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Preparation and Characterization of Phytosomal-Phospholipid Complex of P. Amarus and its Tablet Formulation

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Abstract

Present investigation was aimed at formulation, characterization and evaluation of phytosomal complex tablets for sustained delivery of *Phyllanthus amarus* complex. Phyllanthin, one of the active lignin present in this plant species was isolated from the aerial parts, by silica gel column chromatography employing gradient elution with hexane–ethyl acetate solvent mixture. It was obtained in high yields (1.23%), compared to reported procedures and the purity was ascertained by HPTLC analysis. Phyllanthin was characterized for M.P, UV–Visible spectrophotometry, FT-IR, 1H NMR, 13C and NMR analysis. Release kinetics was evaluated by using United States Pharmacopeia (USP)-22 type I dissolution apparatus. Scanning electron microscopy was used to visualize the effect of dissolution medium on matrix tablet surface. HPTLC was carried out for quantitative and qualitative estimation of Phyllanthin in *Phyllanthus amarus* and R_f of phyllanthin was found to be about 0.25. The content was found to be maximum for phytosomal complex of phyllanthus formed by vaccum drying of 1:1 drug excipient ratio. The in-vitro drug release study revealed that optimized formulation sustained the drug release for 12 hr (88.1% ± 4.1% release). Fitting the in vitro drug release data to Korsmeyer equation indicated that diffusion along with erosion could be the mechanism of drug release.

Key words: - *Phyllanthus amarus, tablet formulation, in vitro release*

1 INTRODUCTION

According to the World Health Organization about 80% of the population in many third world countries still uses traditional medicine (e.g., medicinal plants) for their primary health care, due to poverty and lack of access to modern medicine. Since about 80 % of the 6.1 billion people of the world live in less developed countries i,e 3.9 billion people will likely use medicinal plants on a frequent basis. The investigation of plants as potential sources of new drugs to treat cancer, AIDS and malaria requires the search of as many resources as possible. The discovery of phytochemical compounds with, for example, cytotoxic and anti-tumor activity could lead to the production of new drugs for the treatment of cancer (De Silva., 1997).

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Herbal medicines continue to be a popular healthcare choice with the general public not only for health maintenance and wellbeing, minor ailments (e.g. coughs and colds), chronic conditions (e.g. back pain) and serious chronic diseases (e.g. asthma, cancer, depression, diabetes), but also for 'enhancement' of functions or processes, such as the use of *Ginkgo biloba* products for memory enhancement. In an attempt to support the traditional use of herbal drugs with scientific evidences, lot of research has been carried out during past decades for establishing the pharmacological basis of action and clinical use of herbal medicines. On the other side, similar progress has been done in the field of phytochemistry for establishing the extraction procedure, purification/ isolation procedure and chemical structure of active constituents of these herbal medicines. As a net result we are shifting towards "purer forms of herbal drugs (Purified and standardised extracts, single phytoconstituent)" from the "crude" ones (i.e. roots, leaves etc.). The active ingredients of most of the biological plants are polar in nature even then the water solubility of most of the phytoconstituents is not very good as also the bioavailability. This can be either because of complex molecular nature and size of the phytoconstituents that causes the poor bioavailabilty (Dubey *et.al.,2007*).

Phytosome technology has been effectively used to enhance the bioavailability of many popular herbal extracts including milk thistle, ginkgo biloba, grape seed, green tea, hawthorn, ginseng etc and can be utilized for various therapeutic uses or for administration of dietary supplements. *Phyllanthus amarus* has also been shown to work as an antifungal, antibacterial and antiviral agent and reportedly is also used in traditional medicines in India to treat liver diseases, asthma and bronchial infections (Foo *et.al., 1992*). *P. amarus* is also used traditionally in India to treat cardiovascular problems (Chevallier., 2000). This popular medicinal herb is also a remedy around the world for influenza, dropsy, diabetes and jaundice (Foo, 1993).

To examine the various advantages of phytosomes, especially their ability to enhance the bioavailability of hydrophilic phytoconstituents, as well as lipophilic phytoconstituents various therapeutic applications of phytosomes have been explored. Phytosomes are formulated by patented processes in which the standardized extract (having a standardized content of active principles) or active ingredients of herbs (like flavolignans and terpenoids) are bound to the phospholipids like phosphatidylcholine (PC) through a polar end. The phytosome technology produces small cells which protect the valuable components of the herbal extract from destruction by digestive secretions and gut bacteria. (Dubey *et.al, 2007*). Phytosomes are novel complexes which are prepared by reacting 2-3 moles, or preferably one mole of a natural or synthetic phospholipid, such as phosphatidylcholine, phosphatidylethanolamine or

phosphatidyiserine with one mole of phytoconstituent component, either alone or in the natural mixture, in aprotic solvent such as dioxane or acetone (Bombardelli *et.al*.,1993). From this, phytosomal complex can be isolated by precipitation with non-polar solvent such as aliphatic hydrocarbons or lyophilization or by spray drying (Mascarella., 1991). In the complex formation of phytosomes, the ratio between these two moieties is in the range from 0.5-2.0 moles (Jose *et.al.,1987*).

