

3.6 FTIR: - chemical integrity

The formation of the complex was confirmed by comparing FT-IR spectra of the phytoconstituent, the phospholipid and their herbosomes. FTIR spectroscopy is also a useful tool for the control of the stability of herbosomes. The free hydroxyl group interacts with the choline part of phospholipid. The peak corresponding to the free hydroxyl group changes and a broad peak appears instead. The FTIR spectroscopy revealed shifting of hydroxyl (OH) group to a lower frequency in the spectra as compared to that of extract of UD and either phospholipid investigated, indicating the formation of strong hydrogen bonding between hydroxyl groups of the phospholipids and the UD constituents in the herbosomes form. The band of choline N-$(CH_3)_3$ groups in PC spectra is shifted to higher frequency in herbosome suspension of UD spectra with decreased intensity, indicating that the interaction between PC and extract of UD is also at the level of the choline moiety.

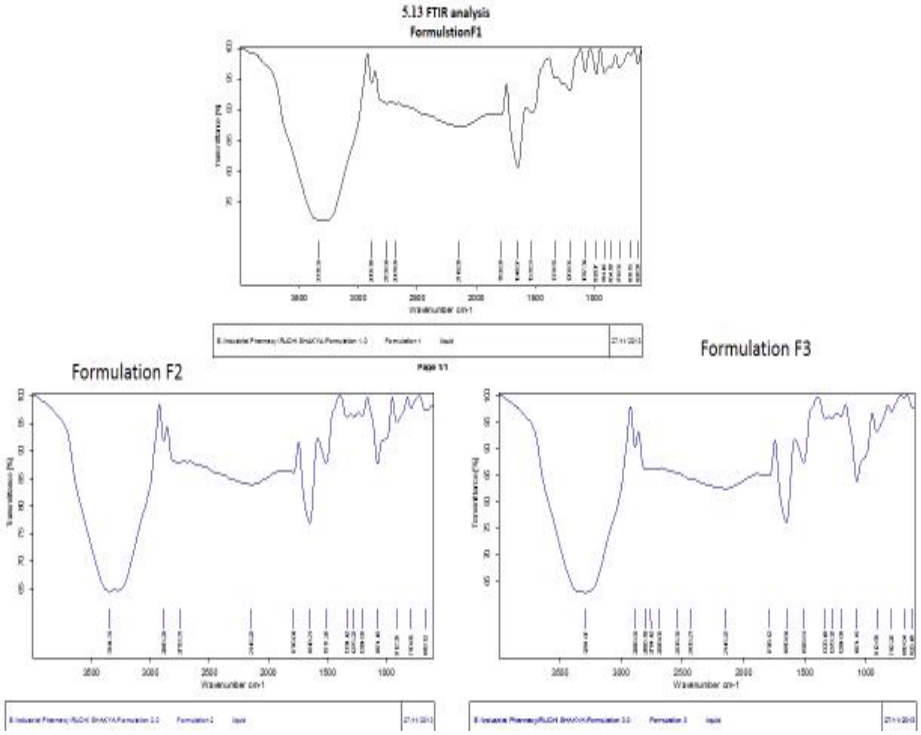


Fig 3: The complex formation confirm by comparing FT-IR spectra.

