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Research Article

FORMULATION AND EVALUATION OF CAPSULES OF *Syzygium cumini* PHYTOSOMES

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ABSTRACT

The objective of the study was to develop a novel Phytosome formulation of *Syzygium cumini* capsules by incorporation of phospholipids, for the improved permeability, solubility and better physical characteristics. The *Syzygium cumini* phytosome capsules were prepared by using Thin Film Hydration Technique method and were optimized. The formations of phytosomes were analyzed for microscopic view, SEM, TEM, measurement of particle size & zeta potential, drug entrapment efficiency, drug content, *In vitro* dissolution studies and also the release kinetics of *Syzygium cumini* phytosomes complex. The *Syzygium cumini* phytosome capsules prepared by using Thin Film Hydration Technique showed a good microscopic view and practical yield, the drug content, SEM, TEM, measurement of particle size & zeta potential and other *in vitro* studies were resulted as anticipated. The *Syzygium cumini* phytosome capsules were found to show better solubility and compatibility with the excipients, it is concluded that *Syzygium cumini* extract phytosomes has better physical characteristics and improved permeability, solubility than that of extract to overcome ability to cross lipid-rich biological membranes and which results in increase oral bioavailability.

KEYWORDS: *Syzygium cumini* phytosome, Thin Film Hydration Technique method, FTIR, SEM & TEM.

INTRODUCTION

Even in area where modern medicines are used now a day, the interest on herbal medicines and its phytonutrients utilization have been increasing rapidly in recent years for treatment of various health aliments. The plant derivatives like *Echinacea* (stimulate the immune system and herpes), *Dong quai* (gynecological complaints and lower blood pressure), *Garlic* (reduce the risk of heart disease by lowering levels of blood fats and cholesterol, antibiotic and antiviral properties),*Ginger* (treating nausea, including motion sickness and morning sickness),*Ginkgo biloba* (treat poor blood circulation and tinnitus),*Ginseng* (treat weakness used to reduce blood pressure and cholesterol levels) and *hypericum* (treating mild to moderate depression & anxiety and insomnia) were used to cure various diseases. Recently developing countries are mostly relying on traditional medicines and according to the World Health Organization, 75% of the world's populations are using herbs for various basic healthcare needs[1]. From the traditional herbal medicines a wide range of bioactive constituents can be obtained through various extractions namely artemisinin, camptothecin, paclitaxel, reserpine, vinblastine and vincristine. Most of the extracted components of biologically active constituents of plants have polar molecules which are of water-soluble phytoconstituents like flavonoids, tannins, glycosidal aglycones etc., are poorly absorbed due to physico chemical property, macromolecular size, due to which cannot be absorbed by passive diffusion or due to their poor lipid solubility, thereby less ability to cross lipid-rich biological membranes, resulting in their poor bioavailability[2]. The Phytosome technology, a novel drug delivery system, can overcome the above problems from the hydrophilic environment into the lipid-friendly environment of the enterocyte cell membrane to the cell. The Phytosome patented technology, is developed by Indena S.P.A of Italy[3]. It involves incorporation of standardized plant extracts into phospholipids to produce lipid compatible molecular complexes.

Phytosomes are defined "Phyto" means plants and some means cell-like, which is a novel drug delivery system in which hydrophilic choline moiety (head) binds to phytoconstituents (polar) and lipophilic phosphatidyl moiety surrounds choline bound phytoconstituents or form outer layer, therefore phytoconstituents become lipid soluble[4]. Phytosomes were found to have improved pharmacokinetics and pharmacological parameter[5-7].

Syzygium cumini (L.) is belonging to the family Myrtaceae having synonym of *Syzygium cumini Lam* and common name – Jamun, is a well known tree of Indian subcontinent and adjoining regions of Southeast Asia, Australia. The Large trees cultivated throughout India for the edible fruits (Black Plum) and are reported to contain vitamin C, gallic acid, tannins, anthocyanins, includes cyanidin, petunidin, malvidin glucoside and other components[8-9]. *Syzygium cumini* is a medicinal plant, whose parts were pharmacologically, proved to posse's antiinflammatory,

hepatoprotective, antihyperlipidemic, diuretic, hypoglycemic, antibacterial, anti – HIV activity and anti- diarrheal effects[10-13].

MATERIALS AND METHODS

Phosphatidylcholine (soy lecithin) & Cholesterol (Germany), solvents (dichloromethane, ethanol, and methanol) used were of analytical grade. All the glassware used was BOROSIL®. Equipments: UV-Visible spectrophotometer (Shimadzu 1700), centrifuge (Remi), Particle size analyzer (Malvern Instruments Ltd, UK), FTIR (Shimadzu), Thin Film Hydration Technique using Rotary Flash Evaporator (Roteva, Medica Mfg. Co.,)

Preparation of plant extract

The seeds of the *Syzygium cumini* were processed by the removal of the fruits outer coating and the inner kernel were taken, dried under shade and powdered well. The preparation of hydro alcoholic extracts in the ratio 70:30 % v/v. The extraction was carried out by using Soxhlet's apparatus for 48 hrs. The *Syzygium cumini* seeds hydro ethanolic extract yields obtained were 9.1%w/v. The hydro ethanolic *Syzygium cumini* extract was used for further studies.

