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Research Article

DEVELOPMENT AND *IN-VITRO* EVALUATION OF PHYTOSOMES CONTAINING HERBAL EXTRACT OF *CENTELLA ASIATICA* FOR ANTIULCER AND ANTIOXIDANT ACTIVITY

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ABSTRACT
Herbal medications have a diverse range of active constituents allowing us to use them in a variety of ways, but active constituents are poorly absorbed due to their strong polarity and low lipophilicity, resulting in low bioavailability. The aim of this research was to improve bioavailability by development and *in-vitro* evaluation of phytosomes containing herbal extract of *Centella asiatica* for its antioxidant and gastroprotective activity. Phytosomes of *Centella asiatica* were prepared by reflex method and further it is characterized and evaluated. The complex formation was estimated by FTIR analysis and drug content and drug entrapment efficiency of phytosomes was achieved to be 91.6% and 84.3% respectively. The mean diameter was found to be 854.2 nm and zeta potential 28.4 mV was found. It indicates that the *in-vitro* drug release of *Centella asiatica* were higher in comparison to the formulation complex i.e., 100% and 77.6%. The release kinetics of the optimized phytosomal formulation (F3) best fitted and the R^2 value was found to be 0.9879. The anti-oxidant activity of *Centella asiatica* phytosomes was superior than its hydroalcoholic extract i.e., % inhibition of phytosomal formulation is 83.55 having IC_{50} value 1.99 and % inhibition of hydroalcoholic drug extract was 85.31 having IC_{50} value 2.77. In anti-ulcer activity phytosomes was found to neutralize acid more significant as compare to standard and hydroalcoholic extract of *Centella asiatica*. The results indicated that the prepared phytosome could be a promising candidate for effective delivery of active constituents.

Keywords: Bioavailability, Gastroprotection, Reflex method, Antisolvent precipitation method.

1. INTRODUCTION
Ulcer is the breakage in lining of mucous membrane or skin characterized by sloughing of inflammatory dead tissue. There are many types of ulcer viz. oral, oesophageal, peptic and genital ulcer. Among all, peptic ulcer is the most prevalent type. Peptic ulcer is erosions found in the mucosal lining of the digestive tract, typically in the stomach or duodenum. Gastric ulcers are located in the stomach, characterized by pain which aggravates on food intake. Weight loss, hematemesis, melena, nausea and vomiting are probable additional symptoms [1].

Centella Asiatica is a clonal, perennial herbaceous creeper, belonging to the Umbelliferae (Apiaceae) family. *Centella asiatica* is used for blood purification, hypertensive individuals, and memory enhancement. It also re-energizes nerves and brain cells which is mentioned in Ayurveda [2]. The important chemical components responsible for therapeutic activity are triterpenes such as asiaticoside, madecassoside, asiatic acid and madecassic acid. *Centella asiatica* triterpenoid has significant effect on improving digestive disorder as indicated by improvement in liver health and reducing *H. pylori*-associated gastric ulcer.

Different researches demonstrate wide nutritional impacts of flavonoids on antioxidant activity. Majority of antioxidant chemical experiments have shown that they have free radical scavenging activity. Antioxidants are molecules that protect animal, human and plant cells from the harmful possessions of reactive oxygen species. The functional groups arranged in the nucleus of flavan determine antioxidant activity [3]. Herbal drugs have found to shown stunning efficacy *in-*

vitro but poor efficacy *in-vivo* owing to their low lipid solubility. A greater knowledge of biopharmaceutics, pharma-cokinetics of herbal medicine may also help in the development and calculation of rational dose regimen [4]. Phytosomes are a new vesiscular lipid-based drug delivery system, they are cell-like structures and are formed by the reaction of phospholipid and bioactive constituents in a non-polar solvent. Different phytoconstituents like alkaloids, glycosides, polyphenols, and flavonoids are observed to have various biological interest like antihypertensive, antioxidant, cardio-protective, anti-cancer, anti-inflammatory, antilipidemic an immunomodulator activity. Lipid (Phosphatidyl-choline) serves as a carrier for phytosomes, but it also possesses liver protective activity resulting in a synergistic effect when combined with hepatoprotective drugs. When compared to the free active components, Phytosomal complexes are more easily absorbed and produce better bioavailability. It is now well known that the use of phytosomes has controlled the problem of low bioavailability for several active ingredients [5]. The herbal novel drug delivery system is an advanced form for phytoconstituents to upgrade the drug delivery system. In recent years bioactive components have been used to develop different kinds of novel formulations such as Polymeric nanoparticle, Nano capsule, Niosomes, Liposomes, Phytosomes, Microspheres, Ethosomes, and Transferosomes [6]. This study revealed it's antiulcer and antioxidant effect with improved bioavailibity of active constituents.

2. MATERIAL AND METHOD

2.1. Material

Centella asiatica extract were collected from Natural Hub, New Delhi, Soya lecithin from Yarrow pharma, DCM (Dichloromethane) & N-Hexane from Fisher Scientific (Mumbai) & Methanol, Ethanol N-Octanol or DMSO (Dimethyl sulfoxide) from Loba. All other solvents and reagents were of analytical grade.

2.2. Preformulation studies

2.2.1. Determination of absorbance maxima for phyto constituent of Centella asiatica

Accurately measured 100 mg CA was transferred into 4 different volumetric flask of 100ml. Then the drug was properly dissolved in hydro-alcoholic solution, 7.4pH phosphate buffer, methanol and water then volume make up to the mark with blank solution. The concentration of the solutions was found to be 1000 microgram per ml also called as stock solution. Then 1 ml was pipetted out from each stock solution and transferred into different 100 ml volumetric flask and volume was madeup 100 ml with respective solutions. The concentration of the solutions was found at 10 microgram per ml. The sample was scanned in UV-visible spectrophotometer within the range of 200-400 nm (Fig. 1).

2.2.2. Standard calibration curve for phyto constituent of Centella asiatica

Centella asiatica (100 mg) was measured accurately and transferred separately into 4 different volumetric flasks of 100ml and dissolved in hydro-alcoholic solution, 7.4pH phosphate buffer, methanol and water respectively, then volume was made up to the mark. The concentration of the stock solution was found to be 1000 microgram per ml in each solution. Further stepwise dilutions were prepared of different concentrations of 2, 4, 6, 8, 10, and 12 microgram. Absorbance of the solution was measured by UV-visible spectrophotometer at 282 nm and calibration curve was obtained by projecting the graph between absorbance vs concentration.

2.2.3. IR studies

IR studies were completed with the help of KBr press and press pellet approach. To form the pellet dried KBr, drug extract and soya lecithin (phosphatidylcholine) were compressed. Pallet was then placed into the sample holder and retained in apparatus to measure the IR spectra. IR spectra of plant extract and excipient were performed by Shimadzu IR spirit Instrument at Devsthali Vidyapeeth College of Pharmacy, Lalpur, Rudrapur Uttarakhand.

2.2.4. Solubility analysis

For the determination of solubility due to complexation, the apparent solubility of herbal extract was calculated by dissolving the excess amount of drug extract in 10 ml solvent (such as distilled water, ethanol, methanol, 0.1N HCl, 6.8 pH phosphate buffer or 7.8 pH phosphate buffer) kept in tight closed capped vials. All the volumetric flasks were shaken properly till the saturation point attained and kept all the samples for 24 hours at 25°C temperature. When the equilibrium had been established, centrifuged the saturated solution for 30 minutes at 1000 rpm to remove the excess amount of drug from solution. Afterwards supernatant was filtered promptly with the same suitable solvent to avoid the crystallization. The filtrate solution was analyzed in UV spectrophotometer at 282 nm.

2.2.5. Partition coefficient

For the determination of partition coefficient two phases (oil and aqueous phase) are required. N- octanol is used as an oil phase and in aqueous phase water is used. Accurately measured 50 ml octanol and 50 ml water were transferred into the separating funnel then 100mg *CA* was added to it, continuously shaken the mixture for the duration of 2 hours until the equilibrium was attained. After that, the assembly was permitted to stand overnight. After 24 hours, oil phase and aqueous phase were separated and both the phases were tested for drug content by analyzing the absorbance in UV spectrophotometer at 282 nm.

2.3. Formulation of CA Phytosomes

Phytosomes of *Centella asiatica* were prepared by antisolvent precipitation method. The phospholipid was accurately weighed and properly dissolved in dichloromethane (DCM) and poured into the RBF. After that, drug was dissolved in liquid solution, refluxed the mixture for 2 hours at 50°C temperature. Afterwards mixture was concentrated then the assembly was detached and added n- hexane into the mixture with continuous agitation to get precipitate. The dispersion was sonicated by probe sonicator by 8 cycles of 30 seconds to form the phytosomes. Seven different formulations were prepared.

2.4. Evaluation of *Centella asiatica* phytosomes

2.4.1. Particle size and zeta potential

The mean particle size and zeta potential of the optimised formulation was estimated by Malvern Zeta meter. Sample analysis was done by diluting it with the double distilled water to attain an appropriate concentration before the measurement [7].

2.4.2. DSC

The thermal analysis of the samples *Centella asiatica* extract, Phospholipid (Soya lecithin), physical mixture and prepared phytosomes was carried out using a Differential Scanning Calorimeter (Mettler Toledo, USA). Sample were analysed in crimped aluminium pans heated at 40-260°C at a linear heating rate 10°C min^{-1} to test the purity of drug results obtained compared with the literature record.

2.4.3. Drug content analysis

Phytosomal suspension was dissolved in a 100 ml 6.8 pH phosphate buffer and continuously shaken for the duration of 2 hours by assembling the beaker on a magnetic stirrer. After that resultant solution was filtered, 1 ml of sample was pipetted out from the stock solution and diluted up to 10 ml in 10 ml volumetric flask. The absorbance of sample solution was recorded by using UV spectrophotometer at 282 nm.

2.4.4. Entrapment efficiency

The entrapment efficiency of the *Centella asiatica* can be determined by ultracentrifugation technique. Entrapment efficiency relates the percentage of drug encapsulate or entrapped within or absorbed in the phytosome. For the estimation of entrapped drugs, 1 ml phytosome in a volumetric flask and sample were taken and diluted with 6.8 pH phosphate buffer and volume madeup up to 10 ml. Diluted sample was then centrifuged at 1500 rpm for 60 min to separate out the aqueous and oil phase. Filtered the supernatant with 0.2 Micron membrane filter and reported the absorbance by using UV spectrophotometer at 282 nm [8].

2.4.5. In vitro release study

Drug release from the phytosome was reported by using the dialysis membrane. 0.1N HCl and 6.8 pH PO_4 buffer was used as a dissolution media and the whole assembly was set up on the magnetic stirrer and temperature was maintained at 37°C. The solution was continuously stirred by using a magnetic bead. 0.1N HCl dissolution media was used for the first 2 hours and then for the next 10 hours a 6.8 pH phosphate buffer is used as a dissolution media.1 ml of solution was then pipetted out from the dissolution media and the same amount of fresh dissolution media was transferred for the quantity withdrawn. The withdrawn sample was then analyzed in UV spectrophotometer at 282 nm and calculated the % CDR.

