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FORMULATION AND EVALUATION OF SUPER SATURABLE SELF EMULSIFYING DRUG DELIVERY SYSTEM OF *BACOPA MONNIERI* METHANOLIC EXTRACT

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Abstract:

The objective of the present study was to develop a super saturable self-emulsifying drug delivery system of *Bacopa monnieri* to enhance its solubility and its oral bioavailability. The herbal drug *Bacopa monnieri (*Family-Scrophulariaceae) is a creeping marsh plant used in Ayurveda for neurological rejuvenation, and has implications for memory enhancement and anxiety. *Bacopa monnieri* is an herbal drug with poor aqueous solubility. Solubility of *Bacopa monnieri* in various oils was determined to optimize the oil phase of an S-SEDDS. Various surfactants and co-surfactants were screened for their emulsification ability with the selected oil. Pseudo ternary phase diagrams were constructed using TRIPLOT V 14 software to identify the self-emulsification region. SEDDS were prepared using Isopropyl myristate as oil, tween 80 as surfactant and Transcutol P as co-surfactant. To overcome the problems with SEDDS they are converted to super saturable SEDDS using HPMC. Formulated S-SEDDS were evaluated for drug content, *in-vitro* drug release and its stability. Results showed that the prepared S-SEDDS have 95.57% drug content. Dilution studies showed the spontaneous micro emulsification and no sign of phase separation. Drug release from S-SEDDS was found to be significantly higher compared to the SEDDS and the Bacopa monnieri Methanolic extract. From the present study it is clear that the formulated S-SEDDS can improve the solubility and bioavailability of an herbal drug with poor aqueous solubility.

Key Words: Super saturable self-emulsifying system, *Bacopa monnieri*, Oral bioavailability, Isopropyl myristate, Tween 80 and Transcutol P.

Introduction:

Oral route has been the major route of drug delivery for the chronic treatment of human diseases. Approximately 40% of new drug candidates have poor solubility and the oral delivery of each drug is frequently associated with low bioavailability, high intra and inter subject variability and a lack of dose proportionality. To overcome these problems various formulation strategies are exploited including the use of surfactants, lipids permeation enhancers, micronisation, and salt formation, complex formation with cyclodextrins, liposome formation, nanoparticles and solid dispersions.

Recently, much attention has been paid to lipid-based formulations with particular emphasis Self-Emulsifying Drug Delivery System (SEEDS) to enhance the solubility of drug and to improve the oral bioavailability of lipophilic drugs. SEDDS may be defined as isotropic mixture of oils, surfactants and co-surfactants. SEDDS formulation upon administration through an oral route, they spontaneously form oil in water emulsion in the GIT tract which disperse into fine droplets. The finer droplets provide a higher surface area for the drug to dissolve or permeate in surrounding medium.

The herbal drug *Bacopa monnieri (*Family-Scrophulariaceae) is a creeping marsh plant used in Ayurveda for neurological rejuvenation, and has implications for memory enhancement and anxiety. One of the major problem with this drug is its low aqueous solubility. Poor solubility of *Bacopa monneri* leads to poor dissolution and hence poor bioavailability. Aqueous solubility can be increased by formulating it into SEDDS. Hence, main objective of the present study is to formulate and evaluate the super saturable self emulsifying drug delivery system of Bacopa monnieri.

Materials and Methods:

Drug and chemicals:

Bacopa monnieri methanolic extract was obtained from Chakrapani ayurvedic and research clinic, Jaipur, Rajasthan. Isopropyl myristate (Isopropyl tetradecanoate), Tween80 (polyoxyethylene sorbitan mono laurate), was obtained from S.D Fine chemicals (Mumbai) and Transcutol-P (Diethylene glycol mono ethyl ether) was obtained as a gift sample from Gatteffose, Mumbai.

Method:

In brief, oil was added to previously weighed Bacopa monneri extract (unit dose 150mg). The components were then kept in a sonicator at 37ºC until drug completely dissolved in oily phase. Surfactant and co-surfactant were then added to the prepared composition and were magnetically stirred until clear emulsion was formed. The prepared microemulsions were stored in the suitable container at ambient temperature for further studies.

Self Emulsifying Drug Delivery System:

Selection of components based on solubility studies:

Oils, Surfactants and Co-surfactants:

Solubility of *Bacopa monnieri* in various oils, surfactants and co-surfactants were studied using shake flask method. Solubility studies were performed by adding excess amount of drug into 2ml of each excipient followed by sealing in vials. These vials were then kept on Rota shaker for 72 hrs for attainment of equilibrium.vials were centrifuged at 15000 rpm for 10mins using a centrifuge followed by filtering it through membrane filter (0.45µm). Samples were suitably diluted with methanol at 278nm by a UV visible double beam spectrophotometer, using methanol as a blank.

Based on emulsification studies:

Surfactant

Various surfactants (Cremophor EL, Span 20, Span 80, Tween 20 and Tween 80) were screened for their emulsification ability of selected oil phase. The selection of surfactant is based on the transparency and ease of emulsification. Briefly, 300mg of the surfactant were added to 300mg of oil phase. The mixture was gently heated at 50ºC for the homogenation of the components. Each mixture, 50mg was then diluted with distilled water to 50ml in a stoppered conical flask. Ease of emulsification was judged by the number of flak inversions required to yield a homogenous emulsion. Emulsions were allowed to stand for 2hrs and their percentage transmittance was measured at 560nm by a double beam UV spectrophotometer using distilled water as a blank.

Co-Surfactant:

Different co-surfactants namely, (PEG 600, Propylene glycol, Ethanol, Capmul, Glycerol, PEG 400 and Transcutol-P) were screened for the emulsification ability of selected oily phase. Co-surfactant selection was

done on the basis of percentage transmittance and ease of emulsification. Briefly, 200 mg of the surfactants were mixed with 100 mg of the co-surfactant. Then 300 mg of the selected oily phase was added to this mixture. The mixtures were gently heated at 50ºC the homogenization of the components. Each mixture, 50 mg was diluted with water to 50 ml and ease of emulsification was judged by number of flask inversions required to yield a homogenous emulsion. Emulsions were allowed for 2hrs and their percent transmittance was evaluated spectrophotometrically at 560nm by a double beam UV spectrophotometer using distilled water as a blank. The emulsions were further observed visually for any turbidity or phase separation.

