



Formulation And Evaluation Of Phytosome Containing Cumin Seeds

Pranita S. Kavitate^{1*}, Pooja S. Sarje², Vijay B. Sanap³, Rutuja Y. Sawant⁴

Department of Pharmaceutical analysis

JBVP's Vidya Niketan College of Pharmacy Lakhewadi. Tal. Indapur, Dist. Pune. 413103

❖ Abstract :

Cumin is a flavouring and antioxidant ingredient. In addition to these benefits, it treats diarrhoea, spasms, stomach problems, and inflammation while also having antibacterial, analgesic, anti-inflammatory, and sedative effects. Nowadays, natural medications are used to treat most common ailments and nutritional deficiencies. Any herbal medicine's effectiveness depends on how well the therapeutically active ingredient is delivered at an effective level. However, whether applied topically or taken orally, their bioavailability is severely limited. Phytosomes are advanced herbal preparations that have the phytoactive components that are derived from herbs and can convert the hydrophilic to the lipophilic state of the cell membrane. They can be made into tablets, gels, creams, suspensions, and other pharmaceutical forms. Phytosomes are now a great alternative for treating many ailments. By making a highly lipophilic medication more hydrophilic, cumin phytosomes dramatically improve absorption and bioavailability; this makes the phytosome technique perfect for drug delivery.

Keywords : phytosome ,Bioavailability ,Liposome, Cumin seed, Absorption.

❖ INTRODUCTION:

A. Introduction of drug

Phytosome technology developed by Indina Corporation. Italy [1]. Phospholipid complexation may be a patented technology that involves incorporating plant samples or soluble plant dihydrogen monoxide into phospholipids to provide lipid-compatible molecular complexes. The nutritional process that forms hand tissue is the main product of the plant and prevents damage to digestive and intestinal bacteria. Phospholipid complexes improve pharmacokinetic and pharmacological parameters. The seeds are used in traditional medicine and as food flavoring. Previous pharmacological studies have shown that cumin has anti-inflammatory, anti-inflammatory, anti-inflammatory, anti-inflammatory, anti-inflammatory, anti-inflammatory, anti-inflammatory, platelet aggregation, lowering blood pressure, bronchiectasis, anti-inflammatory properties. -inflammatory, anti-inflammatory, anti-amyloid production, anti-inflammatory. Osteoporosis, aldose reductase, $\hat{\pm}$ -glucosidase and other effects. This review focuses on the chemical composition and pharmacological properties of cumin (Cuminum cyminum) (1)

Cuminum cyminum and Carum carvi are sources of cumin and coriander seeds, which have been widely used in traditional medicine since ancient times in the treatment of various indications. Cumin and coriander seeds are rich in essential oils, and their chemical composition and biological activities have been studied. In recent years (especially in the last three years) progress has been made in confirming its

medicinal properties through various studies. Many new biological activities were revealed in this experiment. This review highlights the importance of cumin and coriander as sources of various natural products and their medicinal uses.

PLANT PROFILE :

Synonyms:

