

Formulation and Evaluation of Herbal Drug Loaded Self Nano Emulsifying Drug Delivery System (SNEDDS)

Vishal N Kushare^{*1,2}, Saravanan S²

¹Department of Pharmaceutics, Maratha Vidya Prasarak Samaja's Institute of Pharmaceutical Sciences, Adgaon, Nashik-422003, Maharashtra, India

²Department of Pharmaceutical Sciences, Annamalai University, Annamalai Nagar, Chidambaram-608002, TamilNadu, India



Article History:

Received on: 04 Oct 2018
Revised on: 06 Nov 2018
Accepted on: 18 Dec 2018
Published on: 28 Dec 2018

Volume: 3 Issue: 2

Keywords:

Coriandrumsativum, self nanoemulsifying drug delivery system, poly dispersity index, dissolution studies.

ABSTRACT

The goal of this research was to formulate and test *invitro* the self-nano emulsifying drug delivery system (SNEDDS) of poorly water-soluble herbal material. Linalool, an essential of *Coriandrum sativum* with anti-epileptic activity, was isolated from *Coriandrum sativum* by using Soxhlet extraction method followed by column chromatography and fractionates are concentrated under reduced pressure by using rotary flash evaporator. It is low water soluble material; unpredictable dissolution and low bioavailability make it very difficult to administer linalool orally. The captex-200 oil was exhibited maximum solubility of linalool. Thus, it was chosen as the oil phase, while Tween 80 and PEG-200 were chosen as surfactant and co-surfactant respectively for the preparation of linalool SNEDDS. For the determination of existence zone of nanoemulsion, pseudo ternary phase diagram was developed using the Prism Software by using water titration method. Self-nanoemulsion are evaluated for scanning electron microscopy (SEM), particle size analysis, polydispersity index, zeta potential and *invitro* drug release. The s9 formulation showed 97.72% cumulative release higher than other selected formulations (S4-S8). The S9 formulation showed promising result on droplet size, zeta potential, polydispersity index, *invitro* drug dissolution. It was concluded that SNEDDS formation from captex-200, tween 80, PEG-200, S_{mix} (4:1), is a promising approach to enhancing substance solubility and the pace of dissolution.

*Corresponding Author

Name: Vishal N Kushare
Phone: 7744889098
Email: vishalkushare7@gmail.com

eISSN: 2455-8842

DOI: <https://doi.org/10.26452/ijpib.v3i2.1278>



Production and Hosted by

ScienZTech.org

© 2018 | All rights reserved.

INTRODUCTION

Selfnanoemulsion drug delivery systems (SNEDDS) are defined as isotropic mixtures of oil, surfactant, co-surfactant and active pharmaceutical ingredient that form o/w selfnanoemulsion. It is very difficult to deliver hydrophobic and lipophilic medication in oral route are limited to 40-50%, due to dose proportionality, unacceptable patient variability, poor solubility and bioavailability. The designing of appropriate dosage form to overcome this problem is very big challenge for pharmaceutical research and development sector. Amongst the various drug delivery systems colloids like nanoemulsion, micro emulsions, liposomes and nano particles

offers solution for troubleshoot raised in formulation of poor water soluble drugs [1, 2].

Successfully designed to deliver hydrophobic medications, self-nanoemulsion has been shown to improve their oral absorption and bioavailability, as well as the dissolution rate profile [3, 4]. The mixtures are transparent and isotropic nano emulsions that are either small drops or globules below 100 nm. When these Self Nanoemulsions are used in the drug delivery system, drugs are embedded in the oil or surfactant and then water is incorporated to create Self Nanoemulsion [5-7].

Coriander (*Coriandrum Sativum* L.) is a well-known medicinal aromatic plant that grows in Mediterranean countries. Seeds are used in herbal medicine for treating stomach disorders, rheumatism, anti-convulsant, antipsychotic and joint pains. The coriander seeds have essential oil compounds: linalool (up to 70%), geranyl acetate (up to 11%), geraniol, borneol, citronellol, α -pinene [8-10].

This research is to formulate Self-Nanoemulsifying formulation to improve the solubility of low soluble Coriandrol from coriander sativum and to evaluate its Zeta potential, Droplet Size Distribution, Poly Dispersive Index (PDI) and SEM (Scanning Electron Microscopy) [11, 12].

MATERIALS

The following materials are used in the experiment are of laboratory and industrial grade. All chemicals were of analytical reagent grade. Tween 80, Polyethylene glycol-200 (PEG-200), Captex are acquired from Sd fine chemicals limited Mumbai.

METHODS

Extraction of Linalool

Extraction by soxhlet apparatus-Dichloromethane extraction process

Sample of coriander seeds (100g) is harvested using Soxhlet apparatus using methylene chloride (500 mL). The solvent was evaporated under vacuum after 6 cycles of the extract and the extract obtained was dried under vacuum (50°C, 24 hours), resulting in liquid (oil-like) extract [13].

Column chromatography for isolation

Approximately 30 gm of the extract was poured over the activated silica gel that was packed into a glass column (5x54 cm). The column was eluted with a hexane solvent gradient: ethyl acetate (9:1 v / v ratio) with a flow rate of 1mL / min. The column was then washed with 100% ethyl acetate, extracting and concentrating all fractions of approximately

500 mL each using rotary evaporation [14, 15].