Therefore present investigation was aimed at formulation, characterization and evaluation of phytosomal complex tablets for sustained delivery of P*hyllanthus amarus* phytosomal complex.

2. MATERIAL AND METHOD

2.1 Materials

Standardized extract of P*hyllanthus amarus was* procured as gift sample from *natural* Remedies Pvt. Limited, Bangalore and Phospholipon 85G from Lipoid, Switzerland. All other materials and chemicals used were of either pharmaceutical or analytical grade.

2.2 Authentication

2.2.1 Nuclear magnetic resonance (NMR)

The NMR (Bruker) spectrum of Phyllanthin was recorded using tetramethylsilane as internal standard

2.2.2 High Performance Thin Layer Chromatography (HPTLC)

Chromatography was performed using commercially-prepared, Precoated silica gel HPTLC plates (20 × 20 cm, GF_{254} Merck, Germany). A Linomat V (Camag, Muttenz, Switzerland) automatic TLC applicator was used to apply samples and standards onto the TLC plate under a flow of nitrogen gas with dosage speed 200 nL/s. The samples were applied as 6 mm wide bands at 12 mm from the bottom and 15 mm from both sides. The syringe used was Hamilton micro liter (100µL) syringe. Each TLC plate was developed to a height of about 10 cm with a mobile phase of hexane: acetone: ethyl acetate (74:12:8) under laboratory conditions (25– 30°C and 40–50% relative humidity). Stock solution was prepared in methanol (1 mg/mL). Working solutions of standard were prepared by appropriate dilutions of the stock solution with methanol in concentration range of 800ng/ml, 1000ng/ml, 1200ng/ml, 1400ng/ml, 1600ng/ml, 1800ng/ml and these concentrations were used to prepare calibration curve for HPTLC.

2.3 Preparation and evaluation of phytosomal complex

Phytosomes were formulated by Indena's patented processes (www.indena.com). Complex was prepared with standardized extract of *Phyllanthus amarus* and phospholipon 85 G at a molar ratio of 1:1 and 1:2. Weighed amount of standardized extract of *Phyllanthus amarus* and phospholipon 85 G were taken in a 100 ml round bottom flask and 20 ml of dichloromethane was added. The mixture was refluxed at a temperature not exceeding 40°C for 2 h. The resultant clear solution was evaporated and 10 ml of n-hexane was added to it with continuous stirring. One of the batch of drug–phospholipid complex was precipitated and the precipitate was filtered and dried under vacuum to remove traces of solvents and the other batch was subjected to rota evaporation resulting in a thin film formation. This thin film was separated. The resultant drug–phospholipid complexes were kept in an amber colored glass bottle, flushed with nitrogen and stored at room temperature.

2.3.1 Microscopic view of the complex

Olympus (CH 20i) microscope was used for microscopic characterization of the complex. The complex was suspended in distilled water and a drop was placed on a slide and covered with a cover slip. Microscopic view of the complex was observed at a magnification of 400X.

2.3.2 Scanning Electron Microscopy (SEM)

The surface morphology of complex was investigated by Scanning Electron Microscope Model JSM6100 (Jeol).

2.3.3 Fourier Transform Infrared Spectroscopy (FTIR)

Fourier transform infrared spectrum (FTIR) was recorded for fractions using infrared spectrophotometer. Samples were prepared in KBr disk (2 mg sample / 200 mg KBr) with a hydrostatic press at a force of 275790.292 Pascal's for 4 min.

2.3.4 Determination of phyllanthin content in complex

The content of phyllanthin in phytosomal complex was determined by solubilizing 10mg/ml of complex in methanol and a 1µl aliquot of the resulting solution was injected into a HPTLC system using precoated silica gel HPTLC plates (20 × 20 cm, GF_{254} Merck, Germany) as stationary phase. The mobile phase was a mixture of hexane: acetone: ethyl acetate (74:12:8)**.** Eluent was monitored at 220 nm.

2.4 Formulation of phytosomal complex tablets

2.4.1 Formation of granules

Tablets of *Phyllanthin amarus* were prepared by dry granulation technique using different polymers. Accurately weighed quantities of presieved drug and granulation materials [diluents (DCP) about 4%, phytosomal complex about 50%, binder (MCC) 10% and glidant (Magnesium Stearate) 2%] were mixed & slugs were prepared. Blend was then subjected to Dry granulation, using flat faced punch.

Various parameters optimized were as follows: (Brook and Marsha, 1968).