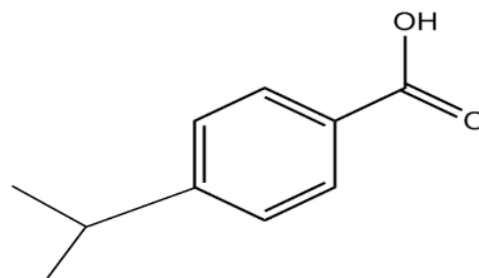
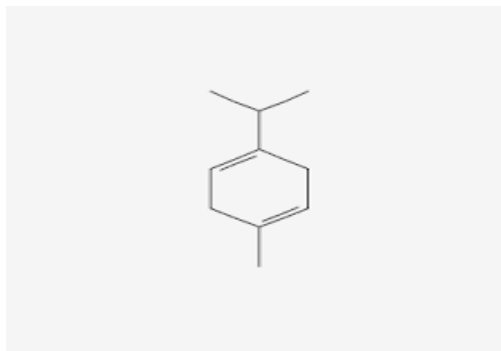
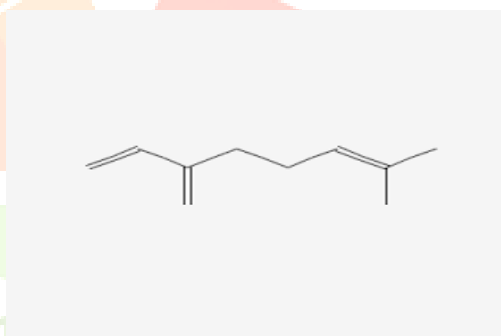
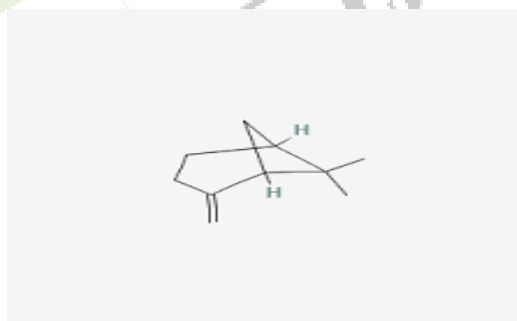
Cuminum cyminum J. F. Gmel., *Cuminum aegyptiacum* Mérat ex DC., *Cuminum hispanicum* Mérat ex DC., *Cuminum odorum* Salisb., *Cuminum sativum* J. Sm., *Cuminum longinvolucellatum* St.-Lag. Taxonomic classification: Kingdom: Plantae; Subkingdom: Viridiplantae; Infrakingdom: Streptophyta; Superdivision: Embryophyta; Division: Tracheophyta; Subdivision: Spermatophytina; Class: Magnoliopsida; Superorder: Asteranae; Order: Apiales; Family: Apiaceae; Genus: *Cuminum*; Species: *Cuminum cyminum*. Nomenclature and Common names: The word cumin was derived from the Latin *cuminum*, which itself was derived from Greek (*kyminon*). The common names of the plant were: Arabic: Kamoun, Kamun; Chinese: Ou shi luo, Ma qin (Ma ch'in), Xian hao, Xiang han qin, Zi ran.; English: Cumin, Roman caraway; French: Cumin, Cumin de Malte, Cumin blanc, Cumin du Maroc, Faux anis; German: Kreuzkümmel, Römischer Kümmel, Weißer Kreuzkümmel; Greek: Kimino, Kiminon; India: Jiiraa (Jeera), Zeera (zira, ziira), afed ziiraa (Safed zira), Safed jiiraa (Safaid jeera); Italian: Cumino; Japanese: Hime unikyoo, Kumin; Portuguese: Cominho; Russian: Kmin, Kmin rimskii, Kmin tminovyi (Kmin tminovyj); Spanish: Comino; Swedish: Spiskummin(2)

B. Phytosome method

- 1) solvent evaporation method
- 2) Mechanical Dispersion method
- 3) Saiting out technique
- 4) Lyot Lyophilization method
 - Anti - solvent precipitation process
 - Rotary evaporation process.(Refrence) (4)

C. Basic introduction of drug

Drug Name	Cumin Seed
Synonyms	Edible seed , <i>Cuminum Cyminum</i> Jeera (Hindi)
Biological source	Cumin seeds are Obtained from seeds of herb <i>cuminum Cyminum</i> belong in to the Family Apiaceae
Chemical constituents	<i>Cumin (cuminum cyminum L)</i> The major compounds present in cumin oil include cuminaldehyde(23-18),B- pinene (12-47),B- myrcene (0-96), α -cymene(6-17), γ - terpinene (20-47) & P-metha-1,4-diene-7-ol
Structure	a) Cumina

b) γ -Lerpinenec) β -myrcened) β -Pinene**Boiling point**

Cuminaldehyde (235-236°C)

2) β -pinene (165-167°C)3) β -myrcene (167°C)4) α -cymene (177°C)5) γ -terpinene (183°C)

Melting Point	Cuminaldehyde (97°C) 2) B-pinene (-61.54°C) 3) B-myrcene (-10°C) 4) R-cymene (-68°C) 5) γ-terpinene (60-61°C)		
Solubility	Chemical	Soluble	Insoluble
	a) Cuminaldehyde	ethanol, ether, toluene	Water
	b) B-pinene	alcohol	Water
	c) B-myrcene	Alcohol	Water
	d) P-Cymene	Alcohol, Ether, Chloroform, Acetone	Water
Uses	<p>a) Cinnamaldehyde: A flavouring agent used in perfumes and other products containing fragrance.</p> <p>b) B-pinene in conjunction with other chemicals obtained from plants to treat kidney, bladder, and urinary stones</p> <p>c) B-myrcene: anabolic, anti-inflammatory, fragrance, and flavouring agent</p> <p>d) The flavouring ingredient in cough syrup is P-cymene. raw ingredient used in the manufacturing of pesticides.</p>		