Thin Layer Chromatography (TLC)

In our laboratory, glass sheets (10x10 cm) were coated using Silica G gel, thickness 0.25 mm. Essential oil samples have been dissolved in methylene chloride (ratio 1: 10) and essential oil solutions (approximately 20 μ L) have been found as a reference point or line on the counter. The mobile phase was toluene: ethylacetate (93:7 V/V). The development was undertaken in a glass chamber at room temperature (approx. 20°C). Mobile phase was toluene (93:7V/V): ethylacetate. The development was undertaken in a glass chamber at room temperature (approx. 20°C). Detection was conducted by spraying the plate with 1% vanillin solution (1g vanillin was dissolved in 99 g mixture of 95 % ethanol and sulphuric acid, ratio 9:1; w / w). The plate was heated at 110°C for 5-10 min after sprinkling [16, 17].

Screening of phytochemical constituents of crude extract

Test for alkaloids

Dragendorff's test: Alkaloids with Dragendorff's reagent (potassium bismuth iodide solution) give reddish brown precipitate.

Mayer's test: With Mayer's reagent (Potassium mercuric iodide solution), alkaloids give precipitate cream colour.

Test for tannins

Ferric chloride test: Treat the extract with a solution of ferric chloride, blue colour appears when there are hydrolysable tannins and green colour appears when there is condensed tannins.

Test for steroids

Sulfur powder test: Tiny amount of sulphur powder is applied to the test solution, it sinks downwards.

Test for amino acids

Ninhydrine test: To the test solution add Ninhydrine solution, boil, violet colour indicates presence of amino acid.

e) **Test for inulin:** Transfer the α -naphthol and sulphuric acid solution to the test solution and its form a brownish red colour.

f) **Test for mucilage:** Treat the test solution with red solution of ruthenium, producing pink colour.

g) **Test for naphthoquinones**

Dam-Karrer test: Add 10 per cent potassium hydroxide solution produces blue colour to the chloroformic plant extract.

h) **Test for acidic compounds:** After treatment with sodium bicarbonate alcoholic extract of the drug causes effervescence.

i) **Test for hydroxyl anthraquinone:** Treat with solution of potassium hydroxide to the sample

j) **Test for cardiac glycoside**

Baljet's test: Treat the test solution with picric acid or sodium picrate, and form an orange colour [18]

Preformulation

Preparation of calibration curve of Linalool (coriandrol) in Dichloromethane

10g of isolated Linalool was accurately weighed and dissolved in 10ml of Dichloromethane. This pipette out 0.4, 0.8, 1.2, 1.6, 2.0 ml into 10ml volumetric flask and make up the volume with Dichloromethane. Ultraviolet scan was taken between the wavelengths 400-800nm against Dichloromethane as the blank which gave a highest peak at 665 nm and the same was selected as λ_{max} of Linalool [19].

Identification of drug by uv-spectro photometric method

Preparation of standard calibration curve of Linalool (coriandrol) in Dichloromethane

10g of isolated Linalool was accurately weighed and dissolved in 10ml of Dichloromethane. This pipette out 0.4, 0.8, 1.2, 1.6, 2.0 ml into 10ml volumetric flask and make up the volume with Dichloromethane. Ultraviolet scan was taken between the wavelengths 400-800nm against Dichloromethane as the blank which gave a highest peak at 665 nm and the same was selected as λ_{max} of Linalool [20].

Identification of drug by IR- spectrophotometric method

Each chemical or drug's infrared spectrum provides details about the functional groups found in that particular substance. A spectrophotometer for recording the spectrum in the infrared region consists of an optical device capable of delivering 400-4000 cm^{-1} for the monochromatic light in the scanning range and 2 cm^{-1} resolution. Attenuated Absolute Reflection (ATR) is used for liquid and semi-soil analysis

Screening of excipients based on solubility

The excipients selection is focused on the solubility of the drugs, lipids, surfactants and co-surfactants. the solubility of drug in various oils (Arachis Oil, Castor Oil, Captex-200p, Sunflower Oil, Captex-300, And Captex-350), Surfactants (Tween-20, Tween40, Tween80, Span-20, Span-80), co-

surfactants (Ethanol, PEG-200, Propylene glycol) was determined by dissolving an excess of the drug in 1 g of the chosen vehicle. Dissolving an excess of the drug in each vial containing 1 g of the chosen vehicle was estimated. For 5min mixtures had been centrifuged at 5000 rpm and then supernatant was taken and filtered. The filtrate was diluted with methanol and a drug concentration was calculated by UV-spectrophotometer in each liquid, surfactant and co-surfactant [21].

Preparation of self nanoemulsifying systems:

Captex-200 as oil, Tween80 as surfactant and PEG-200 as co-surfactant were used to prepare a range of SNEDDS. The quantity of linalool was kept constant in all the formulations. Precisely weighted Linalool was put in a beaker and added oil, surfactant, and co-surfactant. The components were combined by gentle stirring with a magnetic stirrer and the resulting mixture was put about 10-15 min for size reduction in ultra-sonication. The mixture was then heated at 40°C, until the substance was dissolved completely. The homogeneous mixture was maintained at ambient temperature for further use [22, 23]. Table 1

Phase separation study

Accurately about 1 ml of Linalool SNEDDS was added to 100 ml of water (distilled) in a beaker at 37°C and mixed for 2min. the blend was stored at 37°C (Room Temperature) a period of 2 hrs and observed visually for any phase separation.

Scanning electron microscopy (SEM)

The surface morphology of SNEDDS is distinguished by SEM. The samples in the HUS-5 GB vacuum evaporator were placed on alumina stubs using double adhesive tape. The sample was then observed in Hitachi S-3000N SEM at a 10KV acceleration voltage and 5000X magnification [24, 25].