Construction of Pseudo ternary phase diagram:

Based on the solubility and emulsification studies isopropyl myristate, Tween80, Transcutol-P were selected as oil, surfactant and cosurfactant respectively. To determine the required concentration of components for the SEDDS preparation, pseudo ternary phase diagrams was constructed using water titration method at ambient temperature (25ºC). The surfactant and cosurfactant were mixed in different volume ratios (1:1, 1:2, 1:3, 1:4, 4:1, 3:1, 2:1). Oil and S_{mix} (surfactant and cosurfactant mixture) were mixed thoroughly in different volume ratios (1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2, 9:1) and titrated with water by adding in a drop wise manner under gentle agitation. The ratio of one excipient to another in the SEDDS formulation was analysed and the pseudo ternary plot was constructed using TRIPLOT V14 (4.1.0.2) software. Phase diagrams were constructed using IPM as oil, Tween-80 as surfactant and Transcutol-P as co-surfactant.

Formulation:

Preparation of SEDDS:

A series of SEDDS formulations for Bacopa monnieri were prepared based on solubility studies, Pseudo ternary phase diagram and visual observation. In our study Isopropyl myristate was used as oil, Tween 80 as surfactant and Transcutol P as co-surfactants. In brief, oil was added to previously weighed Bacopa monneri extract (unit dose 150mg). The components were then kept in a sonicator at 37ºC until drug completely dissolved in oily phase. Surfactant and co-surfactant were then added to the prepared composition and were magnetically stirred until clear emulsion was formed. The prepared micro emulsions were stored in the suitable container at ambient temperature for further studies.

Characterisation and Evaluation of Sedds:

Self-Emulsification time and Dispersability tests :

The efficiency of dispersability was assessed using a USP dissolution apparatus II. Each formulation (0.5 ml) was added to 500 ml distilled water maintained at 37±0.5ºC, with paddle rotating at 50rpm for gentle agitation. The *in vitro* performance of the formulations was visually assessed using the grading system as shown below.

- **Grade A**: Rapidly forming (within 1 min) emulsion, having a clear or bluish appearance.
- **Grade B**: Rapidly forming, slightly less clear emulsion, having a bluish white appearance.
- **Grade C**: Fine milky emulsion that formed within 2 min.
- **Grade D**: Dull, greyish white emulsion having slightly oily appearance that is slow to emulsify (longer than 2 min).
- **Grade E**: Formulation, exhibiting either poor or minimal emulsification with large oil globules present on the surface.

Thermodynamic stability tests:

Selected formulations were subjected to different thermodynamic stability tests (Heating cooling cycle, Centrifugation and Freeze thaw cycle), to overcome selecting metastable formulation.

Heating cooling cycle: Heating and cooling cycle was done in refrigerator, the temperature ranging between 4°C for 48hrs. The formulations which were stable at these temperatures were subjected to centrifugation test.

Centrifugation: Selected formulations from phase diagrams were centrifuged at 3500 rpm for 30 min and observed for phase separation, creaming and cracking. Formulations that are stable were taken for Freeze thaw cycle.

Freeze thaw cycle: Three freeze thaw cycles were carried out between -4°C and +40°C, where the formulation was stored for not less than 48 hours at each temperature. Those formulations, which passed these thermodynamic stress tests, were selected for further study.

Effect of pH and Robustness to dilution: Dilution and pH of the vehicle have considerable effect on the phase separation of the spontaneously emulsifying systems. Drug loaded SEDDS were diluted with 10, 100 & 1000

times 0.1 HCl. The resulting emulsions were stored for 24 hrs at room temperature and observed for any signs of phase separation or drug precipitation.

Viscosity Determination: Brookfield LVDV II + P ultra V6.0 (Brookfield Engineering Laboratories, Inc, Middleboro, MA, spindle # CPE40) was used to determine the viscosity of different formulations by using spindle no.34 at 25±1.0°C for 100 rpm.

Drug Content Estimation: SEDDS containing Bacopa monneri equivalent to one dose was added in 100 ml volumetric flask containing 0.1 N HCl and mixed thoroughly to dissolve the drug. 1ml of above solution was withdrawn and added to 10ml of methanol which was quantified with UV-visible spectrophotometer at 278nm.

Preparation of Super Saturable Sedds (S-SEDDS): S-SEDDS were prepared by adding HPMC to the liquid SEDDS containing Bacopa monneri extract. In brief HPMC is added to the liquid SEDDS and mixed homogenously using glass rod to ensure uniform distribution of formulation. The resultant suspension is filled into hard gelatin capsule of zero size and stored until further use.

Characterisation of S-Sedds.

Drug excipient compatibility studies:

FT-IR provides information about the structure of molecule and offers the possibility of chemical identification. The infrared analysis was carried out to find out the presence of drug–excipient interactions used in the preparation of S-SEDDS. IR spectra were studied for the pure drug and the optimized formulation was studied in the range from 400-4000cm^{-1}.

***In-vitro* dissolution studies:**

Invitro dissolution studies were carried out to assess drug release from oil phase into aqueous phase by USP type I dissolution apparatus using 900ml of 0.1N HCl for 1hr at 100 rpm and temperature was maintained at 37±0.5°C. 5ml of samples were withdrawn at specified intervals of time and it is replaced with fresh medium to maintain the sink condition. Samples taken were then analyzed at 278 nm using UV spectrophotometer.

Drug content: Bacopa monneri content in the S-SEDDS was determined using the UV method. The S-SEDDS formulation was dissolved in sufficient amount of methanol, it is then subjected to sonication for 10mins and filtered. The absorbance of the filtrate was determined by UV-Visible spectrophotometer at 278nm.

Results And Discussion: The main objective of the study is to develop super saturable self-emulsifying drug delivery system (S-SEDDS) of Bacopa monnieri extract using various concentrations of Isopropyl myristate (oil), Tween 80 (surfactant) and Transcutol-P (Co-surfactant).

Drug excipient compatibility studies:

FTIR analysis was conducted to verify the possibility of interaction of chemical bonds between drug and other excipients of the formulation. FT-IR analysis of optimized formulation and the drug were studied for the interaction of the excipients and the drug in the final formulation. Similar peaks were observed in spectra of different combinations of excipients and in optimized formulation along with absence of interfering peaks indicating there is no unwanted reaction between the drug and excipients used in the studies. From figures 1.1 and 1.2 & tables 1.1 and 1.2 it can be interfered that there was no appearance or disappearance of any characteristic peaks. This shows that there is no interaction between the drug and excipients used in S-SEDDS preparation.