Table 1- Basic introduction of drug

D. Pharmacological action of drug

I. Antioxidant

Cumin and coriander products (oils and their aqueous and solvent extracts) have been shown in various tests to have significant antioxidant properties. These effects have been documented by their ability to kill hydroxyl radicals, 1,1-diphenyl-2-trinitrophenylhydrazine (DPPH) radicals, and lipid peroxides. Other tests used include the ferric thiocyanate method in the linolenic acid system, Fe²⁺ ascorbic acid-induced rat liver microsomal lipid peroxidation (LPO), soybean lipoxigenase-dependent lipid peroxidation, and iron reducing capacity (2).

II. Antimicrobial

This antimicrobial effect has been evaluated by many beneficial and Gram-positive and Gram-negative bacteria. Cumin seed oil and alcohol extract inhibited the growth of *Klebsiella pneumoniae* and its clinical isolates, improved cell morphology, capsule appearance, and reduced urease activity. Cumin and coriander oils have been documented to have antimicrobial properties against soil, food, animal, and human pathogens, including dermatophytes, vibrios, yeasts, aflatoxins, and mycotoxins (2).

III. Anticarcinogenic /Antimutagenic

Independent studies have shown that dietary supplements containing cumin and coriander prevented cancer development in mice exposed to the specific carcinogen 1,2-dimethylhydrazine (DMH).

Many studies have linked the anti-cancer properties of cumin and coriander to their apoptotic, anti-mutagenic, and anti-proliferative abilities [2].

IV. Antidiabetic

The antidiabetic effects of cumin and coriander products are well documented. In a blood sugar test in rabbits, cumin increased the area under the blood sugar curve and hyperglycemic peaks. Methanolic extract of cumin seeds, alloxan and streptozotocin (STZ) reduces blood sugar in diabetic rats and inhibits glycosylated hemoglobin, creatinine, blood urea nitrogen and improves blood insulin and glycogen (liver and skeletal muscle). The bioactive component of cumin seed oil was found to be cumene aldehyde, which separately inhibits aldose reductase and alpha-glucosidase in rats (2).

V. Diuretic

The use of cumin as a diuretic has been confirmed in experimental studies where oral administration of cumin aqueous extract (acute and subchronic type) increased urine output in rats for 24 hours and beyond. It was found that urine sodium and potassium levels increased, while plasma sodium and potassium levels were not affected. Cumin extract did not cause nephrotoxicity or other side effects during the study.[2]

VI. CNS

Application of cumin oil inhibits the development and expression of morphine tolerance (measured by the tail kick method). Morphine dependence is also reversed in a dose-dependent manner, as assessed by a reduction in conditioning scores (the acquisition and expression of morphine-induced conditioned place preference) in rats (2). The inhibitory effect of cumin essential oil on $\hat{I}\pm$ -SN fibrillation, which is an important process in the pathophysiology of many neurodegenerative diseases, especially Parkinson's disease, was examined.[1]

VII. Gastrointestinal

In human trials, some coriander-based herbal preparations have been found to reduce symptoms of indigestion. The antispasmodic effect of coriander alcohol extract demonstrates the inhibitory effect of muscle contraction by spasmogens, acetylcholine and histamine.[2]

VIII. Effect on platelet function

Cumin extract inhibits arachidonic acid-induced platelet aggregation. It also inhibits the production of thromboxane B₂ from exogenous (14C) arachidonic acid (AA) in washed platelets, and in addition, a simultaneous increase is observed in the production of lipoxygenase-derived products (1).