Particle size determination

Dynamic light scattering (DLS) has estimated the average particle size of SNEDDS at scattering angle 1730 and the sample holder temperature is approximately 25°C by usage (Nanopartica SZ-100 HORIBA, Japan). The dispersion assay was diluted to 1:2500 v/v with double distilled water to ensure that the light dispersing rate was within the limits of the instruments [26].

Zeta potential

The potential difference between stationary fluid phases bound to scattered particles to the surface of dispersion is called zeta potential. Colloidal dispersion stability depends primarily on zeta potential; zeta potential has been calculated using a zetasizer (Nanopartica SZ-100 HORIBA Research, Japan).

Table 1: Content of formulation showing linalool self- nanoemulsifying drug delivery systems

Formulation code	Linalool (mg)	Ingredients %w/w	
		Captex-200 (oil)	Tween80+peg-200 (s _{mix}) 4:1
S1	100	10.84	88.50
S2	100	16.53	82.86
S3	100	32.07	67.29
S4	100	32.93	66.51
S5	100	40.43	52.39
S6	100	55.83	43.49
S7	100	64.94	34.42
S8	100	78.90	20.42
S9	100	87.65	11.65

Determination of % drug content

The lipid based dispersed system of linalool were analyzed spectrophotometrically for the drug content at wave length 665 nm with proper dilution of formulations taking dichloromethane as a blank .

RESULTS AND DISCUSSION

By conducting various phytochemical tests as shown in Table 2 , it was confirmed that tannins, flavonoids, steroids, alkaloids and terpenoids are present in *Coriandrum Sativum*. Components like amino acid, glycoside, inulin, mucilage and acidic compounds etc. are absent in the *Coriandrum sativum* crude extract.

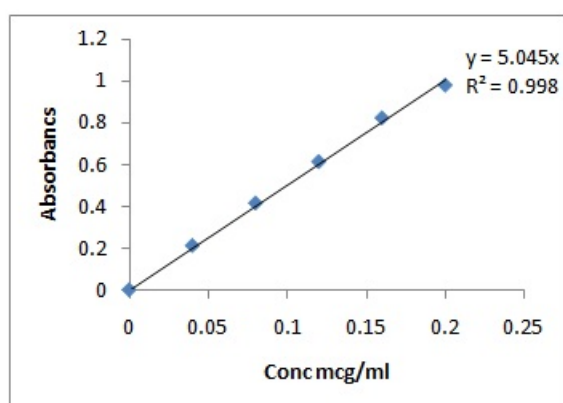


Figure 1: Calibration curve for linalool

The linalool drug was identified with the help of UV and ATR as shown in Figure 1 . The linalool drug exhibited absorption maxima at 665nm, which was complies with the standard as shown in literatures. The calibration curve of linalool was constructed with different concentration and its absorbance was determined at 665nm. The calibration curve was observed to follow Beer's- Lambert 's rule in the

analyzed concentration range (0.04-0.20 g / ml), strong linearity of about 0.999 R² value. In IR spectroscopy, all characteristic functional sharp peaks are present. It also shows all the functional groups are reproducible in SNEEDS formulation as in pure drug which was shown in Table 3 and Figure 2. From the calibration curve linearity and IR spectroscopy results, it shows that the extracted linalool was pure in nature and suitable for formulation.

Preformulation studies were conducted to determine the drug solubility in various excipients like oil, surfactant, and co-surfactant in order to determine the suitability of drug to be incorporated in SNEDDS and its results are shown in Table 4 and Figure 3 . Linalool is practically low soluble in water but freely soluble in Captex-200 (oil), Tween-80 (surfactant) and appreciably soluble in PEG-200 (co-surfactant). The linalool physicochemical studies indicate it has strong potential for SNEDD preparation.

To formulate nanoemulsion formulation the selection of components is an important criteria and the components must and should be pharmaceutically acceptable, nonirritant and non-sensitizing. A major criteria for the collection of components such as crude, surfactant and co-surfactant is the solubility of poorly water soluble substance in different excipients. The drug's higher solubility in the oil phase is necessary to keep the drug in solubilized form for the nanoemulsion. High HLB (Hydrophilic Lipophilic Balance) surfactants and co-surfactants make the formulation stable. The solubility of linalool was found to be highest in Captex-200 as compared to other oils. For the production of optimum formulation Captex-200 was chosen as the oil phase. The self-nanoemulsification method was prepared by the use of Captex-200 as the oil phase. As the aqueous phase, Tween 80 were chosen as the surfactant and PEG-200 as the co-surfactant and double

Table 2: Phytochemical Test for Dichloromethane Extract of Coriander fruit

S.No	Test	Observation	Result
1.	Test for Tannins Extract was added with water, boil for 5 min and filter it to the filtrate add ferric chlorate solution	precipitation of dark colouration	Confirmation of tannin
2.	0.5 g of extract was added with 3ml of 0.1M NaOH	Residue shows yellow coloration which discoloration after addition of acid.	Confirmation of flavonoid.
3.	Test for steroids Apply small amount of sulphur powder to the crude solution	Visualization of Sulphur powder sinks to the bottom.	Confirmation of steroid
4.	Test for alkaloid Add extract to Wagner 's reagent	Formation of Reddish brown precipitate	Confirmation of alkaloid
5.	Test for terpenoids To 2 mL of extracts add of chloroform (2 mL) and conc. H ₂ SO ₄ (2mL)	reddish brown colour at the interface	Confirmation of terpenoids.
6.	Ninhydrine test add ninhydrine reagent to the test solution and boil.	No violet colour	Absence of Amino acid
7.	Test for inulin Add α -naphthol and sulphuric acid to the test solution	No brownish red colour	Absence of Inulin
8.	Baljet's test: Add picric acid to the test solution	No orange colour	Absence of Cardiac glycoside
9.	Froth formation test: Place 2 ml of drug solution in a test tube of water, and shake well.	No froth formation	Absence of Saponin glycoside
10.	Test for mucilage: Treat the sample with sample of ruthenium violet.	No pink colour	Absence of Mucilage
11.	Dam-Karrer Test: Add 10 per cent potassium hydroxide solution to the Chloroformic plant extract.	No blue colour	Absence of Naphthoquinone