Characterization of powdered drug *Syzygium cumini*

Organoleptic properties & wavelength maxima

Syzygium cumini extract was observed for its organoleptic properties like color, solubility. Concentration 100µg/ml of *Syzygium cumini* extract dissolved in phosphate buffer (pH6.8) scanned over a wavelength range of 200-400nm respectively in UV-Visible spectrophotometer (Shimadzu 1700) to get the wavelength maxima.

Solubility profile of *Syzygium cumini*

Solubility of *Syzygium cumini* extract was determined in different solvents such as water, ethanol, methanol, DMSO (Dimethyl sulfoxide) and in phosphate buffer at pH 6.8.

Compatibility studies

FTIR spectroscopy studies were carried out to predict the physicochemical interactions due to the formation of a complex between them between *Syzygium cumini* extract, cholesterol and soy lecithin in the prepared formulation. The *Syzygium cumini* cholesterol and soy lecithin were triturated well with potassium bromide (KBr) pellets in the ratio of 1:100. Then the mixture was introduced in the sample holder and scanned to obtain the graphs in the range of 4000–400 cm^{-1}. FTIR spectrum obtained for the physical mixture of *Syzygium cumini* extract, cholesterol and soy lecithin was compared with *Syzygium cumini* extract and the prepared formulations.

Preparation of *Syzygium cumini* phytosomes complex

Trial formulations of hydroethanolic extract of *Syzygium cumini* was prepared by Thin Film Hydration Technique using Rotary Flash Evaporator, stirred at 50 to 100 rpm for 30 min (Roteva, Medica Mfg. Co.,) to get spherical vesicles. Appropriate amount of cholesterol and lecithin were taken in round bottom flask, dissolved by addition of chloroform and methanol in the following ratios (1:2; 1:1; and 2:1). The flask was rotated at above 1.5cm above a water bath at 40 ± 2ºC under pressure, until all the organic phase evaporated and a thin layer was formed on the wall of the round bottom flask.

The hydroethanolic extract of *Syzygium cumini* (10mg) was dissolved in 20 ml of distilled water and hydrated with dried layers of cholesterol (15 mg) and lecithin (40 to 60mg) in the round bottom flask the mixture was again rotated in a water bath at 40 ± 2ºC for 1 hr. The complex was then sonicated using 3 mm spindle ultra sonicator (Vibronics). The phytosome vesicle containing *Syzygium cumini* extract were subsequently formed, further subject to ultra sonication for 10 to 20min to get spherical vesicles. [The formed Phytosomal suspension was freeze dried to obtain dry powder by using (Lark, Haryana, India)].The prepared phytosomes were stored in refrigerator (10 to 20◦ C) for further evaluations. During the preparation of phytosomes, various parameters were optimized to get a stable formulation[14].

Characterization of *Syzygium cumini* Phytosomes

Microscopic view

Optical microscopy was used for characterization of the *Syzygium cumini* phytosomes complex. The complex was suspended in water and a drop was placed on a glass slide and covered with a cover slip. Microscopic view (ALCO, AMBALA CANTT) of the complex was observed at a magnification of 200X and shown in fig: 7.

Transmission Electron Microscopy (TEM)

Morphological examination of was done for the prepared *Syzygium cumini* phytosomes formulation. The sample was prepared by centrifuging the phytosomes dispersion. A drop of the resultant phospholipids' complex dispersion was placed onto a carbon – coated copper grid, leaving, a thin liquid film was dried and finally viewed for the mean particle size for vesicles was measured and photographed using TEM Fig :8 (Technai, Philips, Netherlands)

Scanning Electron Microscopy (SEM)

Scanning electron microscopy (Model Jeol-5600, Japan) study was done to determine the surface morphology, size and shape of prepared *Syzygium cumini* phytosomes formulation. The optimized freeze dried Phytosome, was subjected for Scanning electron microscopy and photographed in fig: 9& 10.

Measurement of particle size

The particle size of *Syzygium cumini* phytosomes was measured by particle size analyzer (Malvern Instruments Ltd). For the measurement, 100 µl of the formulation was diluted with an appropriate volume of distilled water and the diameter of the vesicle was determined and shown in fig: 11.

Measurement of zeta potential

Zeta potential is the most important parameter for physical stability of phytosomes. The higher the electrostatic repulsion

between the particles the greater is the stability. Zeta potential measurement of the optimized phytosome *Syzygium cumini* suspension was done. (Malvern Instruments Ltd). For the measurement, 1ml of the sample was diluted to 10ml with water, 5ml of this diluted sample was transferred to a cuvette and the zeta potential was measured and shown in fig: 12.

Drug entrapment efficiency

Syzygium cumini phytosome complex was diluted 1-fold with phosphate buffer, and centrifuged at 18,000 rpm for 1/2 h at 5°C using cooling centrifuge (Meditech Technologies India Private Limited, Chennai). The supernatant was isolated and the amount of free drug was determined by UV spectrophotometer at 254nm. To determine the total amount of drug, 0.1 ml of the phytosome suspension was diluted in methanol, adjusting the volume to 10 ml and shown in table 8 & fig: 13.