(I) Bulk Density (Db)
(II) Tapped Density (Dt)
(III) Angle of Repose Carr's Index
(IV) Hausner Ratio (H)

Dry granulation method

The slugs prepared were milled and passed through scree of 10 mesh size aperture. The granules were sieved. The final granules were blended and compressed using round flat punches tablet press (Multi Punch type, AK Industries, Nakodar, Punjab). Six batches of tablets were prepared for each formulation.

2.4.2 In vitro evaluation of tablets (Indian Pharmacopoeia., 1996)

Thickness

The thickness of the tablets was measured by vernire caliper and expressed in mm.

Hardness

The hardness of the tablet was determined using a Monsanto hardness tester (Interlabs, Ambala, India) and expressed in Kg / cm^2.

Tensile Strength

The load (P) required to cause diametral fracture in a tablet was determined using the Monsanto hardness tester (Interlabs, Ambala, India). Ten tablets randomly selected from a given size fractions were used for the determination. The mean fracture load was used to calculate the tensile strength (T) using the expression below:

$$T = \frac{2P}{\pi Dt}$$

Where, t and D represent the thickness and diameter of the tablet respectively. Triplicate determinations were carried out for the various size fractions and mean determinations.

Friability (F) (James Sworbrick *et.al*)

The friability of the tablet was determined using Roche Friabilator (model no 902). It is expressed in percentage (%). 10 tablets were initially weighed ($W_{initial}$) and transferred into the friabilator. The friabilator was operated at 25 rpm for four mins. The tablets were weighed again (W_{final}). The percentage friability was then calculated by:

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

It is reported in Table 6.

Weight Variation

Ten tablets were selected randomly from the lot and weighed individually to check for weight variation. IP limit for weight variation in case of tablets weighing upto 200mg is ± 7.5%.

In Vitro Disintegration Time

Water was used as disintegration medium. The apparatus was operated for 15 mins with discs after which the state of tablets was examined. If the tablet failed to comply because of adherence to the discs, the test was repeated further with 6 tablets omitting the discs.

In-vitro dissolution studies

In vitro dissolution studies for all the prepared tablets was carried out using USP paddle dissolution apparatus (model no DS 3000) at 50rpm in 500ml of phosphate buffer pH 6.8 as dissolution media, maintained at 37±0.5ºC. 5ml aliquots were withdrawn at the specified time intervals for 12 hr, filtered through whatman filter paper and assayed spectrophotometrically at 220nm. An equal volume of fresh medium, which was pre-warmed at 37±0.5 ° C, was replaced into the dissolution media after each sampling to maintain the constant volume thought the test. The same procedure was repeated for F1,F2,F3,F4,F5,F6.

Scanning Electron Microscopy (SEM)

After 12 hr of dissolution study optimized formulation F4 tablet was allowed to swell for 2 hr in PSB (pH 6.8). Tablet was than dried in desiccator and observed for any alteration in surface morphology using Scanning Electron Microscope Model (JSM6100 Jeol).

Stability studies

Stability studies were carried out for two months on the optimized formulation of sustained release phytosomal tablets. For stability study thirty tablets of optimized formulation were placed in humidity chamber (Sonar) at 75% RH, 45°C. After two months, the optimized formulation was evaluated for weight variation, hardness, friability, disintegration and percentage drug content.

3 RESULTS AND DISCUSSION

3.1 Spectroscopic data for P. amarus extract

3.1.1 NMR Spectroscopic Data for Phyllanthus amarus extract.

The ^{1}H-NMR data of the P*hyllanthus amarus* was represented by distinctive aromatic hydrogen region [H-Ar: δ 6.72 – 6.53 (m)]; methylenedioxy moieties [O-CH_2-O: δ 5.85 (s)]; methoxyl groups bonded to the aromatic ring (OMe-Ar: δ 3.81 – 3.73, 3.51); methoxyl groups bonded to the alkyl moieties (OMe-alkyl: δ 3.31 – 3.19); methynic groups [CH: δ 2.00 – 1.94 (m)]; methylenic groups [CH_2: δ 3.00 – 2.54, 2.26 (m)]; The observed ^{1}H-NMR and ^{13}C-NMR of phyllanthin were reported as in Figure 1.

