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# Formulations and Characterization of Liquid SMEDDS of Dexlansoprazole

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**Abstract:**
Dexlansoprazole is a second-generation proton pump inhibitor (PPI) used in the treatment of symptoms of gastroesophageal reflux disease (GERD) and erosive esophagitis (esophageal damage caused by acid in stomach), but because of poor solubility, stability and oral bioavailability. The objective of our research was to formulate a self-micro emulsifying drug delivery system (SMEDDS) of Dexlansorazole by minimum surfactant concentration which would improve its solubility, stability and oral bioavailability. Optimized formula [C7IIB] composition includes Capryol 90 as oil, Labrasol as surfactant and Captex 500 as cosurfactant containing 30 mg of Dexlansoprazole showing drug release for liquid SMEDDS formulation (99.9%), droplet size (9.10 nm), Zeta potential (-23.9), viscosity (0.9141 cP) and infinite dilution capacity. In-vitro drug release of C7IIB was extremely high ($p < 0.05$) compared with marketed conventional capsules (M). C7IIB was also employed to develop various SMEDDS formulations (Powder-filled capsule).

Key words: Dexlansoprazol, SMEDDS, solubility
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## Introduction

Self-micro emulsifying drug delivery system are prepared in different dosage forms, in which one of the filling in soft and hard hard gelatin capsules resulted in leakage and difficult in manufacturing and loss of material. Therefore, the conversion of liquid Self-micro emulsifying drug delivery system in to solid Self-micro emulsifying drug delivery system such as pellets, tablets, capsules, powder etc. and also they extend the shelf life of drug also to over come the manufacturing problem and leakage problem also. Conversion of free flowing powder and pellets to tablets or capsules and the enhances the ace capacity of dosage form to easy for patient compliance also1. Self-micro emulsifying drug delivery system are basically discovered for BCS class-II drugs, because of drug with low solubility and high permeability i.e. that is results in poor bioavailability such types pf drugs can be improve the solubility. Solubility can be improved by using oil, surfactant, co-surfactant and solvents they can easy to formulate and improve the bioavailability and stability. 2-4

Dexlansoprazole reduces gastric acid production by blocking the final stage of acid secretion. It specifically targets the H/K ATPase enzyme on the surface of gastric parietal cells, which plays a key role in releasing hydrochloric acid. The H/K ATPase acts as a proton pump, exchanging hydrogen ions ($H^+$) from the cell's cytoplasm with potassium ions ($K^+$) in the canaliculus, leading to the secretion of hydrochloric acid into the stomach.5-6

The aim of present study work is to formulate and evaluate a self-micro emulsifying drug delivery system containing drug and to further explore the ability of porous added excipients/ surfactants in the form of solid carriers for Self-micro

emulsifying drug delivery system. Self-emulsify small droplet size between 100-250 nm provides a large interfacial area are gentle agitation of Gastrointestinal tract facilitates Self-micro emulsifying drug delivery system, which ultimately enlarges the activity of pancreatic lipase which acts by hydrolyzing triglycerides and ultimately promotes the faster release of drug.The stability of formulation can be easily increases with the help of Self-micro emulsifying drug delivery system as compare to the emulsion forms, which can be decrease the gastric irritation and thus it can be increase the patient compliance. Oil, surfactant and co-surfactant of SMEDDS play a crucial role in increasing the bioavailability of Self-micro emulsifying drug delivery system.

Material and Methods

Solubility study

The solubility of Dexlansoprazole in various oils and distilled water was determined by adding an excess amount of drug in 2mL of selected oils (capryol 90, isopropyl myristate, Labrafil 1944 CS, captex 200, captex 200 P, captex 355) and distilled water separately in 5mL capacity stopper vials, and mixed using a vortex mixer. The mixture vials were then kept at 25±1.0 o C in an isothermal shaker for 4 h to reach equilibrium. The equilibrated samples were removed from shaker and centrifuged at 3000 rpm for 15 min. The supernatant was taken and filtered through a 0.45 µm membrane filter. The concentration of Dexlansoprazole was determined in oils and water using UV spectrophotometer at 285 nm. 6