The entrapment efficiency was calculated according to the following formula: [15-16]

$$\text{Entrapment efficiency (\%)} = \frac{\text{(Total amount of drug) – (Amount of free drug)}}{\text{(Total amount of drug)}} \times 100$$

Determination of drug content

Drug content of was determined by dissolving accurately weighed quantity of *Syzygium cumini* phytosome dispersion in 10 ml methanol. After suitable dilution absorbance was determined by UV spectrophotometer at 254 nm and drug content was determined by using the formula and shown in table 8 & fig: 13.

$$\text{Drug Content (\%)} = \frac{\text{Actual drug content in Phytosomes}}{\text{Theoretical yield}} \text{X100}$$

In vitro dissolution studies

The prepared *Syzygium cumini* phytosomes was loaded in zero size capsules. *In-vitro* dissolution studies for all the prepared formulations was carried out using type-II apparatus at 50rpm in 900 ml of phosphate buffered saline 6.8 pH as a dissolution media, maintained at 37°C±2°C. 5ml aliquots were withdrawn at the specified time intervals and assayed spectrophotometrically. An equal volume of fresh media was replaced after each sampling to maintain the constant volume. The samples were analyzed at 254nm using UV-visible double beam spectrophotometer (Shimadzu 1700) and shown in fig: 13.

Determination of release kinetics of *Syzygium cumini* phytosomes complex

To study the release kinetics of the *Syzygium cumini* from the best formulation (F2), data obtained from dissolution studies were computed in different kinetics model of (a) zero order (cumulative percent drug released vs. time) (b) first order (Log cumulative percent drug retained vs. time) (c) Higuchi (Log cumulative percent drug released vs. square root of time) (d) Korsmeyer equation (Log of cumulative % release Vs log time). The regression coefficient values of different release kinetics equations were evaluated by computing the data of release profiles of optimized *Syzygium cumini* formulation. The computed *Syzygium cumini* release kinetics was shown in Fig: 15 -18 and the data are summarized in Table: 9, the value of K (release rate constant) was calculated from the slope of the dissolution profiles.

RESULTS AND DISCUSSION

***Syzygium cumini* organoleptic properties**

Syzygium cumini extract was analyzed for the organoleptic property; the extract was brown in nature. *Syzygium cumini* was found to be soluble in ethanol, methanol, phosphate buffer (pH 6.8) and dimethyl sulphoxide.

Determination of wavelength maxima

The wavelength of the concentration 100µg/ml of *Syzygium cumini* extract phytosome in phosphate buffer (pH 6.8) was found to be 254nm in UV-Visible spectrophotometer (**Fig: 1**) and is the typical spectral peak of gallic acid which is present abundantly in *Syzygium cumini* extract.

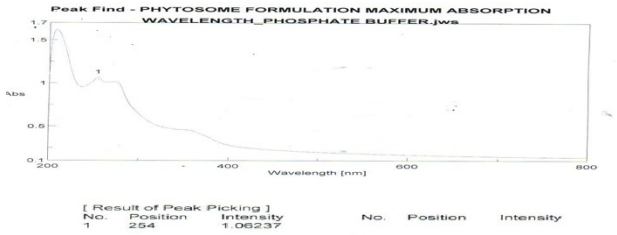


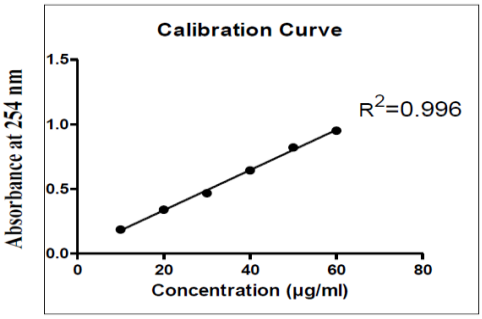
Fig: 1 Results of wavelength measurement of *Syzygium cumini* extract phytosome in phosphate buffer (pH 6.8) in UV-Visible spectrophotometer

Standard calibration curve of *Syzygium cumini* in UV spectrophotometer

The UV absorbance of *Syzygium cumini* standard solution in the range of 10-60µg/ ml of drug in phosphate buffer pH 6.8 showed linearity at λ max 254nm. The linearity was plotted for absorbance against concentration with R^2 value 0.996 and with the slope equation y = 0.0161x (Table: 1 & Fig: 2)

Table: 1 & Fig: 2 Results of Standard calibration curve of *Syzygium cumini* in UV spectrophotometer

Sl No.	Conc. (µg/ml)	Absorbance (nm)
1	10	0.1855
2	20	0.3397
3	30	0.4665
4	40	0.6433
5	50	0.8210
6	60	0.9504



Results of compatibility studies *Syzygium cumini*

The compatibility between the *Syzygium cumini* and cholesterol, lecithin was evaluated using FTIR peak matching method. The interaction *Syzygium cumini* extract with phospholipids'and lecithin due to the formation of a complex between them was found in FT-IR spectroscopy peaks. The FTIR spectroscopy revealed shifting of hydroxyl group (OH) to a lower frequency in phytosome spectra (3451cm-^{1} to 3416cm-^{1}) as compared to spectra of *Syzygium cumini*, indicating the formation of strong hydrogen bonding between hydroxyl group of phospholipids and extract phytoconstituents in *Syzygium cumini* phytosome form. The complex formation in *Syzygium cumini* is a characteristic feature of phytosome formation (Fig: 3-6).