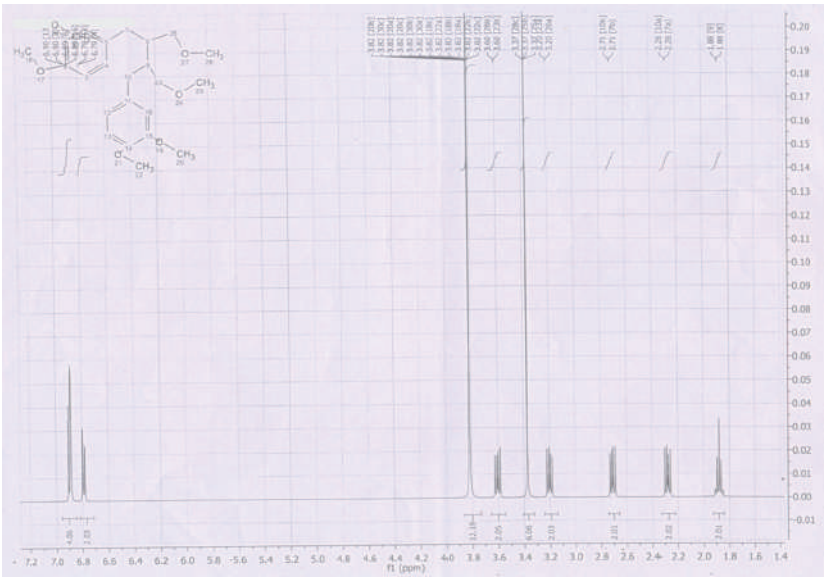

Figure 1: NMR spectra of phyllanthin

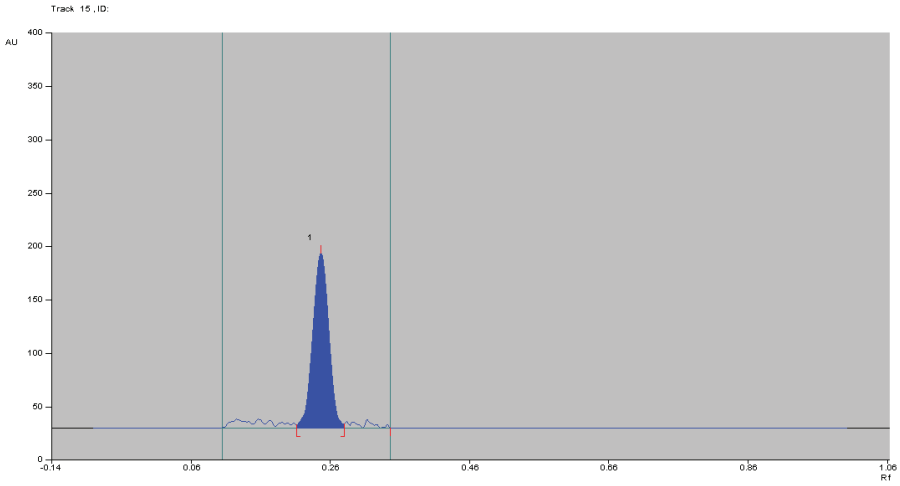

Figure 2: Figure 5.5.HPTLC chromatogram of pure Phyllanthin

1H NMR (500 MHz, $CDCl_3$, TMS):

δ 6.75 [2H-5(5'),d, J = 8.0], 6.65 [2H-6(6'), dd, J = 8.0, 1.9], 6.60 [2H-2(2'), d, J = 1.9], 3.83 [6H-4(4')-OCH_3, s], 3.78 [6H-3(3')-OCH_3, s], 3.30 [6H-9(9')-OCH_3, s], 3.25 [4H-9(9'), m], 2.65 [4H-7(7'), m], 2.05 [2H-8(8'), m].

13C-NMR ($CDCl_3$)

δ: 133.75 (C-1, C-1'), 112.27 (C-2, C-2'), 148.85 (C-3, C-3'), 147.08 (C-4, C-4'), 111.07 (C-5, C-5'), 121.25 (C-6, C-6'), 35.11 (C-7, C-7'), 40.88 (C-8, C-8'), 72.78 (C-9), 72.66 (C-9'), 55.92, 56.00 (OMe-Ar), 58.98 (OCH_3-9, 9').

3.1.2 High performance thin layer chromatography of Phyllanthus **amarus extract**

HPTLC was carried out for quantitative and qualitative estimation of Phyllanthin in *Phyllanthus amarus* and R_f of phyllanthin was found to be about 0.25 and found to be in accordance with results as reported and as shown in the chromatogram Figure 2.

3.1.3 Preparation of Calibration curve by HPTLC

HPTLC was carried out using various concentrations of Phyllanthin stated in the Table 1, and a calibration plot was prepared plotting concentration vs. area under curve as shown in Figure 3

Table 1: Statistical data of conc of phyllanthin and AUC

S.No.	Concentration (ng)	AUC	Statistical parameter
1.	0	0000	y = 3.7319x + 327.93 R^2 = 0.9852
2.	800	3537	
3.	1000	4317	
4.	1200	5040	
5.	1400	5666	
6.	1600	6175	
7.	1800	6669	