Preparation of Dexlansopazole SMEDDS:

A series of SMEDDS formulations were prepared using various oil, Surfactant and Co-surfactant as shown in Table 6.13. In all the formulations, the level of Dexlansopazole was kept constant (i.e. 30 mg). The amount of SMEDDS should be such that it should be solubilize the drug (single dose) completely. The Dexlansopazole (30 mg) was added in the mixture. Then the components were mixed by gentle stirring and vortex mixing, then heated at 40˚C.The mixture was stored at room temperature until further used.7

Table 1 Formulation of Dexlansoprazole SMEDDS

| Ingredients | I | | | | II | | | | III | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | A | B | C | D | A | B | C | D | A | B | C | D |
| Dexlansoprazole | 30 mg | | | | | | | | | | | |
| C 1 | | | | | | | | | | | | |
| Ca 90 | 5 | 5 | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 15 | 15 |
| PO | 47.5 | 60 | 35 | 70 | 45 | 60 | 30 | 70 | 42.5 | 56.6 | 28.4 | 70 |
| Peceol | 47.5 | 35 | 60 | 25 | 45 | 30 | 60 | 20 | 42.5 | 28.4 | 56.6 | 15 |
| C 2 | | | | | | | | | | | | |
| Ca 90 | 5 | 5 | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 15 | 15 |
| Tr-P | 47.5 | 60 | 35 | 70 | 45 | 60 | 30 | 70 | 42.5 | 56.6 | 28.4 | 70 |
| Lauroglycol | 47.5 | 35 | 60 | 25 | 45 | 30 | 60 | 20 | 42.5 | 28.4 | 56.6 | 15 |
| C 3 | | | | | | | | | | | | |
| Ca 90 | 5 | 5 | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 15 | 15 |
| Lauroglycol | 47.5 | 60 | 35 | 70 | 45 | 60 | 30 | 70 | 42.5 | 56.6 | 28.4 | 70 |
| Tr-P | 47.5 | 35 | 60 | 25 | 45 | 30 | 60 | 20 | 42.5 | 28.4 | 56.6 | 15 |
| C 4 | | | | | | | | | | | | |
| Ca 90 | 5 | 5 | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 15 | 15 |
| Capmul MCM(C8) | 47.5 | 60 | 35 | 70 | 45 | 60 | 30 | 70 | 42.5 | 56.6 | 28.4 | 70 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Labrasol | 47.5 | 35 | 60 | 25 | 45 | 30 | 60 | 20 | 42.5 | 28.4 | 56.6 | 15 |
| C 5 | | | | | | | | | | | | |
| Ca 90 | 5 | 5 | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 15 | 15 |
| Cap MCM(EP) | 47.5 | 60 | 35 | 70 | 45 | 60 | 30 | 70 | 42.5 | 56.6 | 28.4 | 70 |
| Labrasol | 47.5 | 35 | 60 | 25 | 45 | 30 | 60 | 20 | 42.5 | 28.4 | 56.6 | 15 |
| C6 | | | | | | | | | | | | |
| Ca-90 | 5 | 5 | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 15 | 15 |
| Acconon CC- 6 | 47.5 | 60 | 35 | 70 | 45 | 60 | 30 | 70 | 42.5 | 56.6 | 28.4 | 70 |
| Tween 80 | 47.5 | 35 | 60 | 25 | 45 | 30 | 60 | 20 | 42.5 | 28.4 | 56.6 | 15 |
| C7 | | | | | | | | | | | | |
| Ca-90 | 5 | 5 | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 15 | 15 |
| Captex 500 | 47.5 | 60 | 35 | 70 | 45 | 60 | 30 | 70 | 42.5 | 56.6 | 28.4 | 70 |
| Labrasol | 47.5 | 35 | 60 | 25 | 45 | 30 | 60 | 20 | 42.5 | 28.4 | 56.6 | 15 |
| C8 | | | | | | | | | | | | |
| Ca-90 | 5 | 5 | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 15 | 15 |
| Acconon CC-6 | 47.5 | 60 | 35 | 70 | 45 | 60 | 30 | 70 | 42.5 | 56.6 | 28.4 | 70 |
| Labrasol | 47.5 | 35 | 60 | 25 | 45 | 30 | 60 | 20 | 42.5 | 28.4 | 56.6 | 15 |

Where; various ratios of S/CoS are A-1:1; B-2:1; C-1:2 and D-3:1; I-5% oil conc.; II – 10% oil conc. and III-15% oil conc.