Table 3: ATR spectra wavelength values of Linalool pure and Linalool SNEDDS formulation

Range	Wave length (cm ⁻¹)		Characterization
	Linalool pure drug	Linalool SNEDDS	
2850-2970	2859.24cm ⁻¹	2864.52cm ⁻¹	C-H stretching (symmetric)
1690-1760	1738.17cm ⁻¹	1737.72cm ⁻¹	C=O stretching
1340-1470	1458.36cm ⁻¹	1456.36cm ⁻¹	C-H bending
1340-1470	1351.43cm ⁻¹	1350.80cm ⁻¹	C=H stretching
1050-1300	1104.63cm ⁻¹	1095.21cm ⁻¹	C-O bending vibrations
675-995	722.10cm ⁻¹	944.55cm ⁻¹	C=H bending

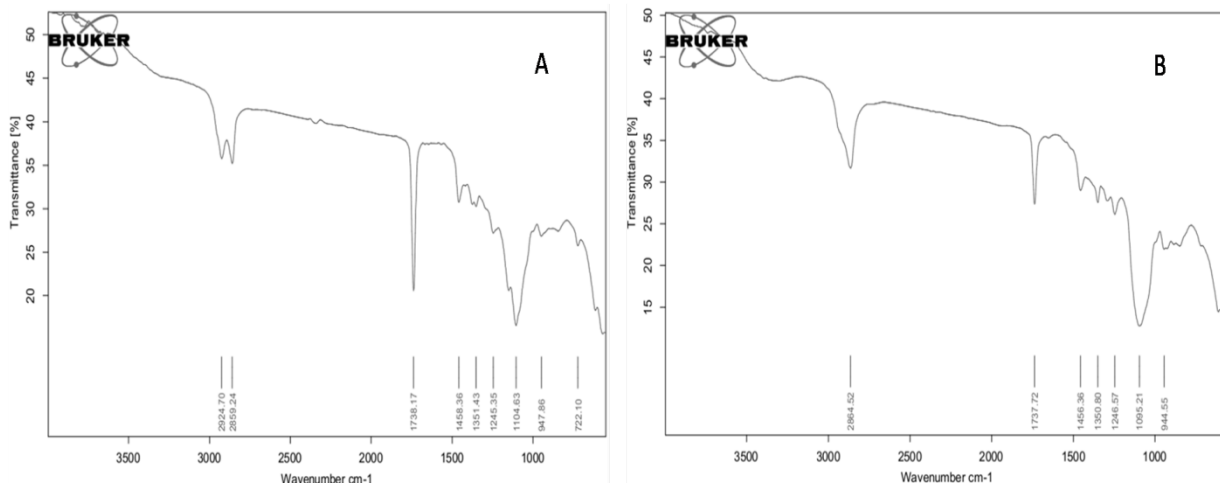


Figure 2: ATR Spectra of (A) Linalool pure drug; (B) Linalool SNEDDS formulation

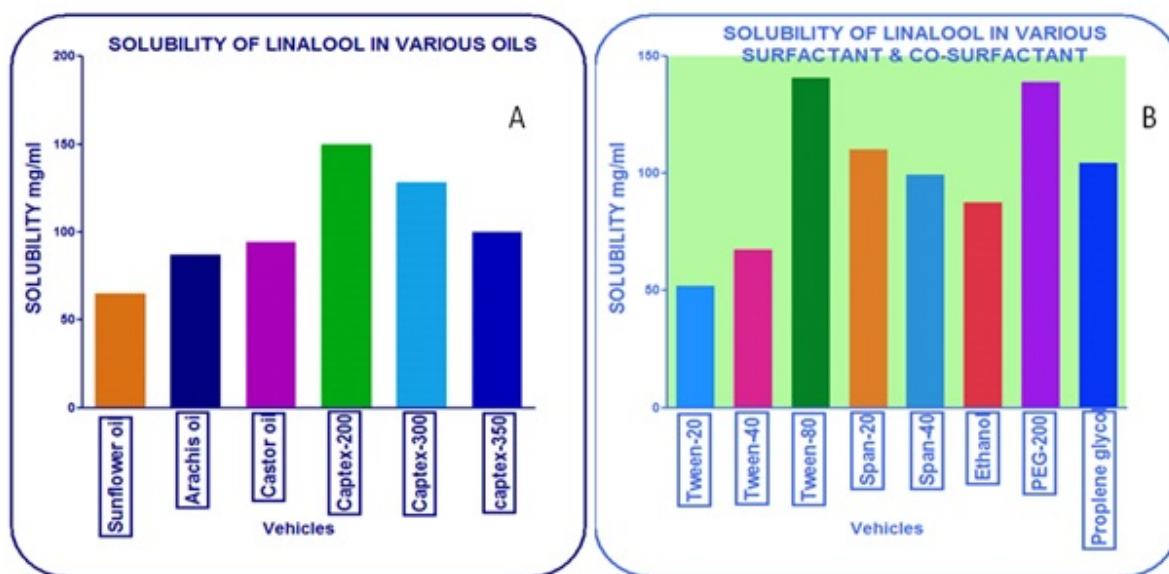


Figure 3: Solubility of in different Linalool oils, surfactant and co surfactant

Table 4: Solubility study of Linalool in oil, surfactant and co-surfactant

S. No	Oil	Solubility (mg/gm.)	Surfactant	Solubility (mg/gm.)	Co-surfactant	Solubility (mg/gm.)
1.	Arachis Oil	87.12±0.55	Tween-20	52.15±0.41	Ethanol	87.64±0.77
2.	Castor Oil	94.31±0.22	Tween-40	67.28±0.41	PEG-200	138.9±0.22
3.	Captex-200	150.11±1.35	Tween-80	140.83±0.30	Propylene glycol	104.32±0.15
4.	Sunflower Oil	65.24±0.69	Span-20	110.32±0.11	-	-
5.	Captex-300	128.32±1.85	Span-80	99.38±0.29	-	-
6.	Captex-350	100.51±0.40	-	-	-	-

distilled water. In this analysis, Tween80 was chosen as a surfactant with HLB value 15, and PEG-200 as a co-surfactant with HLB value > 10.

Pseudo-ternary phase diagram:

By using the selected Captex, tween 80 and PEG, SNEED are prepared by constructing phase diagram. The composition of SNEDDS as well as the phase behavior of mixture can be determined. For each Smix ratio as shown in Table 5 and Figure 4, the pseudo ternary phase diagram constructed separately, so that O/W nano emulsion regions identified and nano emulsion could be optimized.

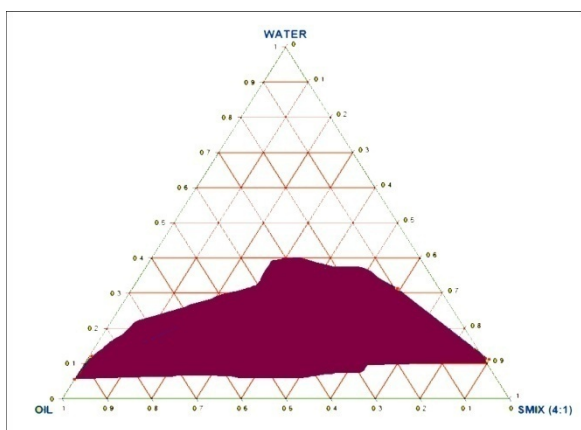


Figure 4: Surfactant /co-surfactant ratio 4:1 shows high region in phase diagram