2.4.6. DPPH radical scavenging activity

Free radical scavenging activity of sample was estimated by preparing solution of DPPH in methanol (6×1^{-5}) for UV analysis. Various concentrations of sample (10-80 microgram per ml) were prepared and add to solutions of DPPH in the ratio of 1:1 by continuous stirring. The sample was placed in the area of dark at ambient temperature. Ascorbic acid and Trolox are used as standard. The percentage inhibition of DPPH radical scavenging capability was calculated by equation given below [9].

Percent inhibition = $[(A_0 - A) / A_0]\times 100$

Where, A_0 is Absorbance of DPPH in absence of sample (control), A is Absorbance of DPPH in presence of sample (test).

2.4.7. In-Vitro Antiulcer Activity

2.4.7.1. Acid Neutralizing Capacity

The value of acid neutralizing capacity of ethanolic extract of *Centella asiatica* (100mg, 500mg, 1500mg) and phytosomal formulation was compared with standard. Aluminium hydroxide [$Al(OH)_3$] and Magnesium hydroxide [$Mg(OH)_2$] (500mg) were the antacid which are used as standard. Water was added to the 5 ml quantity of this mixture to make up the complete volume of 70 ml and mixture was then stirred for 1 minute. Afterwards, 30 ml of 0. 1 normal HCl was added into both the preparations of standard and test and agitated for 15 minutes. Then few drops of phenolphthalein solution were added and mixed the solution. Excess of HCl was titrated with sodium hydroxide solution of 0.5N drop by drop till the pink colour developed [10].

The moles of acid neutralized is considered by the formula-

Percent inhibition = $[(A_0 - A) / A_0] \times 100$

3. RESULTS AND DISCUSSION

3.1. Determination of absorbance maxima for active constituent of *Centella asiatica*

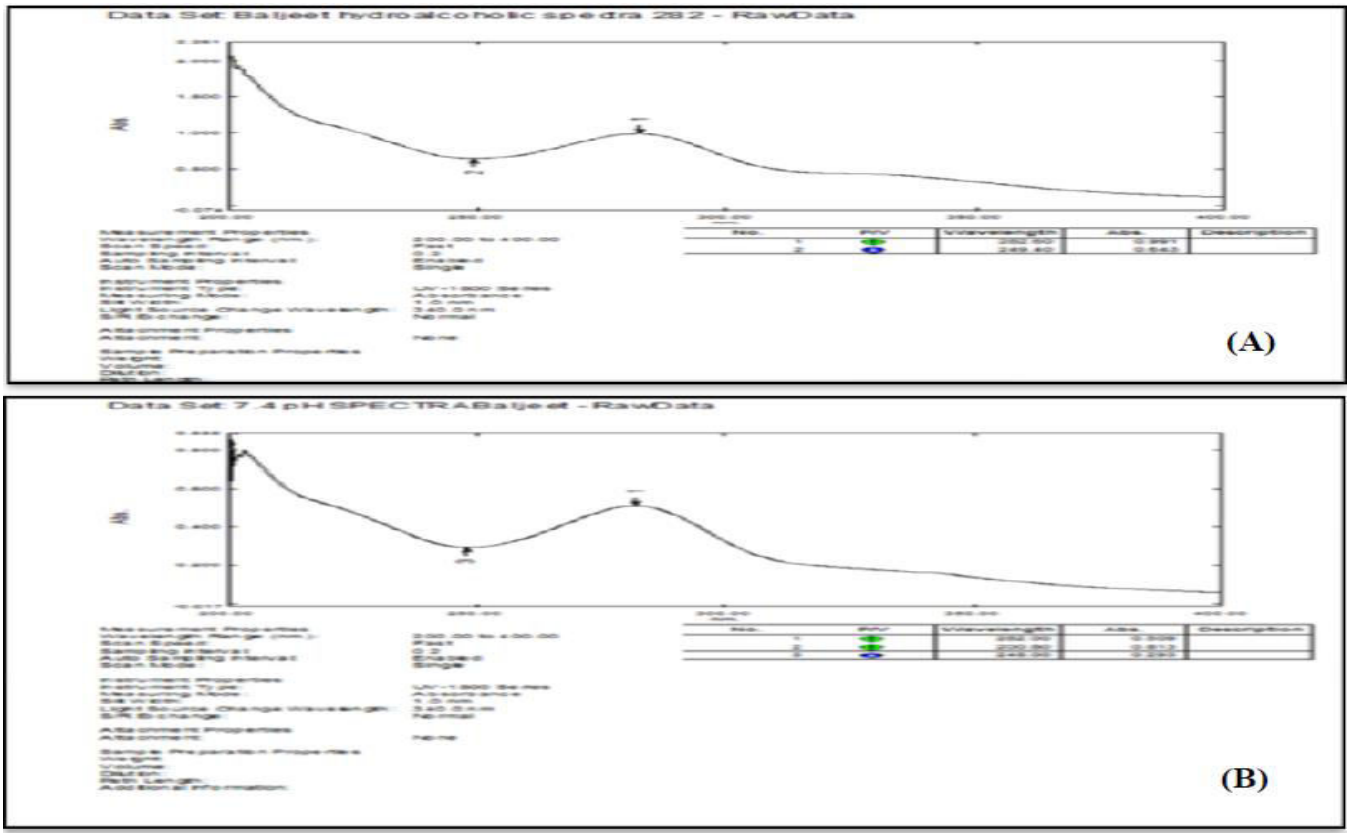
Stock solution of 1000 microgram per ml was prepared by dissolving the *Centella asiatica* extract in hydroalcoholic solution, 7.4 pH phosphate buffer, methanol and distilled water. The sample was scanned in a UV spectrophotometer in the wavelength range of 200 to 400 nm. The maximum wavelength was found to be 282 and 278 and used for further studies. Results are shown in Fig. 1.

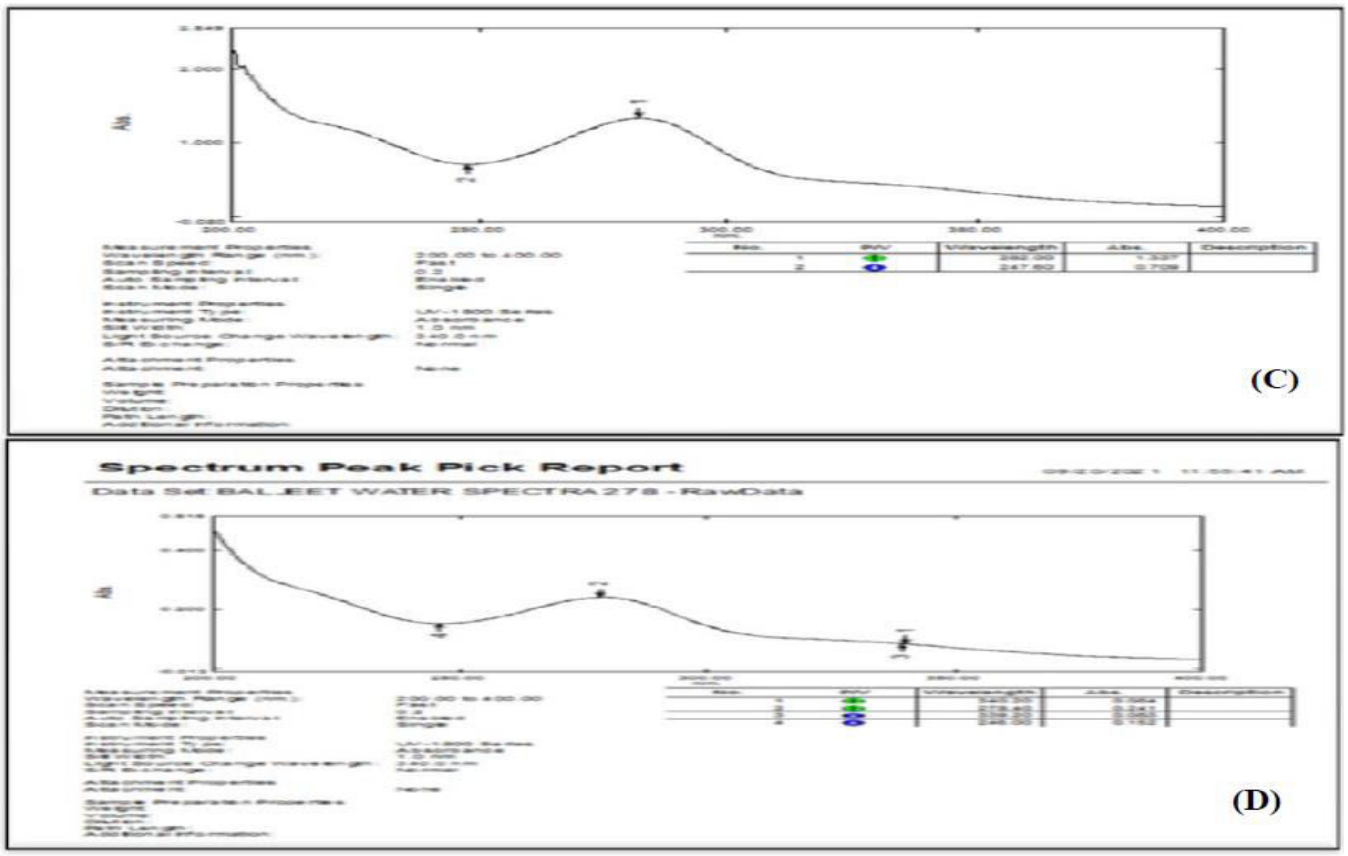
3.2. Standard Calibration Curve for active constituents of *Centella asiatica*

The maximum absorbance data in hydroalcoholic solution, 7.4 pH phosphate buffer, methanol was found to be 282 nm and in water it was 278nm, when scanned in the range of 200 to 400 nm. The calibration curve of *Centella asiatica* extract was prepared by dissolving it in hydroalcoholic solution, 7.4 pH phosphate buffer, methanol and water respectively. The linearity over the concentration range of 2-12(µg/ml) passing through origin and it follows the beer Lambert law. Results are shown in Fig. 2.