Drug and surfactant compatibility study

Physical compatibility of the water-insoluble drug with surfactants should be used in surfactant selection procedure. Physical compatibility may include precipitation/crystallization, phase separation and color change in the drug - surfactant solution during course study. Chemical compatibility is primarily regarded as the chemical stability of the drug in a surfactant solution. A surfactant was considered for further development only if it was physically and chemically compatible with drug.8

Pseudoternary phase diagram:

The mixture of oil and surfactant/cosurfactant at certain weight ratios were diluted with water in a dropwise manner. Distill water was used as an aqueous phase for the construction of phase diagrams. Oil, surfactants and co surfactants were grouped in four different combinations for phase studies. Surfactant and cosurfactant (Smix) in each group were mixed in different weight ratios (1:1, 2:1, 1:2, 2:1, 3:1). These Smix ratios were chosen in increasing concentration of surfactant with respect to cosurfactant and increasing concentration of cosurfactant with respect to surfactant for detailed study of the phase diagrams for formulation of SMEDDS (Fig.8.6). For each phase diagram, oil and specific Smix ratio was mixed thoroughly in different weight ratios from 1:1 to 3:1 in different glass vials. Twelve different combinations of oil and Smix were made so that maximum ratios were covered for the study to delineate the boundaries of phases precisely formed in the phase diagrams. Pseudo-ternary phase diagrams were developed using aqueous titration method. The concentration of water at which turbidity-to-transparency and transparency-to-turbidity transitions occurred was derived from the weight measurements. These values were then used to determine the boundaries of the microemulsion domain corresponding to the chosen value of oils, as well as the S/CoS mixing ratio. On the basis of the solubility studies of drug, Capryol 90 was selected as the oil phase. The physical state of the SMEDDS was marked on a pseudo-three-component phase diagram with one axis representing aqueous phase, the other representing oil and the third representing a mixture of surfactant and cosurfactant at fixed weight ratios (Smix ratio).

Characterization of SMEDDS of Dexlansoprazole9-10

Viscosity and pH: The viscosities were measured to determine rheological properties of formulations. Brookfield LVDV

111+ CP viscometer at 30˚C with a CPE 42 spindle at 5 rpm was used to serve this purpose. The pH of the formulations was measured using pH meter.

Thermodynamic stability:

Heating cooling cycle: Six cycles between refrigerator temperature 4˚C and 45˚C with storage at each temperature of not less than 48h was studied. Those formulations, which were stable at these temperatures, were subjected to centrifugation test.

Centrifugation: Passed formulations were centrifuged at 3500 rpm for 30min. Those formulations that did not show any phase separation were taken for the freeze thaw stress test.

Freeze thaw cycle: Three freeze thaw cycles between 4˚C and +25 ˚C with storage at each temperature for not less than 48h was done for the formulations. Those formulations, which passed these thermodynamic stress tests, were further taken for the dispersibility test for assessing the efficiency of self-emulsification. The formulations were observed visually for any phase separation or color change.

Dispersibility test:

The efficiency of self-emulsification of oral SMEDDS was assessed using a USP dissolution apparatus 2. One milliliter of each formulation was added to 900 ml of water at 37±0.5 ˚C. A standard stainless steel dissolution paddle rotating at 50 rpm provided gentle agitation. The in-vitro performance of the formulations was visually assessed using the following grading system:

Grade A: Rapidly forming (within 1 min) microemulsion, having a clear or bluish appearance.

Grade B: Rapidly forming, slightly less clear microemulsion, having a bluish white appearance.

Grade C: Fine milky microemulsion that formed within 2 min.