Screening of Oils, Surfactant's and Co-surfactants.

Solubility studies:

Solubility studies were conducted to identify a suitable oil phases, surfactant and cosurfactant for the development of the Bacopa monneri S-SEDDS. The solubility of Bacopa monneri in various oils, surfactants, cosurfactants is presented in tables 1.3, 1.4, and 1.5 and shown in figures 1.3, 1.4 and 1.5. Among the various oils that were screened, Isopropyl myristate could solubilize the target amount of Bacopa monneri extract (150mg) at a relatively small amount of oil. And Tween 80 and Transcutol-P was selected as surfactant and co-surfactant due to high solubility of drug. The selection of surfactant and cosurfactant in the further study was governed by the emulsification efficiency.

Based on emulsification study:

Screening of Surfactant: Surfactants were selected based on their ability of ease of emulsification (No. of flask inversions of oil phase and percent transmittance). Surfactants were screened and the results were given in the table 1.6. Isopropyl myristate exhibited highest emulsification ability with Tween 80 (% Transmittance 96.2 and No of flask inversions is 6). Based on these studies Tween 80 is selected as surfactant.

Screening of Cosurfactants:

Screening of cosurfactants was performed and the results are given in the table 1.7. Based on the results of emulsification Transcutol-P was selected as Cosurfactant as they exhibited high percentage transmittance (97.4) with Isopropyl myristate and Tween 80 with less number of flask inversions (03).

Pseudo ternary phase diagram:

The aim of the construction of pseudo ternary phase diagrams was to determine the existence range of self-micro emulsifying region and to select suitable concentrations of oil, surfactant and cosurfactant. The self-emulsification region was found to be highest for formulation SF5 (2:1) represented in figure 1.6. Phase diagram was constructed using isopropyl myristate, Tween 80 and Transcutol- P as oil, Surfactant and Co-surfactant respectively.

Assessment of Self emulsification time and dispersability:

Emulsification time is an important index for the assessment of emulsion formation. SEDDS disperse completely and rapidly when subjected to aqueous dilution under mild agitation. The decrease in self-emulsification time can be assumed to be due to the relative decrease in surfactant concentration, leading to decreased viscosity of the formation. S1 & S4 showed Grade A results by rapidly forming (within 1min) microemulsion, having a clear or slightly bluish color, S2 showed Grade B results in rapidly forming, slightly less clear emulsion in bluish color and S3 & S5 showed Grade C results in fine milky emulsion that formed within 2 mins.

Centrifugation:

The formulation S1, S3 and S4 were found to be stable after centrifugation test because of no phase separation, but S2 and S5 were failed due to phase separation and reported as unstable given in table 1.10. The formulations S1, S3 and S4 were further subjected to freeze thaw cycle.

Viscosity determination: The viscosities of the various formulations were determined by Brookfield viscometer using spindle no.S-34 formulation F4 (2:1) has the minimum viscosity due to the reduced surfactant and co-surfactant levels. The viscosities of various formulations are given in table 1.9. Among all the formulations S4 was found to have lowest viscosity.

Drug content:

Drug content of different formulation were shown in the above table 1.9. It was observed that the formulation S4 have highest drug content.

***Invitro* drug release:**

In-vitro dissolution studies were carried out using type II dissolution apparatus for all the formulations. It is observed that within 1hr, 90.51% drug was released from the optimized formulation (S4) in 0.1N HCl. The results of dissolution profile of o/w nanooemulsion formulation were shown in table 1.11 and fig 1.7.

Evaluation of Super Saturable Sedds:

Percent cumulative drug release of super saturable SEDDS (S4H1 to S4H3)

Invitro dissolution studies were carried out by using USP type II apparatus (basket type) for different formulations. From the results of Invitro dissolution studies, it can be observed, that formulations S4H3 (2:1) containing (20%) HPMC showed greater drug release (96.04) in 1hr, when compared to other formulations and where shown in the table 1.12 and figure 1.8 .

Comparison of *invitro* drug release between *Bacopa monnieri* SEDDS, S-SEDDS and Extract.

Supersaturable SEDDS of formulation S4H3 (2:1) containing 20% HPMC was compared with *Bacopa monneri* extract were represented in table 1.13 and figure 1.9. The percent drug release of SEDDS formulation is 90.51%, S-SEDDS formulation is 95.57% and the extract is 78.89%. S-SEDDS formulation S4H3 showed better drug release when compared to SEDDS formulation and the extract.

Zeta Potential and Droplet Size:

1ml of suspension was taken in disposable syringe and inserted into one of the zeta cell of Malvern Zetasizer. Zeta potential of optimized formulation was found to be -15 MV. The value 0 to ±10mV indicates instability, ±10mV to ±30Mv indicates good stability, and ±30mV to ±60mV indicates excellent stability. -15mV indicated that particles were negatively charged and there was no flocculation. The formulation was found to be stable. Zeta potential and droplet size were represented in figure 1.10.

Polydispersive Index and Droplet Size.

Size and poly dispersivity index of SEDDS were determined using He-Ne laser at scattering angle of 175º at 25ºC by Horiba SZ 100Z. Polydispersity index was found to be 0.260 and its particle size was 30.0nm as shown in 1.11. PI value from 0 to 0.08 indicates standard monodisperse, 0.08 to 0.7 is mono-disperse and greater than 0.7 is polydisperse.

Stability Studies:

During the 12 weeks of stability study, none of the stored samples showed phase separation or rapid precipitation indicating that prepared formulations were physically stable under all storage conditions. They showed no signs of breaking or cracking when subjected to freeze thaw cycles. No significant difference was found between the emulsification time and drug content of diluted S-SEDDS at zero time and under all storage conditions throughout the 12 weeks. This indicates the stability of the S-SEDDS dosage forms.