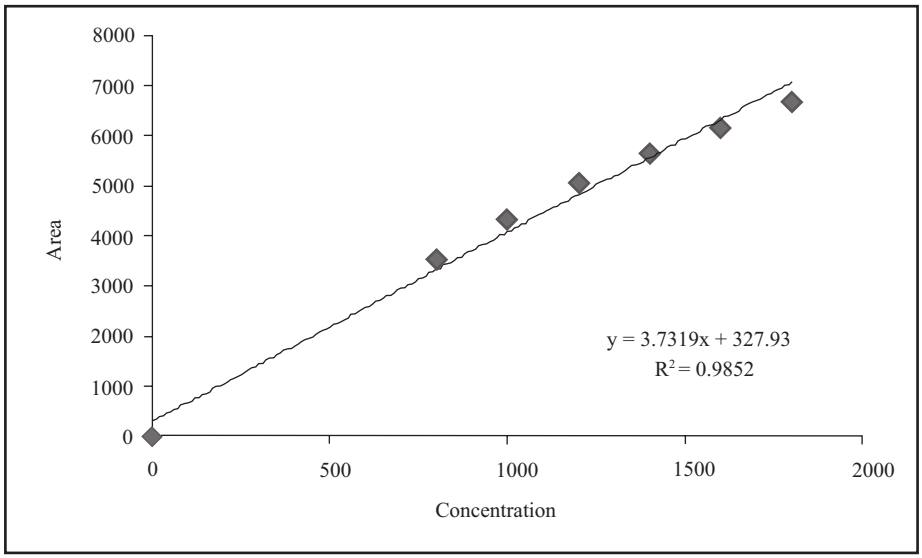

Figure 3: Calibration curve of phyllanthin by HPTLC

3.2 Preparation of Phytosomal Complex

The prepared complex was subjected for further evaluation parameters such as scanning electron microscopy, high performance thin layer chromatography, fourier transform infrared spectroscopy. Phyllanthus–phospholipid complex with different molar ratio 1:1 and 1:2 were analysed for content and surface morphology as shown in Table 2 and Figure 5.

Table 2: Content estimation of phyllanthin in phytosomal complex

Sr. no.	Extract	% of phyllanthin
1	Standardized extract	0.67
2	Phyllanthus 1:1 (Vaccum)	2.8
3	Phyllanthus 1:2 (Vaccum)	1.1
4	Phyllanthus 1:1 (Rota)	1.2
5	Phyllanthus 1:2 (Rota)	1.5

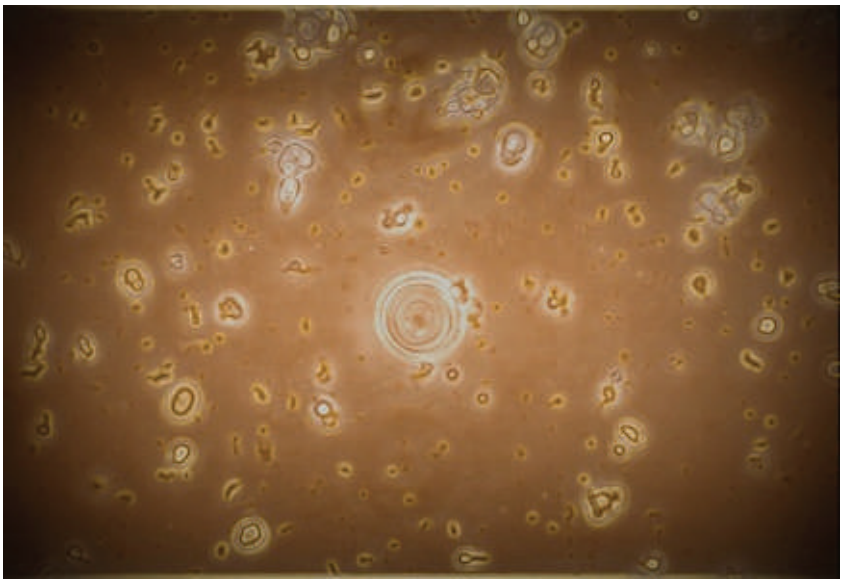

Figure 4: Microscopic view of phytosomal complex at 400X magnification.

Results showed that complex with molar ratio 1:1 showed more content (2.8%) in comparison to 1.2% in 1:2 and morphology was more even and spherical in 1:1 molar ratio. Therefore 1:1 was selected as optimized ratio for further evaluation.

3.2.1 Microscopic view

Optical microscopy was used for the surface morphology of phytosomal complex. The microscopic view, as shown in figure 4 indicated the presence of spherical structures of the complex. The vesicles consisted of Phosphotidyl choline 85G and phytosomal complex were intercalated in the lipid layer as shown in Figure 4.

3.2.2 Determination of Phyllanthin Content in Complex

Content of Phyllanthin in the phytosomal complex was determined by HPTLC, by the HPTLC method as described in section below**.**The content is estimated by HPTLC method by different methods such as vaccum drying and rota evaporation in different ratios such as 1:1 and 1:2. The content was found to be maximum for phyllanthus formed by vaccum drying of 1:1 as shown in Table 2. Thus it was taken as optimized formulation for further evaluation.