This pseudo ternary phase diagrams were built with combination of oil and Smix ratio from 1:9 to 9:1 like 1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2, and 9:1. Each ratio of Smix and oil ratio represents separate phase diagram individually. On which ratio of oil and Smix gives highest region of nano emulsion was identified and select that ratio for main formulation of SNEDDS preparation. In this study we found that 4:1 (Surfactant: co-surfactant) ratio gives high region area for nano emulsion preparation so 4:1 Smix taken as optimized ratio.

Characterization of self-nano emulsions:

Physical appearance characterization:

Physical appearance (colour, clarity and separation between phases) of optimized formulation analyzed on S4 to S9. Formulations appeared identical in colour and clarity, as well as no phase separation observed under standard storage conditions ($37 \pm 2^{\circ}\text{C}$) under one month observation. The results are shown in Table 6.

Linalool SNEDDS concentration was diluted with purified water ($100 \mu\text{l}$ in 250 ml) and gently stirred with magnetic stirrer. Temperature should be 37°C the selected nano emulsion formulations (S4, S5, S6, S7, S8, and S9) were clear and slightly bluish appear-

ance. So these formulations were good and stable formulations.

Scanning Electron Microscopy (SEM) Evaluation

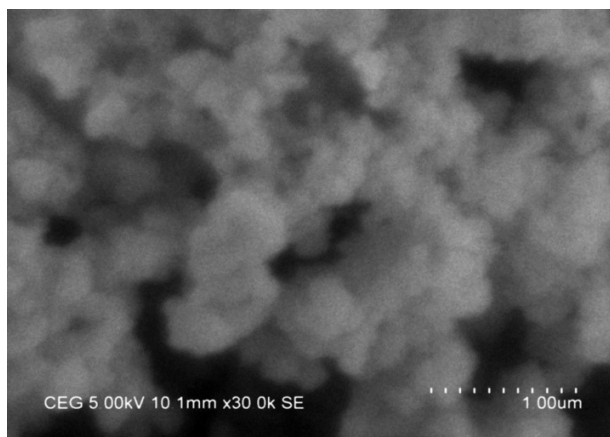


Figure 5: Sem Image Of S9 linalool Sneed's Formulation.

Using Hitachi S-3000N SEM at a 10KV acceleration voltage and 5000X magnification, the surface morphology and self-nanoemulsion structure formulated with optimised parameters were observed. The study revealed that the majority of the self-nanoemulsion was in shape relatively spherical, the particle surface had a characteristic smoothness and the particle size was in non-metric scale, as shown by SEM. Some of the particles appear clumsy as seen in Figure 5.