List of figures:

Tables And Figures:

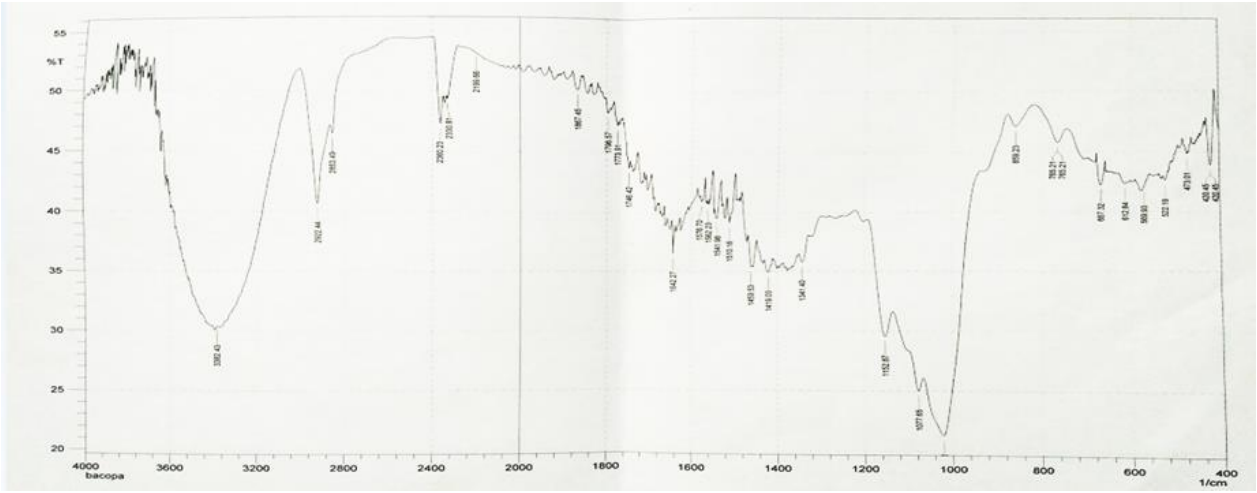

Figure: 1.1:- represents FTIR spectra of *Bacopa monneri* extract.

Table: 1.1:- Represents FTIR peaks of *Bacopa monneri* extract.

Functional group	Reported Value (cm^{-1})	Observed Value (cm^{-1})
=C-H	2960-2850	2853.49
C=C	1650-1450	1459.53
N-H	3500-3300	3382.43
C=0	1760-1680	1746.42
O-H	3570-3350	3382.43

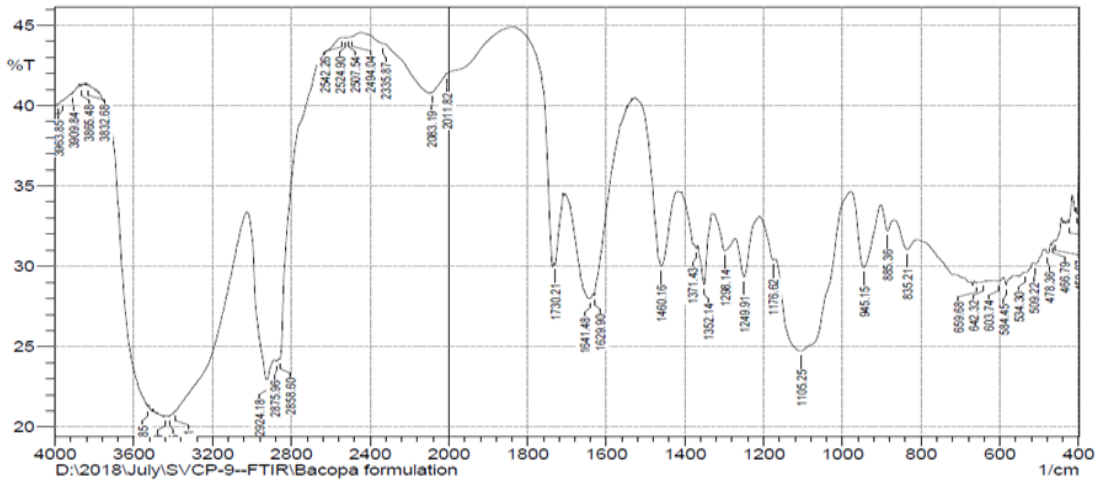

Figure: 1.2:- FTIR spectra of optimized super SEDDS formulation S4H3.

Table: 1.2:- Represents FTIR peaks of optimized formulation.

Functional group	Reported Value (cm^{-1})	Observed Value (cm^{-1})
=C-H	2960-2850	2858.60
C=C	1650-1450	1460.53
N-H	3500-3300	3387.11
C=0	1760-1680	1730.21
O-H	3570-3350	3387.11

Table: 1.3:- Solubility of *Bacopa monnieri* extract in different oils.

S.No	Type of Oil	Solubility (mg/ml)
1.	Oleic acid	9.272
2.	Olive oil	2.181
3.	Isopropyl myristate	13.295
4.	Labrafac	0.477
5.	Sunflower oil	3.931
6.	Castor oil	0.522
7.	Arachis oil	6.477

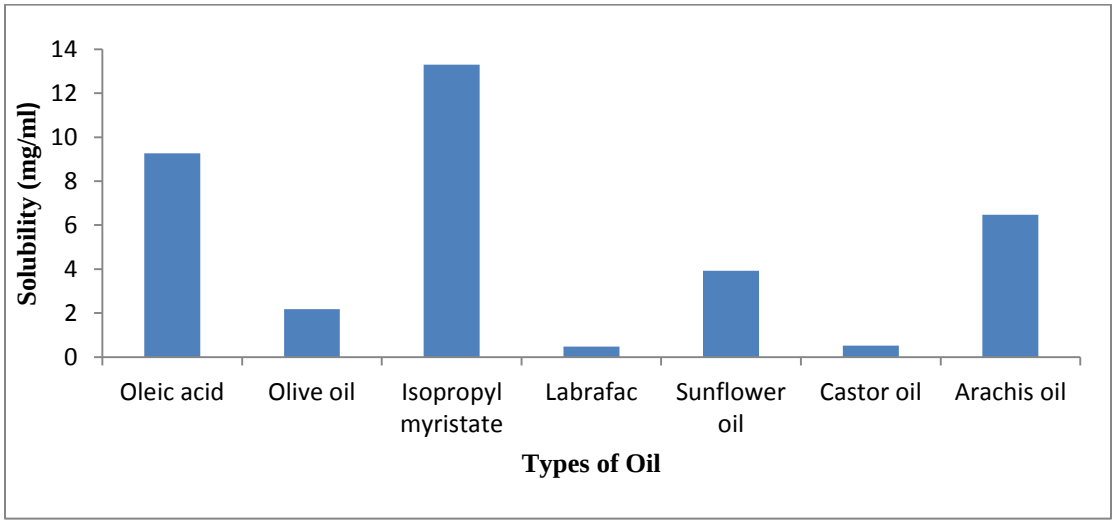

Figure: 1.3:- Solubility of Bacopa monnieri extract in different oils.