3.3.3 Scanning Electron Microscopy (SEM)

The surface morphology of phospholipids and phytosomal complex as examined by SEM is Figure 5. Phytosomal complex was made up of phospholipids and drugs and appeared irregular spheres shape.

3.3.4 Fourier Transform Infrared Spectroscopy (FTIR)

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 and phytosomal complex was negligible as shown in Figure 6.

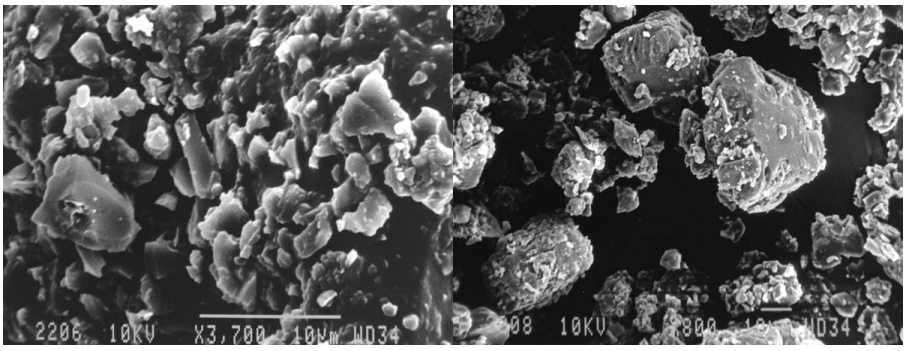

Figure 5: SEM of phytosomal complex of ratio 1:1 (left) 1:2 (right)

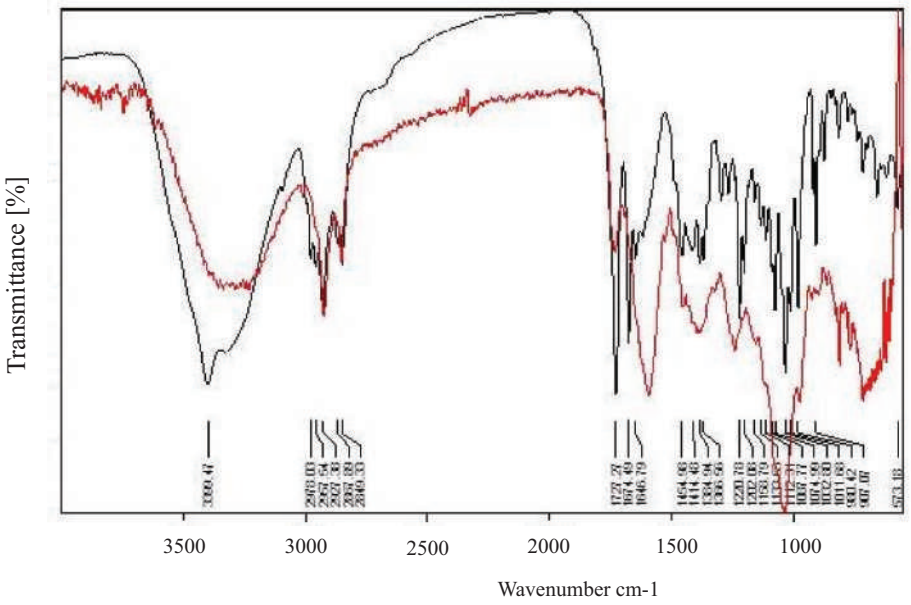

Figure 6: FTIR spectra of phytosomal complex

Table 3: Composition of Different formulations

Formulation	DiCalcium Phosphate(mg)	Phytosomes (mg)	Microcrystalline cellulose(mg)	Magnesium Stearate(mg)
F1	80	100	-	1
F2	70	100	20	2
F3	80	100	10	2
F4	80	100	20	2
F5	80	120	20	2
F6	80	80	20	2

3. 4 Formation of granules

Six batches of granules (F1-F6) were prepared by process of dry granulation with different composition of polymers as shown in Table 3.

The prepared granules were then subjected to various evaluation parameters such as bulk density, tapped density, angle of repose, Carr's index, Hausner's ratio. The results obtained for the different evaluation parameters were summarized in Table 4.