3.3. Drug excipient compatibility study

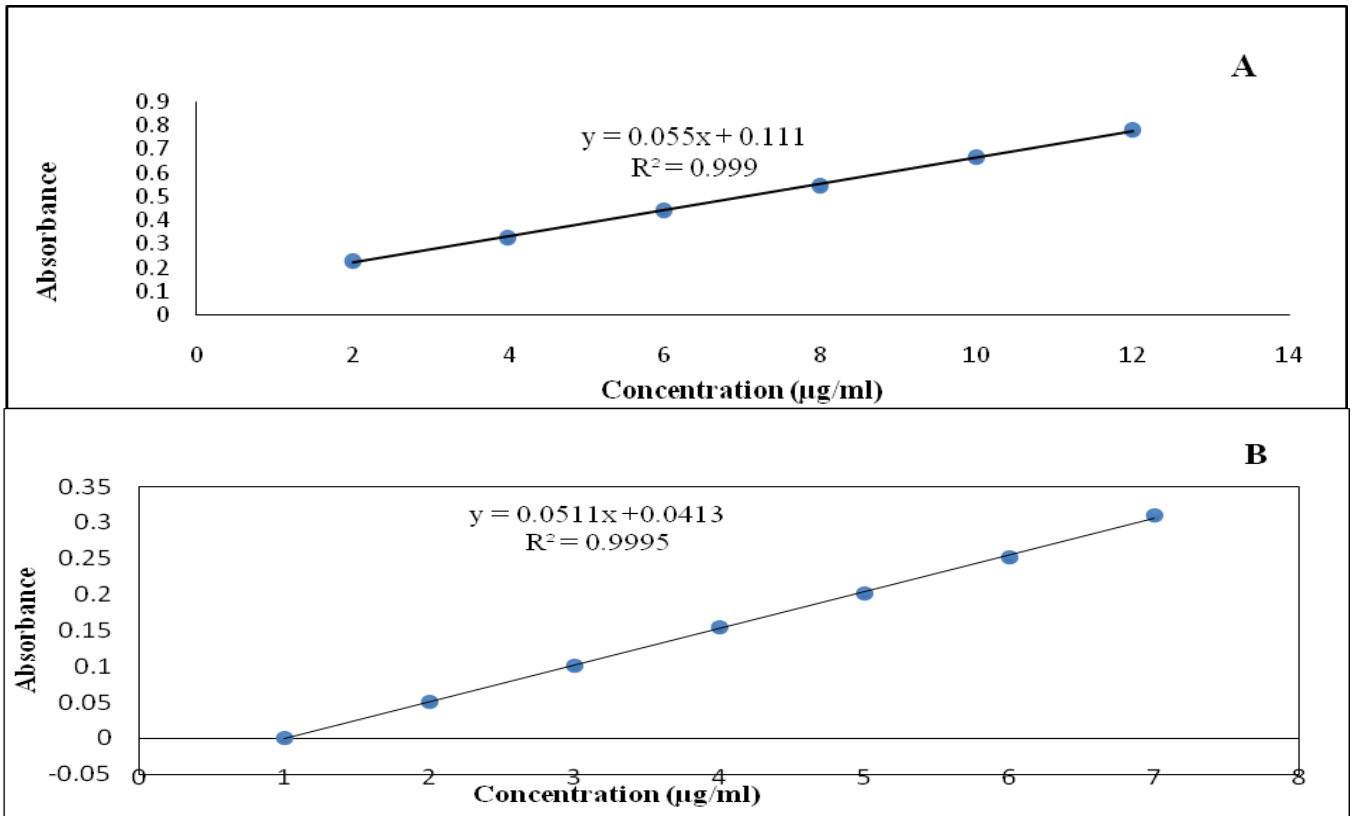
The Infra-red spectra of *Centella asiatica* as well as herbal extract with lipid display characteristic peaks. All the peaks of *Centella asiatica* were present in the spectra thus indicating compatibility between drug and lipid. It indicates that there is no major change in the drug extract. The results are shown in Figs. 3-6.