Table: 1.4:- Solubility of *Bacopa monnieri* extract in different surfactants.

S.No	Type of surfactant	Solubility (mg/ml)
1.	Span 20	4.272
2.	Cremophor RH	0.568
3.	Span 80	1.632
4.	Tween 20	6.659
5.	Tween 80	9.068

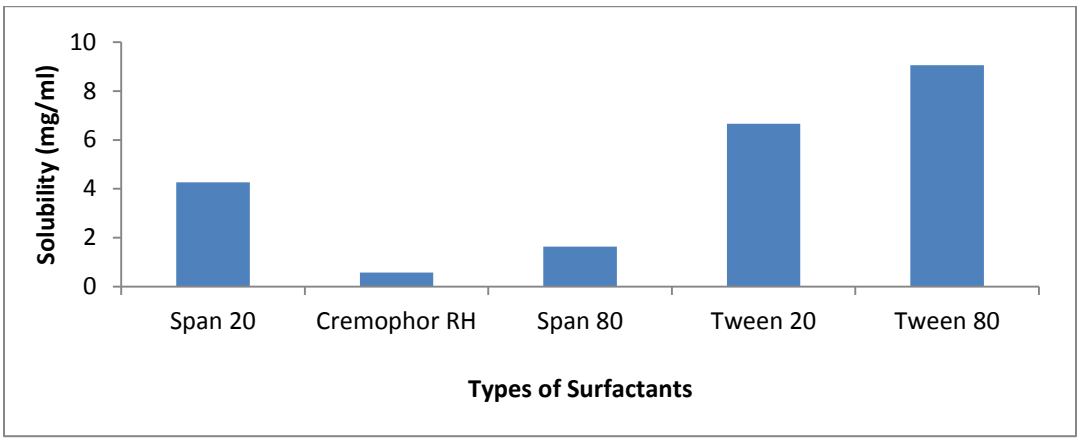

Figure: 1.4:- Solubility of *Bacopa monnieri* in different surfactants.

Table: 1.5:- Solubility of *Bacopa monnieri* extract in different Co-surfactants.

S.No	Type of Cosurfactant	Solubility (mg/ml)
1.	PEG 600	4.271
2.	Propylene glycol	2.681
3.	Ethanol	20.04
4.	Capmul	1.863
5.	Glycerol	2.295
6.	PEG 400	2.750
7.	Transcutol-P	20.36

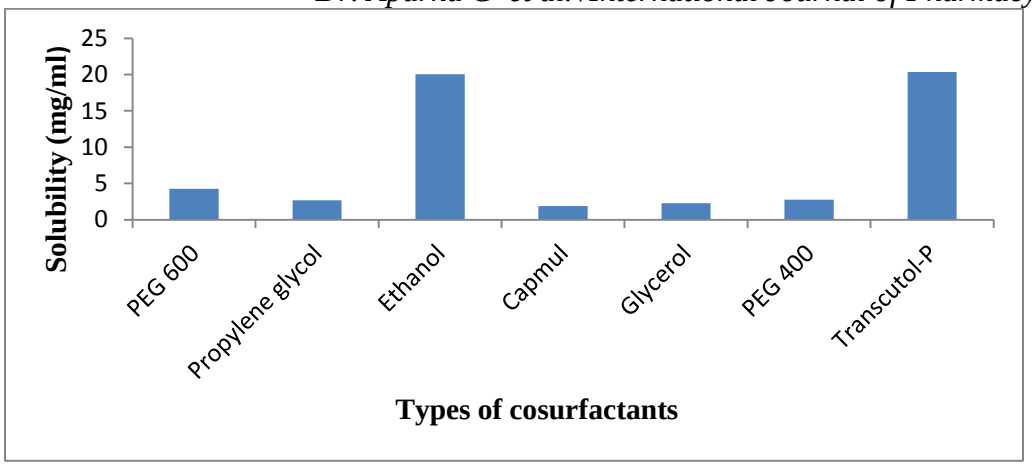

Figure: 1.5 Solubility of *Bacopa monnieri* in different Cosurfactants.

Table: 1.6:- Screening of surfactant based on emulsification.

S.No	Selected oil (300mg)	Type of surfactant (300mg)	No. of flask inversions (Ease of emulsification)	% of transmittance at 278nm.
1.	Isopropyl myristate	Span 20	50+	80.1%
2.		Cremophor RH	07	73.4%
3.		Span 80	40+	56.3%
4.		Tween 20	09	87.2%
5.		Tween 80	06	96.2%
6.		Span 60	40+	42.1%

Table: 1.7:- Screening of co-surfactants based on emulsification.

S.No	Oil	Surfactant	Cosurfactant	No of flask inversions	% transmittance
1.	Isopropyl myristate	Tween 80	Ethanol	05	93.2%
2.			Propylene glycol	07	96.2%
3.			Transcutol P	03	97.4%
4.			PEG 600	05	92.4%
5.			Capmul	14	84.5%
6.			Glycerol	12	92.2%

Table: 1.8:- Percentage of Nanoemulsion region in formulation.