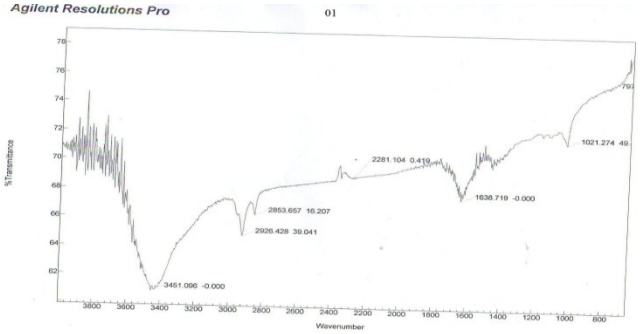


Fig: 3 FTIR spectrum of cholesterol, lecithin.

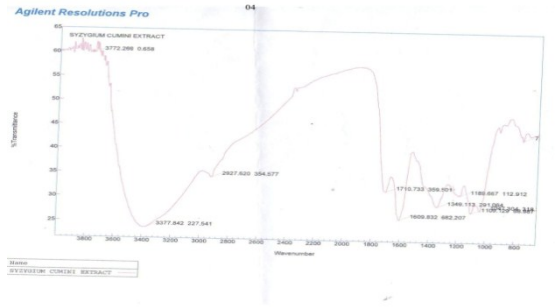


Fig: 4 FTIR spectrum of *Syzygium cumini*

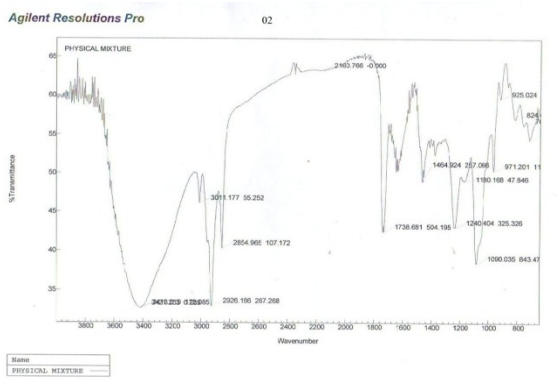


Fig:5 FTIR spectrum of physical mixture of *Syzygium cumini,* cholesterol and lecithin.

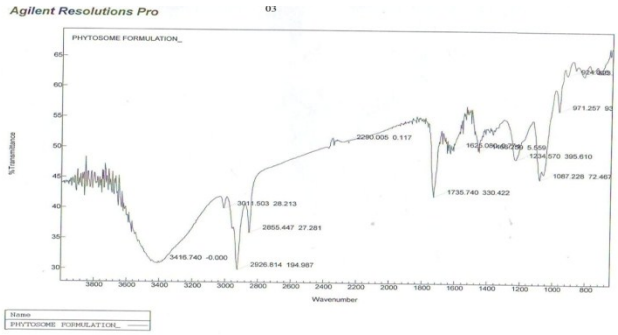


Fig: 6 FTIR spectrum of phytosome formation

Preparation of *Syzygium cumini* phytosomes complex

Syzygium cumini phytosomes complex prepared by Thin Film Hydration Technique method in the ratios of Drug : Cholesterol : Lecithin (1:1.5:4; 1:1.5:5; & 1:1.5:6) and were optimized based on basis of effective concentration of the *Syzygium cumini* drug and phospholipids ratio, amount of solvent, rotating speed, ultrasonication time and temperature during ultrasonication as shown in Table 3-7.

Optimization Parameters

During the preparation of *Syzygium cumini* phytosomes formulation the amount of solvent (methanol and chloroform) were adjusted to get thin uniform film (Table 2). The methanol: chloroform ratios of 1:2; 1:1 and 2:1 were optimized to get thin uniform film of good performance, qualities and suitability of phytosomes. The methanol and chloroform 1:2 ratio results in

thick & non uniform film, 1:1 ratio results forms a thin uniform film of the suitable requirement and the 2:1 ratio took more time to form the phytosomes with less vesicle. And hence the 1:1 ratio (5 ml: 5 ml) of methanol and chloroform were the best optimized solvent ratios to get thin uniform film of *Syzygium cumini* phytosomes complex.