Self-nano emulsion droplet size analysis

Dynamic light scattering (DLS) has calculated the average particle size of SNEDDS at the scattering angle 1730 and the sample holder temperature is approximately 25°C by usage (Nanopartica SZ-100 HORIBA Research, Japan). The dispersion sample was diluted to 1:2500 v/v with double distilled water to ensure that the rate of light dispersion was within the range of the instruments the mean particle size, poly dispersibility index and zeta potential of formulations were tabulated below Table 7.

The mean droplet size of all SNEEDS was shown to be 250 nm in Table 7 and Figure 6, the droplet size decreased with Smix concentration increased in formulations. On the other hand increase in oil phase in the formulation result in increase in particle size nano size to micro size. The droplet size of formulation S9 was significantly lower (55.6 nm) compared with all formulations. The mean droplet size of formulations S4 to S9 was only marginally different, which may be due to increased concentration of Smix in formulation i.e. to formulation. In line with the study, this result is that the addition of surfactant to the self-nanoemulsion system causes the

Table 5: Selected mixture of oil, smix (4:1) and water for building of Pseudo-ternary phase diagram

Formulation code	Captex-200(%)	Tween80/PEG-200(%)	Water (%)	Visual Observation
S1	0.9434	0	0.056	Separation
S2	0.86	0.0047	0.1219	Turbid
S3	0.7231	0.1121	0.1658	Turbid
S4	0.572	0.1923	0.2342	Turbid
S5	0.4263	0.2588	0.3117	Viscous gel
S6	0.3062	0.3579	0.3363	Milk like
S7	0.2584	0.3736	0.3679	Clear but turbid
S8	0.2042	0.4243	0.3705	Transparent and clear
S9	0.1427	0.4921	0.365	Transparent and clear
S10	0.0911	0.5925	0.3132	Transparent and clear
S11	0	0.8984	0.1115	Turbid lightly

Table 6: Visual assessments of linalool SNEEDS formulation

Formulation	Emulsification time	Appearance
S4	Spontaneous, within 52 sec	Bluish less clear
S5	Spontaneous, within 57 sec	Bluish less clear
S6	Spontaneous, within 59 sec	Bluish & clear
S7	Spontaneous, within 59 sec	Bluish& transparent
S8	Spontaneous, within 60 sec	Bluish& transparent
S9	Spontaneous, within 56 sec	Bluish& transparent

Table 7: Particle Size, Polydispersibility Index And Zeta Potential of Various Snedds Formulations (S4 - S9)

Formulation	Mean particle size (nm)	Poly dispersibility index	Zeta potential (mV)
S4	231.8	0.579	-12.7
S5	205.1	0.097	-15.8
S6	192.1	0.446	-13.7
S7	160.7	0.618	-11.1
S8	128.1	0.771	-11.2
S9	55.6	0.931	-31.6

interfacial film to condense and stabilise, while the co-surfactant causes the film to develop. All formulations had droplets in the range that are well evident from the polydispersity values. All self nanoemulsions had values of polydispersity, which indicates the uniformity of droplets in the formulations. Polydispersity value was < 0.9 in the all formulations (0.579-0.931) [27, 28].

Zeta potential measurement

The zeta potential indicates the degree of repulsion in dispersion between contiguous, similarly charged particles. Stability can lead to molecules and particles which are small in size and have a high zeta potential (positive or negative). The attraction exceeds repulsion when the potential is tiny, and the dispersion breakdown and flocculate. All the formulations S4 to S9 having appreciable zeta potential which indicates that all formulations (S4, S5, S6, S7, S8 and S9) stable and having zeta potential, -12.7mV,

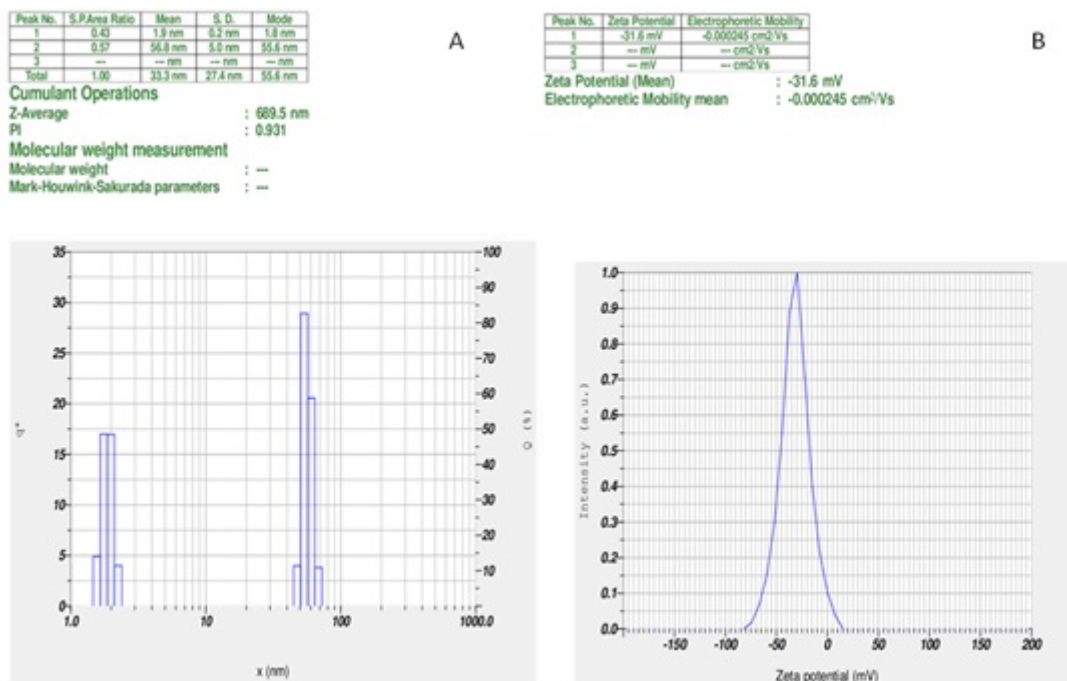


Figure 6: (A) Particle size and (B) zeta potential report for S9 formulation

-15.8 mV, -13.7mV, -11.1 mV, -11.2 mV and -31.6 mV respectively. It was found that the high value of zeta potential of selected self nanoemulsion formulation S9 was measured -31.6 mV.