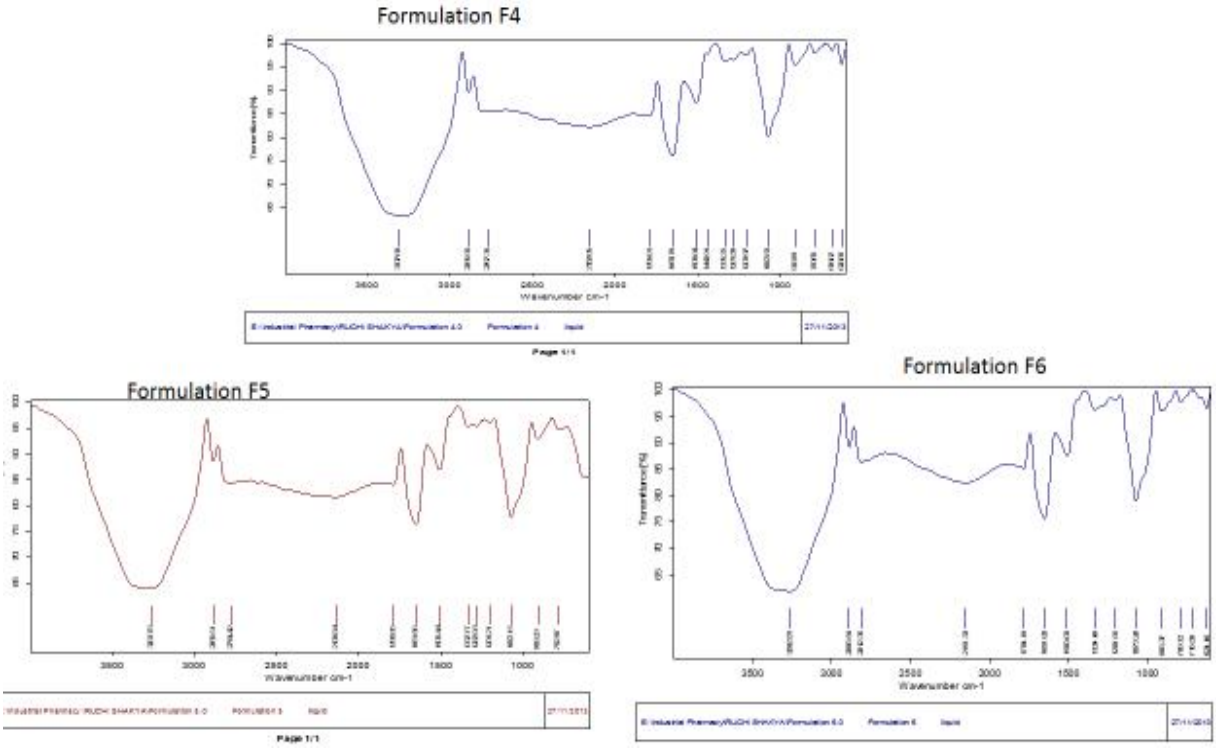


Fig 4: The complex formation confirm by comparing FT-IR spectra.

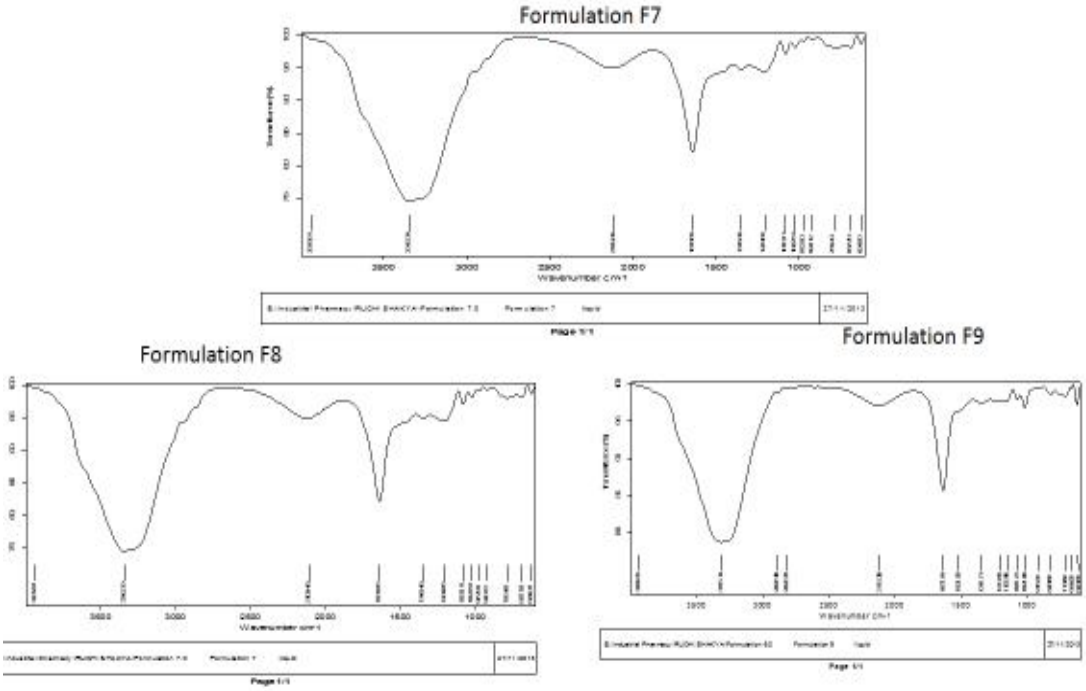


Fig5: The complex formation confirm by comparing FT-IR spectra.

3.7 STABILITY STUDIES

Stability studies were conducted to determine the stability and changes in particle size, surface tension integrity of suspension. Optimized herbosome suspension of *Urtica dioica* (F5) was kept for Stability studies at 2-8°C and at 30±2°C/65±5% RH for two months and showed no change or little decrease in particle size, surface tension integrity of suspension

Table 2: Stability studies of the different parameters.

| Parameters | At 0 day | | |
|---|---|---|---|
| | F5 | 30º C ± 2º C/65% RH ± 5% RH | 2-8°C |
| | | F5 | F5 |
| Particle size | 2.324µm | 2.524 µm | 2.654 µm |
| Surface tension | 43.33dyne/cm | 44.11 dyne/cm | 44.54 dyne/cm |
| pH | 6.8 | 6.8 | 6.8 |

## 4 Conclusion

A novel emerging technique is applied to phytopharmaceutical for the enhancement of bioavailability of herbal extract for medicinal applications as these molecules limits to pass through biological membrane for their absorption in the blood stream. So, herbosomes recent advanced forms of herbal formulations which contain the active ingredients of the herb bounded to phospholipids is developed that have enhanced absorption rate, producing better bioavailability than conventional herbal extracts .The results indicated that the herbosome suspension depend on Drug: Phospholipid ratio. It directly effects on the physicochemical parameters. During *in-vivo* comparative study, the result have shown that herbosomal suspension of *Urtica dioica* were better than powdered market formulation of *Urtica dioica*.

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