Table: 2 Optimization of Solvent for the preparation of *Syzygium cumini* phytosomes complex

Amount of methanol and chloroform	Observation
1:2 (5 ml : 10ml)	Thick, non uniform film
1:1 (5 ml : 5 ml)	Thin uniform film
2:1 (10 ml : 5 ml)	Took more time, less vesicle

In the preparation of *Syzygium cumini* phytosomes formulation the rotating speed of rotary flash evaporator - stirrer was adjusted in order to get spherical vesicles to get thin uniform film (Table 3). At a speed 50 ± 5 rpm results in clumps of *Syzygium cumini* phytosome, 100 ± 5 rpm speed forms good spherical vesicles of expected design, and with >100 rpm speed irregular shaped vesicles was seen. Hence, the optimized rotating speed of rotary flash evaporator stirrer was adjusted of 100 ± 5 rpm which results in uniform spherical vesicles of *Syzygium cumini* phytosomes of desired vesicles.

Table: 3 Optimization rotary flash evaporator stirrer speed for the preparation of *Syzygium cumini* phytosomes complex

Rpm	Observation
50 ± 5	Clumps
100 ± 5	Spherical vesicles
>100	Irregular shaped vesicles

Table:4 Optimized formula for the preparation of *Syzygium cumini* phytosomes complex

Formulation Code	Drug (mg)	Cholesterol (mg)	Lecithin (mg)	Methanol (ml)	Chloroform (ml)	P.water (ml)	Drug: Cholesterol: Lecithin
F1	10	15	40	5	5	20	1:1.5:4
F2	10	15	50	5	5	20	1:1.5:5
F3	10	15	60	5	5	20	1:1.5:6

Optimized formula for the preparation of *Syzygium cumini* phytosomes complex was shown below (Table 5). A trial and error method was done to get desired performance, better qualities and optimum suitability of *Syzygium cumini* phytosomes. Three trials formulation (F1,F2& F3) of *Syzygium cumini* phytosomes were formulated, and contains a constant drug - *Syzygium cumini* extract (10mg), cholesterol (constant 15mg) in all batches, lecithin (in varying quantity of 40- 60mg), methanol and chloroform (each 5 ml in all batches), purified water (20ml in all formulation) were added. The drug: cholesterol: lecithin ratio was 1:1.5:4 (F1); 1:1.5:5 (F2) and 1:1.5:6 (F3). The amounts of solvent, rotating speed of rotary flash evaporator stirrer were optimized previously.

Table: 5 Optimization of Drug Vs Cholesterol and Lecithin for the preparation of *Syzygium cumini* phytosomes complex

Formulation Code	Drug (*Syzygium cumini* extract)	Cholesterol	Lecithin
F1	1 (10 mg)	1.5 (15 mg)	4 (40 mg)
F2	1 (10 mg)	1.5 (15 mg)	5 (50 mg)
F3	1 (10 mg)	1.5 (15 mg)	6 (60 mg)

Further in the preparation of *Syzygium cumini* phytosomes complex the ultrasonication time and temperature during ultrasonication were optimized (Table 6). In order to get good spherical vesicles with required entrapment efficacy the ultrasonication time was set in between 10, 15 and 20 min. At 10 and 20 min of ultrasonication time incomplete and large sized vesicles & broken vesicles were obtained respectively. The desired spherical vesicles were obtained at the ultrasonication time of 15min.

The optimization of temperature during Ultrasonication was also adjusted to get numerous vesicles of moderate of desired size (Table 7). During 5 to 10°C and room temperature (25±2° C) Small size vesicles & large size vesicles, aggregates were formed respectively. The better qualities and optimum suitability of spherical vesicles were obtained at 10 to 20° C.

Table: 6 Optimization of Ultrasonication time in the preparation of *Syzygium cumini* phytosomes complex

Time (min)	Observation
10	Incomplete and large sized vesicles
15	Spherical vesicles
20	Broken vesicles

Table: 7 Optimization of temperature during Ultrasonication in the preparation of *Syzygium cumini* phytosomes complex

Temperature (° C)	Observation
5 to 10	Small size vesicles
10 to 20	Numerous vesicles of moderate size
Room temperature (25±2° C)	Large size vesicles, aggregates

CHARACTERIZATION OF *Syzygium cumini* PHYTOSOMES COMPLEX

Microscopic view

The prepared and optimized *Syzygium cumini* phytosomes under optical microscopy showed the characteristic features of presence of sphere shaped vesicles at the magnification of 200X. The phytosomes complex was thin uniform film of numerous vesicles of moderate, with uniform sizes were seen (Fig: 7).

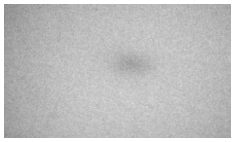


Fig:7 Microscopic view *Syzygium cumini* phytosomes

Transmission Electron Microscopy (TEM)

TEM is a vital characterization tool for directly imaging of the *Syzygium cumini* phytosomes capsules, quantitative measures of particle, size, size distribution and morphology in a two dimensional projection of the sample. Electron beam passes the TEM grids at half way down the column of the thin sample which shown the particle of spherical size ranges from 0.01 to 0.02µm (Fig: 8).