Summary and conclusion

Linalool (coriandrol) crude extract is extracted from coriandrumsativum seeds by using dichloromethane (Soxhlet method) and linalool is isolated by using column chromatography and concentrated under reduced pressure by using rotary flash evaporator. By testing various chemical tests, the confirmation of linalool was achieved. The drug and excipients compatibility study was done by using Bruker-Ftir-Atrspectrophotometer and conformed there no incompatibility between drug and excipients. Different oils, surfactant and co-surfactant were taken for solubility studies and it was found that captex-200 exhibited maximum solubility of linalool. Thus it was selected as the oil phase, while for the formulation of linalool SNEDDS between 80 and PEG-200 were selected as surfactant and co-surfactant respectively. Different ratios of surfactant (tween80) and co-surfactant (PEG-200) in fixed ratios (1:1, 1:2, 1:3, 1:4, 2:1, 3:1 and 4:1) were used to prepare self-nanoemulsions. Pseudo ternary phase diagram was constructed using water titration method for the determination of the existence zone of nanoemulsion. It was found that S_{mix} ratio 4:1 exhibited maximum area out of all the ratios. This is due to the fact that the interfacial

tension was reduced to a very low level when surfactant was applied, and very limited free energy was obtained which helped in the phase diagram to exist in a larger area of nanoemulsion. The main summarized results of best S9 SNEEDS are shown in Table 8.

Table 8: The best Linalool self-nanoemulsion formulation S9 given following characterization results

S.NO	Parameter	Observation
1.	Particle Size Distribution	55.6 d.nm
2.	Zeta Potential	-31.6mV
3.	Polydispersity Index	0.931
4.	Drug content	99.23±0.45%
5.	Emulsification time	Spontaneous, within 56 sec

CONCLUSION

To improve the bioavailability of hydrophobic/lipophilic drugs orally, SNEDDS is the most promising approach to overcome formulation difficulties towards dissolution/solubility. In terms of droplet size, polydispersity index, dissolution and diffusion studies, S9 formulation showed promising results. Finally concluded that SNEDDS

formation from captex-200, tween 80, PEG-200 is promising method for improving herbal linalool drug solubility.

FUNDING SUPPORT

The authors declare that they have no funding support for this study.

ACKNOWLEDGEMENT

The authors are thankful to all who have extended their constant support for the completion of the work.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

REFERENCES

- [1] Patel ND, Patel KV. An Emerging Technique for Poorly Soluble Drugs: Self-Emulsifying Drug Delivery System. *International Journal of Pharmaceutical & Biological Archives*. 2011;2(2):621–629.
- [2] Madhubabu AB, Prakashrao. Self-emulsifying drug delivery systems. *International Journal of Biological & Pharmaceutical Research*. 2012;3(6):767–774.
- [3] Aissaoui A, El-Hilaly J, Israili ZH, Lyoussi B. Acute diuretic effect of continuous intravenous infusion of an aqueous extract of *Coriandrum sativum* L. in anesthetized rats. *Journal of Ethnopharmacology*. 2008;115(1):89–95. Available from: [10.1016/j.jep.2007.09.007](https://doi.org/10.1016/j.jep.2007.09.007).
- [4] Emamghoreishi M, Khasaki M, Aazam MF. *Coriandrum sativum*: evaluation of its anxiolytic effect in the elevated plus-maze. *Journal of Ethnopharmacology*. 2005;96(3):365–370. Available from: [10.1016/j.jep.2004.06.022](https://doi.org/10.1016/j.jep.2004.06.022).
- [5] Zoranzekovica. Essential oil and extract of coriander (*Coriandrum sativum* L.). *APTEFF*. 2011;42:1–288.
- [6] Shyamala BN, Gupta S, JyothiLakshmi A, Prakash J. Leafy vegetable extracts—antioxidant activity and effect on storage stability of heated oils. Elsevier BV; 2005. Available from: [10.1016/j.ifset.2004.12.002](https://doi.org/10.1016/j.ifset.2004.12.002).
- [7] Sushmag U, Raj K, Rajyalaxmi, Vinayumeshrao, Sudhakar M. solubility enhancement of lamotrigine using solid self-emulsified drug delivery systems. *International Journal of Advances in Pharmaceutical Sciences*. 2013;4:1340–1349.
- [8] ABhagwat D. Formulation and evaluation of solid self micro emulsifying drug delivery system using aerosil 200 as solid carrier. *International Current Pharmaceutical Journal*. 2012;1(12):414–419. Available from: [10.3329/icpj.v1i12.12451](https://doi.org/10.3329/icpj.v1i12.12451).
- [9] SunithaReddy S. Solubility Enhancement of Poorly Water Soluble Drug Efavirenz by Solid Self-Emulsifying Drug Delivery Systems. *International Journal of Pharma Research & Review*. 2014;3(4):20–28.
- [10] Patel K. VidurSarma and PradeepVavia. Design and evaluation of Lumefantrine - Oleicacid self nanoemulsifying ionic complex for enhanced dissolution. *DARU Journal of Pharmaceutical Sciences*. 2013;21:27–27.
- [11] Salimi A, Hemati A, Birgani SA. Design and Evaluation of Self-Emulsifying Drug Delivery System (SEDDS) Of Carvedilol to Improve the Oral Absorption. *Jundishapur Journal of Natural Pharmaceutical Products*. 2014;9(3):16125–16125. Available from: [10.17795/jjnpp-16125](https://doi.org/10.17795/jjnpp-16125).
- [12] Hyma P. Formulation and characterization of novel self-micro emulsifying drug delivery system of glimepiride. *The Experiment*. 2014;24(1):1640–1648.
- [13] Pradeeppatil, Vandanapatil A. Formulation of a self-emulsifying system for oral delivery of simvastatin: In vitro and in vivo evaluation. *Acta Pharm*. 2007;57:111–122.
- [14] MohammadrezaAbbaspour, NegarJalayer. Development and Evaluation of a Solid Self-Nanoemulsifying Drug Delivery System for Loratadin by Extrusion-Spheronization. *Advanced Pharmaceutical Bulletin*. 2014;4(2):113–119.
- [15] AhmadMustafa, Masoudeid. Saringat Haji Baie and Osama Mohammad. The Effect of Surfactant Blends on the Production of Self-Emulsifying System. *IJPFR*. 2012;2(2):21–31.
- [16] GulshanChhabra, KrishnaChuttani, Mishra A, KamlaPathak. Design and development of nanoemulsion drug delivery system of amlodipine besilate for improvement of oral bioavailability. Informa UK Limited; 2011. Available from: [10.3109/03639045.2010.550050](https://doi.org/10.3109/03639045.2010.550050).
- [17] Rajajayaraoy Y, Divyasreek K. A novel technical development and evaluation of Self-emulsifying drug delivery system of Simvastatin. *international journal of research in phar-*