Formulation	% of Nanoemulsion region
a)SF1(1:1)	36%
b)SF2(1:2)	32%
c)SF3(1:3)	25%
d)SF4(1:4)	24%
e)SF5(2:1)	40%
f)SF6(3:1)	31%
g)SF7(4:1)	29%

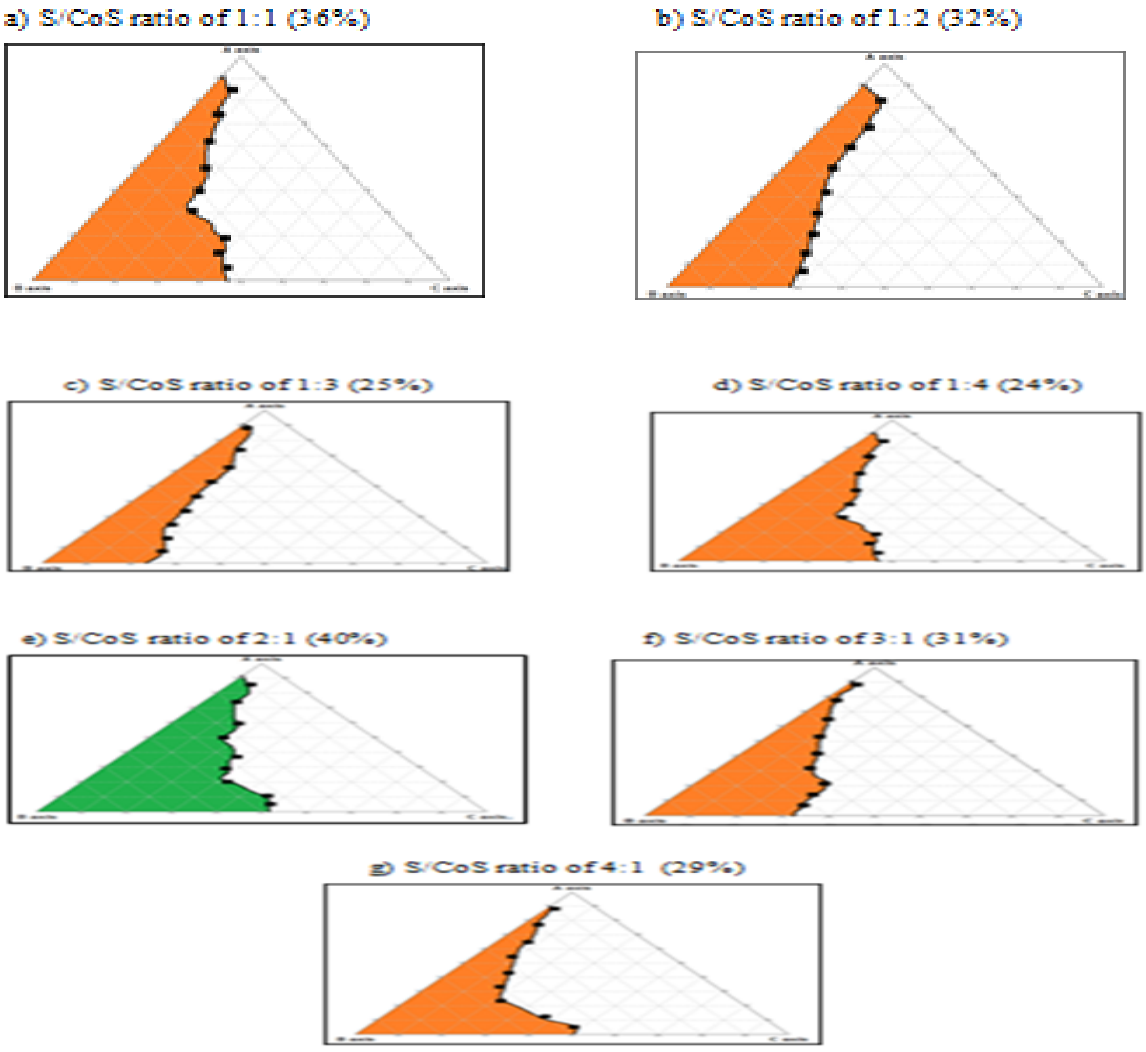

Figure 1.6:- Pseudo ternary phase diagrams constructed Isopropyl Myristate, Tween 80 and Transcutol-P.

Note: A axis- Oil, B axis- Smix and C axis- Water.

Table: 1.9:- Evaluation parameters of SEDDS.

Formulation	Self-emulsification time & dispersibility tests	Effect of dilution	Percentage transmittance	Viscosity (centipoise)	Drug content
S1	Grade A	Pass	92%	43.8	85.79
S2	Grade B	Pass	89%	27.6	86.47
S3	Grade C	Fail	79%	30.6	89.09
S4	Grade A	Pass	95%	24.0	94.50
S5	Grade C	Fail	89%	30.6	82.04

Table: 1.10:- Thermodynamic evaluation parameters.

Formulation	Heating and cooling cycle	Centrifugation test ±SD	Freeze thaw method (-4°C for 2 days and +40ºC for 2 days)
S1(1:1)	Pass	Pass	Pass
S2(1:2)	Fail	Fail	Fail
S3(1:3)	Fail	Pass	Fail
S4(2:1)	Pass	Pass	Pass
S5(3:1)	Fail	Fail	Fail

Table: 1.11:- *Invitro* drug release of different formulations.

Formulation	*Invitro* drug release
S1(1:1)	79.07
S2(1:2)	81.60
S3(1:3)	84.69
S4(2:1)	90.51
S5(3:1)	83.79

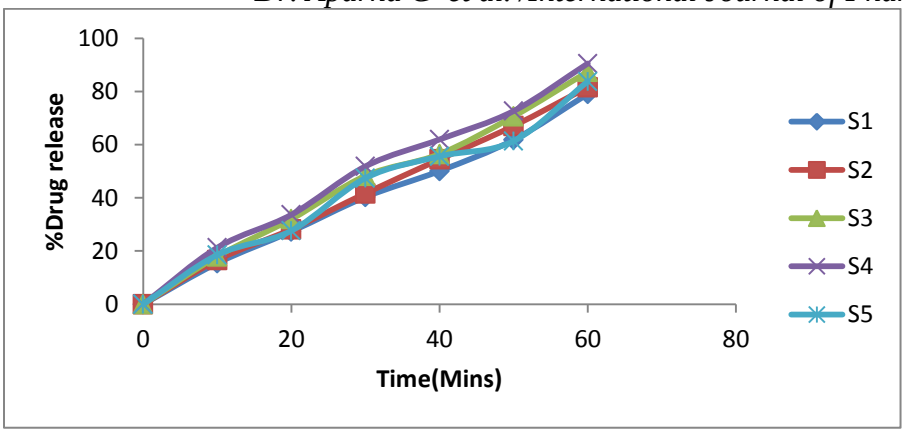

Figure: 1.7:- Percent drug release of SEDDS formulation.

Table: 1.12:- Invitro drug release of various S-SEDDS formulations.