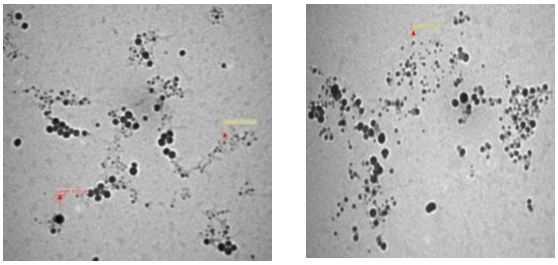


Fig:8 TEM of *Syzygium cumini* phytosomes

Scanning Electron Microscopy (SEM)

Electron gun generates high energy electrons which are focused into a fine beam, which is scanned across the surface of the specimen of the *Syzygium cumini* phytosomes. The image (FIG) obtained was the characteristic feature of the typical phytosome where showed irregular semisolids with different size, with irregular edges were observed. In FIG shows a complete change in the internal crystalline structure due to complex formation (Fig: 9 &10).

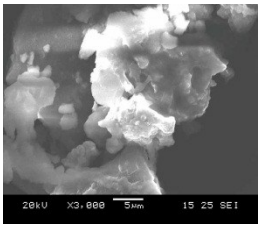


Fig:9 SEM of *Syzygium cumini* phytosomes

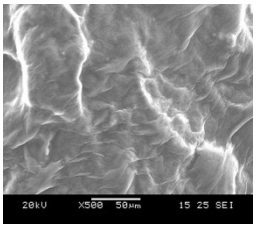


Fig:10 SEM of *Syzygium cumini* phytosomes after dilution in distilled water

Particle size and Zeta potential of optimized Syzygium *cumini* phytosomes

Optimized phytosomes were analyzed for their particle size distribution and zeta potential values. The F2 *Syzygium cumini* phytosomes complex (Fig: 11) was analyzed under for laser light scattering technique in the particle size analyzer by Malvern. It was observed that the average particle size was found to be 143nm for optimized formulation (F2) *Syzygium cumini* phytosomes complex.

Zeta potential is known as the electric potential and is measured in the phytosomal preparation of F2 selected formulation (Fig: 12) and it is the potential difference between the dispersion medium water and the *Syzygium cumini* phytosomes complex. The magnitude of the zeta potential in similarly charged particles of *Syzygium cumini* phytosomes complex confirm the high integrity in the complex and the zeta potential value was found to be -37.7 indicating good stability of the formulation.

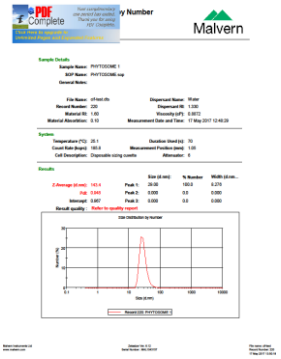


Fig: 11 Particle size

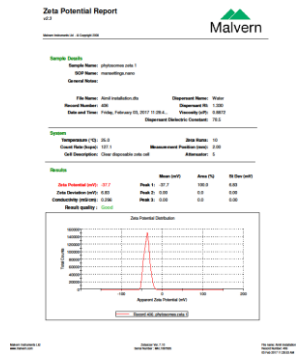


Fig:12 Zeta potential

Drug Content and Entrapment efficiency

Entrapment efficiency is the ratio of weight of drug entrapped into a carrier system to the total drug added in the *Syzygium cumini* phytosomes complex. The *Syzygium cumini* phytosomes entrapment efficiency and release *in vitro* are very important physicochemical characteristics. According to the drug entrapment study conducted the maximum drug entrapment was shown by F2. The entrapment efficiency of all the prepared formulations was given in Table 8 and graphically represented in fig:13. The formulation F2 showed highest drug content of 81% indicating the optimum amount of lipid required for the formation of a *Syzygium cumini* phytosomes. With further increase in the lipid concentration, the entrapment efficiency decreased indicating that the lipid concentration did not help in entrapping the drug into the matrix.

Table: 8 Drug Content and Entrapment efficiency of *Syzygium cumini* Phytosomes

Formulation Code	Drug Content (%w/w)			Avg (%w/w)	Entrapment Efficiency (%)			Avg (%)
F1	65	61	59	**61**	41	33	45	**40**
F2	84	78	82	**81**	63	65	71	**66**
F3	61	67	65	**64**	54	48	52	**51**

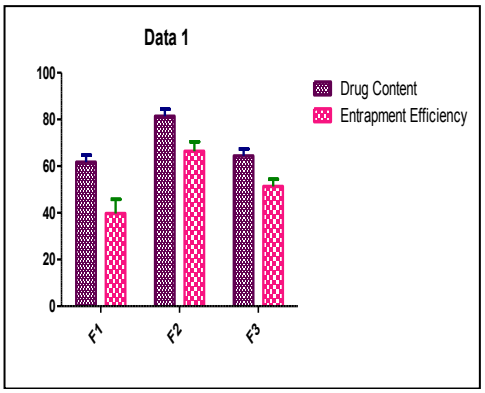


Fig: 13 Diagrammatic representation of drug Content and Entrapment efficiency of *Syzygium cumini* Phytosomes

IN VITRO DISSOLUTION STUDIES

The *Syzygium cumini* phytosomes (F1, F2, F3) was loaded as 250mg capsules and subjected to *in vitro* dissolution studies using USP- type-II apparatus at 50rpm in 900 ml of phosphate buffer (pH 6.8) as a dissolution media, maintained at 37±5° C. The percentage of drug release from the F1, F2 and F3 was calculated and cumulative % drug release compared with all Syzygium *cumini* phytosomes formulations (FI, F2 & F3) and was graphically represented in figure. It was observed that the formulation F2 (92±0.21%) has highest drug release when compared with F1 (70.00±0.15%) and F3 (78.32±0.41%) which was shown in Fig:13.