- macy and chemistry. IJRPC. 2014;4(1):15-25.
- [18] Taha E, SalehAl-Saidan, Samy A, Khan M. Preparation and in vitro characterization of self-nanoemulsified drug delivery system (SNEDDS) of all-trans-retinol acetate. International Journal of Pharmaceutics. 2004;285(1-2):109-119. Available from: [10.1016/j.ijpharm.2004.03.034](https://doi.org/10.1016/j.ijpharm.2004.03.034).
- [19] AhmadMustafaMasoudeid. The effect of surfactant blends on the production of self-Emulsifying system. International Journal of pharmaceutical frontier research IJPFR. 2012;2(2):21-31.
- [20] ShuklaJill, B. Self-microemulsifying drug delivery system. International journal of pharmaceutical sciences. 2010;1:1-9.
- [21] Delaquis P. Antimicrobial activity of individual and mixed fractions of dill, cilantro, coriander and eucalyptus essential oils. International Journal of Food Microbiology. 2002;74(1-2):101-109. Available from: [10.1016/s0168-1605\(01\)00734-6](https://doi.org/10.1016/s0168-1605(01)00734-6).
- [22] Chithra V, Leelamma S. Coriandrum sativum — mechanism of hypoglycemic action. Food Chemistry. 1999;67(3):229-231. Available from: [10.1016/s0308-8146\(99\)00113-2](https://doi.org/10.1016/s0308-8146(99)00113-2).
- [23] Eguale T, Tilahun G, Debella A, Feleke A, Makonnen E. In vitro and in vivo anthelmintic activity of crude extracts of Coriandrum sativum against Haemonchus contortus. Journal of Ethnopharmacology. 2007;110(3):428-433. Available from: [10.1016/j.jep.2006.10.003](https://doi.org/10.1016/j.jep.2006.10.003).
- [24] Chithra V, Leelamma S. Coriandrum sativum — effect on lipid metabolism in 1,2-dimethyl hydrazine induced colon cancer. Journal of Ethnopharmacology. 2000;71(3):457-463. Available from: [10.1016/s0378-8741\(00\)00182-3](https://doi.org/10.1016/s0378-8741(00)00182-3).
- [25] Sumankatteboinaa, Balaji S, Chandrasekhar P. Approaches for the development of solid self-emulsifying drug delivery systems and dosage forms. Asian Journal of Pharmaceutical Sciences. 2009;4(4):240-253.
- [26] Rajesh BV, Reddy TK, Srikanth G, Nivethithai P. Lipid based selfemulsifying drug delivery system (sedds) for poorly water-soluble drugs: a. Review Journal of Global Pharma Technology. 2010;2(3):47-55.
- [27] Kuentz M. Oral self-emulsifying drug delivery systems, from biopharmaceutical to technical formulation aspects. Journal of Drug Delivery Science and Technology. 2011;21(1):17-26. Available from: [10.1016/s1773-2247\(11\)50002-4](https://doi.org/10.1016/s1773-2247(11)50002-4).
- [28] Zoranzekovica D. Essential oil and extract of coriander (Coriandrumsativum L.). APTEFF. 2011;42:1-288.

ABOUT AUTHORS



Vishal N Kushare

Copyright: This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Cite this article: Kushare Vishal N, S Saravanan. **Formulation and Evaluation of Herbal Drug Loaded Self Nano Emulsifying Drug Delivery System (SNEDDS)**. Int. J Pharm. Int. Biosci. 2018; 3(2): 26-36.

ScienZTech

© 2018 ScienzTech.org.