Figure 1: Visual assessment of liquid SMEDDS formulations

Particle size distribution (PSD) and Zeta ( ζ) potential analysis:

SMEDDS formulation was diluted 100 times with distilled water and 0.22M phosphate buffer, at 37 ± 0.5˚C. The resultant emulsions were prepared by gentle agitation for 10 min using a magnetic stirrer. PSD and ζ-potential of the final microemulsion were determined using, Malvern zetasizer.

Transmittance Measurement:

The percent transmittance of various formulations was measured at 285 nm using UV spectrophotometer using distilled water as a blank.

Polydispersibility Index:

The procedure is same as for particle size distribution.

In-vitro diffusion study:

In-vitro drug diffusion study was carried out by using diffusion apparatus. 1 ml of Dexlansopazole SMEDDS diluted with aqueous phase was instilled in dialysis bag and one end was tied with thread and was placed in 50 ml of0.22M Phosphate buffer with 0.01% of SLS as dissolution medium at 37±0.5˚C temperature. The revolution speed of paddle was maintained at a rate of 50 rpm. 104 An aliquot of 2mL was withdrawn at regular time intervals of 0, 10, 20, 30, 60, 75 and 120 min. The SMEDDS formulation was compared with the conventional the suspension of pure drug (S). The samples were analyzed for the drug content using HPLC method at 285nm.

Comparison of In-vitro dissolution of SMEDDS formulation with Marketed formulation

Two criteria for comparison of dissolution:

If both test and reference product show > 85 % of dissolution within 2 hours the profile considered to be similar. If not then,

Calculate f2 value.

The in-vitro drug release profile of prepared batches with Market product's release profile was compared using similarity factor (f2).

$f2= 50 \times \log \{[1+(1/n)\sum t=1n ( Rt- Tt )2]-0.5 \times 100\}$

Where, Rt, Tt are the percentage release of the reference and test profile, respectively, at the t time point. n is total number of sample times. A value of 100% for the similarity factor suggests that the test and reference profiles are identical. Values between 50 and 100 indicate that the dissolution profiles are similar whilst smaller values imply an increase in dissimilarity between release profiles.

Results and Discussion

The solubility of Dexlansoprazole in different oils and water was determined (Table 2). The solubility was found to be highest in oil Capryol 90 (95.25 mg/mL) as compared to other oils while in water it was 0.09 ± 0.01mg/mL. This may be attributed to the polarity of the poorly water-soluble drugs that favor their solubilization in small / medium molecular volume oils such as medium chain triglycerides or mono- or diglycerides. Thus, Capryol 90 was selected as the oil phase for the development of the formulation.

Table 2: Solubility study in various vehicles

| Solvent | Solubility(mg/mL) |
|---|---|
| Transcutol P | 25.1 ± 0.28 |
| Plurol oleique | 69.21 ± 3.18 |
| Labrasol | 24.7 ± 3.52 |
| Capryol 90 | 95.25 ± 1.04 |
| Labrafil 1944 CS | 49.76 ± 1.13 |
| Captex 200 | 5.67 ± 0.68 |
| Captex 200 P | 9.35 ± 0.94 |
| Captex 355 | 25.31 ± 1.02 |
| Capmul MCM | 45.02 ± 1.32 |
| Tween 80 | 93.25 ± 2.85 |
| PEG 400 | 88.13 ± 3.22 |
| IPM | 22.54 ± 0.29 |
| Lauroglycol FCC | 77.05 ± 1.54 |
| Capmul MCM (C8) | 69.70 ± 2.13 |
| Acconon CC-6 | 81 ± 1.76 |
| Captex 500 | 88.35 ± 2.78 |
| Capmul MCM EP | 73.64 ± 1.19 |
| Distill water | 0.09±0.01 |

*Mean±SD, n=3

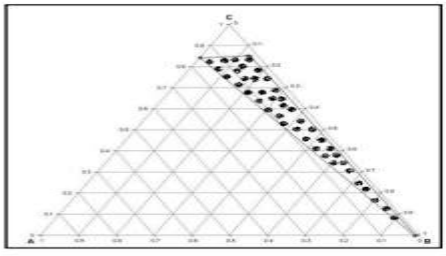
The formulations did not show any changes during the compatibility studies and were found to be stable. Further studies were carried out using this formulation.