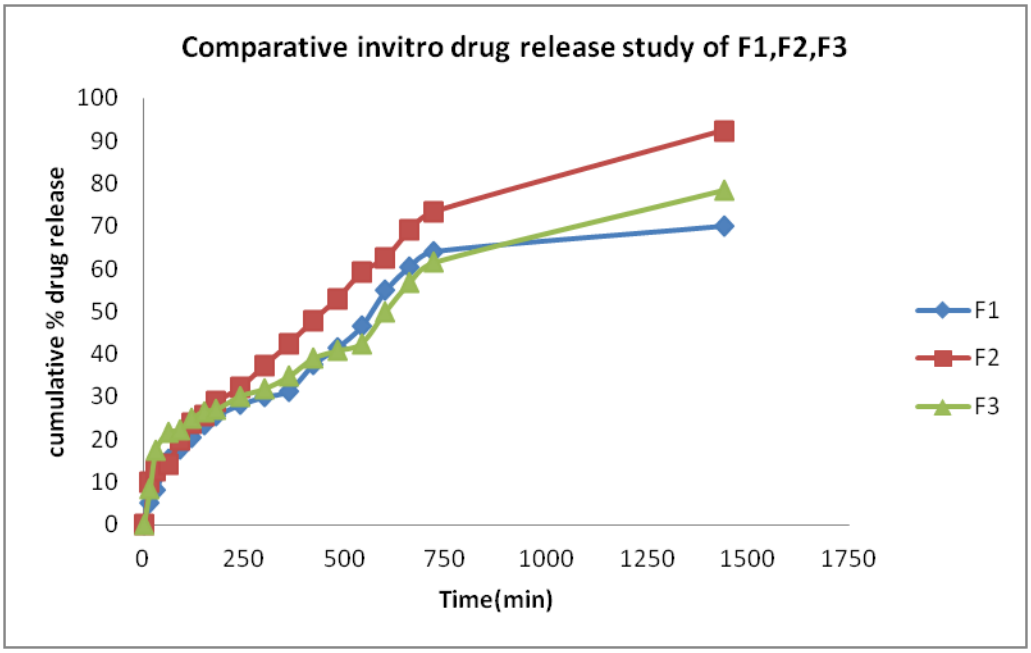


Fig: 14 Cumulative % drug releases from *Syzygium cumini* phytosomes formulation

The release data were computed in different kinetics model of a) zero order b) first order c) Higuchi d) Korsmeyer equation. The regression coefficient values of different release kinetics equations were evaluated by computing the data of release profiles of optimized *Syzygium cumini phytosomes* formulation (Fig: 15-18). The drug release was by diffusion mechanism at a comparatively slower rate, with the increase of release time, square root of release time can be related linearly to % drug released. To confirm diffusion mechanism, the data were fitted into Korsmeyer equation. Effect of erosion on drug release is confirmed by the value of n approaching 1. By Korsmeyer peppas model (R2 =0.9836). Value of release exponent "n" was found to be 0.564. This n value suggests that the release mechanism follows much more Non - Fickian type. The value of n was found with type and concentration of phytosomes complex. And, the drug follows both diffusion and erosion mechanism.

Release kinetics of *Syzygium cumini* phytosomes

Table: 9 Results of *in vitro* release kinetics of optimized formulation F3 of *Syzygium cumini* phytosomes

Batch code	Zero Order R^2	First Order R^2	Higuchi R^2	Korsmeyer peppas R^2
F3	0.7109	0.9754	0.9755	0.9836

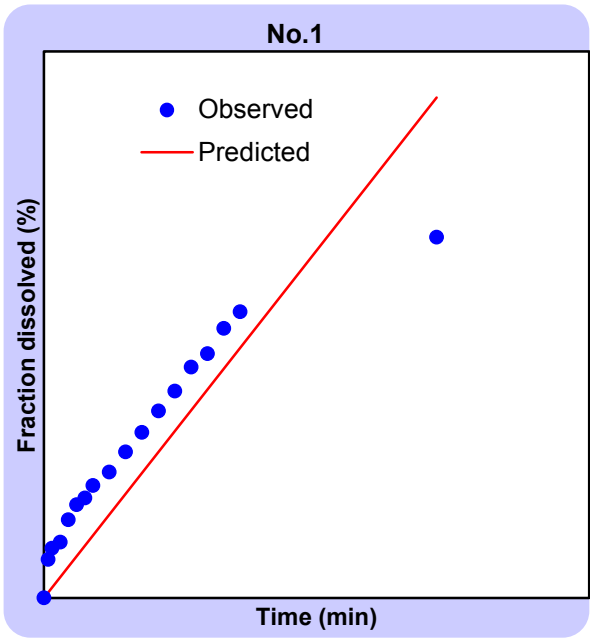


Fig:15 Zero order release (0.7109)