Table 4: Various Characteristic parameter of different formulations

S.No	Formulation Code	Bulk Density	Tapped density	Angle of repose	Carr's index	Hausner's ratio
1	F1	0.352 ±0.0006	0.431 ±0.003	32.5 ±0.252	11.2 ±1.907	1.227±0.008
2	F2	0.363 ±0.0013	0.437 ±0.005	35.5 ±0.321	16.8 ±0.964	1.202±0.014
3	F3	0.358 ±0.0006	0.448 ±0.005	37.4 ±0.153	20.1 ±0.870	1.251±0.014
4	F4	0.351 ±0.004	0.392 ±0.008	29.5 ±0.252	10.4 ±0.316	1.126±0.024
5	F5	0.362 ±0.0012	0.424 ±0.011	33.5 ±0.306	14.5 ±2.339	1.170±0.032
6	F6	0.359 ±0.0008	0.401 ±0.002	32.5 ±0.252	18.5 ±0.530	1.116±0.004

Table 5: Evaluation parameters of different tablet formulations

S.No	Formulation code	Tablet thickness	Hardness	Tensile strength	Disintegration Time (sec)
1	F1	0.521 ±0.003	3.833 ±0.321	6.881 ±0.456	12.637 ±1.982
2	F2	0.520 ±0.005	4.200 ±0.265	6.025 ±0.330	28.650 ±1.660
3	F3	0.520 ±0.001	4.133 ±0.306	5.929 ±0.427	18.487 ±2.667
4	F4	0.510 ±0.003	6.233 ±0.899	9.129 ±0.432	5.263 ±0.934
5	F5	0.511 ±0.003	5.200 ±0.400	7.593 ±0.568	9.427 ±1.602
6	F6	0.517 ±0.004	5.300 ±0.200	7.622 ±0.252	24.390 ±1.480

3.4.1 Preparation of tablets

Six different batches with different composition were prepared by dry granulation process as show in table 4. The tablet thickness, hardness, tensile strength, disintegration time were determined the results are summarized in Table 5.

3.4.2 Evaluation parameters of different tablet formulations

When dissolution drug release was plotted into zero order, first order, Higuchi model it was found that optimized formulation F4 was best fitted into zero order model.

For F1 formulation % cumulative release during 1st hour is 34.09% and 12th hour is 110.59%

For F2 formulation % cumulative release during 1st hour is 33.41% and 12th hour is 111.26%

For F3 formulation % cumulative release during 1st hour is 32.29% and 12th hour is 111.94%

For F4 formulation % cumulative release during 1st hour is 39.71% and 12th hour is 112.28%

For F5 formulation % cumulative release during 1st hour is 38.03% and 12th hour is 110.70% and. For F6 formulation % cumulative release during 1st hour is 37.13% and 12th hour is 109.01%

Because the graphs show cumulative drug release, the errors involved in the drug analysis are also cumulative. Therefore, the mean values showing more than 100% drug release reflect these cumulative errors in drug analysis. Further in the case of F4 optimized formulation release was prolonged to 12 hr hence the proposed phytosomal complex tablet can act as sustained release dosage form. Based upon the results the study can be further subjected for in vivo evaluation to explain its therapeutic potential.

3.4.3 Kinetic analysis of dissolution data

The kinetics of drug release of *Phyllanthus amarus* was determined by Higuchi's model, zero order and first order kinetics as shown in Table 6. The different formulation followed Zero order as their r^2 values were between 0.990 to 0.998.

Table 6: Regression coefficient (r2) values of drug release data obtained from various kinetic models and n value according to Korsmeyer-Peppas model

Formulation Code	Zero order	First Order	Higuchi Model
	r^2	r^2	r^2
F1	0.992	0.973	0.954
F2	0.995	0.968	0.977
F3	0.991	0.912	0.981
F4	0.998	0.967	0.973
F5	0.988	0.955	0.979
F6	0.990	0.973	0.964

Table 7: Evaluation parameters of optimized formulation, at 75%, 45°C RH, for two months.

Parameter	Observation	
	At 0 day	After two months
Weight variation (mg) n=5	910±4.25	910±3.76
Hardness (kg/cm^2) n = 5	4.78±0.32	4.78±0.28
Friability (%) n = 5	0.06	0.469
Drug content (%) n = 5	2.46	2.30

Table 8: Cumulative percentage of drug release from optimized formulation at 75% RH, 45 °C after two months.

Time(days)	% Drug release
0	0
15	110.38
30	110.49
45	110.52
60	110.67

3.4.4 Scanning electron microscopy

Scanning electron microscopy (SEM) provides a qualitative assessment of size, shape, morphology, porosity, size distribution, crystal form, and consistency of powders or compressed dosage forms (Figure 5). This information can be correlated to assess dissolution behavior, bioavailability, and crystalline structure. SEM images also help analysts determine whether particles are maintaining desired physical characteristics during processing, including after compaction or direct compression. The surface morphology of phytosomal tablet after 0 hr and 12 hr as examined by SEM as in Figure 8.

It is reported in the literature that more than 30% release of drug in the first hour of dissolution indicates the chance of dose dumping.

3.4.5 Stability studies

The observed results of stability studies on optimized formulations after two months are given in Tables 7 & 8.