Table 3: Drug surfactant compatibility study

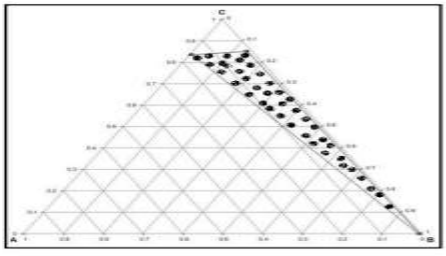
| Formulation | Precipitation | Crystallization | Phase separation | Color change |
|---|---|---|---|---|
| C1 | √ | √ | √ | √ |
| C2 | √ | √ | √ | √ |
| C3 | √ | √ | √ | √ |
| C4 | √ | √ | √ | √ |
| C5 | √ | √ | √ | √ |
| C6 | √ | √ | √ | √ |
| C7 | √ | √ | √ | √ |
| C8 | √ | √ | √ | √ |

Where, √-Passed and ×-Failed

The relationship between the phase behavior of a mixture and its composition can be found with the aid of a phase diagram. Pseudo-ternary phase diagrams were constructed separately for each group (Fig. 2), so that SMEDDS regions could be identified. It can be observed that when Transcutol-P was used along with lauroglycol as S/CoS mixture, amount of oil (10-15%w/w) could be solubilized at a high concentration (85%w/w) of surfactant. It was observed that increase in the concentration of surfactant increased the microemulsion region in this formulation. In Figure 7.1 formulation C4 is shown. Labrasol and Capmul MCM(C8) was used as S/CoS mixture. The amount of oil solubilized was 15%w/w by 70%w/w of surfactant. The lower concentrations of surfactant give a smaller microemulsion region. In Figure 7.1 the formulation C8 is shown in which 5-15% of oil can be solubilized by using 35-70% of surfactant. With the decrease in concentration of surfactant, increase in microemulsion region can also be observed. In Figure 7.1 formulations C7 was observed which gave the appropriate microemulsion region in all the concentrations. The results of visual assessment showing the amount of water required for dilution are as shown in Table 4.In the present study Capryol 90 was tested for phase behavior studies with Labrasol and Captex 500 as the S/CoS mixture. As seen from the ternary plot C7IIB gave a wider microemulsion region at all S/CoS ratios. The microemulsion area increased as the S/Cos ratios increased. However, it was observed that increasing the surfactant ratio resulted in a loss of flowability. Thus, an S/CoS ratio 10% 2:1 was selected for the formulation study.



C2IIID



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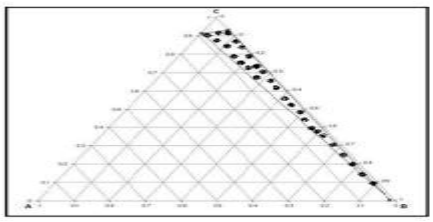
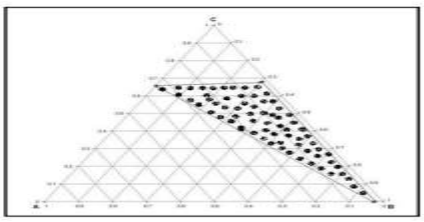