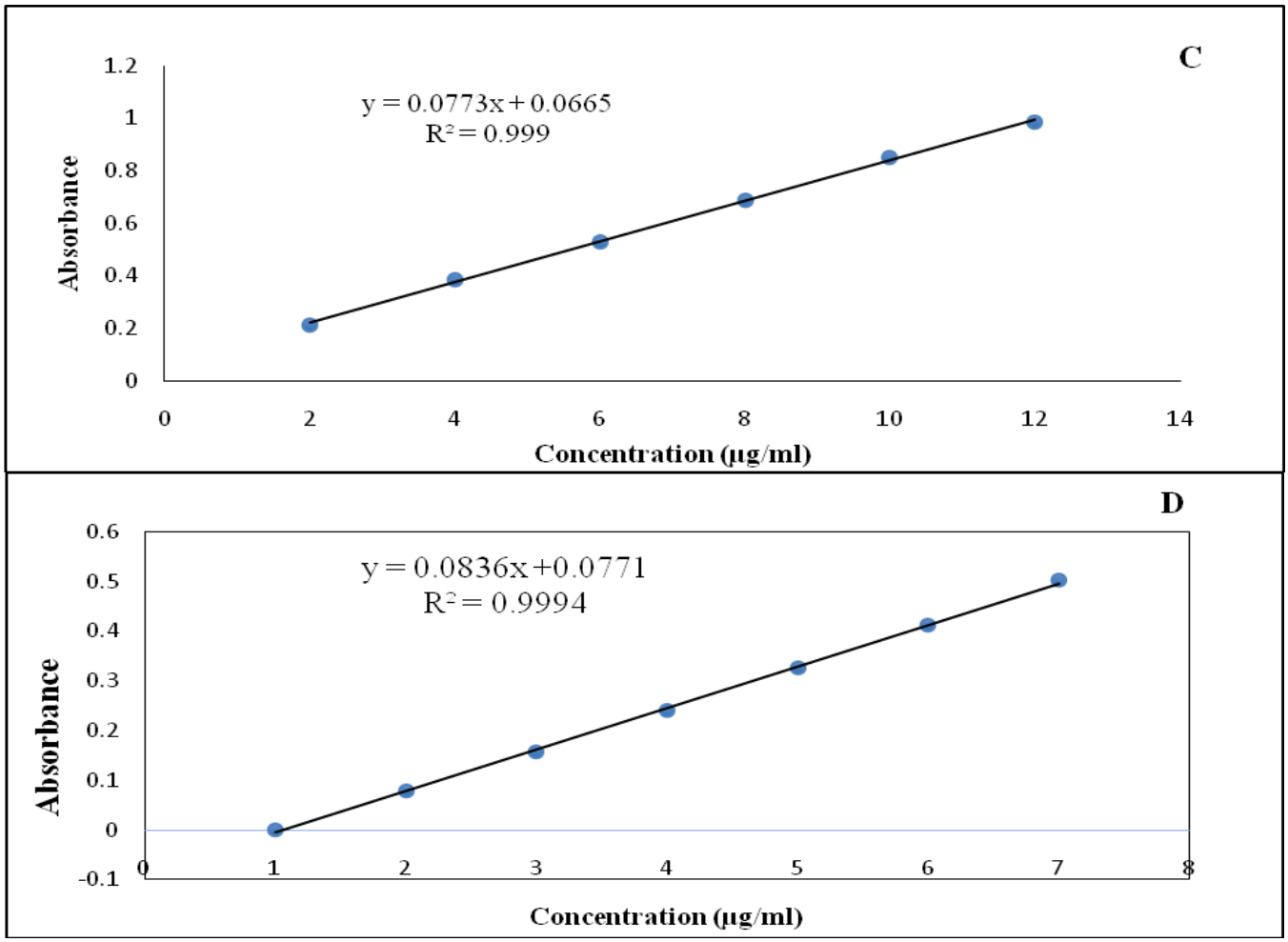




(A) Hydro-alcoholic solution (B) 7.4 pH phosphate buffer (C) Methanol (D) Water

Fig. 1: UV Spectrum for active constituent of *Centella asiatica*





(A) Hydro-alcoholic solution (B) 7.4 pH phosphate buffer (C) Methanol (D) Water

Fig. 2: Calibration Curve for active constituents of *Centella asiatica*

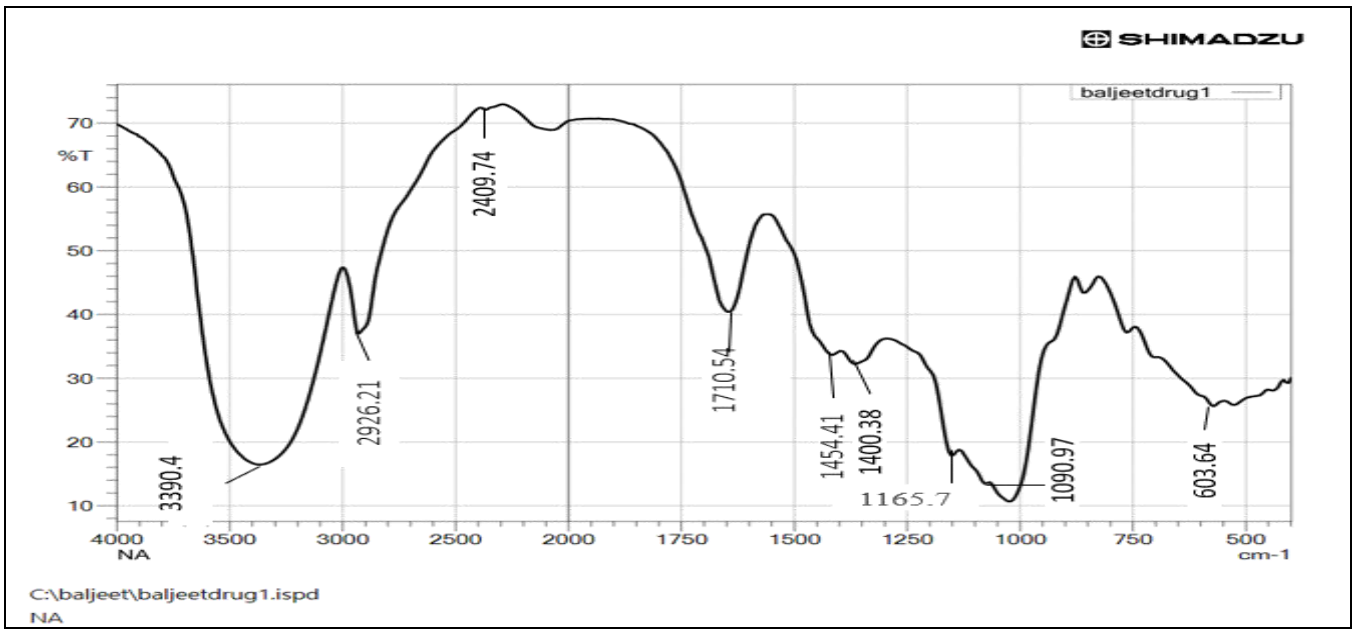


Fig. 3: FTIR Spectra of *Centella asiatica*

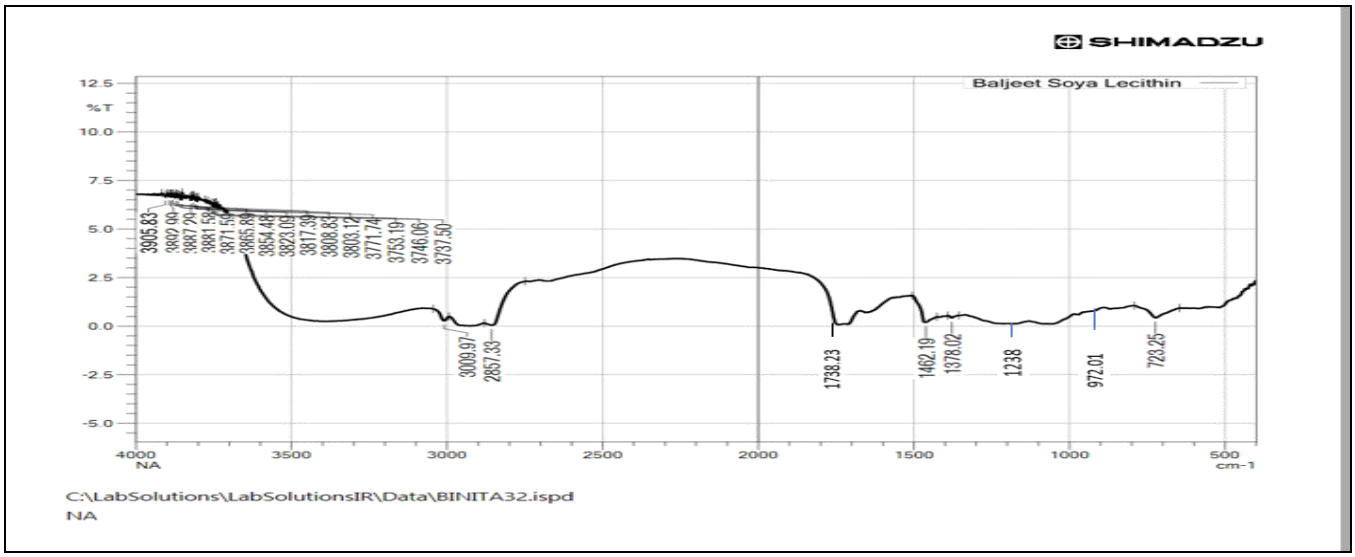


Fig. 4: FTIR Spectra of Soya Lecithin

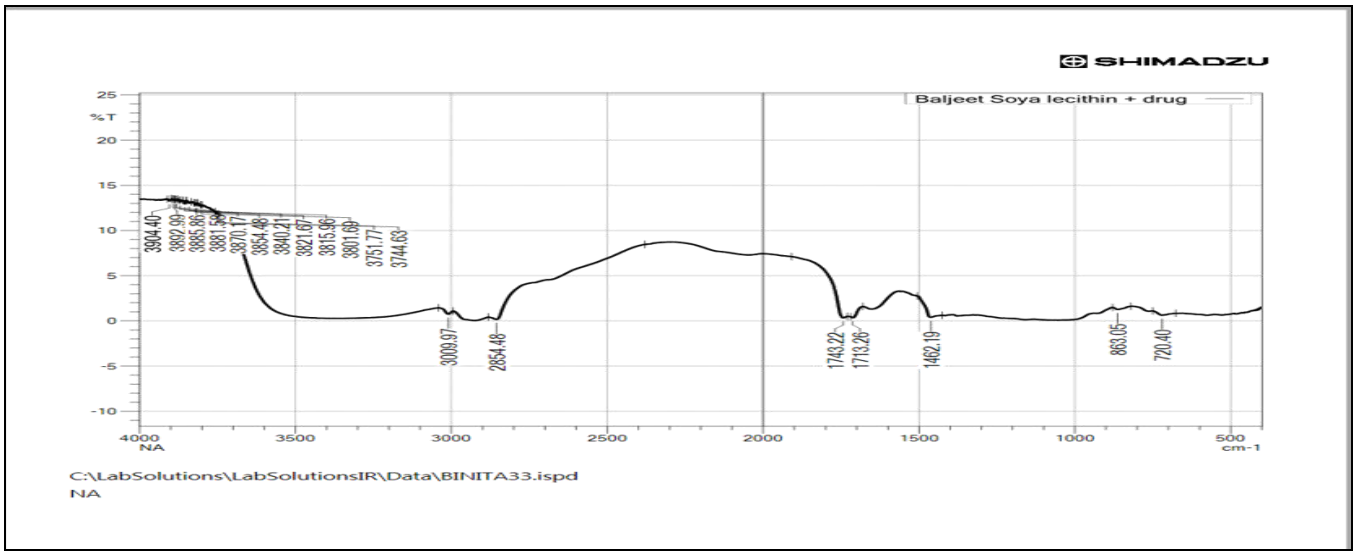


Fig. 5: FTIR Spectra of Soya Lecithin + *Centella asiatica*

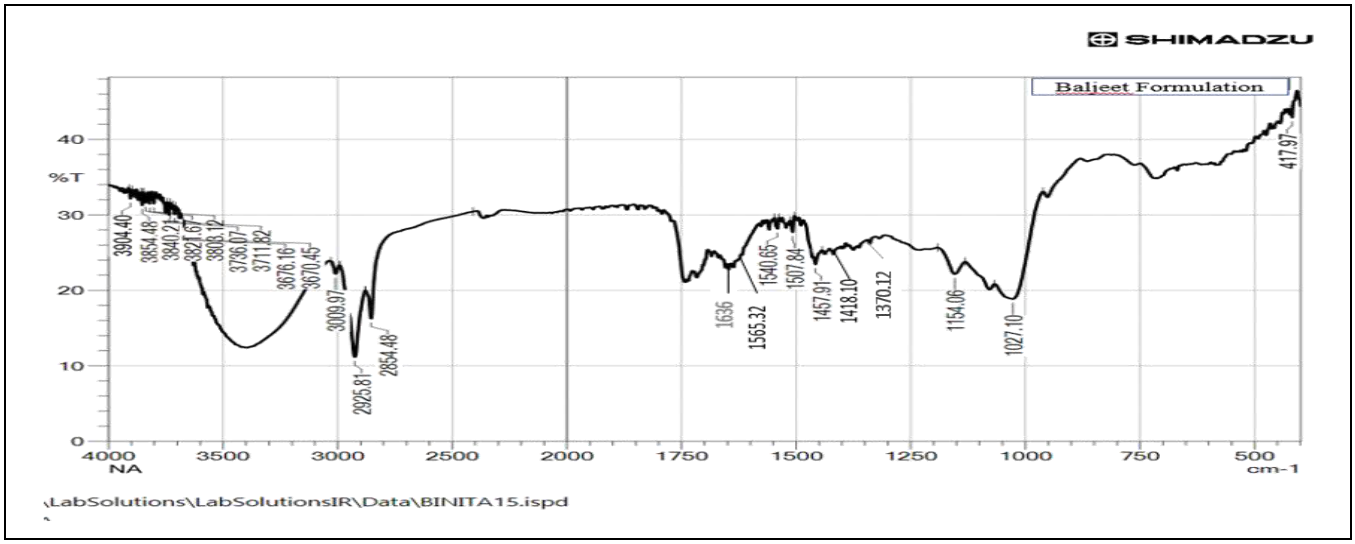


Fig. 6: FTIR Spectra of Formulation

3.4. Solubility Analysis

Determination of solubility of *Centella asiatica* was done in hydroalcoholic solution, 7.4 pH phosphate buffer, 0.1N HCl, methanol and distilled water. From the solubility data analysis of *Centella asiatica* showed highest solubility in Methanol. Solubility of *Centella asiatica* in different solvents are shown in Fig. 7.

3.5. Formulation of Phytosomes of *Centella asiatica*

3.6. Evaluation of Phytosomes of *Centella asiatica*

3.6.1. Particle Size and Zeta potential

The mean particle size and zeta potential of optimized phytosome formulation was estimated by Malvern zeta-sizer. For the analysis, dilutde the sample with double distilled water to reach a suitable concentration before measurement. Results of the analysis were shown in figs.8 and 9.

From the obtained results, it was concluded that F3 formulation has best result and the diameter size of F3 is 854 nm, PDI is 0.437 and zeta potential is 28.4 mV.

Table 1: Composition of phytosomes of *Centella asiatica*

Ingredients	Formulation Code						
	F1	F2	F3	F4	F5	F6	F7
Centella asiatica(mg)	100	100	100	100	100	100	100
Soya lecithin(mg)	50	100	150	200	250	300	350
Dichloromethane(ml)	40	40	40	40	40	40	40
N-Hexane(ml)	10	10	10	10	10	10	10

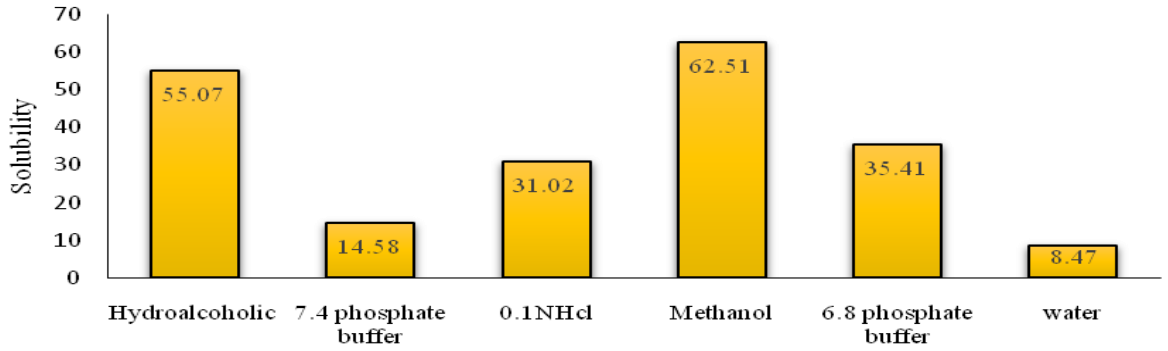


Fig. 7: Solubility Analysis for active constituent of *Centella asiatica* in different solvents (mg/ml)

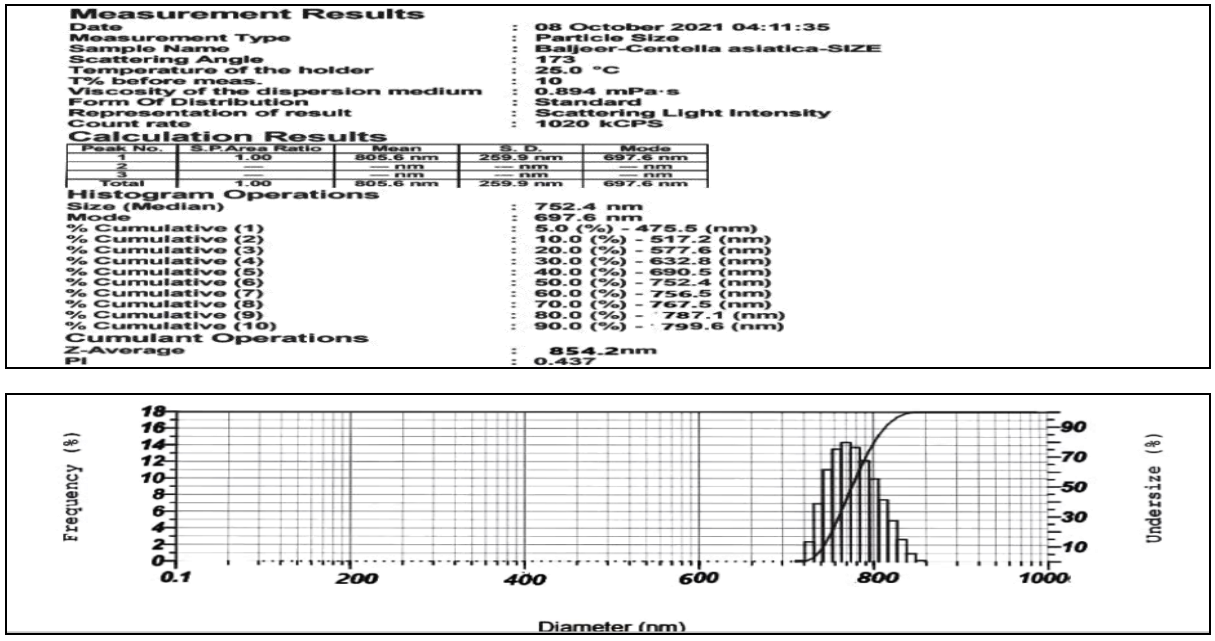


Fig. 8: Polydispersity Index and Diameter Report of Phytosome Formulation (F3)