Time(min)	S4H1	S4H2	S4H3
0	0	0	0
10	25.90	26.18	27
20	32.05	32.6	33.69
30	49.68	51.06	55.73
40	63.04	65.51	67.46
50	79.75	82.23	86.37
60	90.10	92.96	95.57

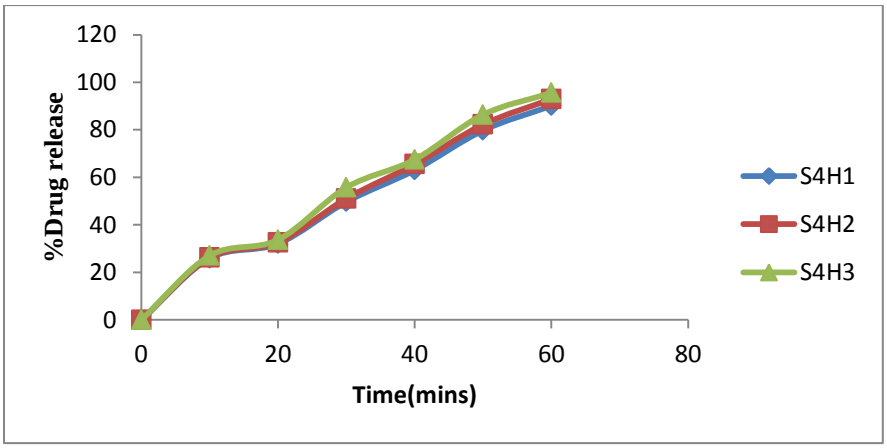

Figure: 1.8:- Percent cumulative drug release of super saturable SEDDS formulation S4H1 to S4H3.

Table: 1.13:- Comparison of *Invitro* drug release between extract, SEDDS and S-SEDDS.

Time (mins)	% Drug release of extract	% Drug release of SEDDS (Formulation-S4)	% Drug release of S-SEDDS (Formulation-S4H1)
0	0	0	0
10	21.81	21.27	27
20	27.66	33.66	33.69
30	39.49	51.85	55.73
40	53.67	61.95	67.46
50	69.78	72.65	86.37
60	78.89	90.51	95.57

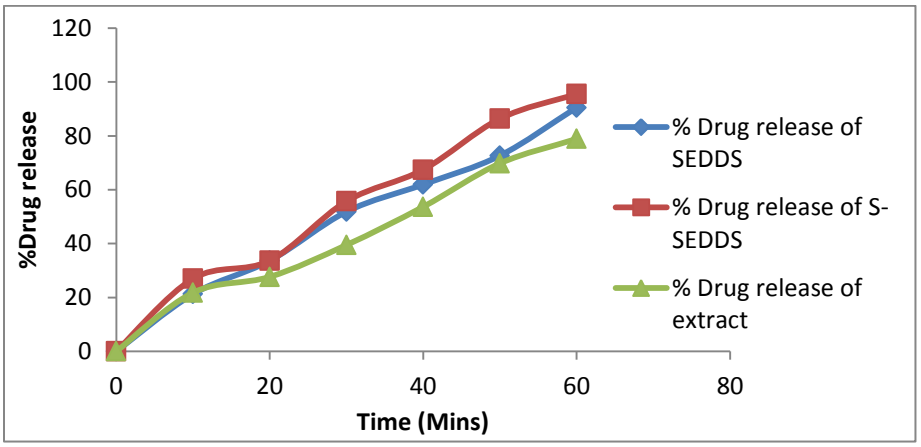

Figure: 1.9:- Comparison of *Invitro* drug release between SEDDS, S-SEDDS and extract.

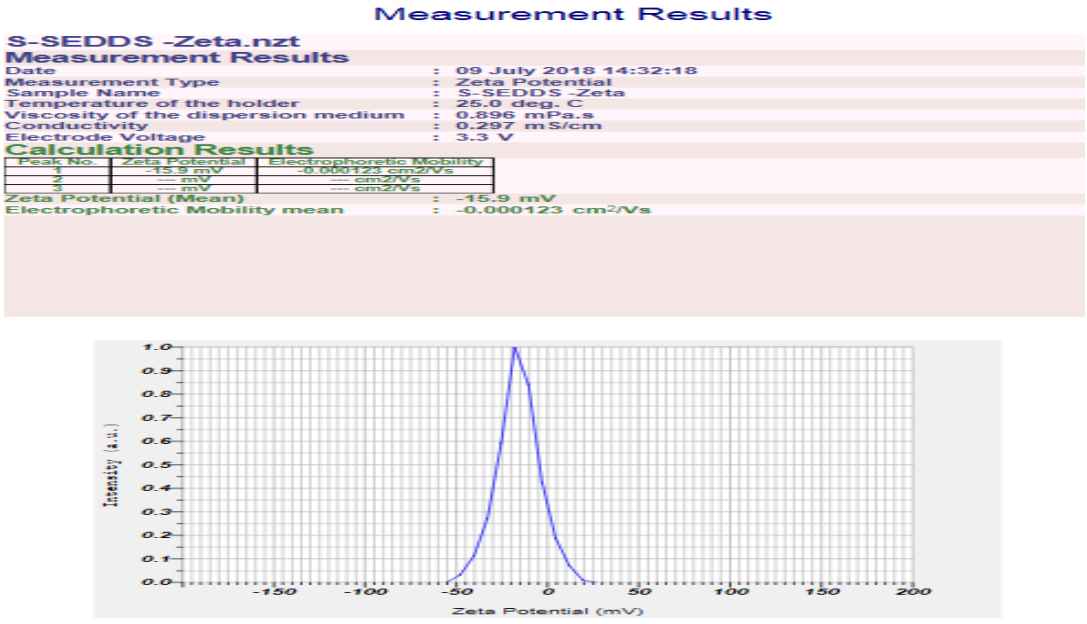

Figure: 1.10:- Zeta potential and droplet size of S-SEDDS of *Bacopa monnieri.*

Table: 1.14:- Stability conditions of formulated Bacopa monnieri S-SEDDS.