❖ Material & Method :

A) Materials used For Preparation of phytosome

1. Phospholipid (i.e Soya lecithin)
2. Dichloromethane (DCM)
3. Chloroform
4. n- hexane
5. Ethanol
6. Cholesterol
7. Phosphate buffer

B) Method With Extraction Procedure

- a) Plant vesicles were prepared using the thin-layer vacuum evaporation technique. Mix the plant stem complex with absolute ethanol in a 250 ml round-bottomed glass. Attach the bottle to the vaporizer area. The solvent evaporates at approximately 60 \hat{A} °C, forming a thin film around the glass. The membrane was hydrated with phosphate buffer, pH 7.4, and the lipid layer was exfoliated in phosphate buffer to form a vesicle suspension. This unit uses a 60% amplitude probe for sonication. The extracted plant will be kept in the refrigerator for 24 hours before characteristic.

- b) React phospholipids (e.g., soy lecithin) and polyphenol extracts in equal proportions with 5 mL of dichloromethane (DCM) and stir until evaporation. After the DCM has evaporated, add 5 mL of n-hexane to the membrane with a whisk and leave it in the fume hood to completely remove the solvent. After complete removal of n-hexane, the film was hydrated and sonicated to obtain the desired phytosome complex.
- c) React phospholipids (e.g., soy lecithin) and polyphenol extracts in equal proportions with 5 mL of dichloromethane (DCM) and stir until evaporation. After the DCM has evaporated, add 5 mL of n-hexane to the membrane with a whisk and leave it in the fume hood to completely remove the solvent. After complete removal of n-hexane, the film was hydrated and sonicated to obtain the desired phytosome complex.
- d) Phospholiposomes can be prepared using the reflux method. Place the polyphenol extract and phospholipids in a 100 mL round-bottom flask and reflux in DCM not to exceed 40°C for 1 hour. The clear solution was evaporated and 15 mL of n-hexane was added until a precipitate was obtained. Declutter and put in the dryer
 Accurately weigh the phospholipids and cholesterol in a beaker, dissolve them in 10 mL of chloroform, and sonicate for 10 minutes using a sonicator bath. Removal of organic solvents can be done by lowering the temperature in the evaporator area (40°C). After all solvents are removed, a thin layer is formed in a field evaporator that is hydrated with the polyphenolic extract of the drug. The phospholipid mixture is sonicated in an ice bath to dissipate heat. The prepared phospholiposomes were stored in an amber vial [55]. An example of this program is shown in Figure 4.

e) **Extraction of Cumin Seed**

Plant material: Cumin seeds are purchased from DMart in Thane, Maharashtra, India, and cumin seed oil is sold online. It is said that cumin oil is found in its leaves and parts and that "part of the plant is used as seeds."

Essential Oil Extraction:- To extract cumin seed essential oil, 125 grams of whole cumin seeds should be weighed. . Place the cumin seed weight in a container and connect it to the distillation condenser. Therefore, cumin seed oil is obtained by hydrodistillation using 700 ml of distilled water. Place the beaker in the heating jacket and gradually increase the temperature from 60°C to 80°C, then from 80°C to 90°C, and finally to 100°C. The extraction process took 3 hours (lots of oil came out of capacitor #1). The oil obtained from whole cumin seeds is called refined cumin oil. Fill the oil into the container. Both extract cumin oil and store it in the refrigerator[3]



Figure 2 Extraction of whole cumin using distillation flask.

C) Method used For Preparation of phytosome

- 1) solvent evaporation method
- 2) Mechanical Dispersion method
- 3) Saiting out technique
- 4) Lyot Lyophilization method
 - Anti - solvent precipitation process
 - Rotary evaporation process.(Refrence) (4)

1. Solvent evaporation technique

Take some kapok leaf extract and soybean lecithin in a 100ml round bottom flask, add 20ml acetone and reflux at 50-60°C for 2 hours. The mixture is concentrated to 5-10 ml to obtain a residue that is filtered and collected. Place the precipitated phospholipid in a dry amber glass vial and store at room temperature (5)

2. Mechanical Dispersion method

In the experiments, lipids dissolved in organic solvents were contacted with water containing the drug (Sikarwar MS et al., 2008). After the removal of organic solvent in the liver, the formation of phospholipid complexes in the plant decreases. Current preparation methods of phospholipid include supercritical fluid (SCF), including gas generator (GAS), compression antisolvent method (PCA), and supercritical antisolvent method (SAS) (Li Y li al., 2008). (4)

3. Salting out technique

An important method of physical preparation is to dissolve PC and plant extracts in a suitable organic solvent and then add n-hexane until the extract-PC complex test forms [7].