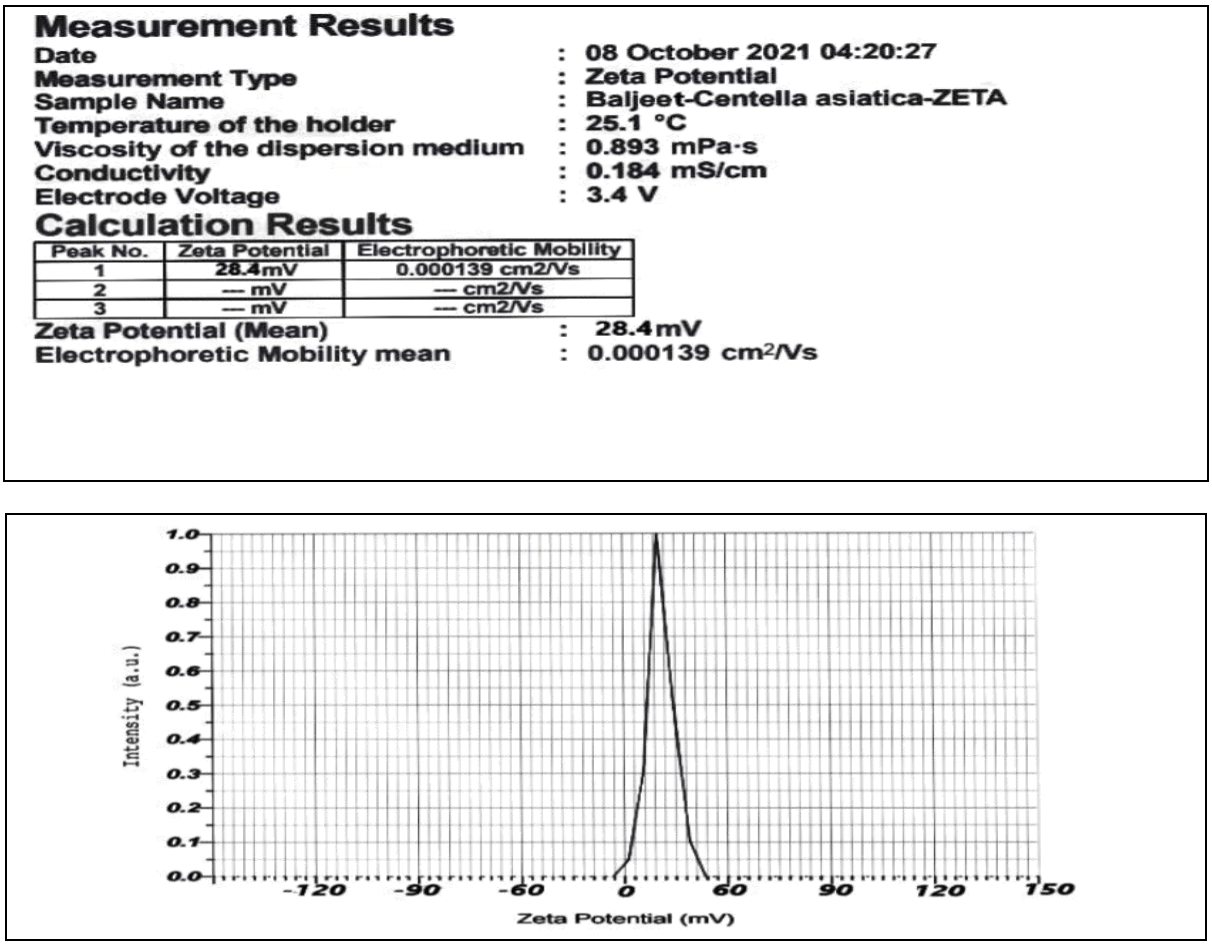


Fig. 9: Zeta Potential Report of Phytosomes Formulation (F3)

3.6.2. Differential scanning calorimetry

DSC of pure drug, soya lecithin, physical mixture and formulation was performed and the results obtained are shown in the Figs. 10-13 given below. Drug shows a characteristic peak at 245.84°C.

3.6.3. Drug Content Analysis

The drug content of *Centella asiatica* extract in phytosome formulation was found to be in the range of 62.4-91.6 which shows the acceptable amount of drug present in the phytosome formulation. Among the phytosome formulations (F1- F7) higher drug content was observed in F3 formulation (91.6%) as shown in fig. 14.

3.6.4. Drug entrapment efficiency

The drug entrapment efficiency of phytosome formulation was calculated from the absorbance obtained from the supernatant solution after centrifugation and the entrapment was found to be in the range of 59.7-84.3. Among the phytosome formulations (F1-F7), highest entrapment efficiency was observed in F3 formulation (84.3) as shown in fig. 15.

3.6.5. In-vitro release studies

In-vitro drug release from the phytosomal formulation was done by using the dialysis membrane. 0.1N HCl was used as diffusion media for the first 2 hours and for the next 10 hours phosphate buffer (6.8pH) was used as diffusion media. The assembly was kept on the magnetic stirrer, and continuous stirring done by using a magnetic bead and temperature was maintained at 37±5°C. At a specific time interval, 1ml sample was withdrawn from the diffusion media and the same amount of fresh diffusion media was transferred for the quantity withdrawn. Procedure was followed for the duration of 12 hours. The collected samples were analysed in a UV spectrophotometer at 282 nm and cumulative percent drug release was calculated and the result concluded that the *in-vitro* drug release of *Centella asiatica* were higher in comparison to phytosome formulation. Results are shown in fig. 16-18.