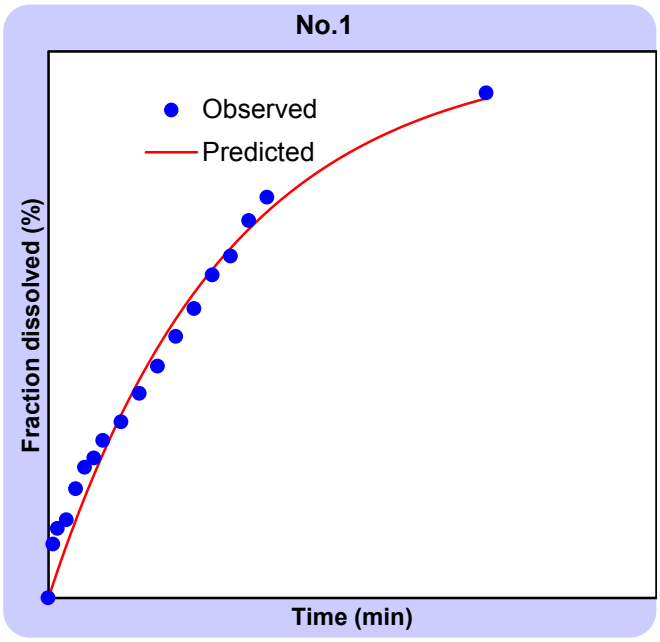


Fig:16 First order release (0.9754)

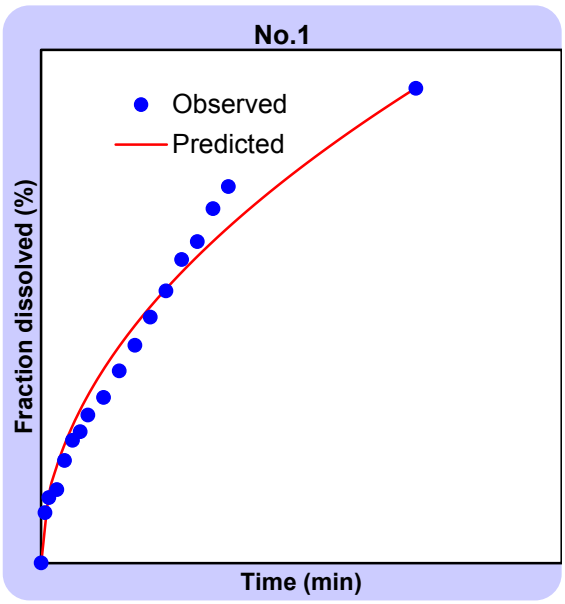


Fig:17 Huguchi (0.9755)

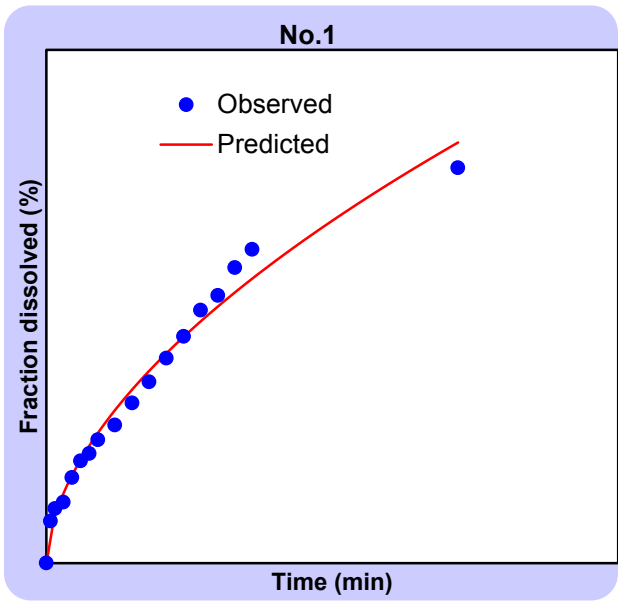


Fig:18 Korsmeyer peppas (0.9836)

Fig: 15-18 The release data were computed in different kinetics model optimized *Syzygium cumini* phytosomes formulation

CONCLUSION

Syzygium cumini phytosomes capsules were successfully formulated using cholesterol and soy lecithin. Soy-lecithin (Phosphatidylcholine) is a phospholipids' are the key component of phytosome process. The prepared phytosomes were formulated in a capsule and was evaluated for *in vitro* drug release. The phytosome was optimized based upon their percentage yield, entrapment efficiency. By FTIR it could be concluded that *Syzygium cumini* and soy lecithin in the complex were joined by non-covalent-bonds, and did not form a new compound. The complex formation in *Syzygium cumini* is a characteristic feature of phytosome formation. The phytosome structure was also evaluated for its spherical size by microscopy, SEM and TEM. From above studies it is concluded that *Syzygium cumini* extract phytosomes has better physical characteristics and proved that phytosomes are more bioavailable as compared to herbal extract

owing to their enhanced capacity to cross the lipid rich biomembranes there by overcome pharmacokinetic variance.

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