4. Lyophilization process

All synthetic and natural phospholipid and botanical products are available in a variety of solvents, and phospholipid-containing compounds are added to other botanical-containing chemicals and mixed until a complex is formed. The product was isolated by lyophilization. The phospholipids used in the phospholipid complexing process have acyl groups, which can be phosphocholine, the phospholipids serine can be the same or different, and the phospholipid acylethanolamine is derived only from stearic acid, oleic acid, palmitic acid, and linoleic acid [cut]. The active components of the plant are structural components[6].

a. Anti-solvent precipitation process:

An amount of plant and phospholipid is refluxed with 20 ml of acetone and other organic solvents at below 50°C for 2-3 hours under certain conditions. The reaction mixture is concentrated to a minimum volume of 10 ml and then a less polar solvent such as n-hexane is added with stirring to obtain a precipitate. The filtrate is stored in a desiccator. Dry the powder and store the powder in a dark amber bottle at temperature.[4]

b. Rotary evaporation process:

The specific gravity of the herbal extract and phospholipids are mixed in an organic solvent such as acetone, miscible with 30 ml of water, in a glass base, and then mixed for two hours in the evaporator area at 50°C. Antisolvents such as n-hexane are usually added to the resulting film after continuous mixing using a stirrer.[4]

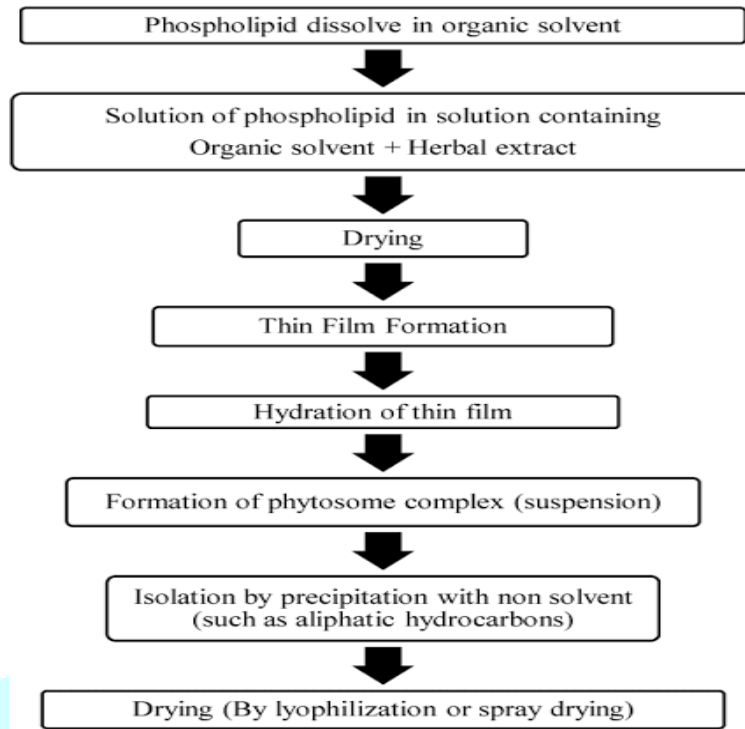


Figure 1 preparation of phytosome

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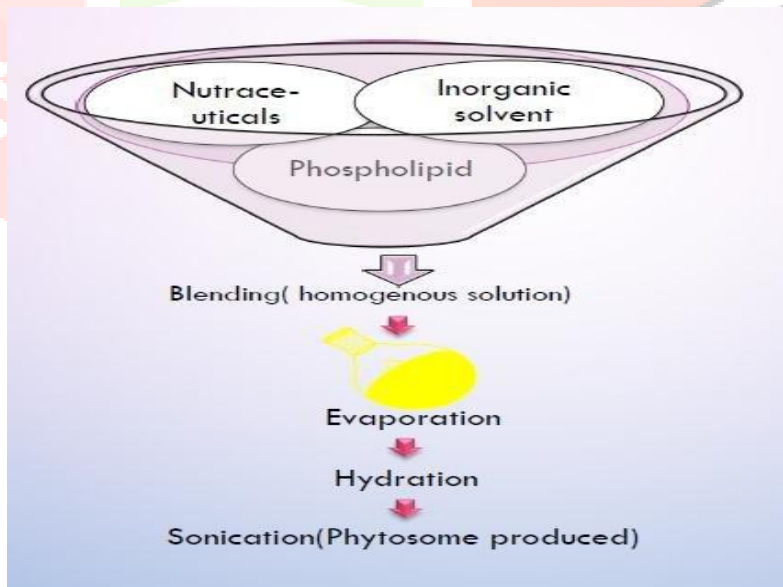