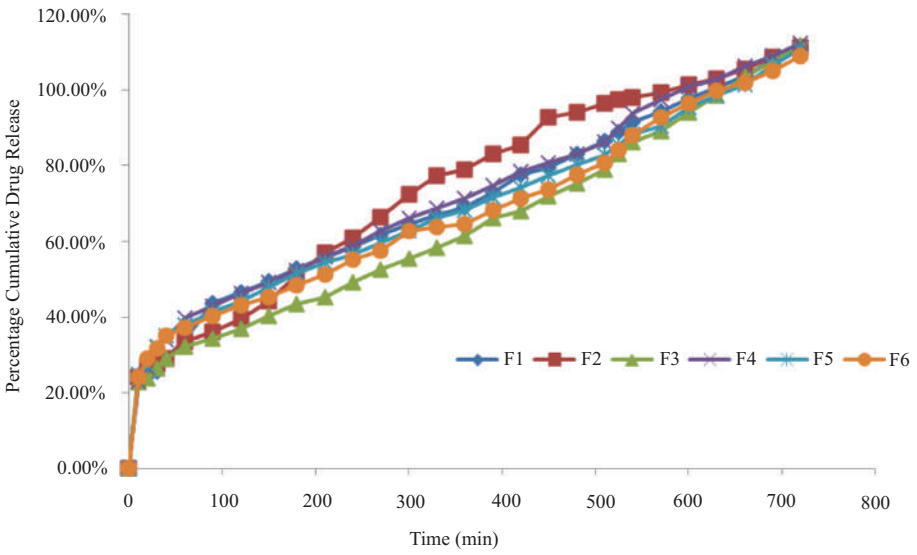

Figure 7: In Vitro Dissolution data of different formulations

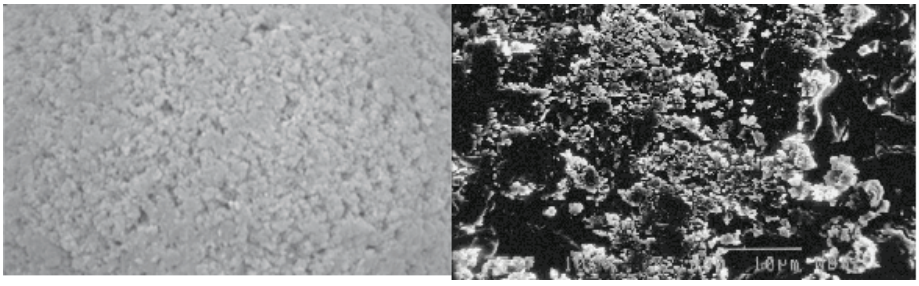

Figure 8: Scanning electron micrographs of tablet at 0hr (left) 12th hr (right)

4 CONCLUSION

HPTLC was carried out for quantitative and qualitative estimation of Phyllanthin in *Phyllanthus amarus* and R_f of phyllanthin was found to be about 0.25. The phytosomal complex was prepared consisting of standardised extract and phospholipid. The microscopic study indicated the presence of spherical structures of the complex. The vesicles consisted of Phosphotidyl choline 85G and phytosomal complex were intercalated in the lipid layer. The content is estimated by HPTLC method by different methods such as vaccum drying and rota evaporation in different ratios such as 1:1 and 1:2. The content was found

to be maximum for phyllanthus formed by vaccum drying of 1:1.The surface morphology of physical mixture of phytosomal complex as examined by SEM. Phytosomal complex was made up of phospholipids and drugs and appeared irregular spheres shape. Fourier Transform Infrared Spectroscopy (FTIR) studies shows that the intensity of the peak was modified but actually shift in the peak was negligible. The physical mixture gives confirmation about their purity and showed no interaction between phytosomal complex and polymers used in the formulations. Phytosomal tablets of phytosomes were successfully formulated by dry granulation method with incorporation of polymers such as DCP, Avicel, Magnesium stearate in combination. DCP was used as a diluent and Avicel as a binder, magnesium stearate as glidant.

The Phytosomal matrix tablet possessed the required physicochemical evaluation such as tablet thickness, hardness, tensile strength, disintegration time weight variation, friability and drug content. The drug content of the prepared formulation was within the acceptable range. The formulation F4 showed maximum drug content.

Scanning electron microscopy (SEM) study was performed on the optimized batch (F4) of phytosomal tablet showed the surface morphology of phytosomal tablet after 0hr and 12hr by SEM studies. It is reported in the literature that more than 30% release of drug in the first hour of dissolution indicates the chance of dose dumping. Among the various formulation batches, F4 showed the maximum drug release at the end of 12hr. The optimized formulation (F4) showed maximum drug release at the end of 1st hour (39.71%) and at the end of 12th hour (112.28%). It was observed that all the formulations were best fitted to zero order and Higuchi model. The stability studies indicated that no change in physical appearance was noticed upon visual inspection of the tablets. All the formulations showed more than 90% of drug content during both accelerated and room temperature storage conditions.

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