C7IC



C7ID

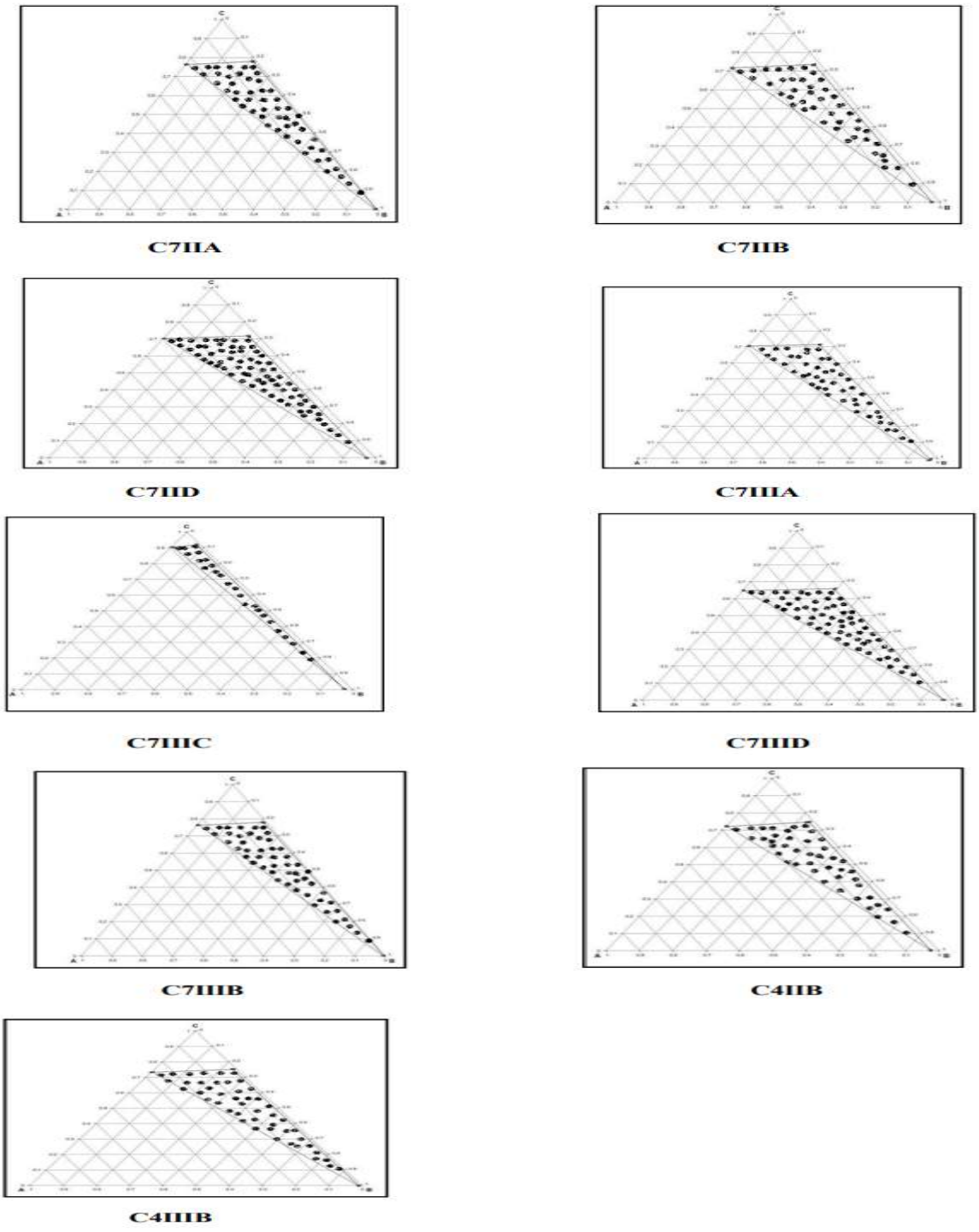



Figure 2: Phase diagrams for various liquid SMEDDS formulations

Table 4: Visual assessment of Dexlansoprazole SMEDDS formulations showing amount of water needed for dilution