Storage conditions	parameters	Initial	1 month	2 month	3 month
40ºC±2ºC/75±5%	Drug content	95.92%	95.89%	95.88%	95.85%
	Emulsification time	Grade A	Grade A	Grade A	Grade A

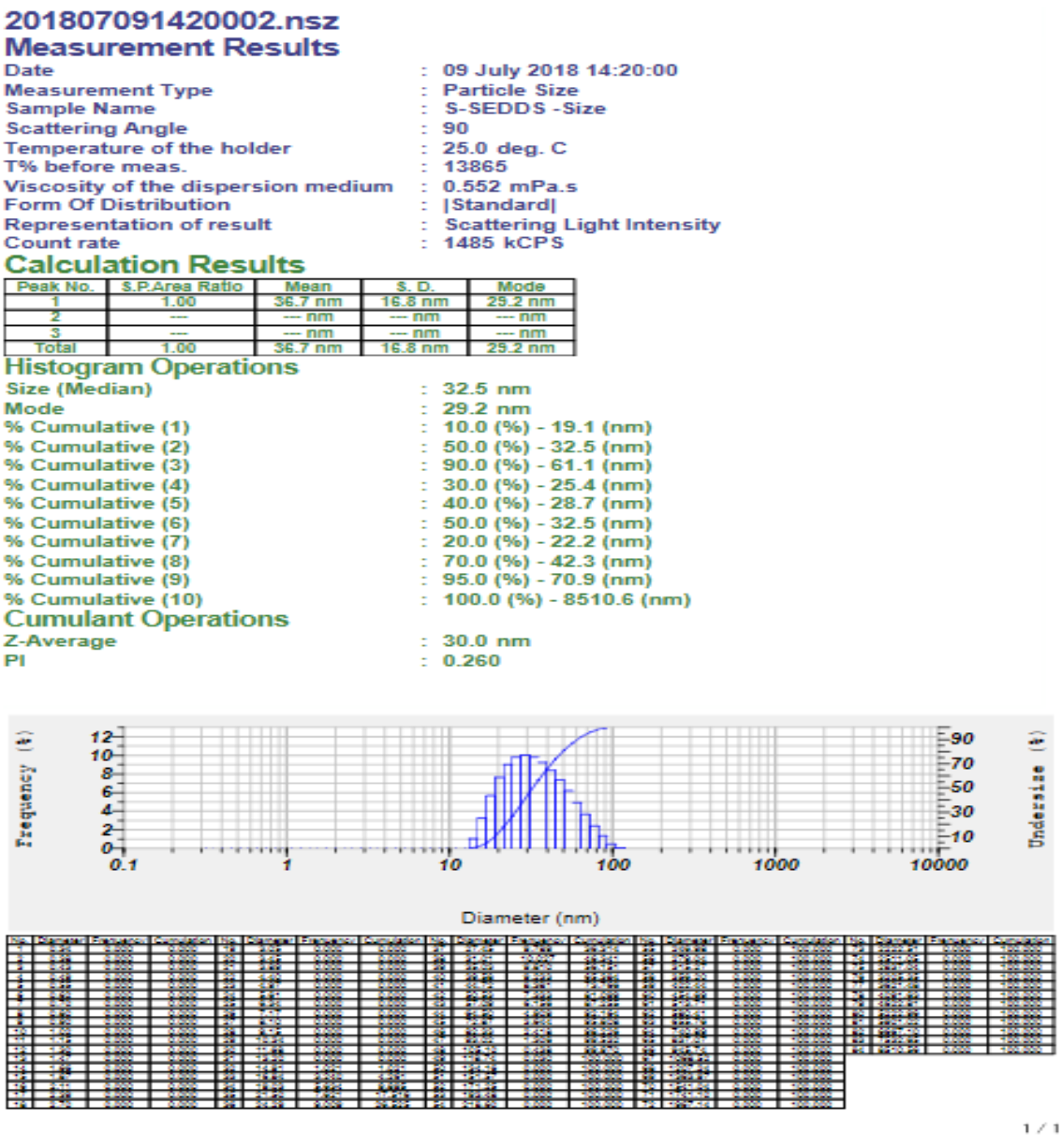

Figure: 1.11:- Polydispersive index and droplet size of *Bacopa monnieri* S-SEDDS

Conclusion:

Bacopa monnieri is an herbal drug possessing many pharmacological activities like anti-oxidant, anti-inflammatory, memory enhancing etc**.,** but its solubility and oral bioavailability are poor. The objective of our investigation was to formulate a super saturable self-emulsifying drug delivery system (SSEDDS) of Bacopa monnieri using minimum surfactant concentration that could improve its solubility, and oral bioavailability. The composition of best selected formulation consist of Isopropyl myristate, Tween 80 and Transcutol-P as oil, surfactant and cosurfactant respectively, containing 150mg of Bacopa monnieri showing drug release for S-SEDDS formulation(95.57%), droplet size(30.0nm), zeta potential(-15.9mV), viscosity(24.0) and infinite dilution capacity. In conclusion, SSEDDS are a promising approach for the formulation of drug compounds with poor aqueous solubility.

- The solubility of *Bacopa monnieri* Methanolic extract was found to be highest in Isopropyl myristate as compared to other oils. Thus, isopropyl myristate was selected as the oil phase for the development of the formulation.
- Addition of higher concentration of co-surfactant as compared to concentration of surfactant showed poor Nanoemulsion.
- From the FTIR studies it can be observed that there is no drug excipient incompatibilities between the drug and the excipients in the SEDDS formulation.
- From the results of pseudoternary phase diagrams it was revealed that the formulation SF5 covers the maximum Nanoemulsion region as compared to other formulations, where as other formulations makes Nanoemulsion which are unstable on dilution and have poor Nanoemulsion region.
- Higher concentration of oil in SSEDDS may provide greater opportunity for the solubilization and incorporation of poor aqueous soluble drug(*Bacopa monnieri*).
- The best selected formulation was found out to have minimum average particle size of 30.0nm and zeta potential of -15.9mV. The zeta potential governs the stability of Nanoemulsion. The high value of zeta potential indicates the electrostatic repulsion between two droplets. DLVO theory states that electric

double layer repulsion will stabilize Nanoemulsion where electrolyte concentration in continuous phase is less than a certain value.

- With further development of this technology, sedds will continue to enable novel applications in drug delivery and solve problems associated with the delivery and solve problems associated with the delivery of poorly soluble drug.

From the above results it can be concluded that the proposed objective of the present research work of enhancing the solubility and drug release was achieved successfully.

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