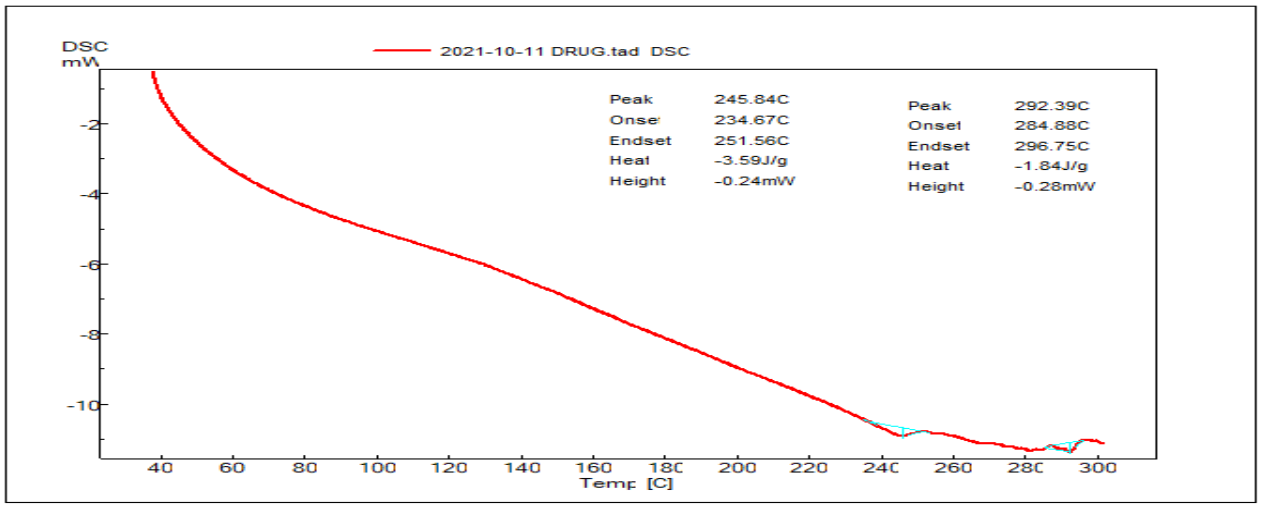


Fig. 10: DSC of *Centella asiatica*

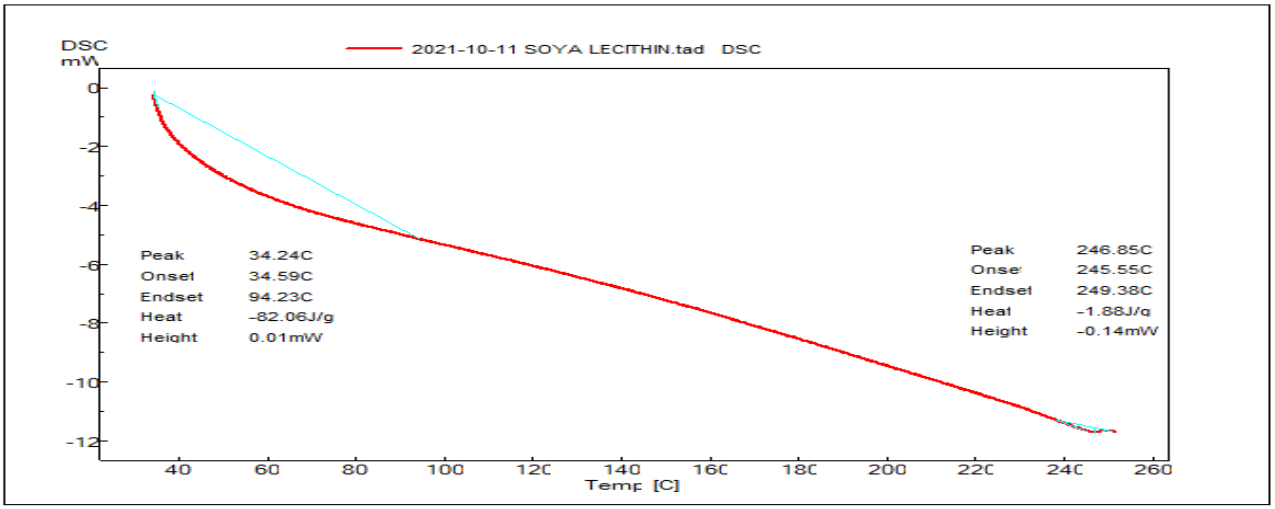


Fig. 11: DSC of soya lecithin

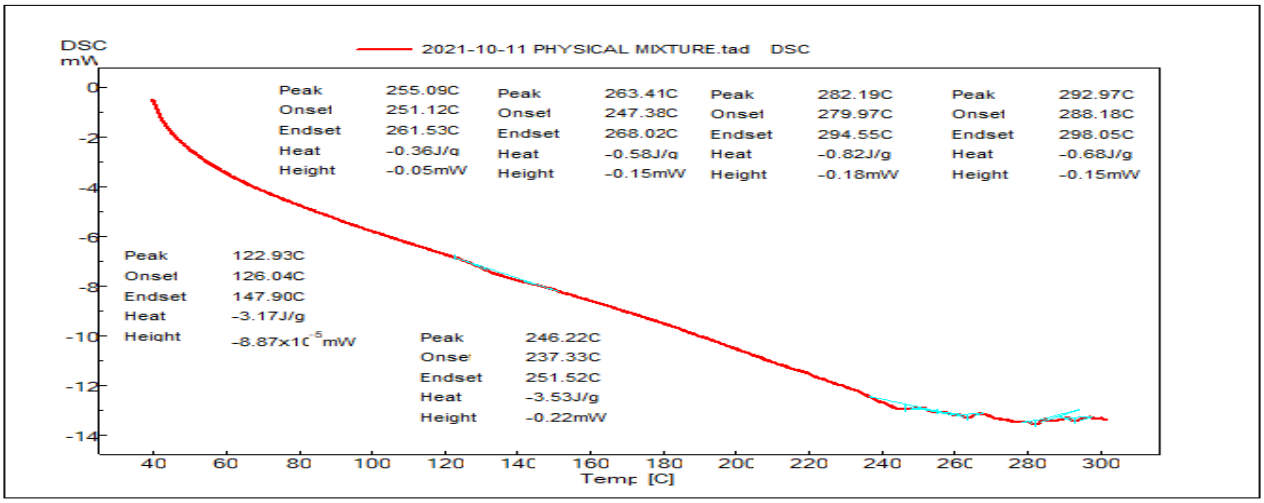


Fig. 12: DSC of*Centella asiatica* + soya lecithin

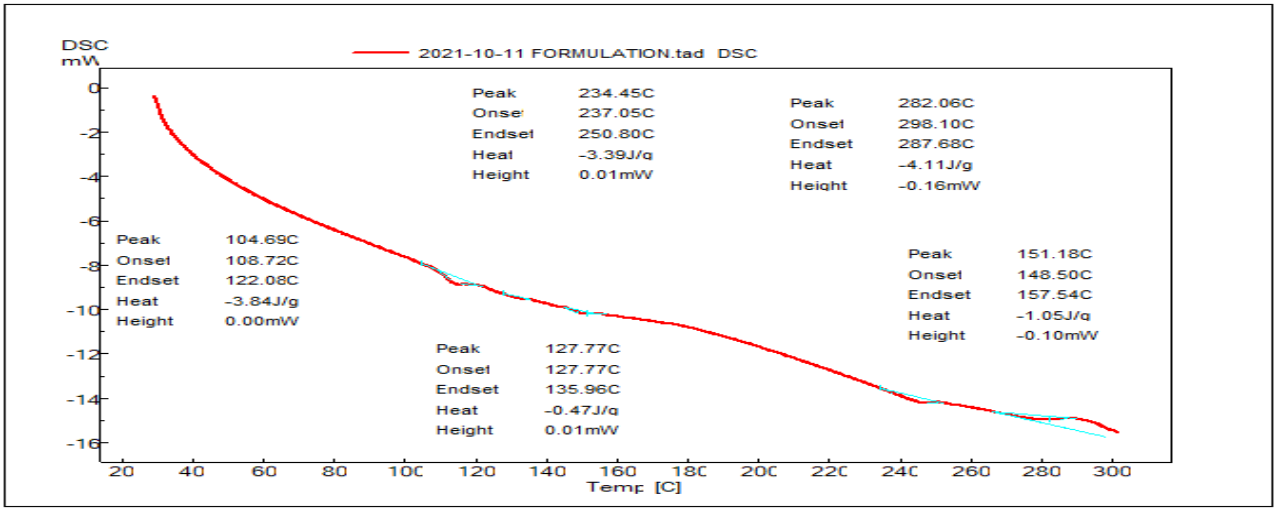


Fig. 13: DSC of formulation

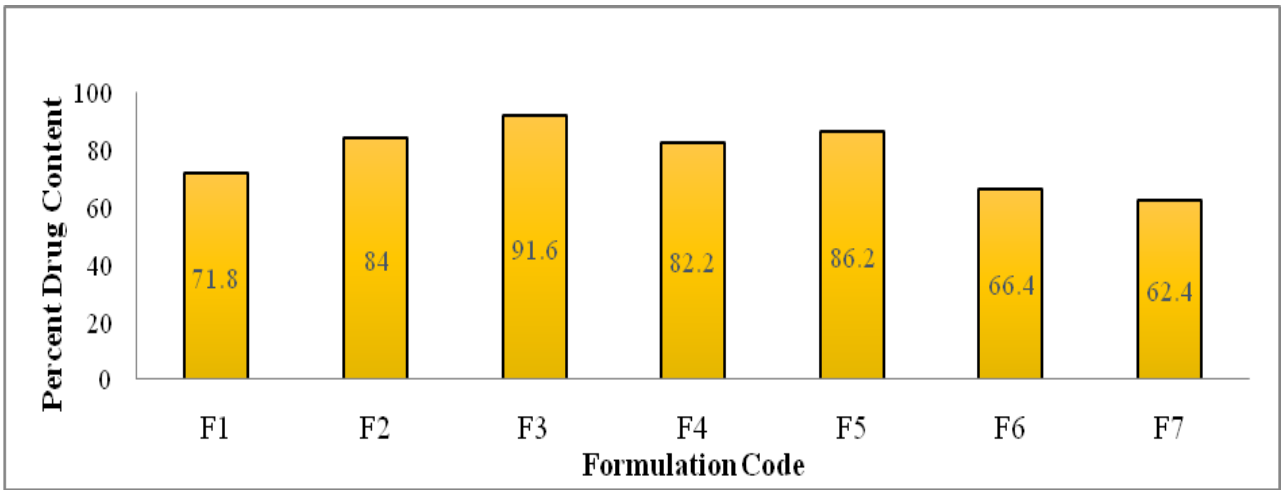


Fig. 14: Percent Drug *Content of* phytosomes formulation

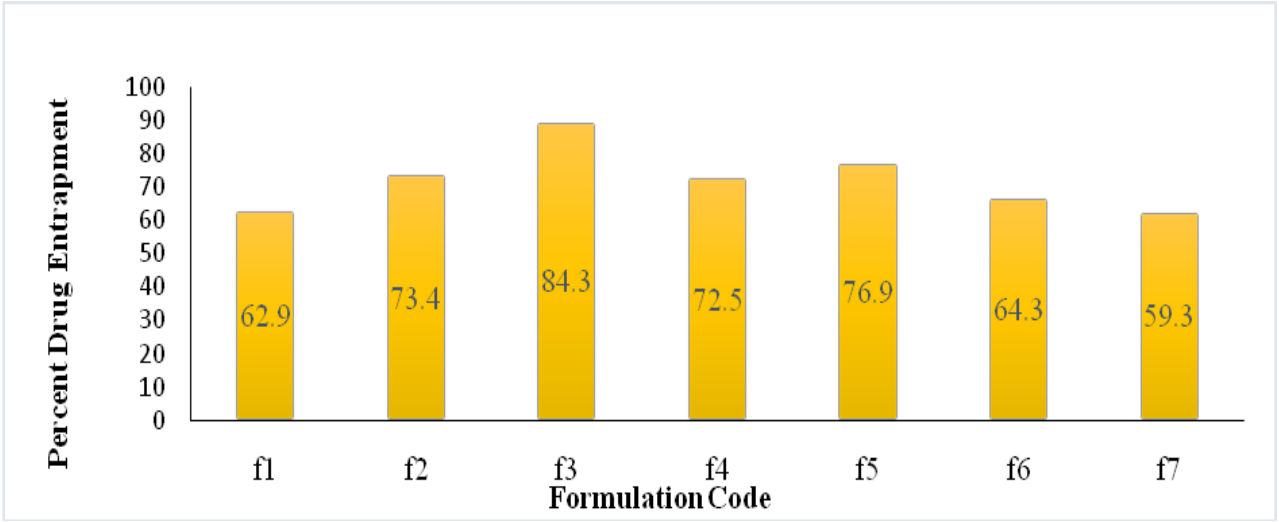


Fig. 15: Percent Drug Entrapment of phytosomes formulation

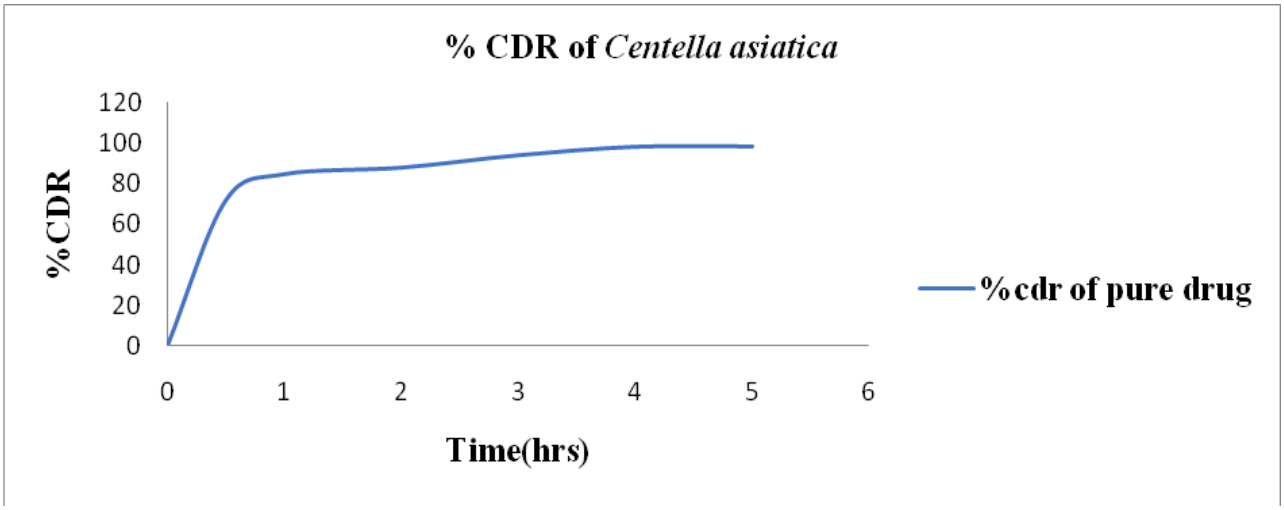


Fig. 16: *In-vitro* Drug Release Profile for active Constituent of *Centella asiatica*