Figure 3- General procedure

❖ **Formulation of phytosome :**

Chemicals	Role
1) Cumin seed oil	It aids in digestion, stimulates secretion of digestive enzymes, and removes gas from the intestine and stomach. Cumin seeds are used in cooking and the oil is used to flavor food and scent cosmetics.
2) Phospholipid	Phospholipids stand widely distributed inside of a plant, an egg yolk, they are, and classified based on their backbones, specifically sphingomyelins and glycerophospholipids. The primary components of glycerophospholipids are Phosphorylcholine, Phosphorylethanolamine, Phosphorylglycerol, Phosphorylserine, Phosphorylinositol, and Phosphodic Acid (PI). Currently, commercially produced phospholipids may be found on the market. The main phospholipids involved in the production of complexes with a hydrophilic head group, two hydrophobic hydrocarbon chains, and are PS, PE, and PC [10]. Due to its amphipathic character, which allows for mild solubilization in aqueous and lipid solutions media, PC is the most preferred phospholipid among them and is used in the creation of phospholipid complexes. PC is also an important a component of cell membranes helps explain why it works well with living things and doesn't harm them.
3) Solvent	A number have been used in the past used by scientists for the synthesis of phospholipid phytocomplexes. In most cases, aprotic solvents such as ethyl acetate, hydrocarbons, cyclic ethers, halogen derivatives, and methylene chloride have all been used towards synthesise complexes of phytophospholipids. However, owing to their success rate, ethanol and methanol are examples of prototic solvents have taken their place. In research to treat inflammatory disorders, the combination of rutin and phospholipids created using methanol. The authors developed a polymeric matrix patch for a better medication retention period over the skin. Results indicated that the improved preparation exhibits 31.32 and 26.56% of the skin penetration, then the patch's anti-inflammatory impact demonstrated its efficiency in a rat-paw oedema model when compared to standard diclofenac gel. In order to improve the absorption of glucose in muscle cells, developed chrysinloaded phytosomes. Solvent evaporation technology is used as a way to create phytosomes that are loaded with chrysin [12]. It was phytosomes created through integrating phospholipids from eggs or soy PC.
4) n-hexane	n-hexane as an antisolvent and drying to get the complex in the form of precipitate

Table 2- Formulation of phytosome❖ **EVALUATION OF PHYTOSOMES:****1) Digital microscopy –**

The prepared phospholipid complex was shaken with water and viewed under a digital microscope with a 400X objective (4)

2) Particle size analysis –

Particle diameter and polydispersity index were recorded by BECKMAN COULTER, Delsa™ Nano. The phospholipid complex preparation was diluted with methanol solvent and then analyzed.[4].

3) Entrapment efficiency

The phospholipid preparation was removed and centrifuged using a cold centrifuge (Remi) at 12000 rpm at 4°C for 1 hour. The absorbance of the solution was measured at λ max 420.0 nm using a UV/visible spectrophotometer (Labindia 3000+). The vesicles are disrupted by applying 1 ml of 0.1% Triton x 100 to the sediment and diluted to 100 ml with phosphate-buffered saline, yielding an absorbance of 420.0 nm. The amount of quercetin in the supernatant and sediment gives the total amount of kapok in 1 ml of dispersion. The encapsulation value is calculated according to the following formula: (5)

4) Particle size and size distribution

Particle size, particle size and zeta potential of optimized phytosome samples were determined by dynamic light scattering (DLS) using a computerized detection system (Malvern Zetamaster ZEM 5002, Malvern, UK). Determine the potential of the plant body, including the Stern layer (zeta potential), by injecting the zeta potential into the body (5)

5) In vitro drug release study

In vitro drug release samples were performed using a USP Type II dissolution apparatus (flap type). Put 900 ml of 0.1N HCl dissolution medium into the dissolution vessel, keep the temperature at $37 \pm 0.5 \text{ }^\circ\text{C}$ and the rotation speed at 50. Operate the machine for 10 hours. Use a 10 ml pipette to withdraw 5 ml of sample every 1 to 10 hours. Replace new dissolution medium ($37 \pm 0.5 \text{ }^\circ\text{C}$) with the same amount of sample each time. 0.5 ml of this was taken and diluted to 10 ml and absorbance spectrometry was used at 420.0 nm [5].