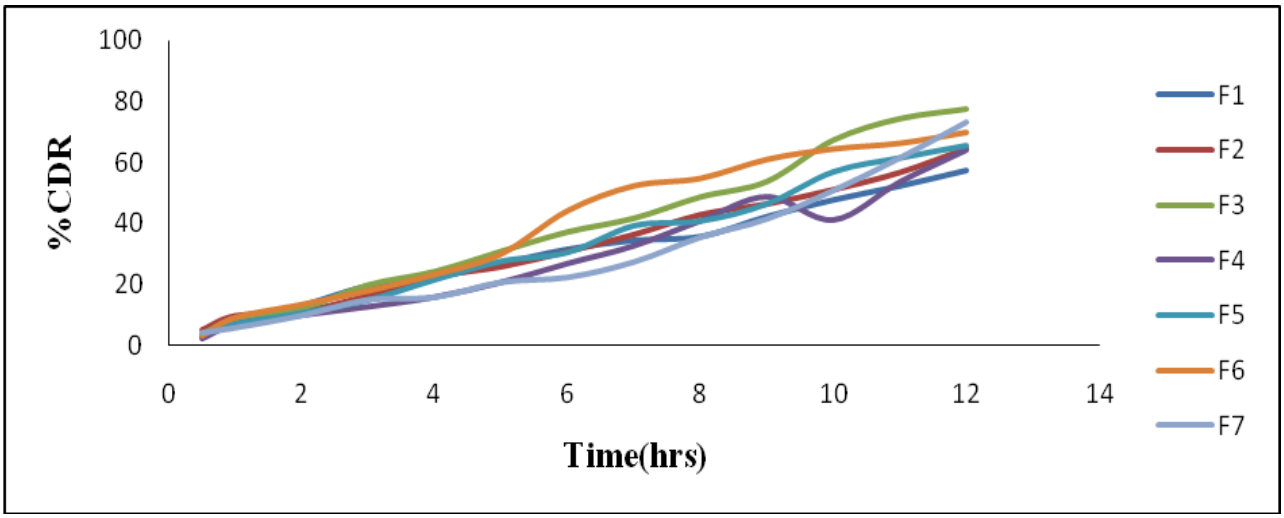


Fig. 17: *In-vitro* Drug Release Profile of Formulation (F1-F7)

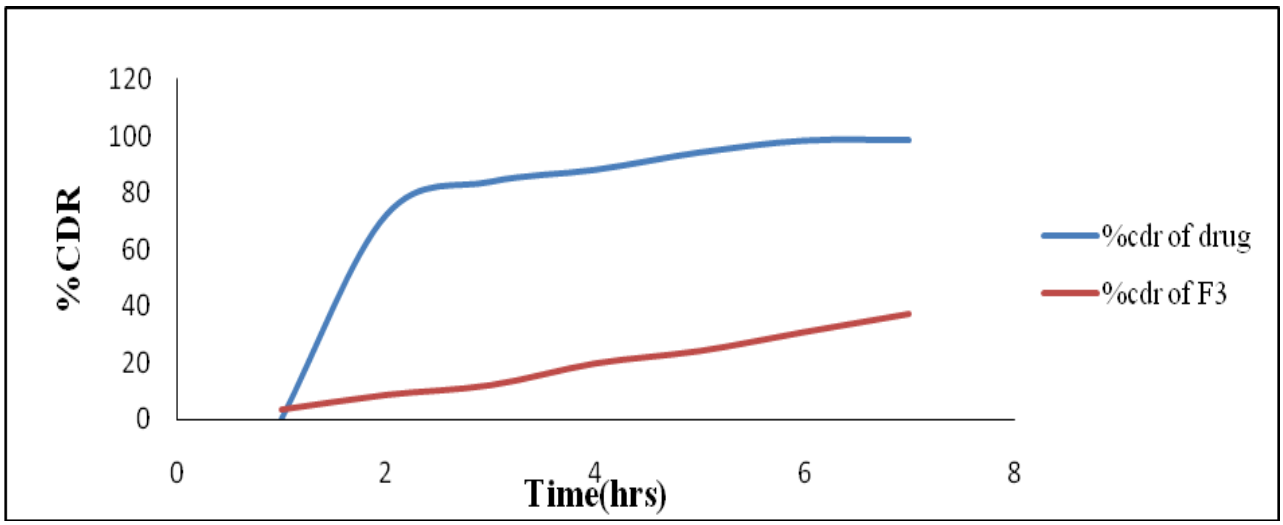


Fig. 18: *In-vitro* Drug Release Profile of Optimized Formulation (F3) & Drug

3.6.6. *In-vitro* Drug Release Kinetics

On the basis of data obtained from *in-vitro* drug release studies, the best formulation F3 was analyzed for the release kinetic studies. The cumulative released data of drug was set into different plots such as zero order, first order and Higuchi model to know about the release pattern of drug and korsmeyer papas' model is used to know about the mechanism of release from the prepared phytosomes. The best released data is selected on the basis of regression coefficient (R^2) value of different models. The release kinetics of the optimized formulation (F3) best fitted in Korsmeyer-peppas model and R^2 value was found to be 0.9879 which is revealed in the tables 2, 3 and Figs. 19-22.

3.6.7. *In-vitro*Antioxidant activity

3.6.7.1. DPPH radical scavenging activity

The radical scavenging capability of DPPH was estimated by drop in its absorbance at range of 517nm induced by the herbal extract passes antioxidant properties. At the concentration of 80µg/ml the IC_{50} value of ascorbic acid, hydroalcoholic extract and prepared formulation was determined. The result concluded in this research that the IC_{50} of phytosomes was lower thus significantly higher free radical scavenging capability to the hydroalcoholic extract and standard. Lower the value of IC_{50} shows the high free radicals scavenging activity. Results are shown in tables 4, 5 and fig. 23.

Table 2: *In-vitro* drug release kinetics of formulation F3

TIME (min)	Log Time	Time$^{1/2}$	%CDR	Log % Cumulative Drug	% Cumulative Drug Remaining	Log% Cumulative Drug Remaining
0	0	0	0	0	100	0
30	1.477121	5.477226	3.8128	0.581244	96.1872	1.983117
60	1.778151	7.745967	8.953406	0.951988	91.046594	1.959265
120	2.079181	10.95445	12.37209	1.088919	87.62791	1.942645
180	2.255273	13.41641	19.98239	1.300647	80.01761	1.903185
240	2.380211	15.49193	24.36077	1.386695	75.639776	1.878785
300	2.477121	17.32051	30.98017	1.477121	69.01983	1.838924
360	2.556303	18.97367	37.32877	1.572044	62.67123	1.797068
420	2.623249	20.4939	41.82788	1.621465	58.17212	1.764719
480	2.681241	21.9089	48.80037	1.688423	51.19963	1.709265
540	2.732394	23.2379	53.86717	1.731415	46.13283	1.664011
600	2.778151	24.4949	67.4644	1.828872	32.5356	1.512358
660	2.819544	25.69047	74.43363	1.871765	25.56637	1.407669
720	2.857332	26.83282	77.604	1.889884	22.396	1.350175

Table 3: Release pattern of phytosomes of *Centella asiatica*

Zero order kinetics	First order kinetics	Higuchi model	Korsmeyer-peppas model
R^2	R^2	R^2	R^2
0.9722	0.9877	0.9559	0.9879

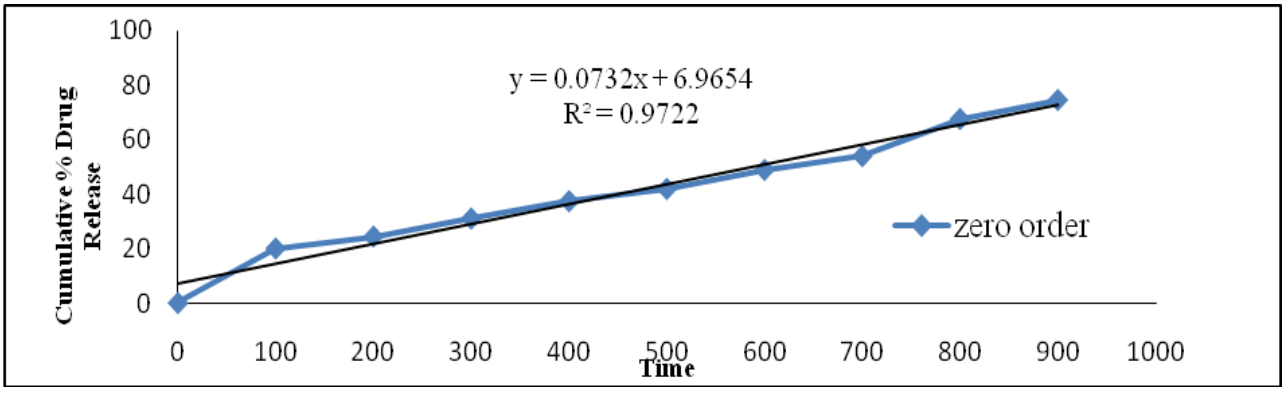


Fig. 19: Zero Order Plot

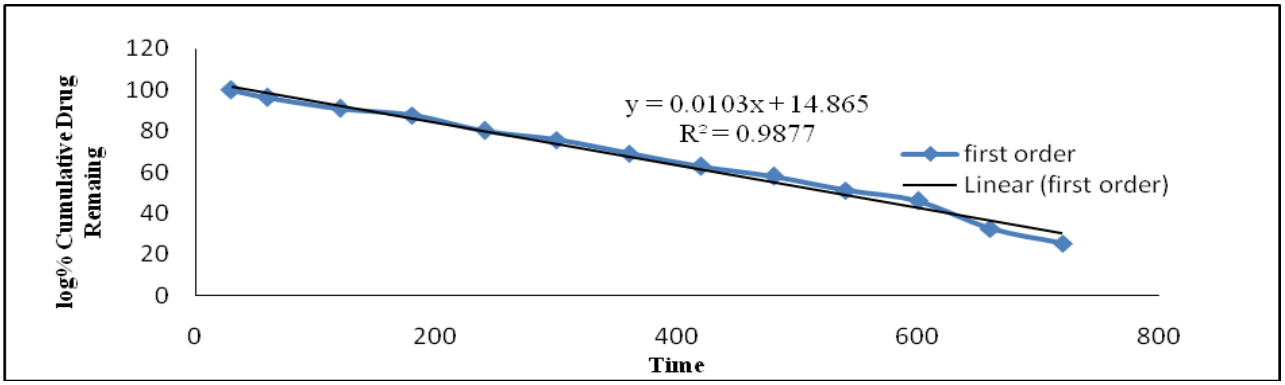


Fig. 20: First Order Plot

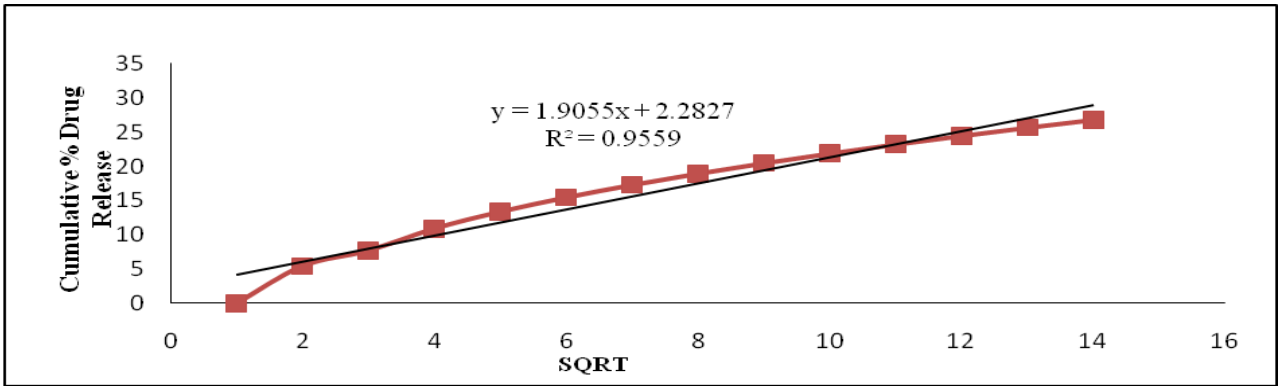


Fig. 21: Higuchi Plot

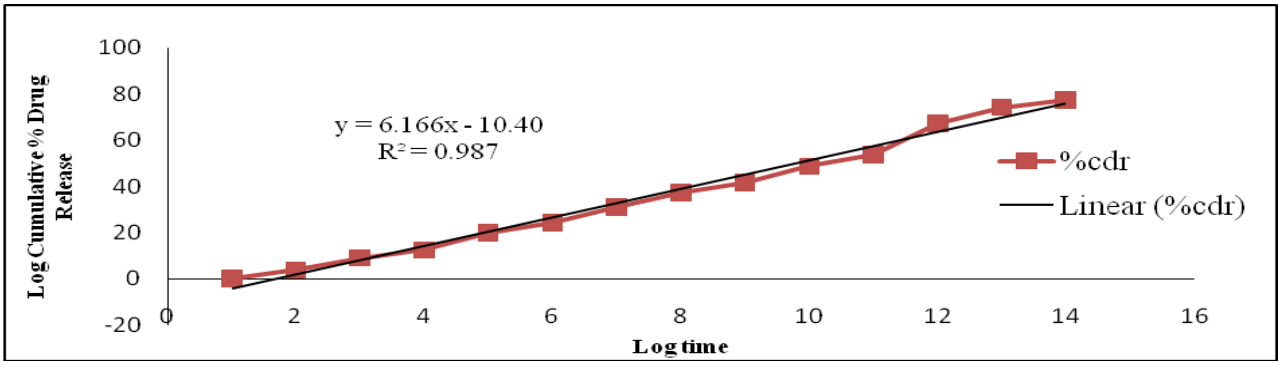


Fig. 22: Korsmeyer-Peppas Plot

Table 4: % Inhibition of DPPH free radical

Concentration (µg/ml)	% Inhibition of DPPH free radical		
	Standard	Hydroalcoholic Extract	Phytosomes
10	42.21	43.55	45.12
20	46.33	47.58	49.33
30	51.59	53.47	54.41
40	59.52	58.71	62.42
50	63.24	62.58	68.65
60	69.7	70.51	75.48
70	75.85	76.8	78.65
80	82.82	85.31	83.55

Table 5: IC_{50} Values of free radical scavenging effect by DPPH method

IC_{50} (µg/ml) of Standard	IC_{50} (µg/ml) of Hydroalcoholic extract	IC_{50} (µg/ml) of Phytosomes
2.54	2.77	1.99

3.6.8. In-vitroAnti-ulcer activity

3.6.8.1. Acid Neutralizing Capacity

The acid neutralizing effect was reported in hydro-alcoholic extract of *Centella asiatica* in various concentrations 100mg, 500mg, 1000mg, phytosomes formulation 1000 mg and in Aluminum hydroxide and Magnesium hydroxide (500mg), they are used in combination as standard. The result found that the phytosome formulation has more significant acid neutralizing effect (10.2) as compared to standard and hydroalcoholic extract. The complete results are mentioned in table 6 and Fig. 24.

Table 6: Effect of *Centella asiatica* extract and phytosomes formulation on ANC

S. No.	Concentration (mg)	Vol. of NaOH consumed	mEq of acid consumed	ANC/gm of antacid
1.	CA-100	39.5	15.0	150
2.	CA-500	42.5	7.75	15.5
3.	CA-1000	30.5	12.35	12.35
4.	Phytosome-1000	41.5	10.2	10.2
5.	Standard-500	45.3	9.21	18.42

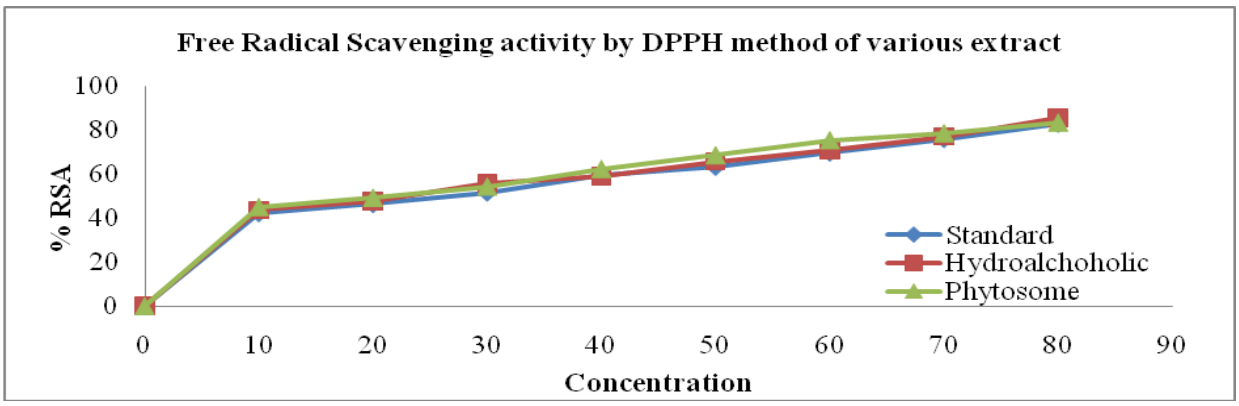


Fig. 23: Curve of free radical scavenging activity by DPPH method

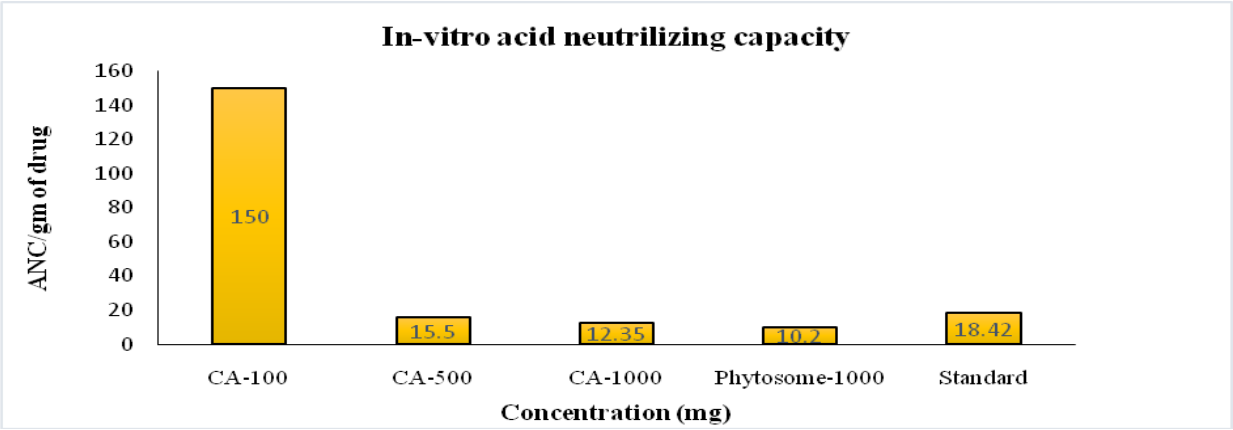


Fig. 24: Effect of *Centella asiatica* extract and phytosomes formulation on ANC

4. CONCLUSION

The optimized formulation (F3) have a considerably higher profile of absorption after administrating orally due to greater lipids solubility, allowing them to permeate biological membrane consequential in increased bioavailability. *Centella asiatica* extract was

obtained to be freely soluble in methanol. The mean particle size and zeta potential of the optimized formulation was found to be 854.2nm and 28.4 mV respectively. DSC shows a characteristic peak of optimized formulation at 245.84°C and drug entrapment efficiency of F3 was found to be 84.3%, highest *in vitro* drug release was observed with formulation F3 (77.6%). The kinetics of F3 best suited with the Korsmeyer-peppas model and R^2 value was obtained to be 0.9879.

The antioxidant activity, radical DPPH scavenging activity of *Centella asiatica* and its phytosome formulation (complex) display that inhibition percentage of hydroalcoholic extract of drug is 85.37% having IC_{50} value 2.77 and percentage inhibition of phytosomes complex was 83.55% having IC_{50} value 1.99 which indicate that phytosomes have greater antioxidant activity than the hydroalcoholic drug extract, it shoes that by the incorporation of lipid the radical scavenging activity of drug increased. Anti-ulcer activity phytosomes was found to neutralize acid more significant as compare to standard and hydroalcoholic extract of *Centella asiatica*. F3 has significant antioxidant properties, gastroprotective activity as well as former pharmacological activitieswith upholding lower side effect better patient compliance.

Future Aspects

The technique of combining phytoconstituent with dietary phospholipid has appeared as a powerful approach for enhancing the pharmacokinetic and pharmacodynamic profile of herbal drugs. It is a new technique which addresses the limitation of traditional delivery system of drug which improves the bioavailability profile of the drug and the drug which poorly absorbed *Centella asiatica* containing antioxidant activity and gastroprotective activity are formulated in the form of phytosomes it helps to regulate the health and prevent disease and support boarding by removing the free radicals from the blood circulation.

Conflicts of interest

None declared

5. REFERENCES

1. Vimala G, Gricilda SF. *Int. J. Micro.*, 2014.
2. Gohil KJ, Patel JA, Gajjar AK. *Int. JPharm. Sci.,* 2010; **72(5)**:546-556.
3. Heim KE, Tagliaferro AR, Bobilya DJ. *J. Nutri. Biochem.*, 2002; **13(10)**:572-584.
4. Lavanya D, Devi AS. *Int. J. Pharm. Sci. Res.,* 2020; **11(6):**2566-2574.
5. Sriya KC, Sai D, Sankar PR. *Int. J. Pharm. Sci. Rew. &Res.*, 2020; **6**:21-26.
6. Patel J, Patel R, Khambholza K, Patel, N. *Asi. J. Pharm. Sci.,* 2009; **4(6):**363-371.
7. Mishra N, Yadav NP, Meher JG, SinhaP. *Asi Pac. J.Tro. Biomed.*, 2012;**2 (3)**:1728-S1734.
8. Dewan N, Dasgupta D, Pandit S, Ahmed *P. J. Pharmacog. Phytochem.*, 2012; **5(4)**:104-108.
9. Ruch RJ, Cheng SJ, KlaunigJE. *Carcinogenesis*, 1989; **10 (6)**:1003-1008.
10. Fatima S, Ramesh C, Qureshi S. *Int.J. Pharmacy*, 2018; **8(12)**:55-59.