6) Stability studies of optimize phytosome formulation

The prepared phospholipid complexes were examined for stability at $40 \pm 2 \text{ }^\circ\text{C} / 75 \pm 5\% \text{ RH}$ and $30 \pm 2 \text{ }^\circ\text{C} / 60 \pm 5\% \text{ RH}$ for 3 months according to ICH guidelines.[5]

❖ Result:

Data size and % encapsulation efficiency are reported in the range of 217-340 nm and 50-71%, respectively, as shown in Table 2 and Figures 3 and 4. The encapsulation efficiency of 71.25% indicates a drug:lipid ratio of 1. : 1.5 as the best ratio for complex formulation. As lipid concentration increases, encapsulation efficiency decreases; This indicates that increasing the lipid concentration does not help encapsulate more drug into the matrix. The best F3 formulation is structurally evaluated by drug release studies and UV spectroscopy of the formulation.

Table 3: Particle size and entrapment efficiency of extract loaded phytosomes

F. Code	Particle size	%Entrapment Efficiency
F1	250.23±1.45	56.25±2.12
F2	245.65±2.65	60.32±3.14
F3	217.90±2.45	71.25±3.52
F4	302.12±2.14	50.12±4.12
F5	340.56±1.56	54.56±3.14
F6	310.25±3.14	56.65±3.12

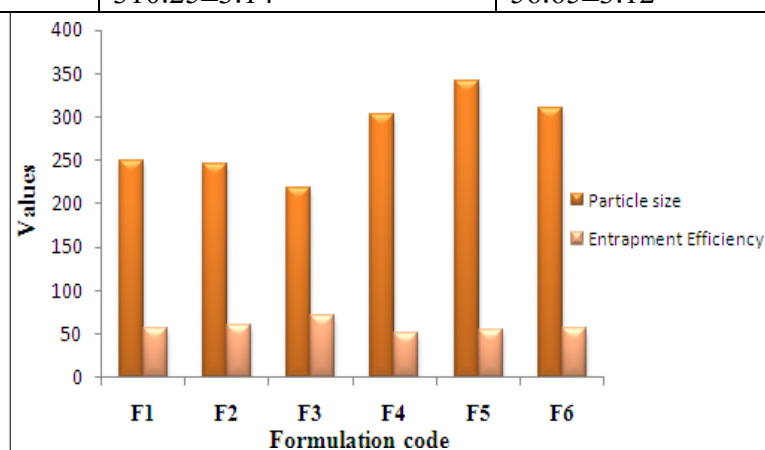


Fig 4: Particle size and entrapment efficiency of extract loaded phytosomes**Table 4: In vitro drug release data for F3**

Time (Hrs)	Cumulative* Percentage Drug Release \pmSD	Log cumulative Percent Drug Remaining
1	20.12	1.902
2	33.65	1.822
4	45.65	1.735
6	53.12	1.671
8	65.45	1.538
12	84.65	1.186

❖ Conclusion:

Fennel leaf extract has hepatoprotective activity. Research on phospholipid complexes may improve treatment and reduce the frequency of drug use. Phytosome is formulated using the solvent evaporation method. In summary, the body of the plant is ready. Phospholipid complexes have improved medicinal properties and have wide applications in the field of cosmetology. The planting method is unconventional, simple and repeatable. In addition, the benefits of phospholipids to the body are also utilized. Among the future prospects of medical practice, many parts of the plant body are still reported. It exhibits a continuous structure with improved free radical scavenging activity. Cumin herb shows hepatoprotective activity and is traditionally used in the treatment of diabetes. Although there are many herbal products on the market, there are many herbal products that have not yet been established in the herbal arsenal that have the best potential to treat life-threatening diseases. More research is generally needed to develop targeted phospholipomas.

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