| I | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Batch | A | VA | B | VA | C | VA | D | VA |
| C2 | 60.4 | b | 52.5 | b | 62.5 | b | 35.9 | c |
| C4 | 18.4 | a | 17.8 | a | 74.6 | b | 14.8 | a |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| C7 | 17.6 | a | 16.7 | a | 68.9 | b | 11.7 | a |
| C8 | 19.5 | a | 18.3 | a | 70.5 | b | 15.5 | a |
| II | | | | | | | | |
| Batch | A | VA | B | VA | C | VA | D | VA |
| C2 | 58.4 | b | 54.5 | b | 59.4 | b | 26.5 | a |
| C4 | 17.2 | a | 15.9 | a | 67.5 | b | 14.3 | a |
| C7 | 15.4 | a | 14.7 | a | 69.2 | a | 13.2 | a |
| C8 | 19.7 | b | 17.7 | a | 64.5 | b | 14.9 | a |
| III | | | | | | | | |
| Batch | A | VA | B | VA | C | VA | D | VA |
| C2 | 54.7 | b | 49.3 | b | 57.2 | b | 28.4 | a |
| C4 | 15.5 | a | 14.8 | a | 65.3 | a | 14.2 | a |
| C7 | 14.2 | a | 12.6 | a | 58.4 | a | 8.5 | a |
| C8 | 16.8 | a | 13.9 | a | 63.8 | a | 12.9 | a |

Where, VA- Visual assessment, a-transparent, and b- Whitish. Values in table indicate Amount of water in ml required to form microemulsion.

All the formulation has viscosity which is highly similar to that of water i.e.1.0. Thus, it shows that SMEDDS forms o/w microemulsion and water remains as external phase. The results of viscosity are as shown in Table 5. All the formulations showed similar pH values in the range of 5.1 to 6.0.

Table 5: Viscosity and pH of various SMEDDS formulations

| Formulation code | Viscosity (cp) | pH |
|---|---|---|
| C4 III D | 0.9148 | 5.14 |
| C7 III D | 0.9145 | 5.68 |
| C4 II B | 0.9143 | 5.92 |
| C7 II B | 0.9141 | 5.25 |

All the formulation that were falling in Grade C, D and E of Dispersibility tests were discarded for further study. Keeping the criteria of increasing oil concentration and minimum amount of surfactant used for its solubilization, one formulation for each percent of oil (5%, 10% and 15%) was selected irrespective of the Smix ratio used for that percent of oil. Optimized formulations were taken for in-vitro release study, globule size and viscosity determination. It was observed that formulation C1, C3, C5 and C6 did not pass the thermodynamic stress tests and thus were dropped for further study .The results are as shown in Table 6.

Table 6: Thermodynamic stability and dispersibility test of different formulations

Formulations I with 5% oil concentration

| Formulation code | Oil:S/CoS ratio | H/C | Cent. | Freeze Thaw. | Disperse. Grade | Inference |
|---|---|---|---|---|---|---|
| C2 | A | X | X | X | Xx | Failed |
| | B | X | X | X | Xx | Failed |
| | C | X | X | X | Xx | Failed |
| | D | X | X | X | Xx | Failed |

| | | | | | | |
|---|---|---|---|---|---|---|
| C4 | A | √ | √ | √ | + | Passed |
| | B | √ | √ | √ | + | Passed |
| | C | X | X | X | Xx | Failed |
| | D | √ | √ | √ | + | Passed |
| C7 | A | √ | √ | √ | + | Passed |
| | B | √ | √ | √ | + | Passed |
| | C | √ | √ | √ | + | Passed |
| | D | √ | √ | √ | + | Passed |
| C8 | A | √ | √ | √ | + | Passed |
| | B | √ | √ | √ | + | Passed |
| | C | √ | √ | √ | + | Passed |
| | D | √ | √ | √ | + | Passed |

Formulations II with 10% oil concentration

| Formulation code | Oil:S/CoS ratio | H/C | Cent. | Freeze Thaw. | Disperse. Grade | Inference |
|---|---|---|---|---|---|---|
| C2 | A | X | X | X | Xx | Failed |
| | B | X | X | X | Xx | Failed |
| | C | X | X | X | Xx | Failed |
| | D | √ | √ | √ | + | Passed |
| C4 | A | √ | √ | √ | + | Passed |
| | B | √ | √ | √ | + | Passed |
| | C | √ | √ | √ | + | Passed |
| | D | √ | √ | √ | + | Passed |
| C7 | A | √ | √ | √ | + | Passed |
| | B | √ | √ | √ | + | Passed |
| | C | √ | √ | √ | + | Passed |
| | D | √ | √ | √ | + | Passed |
| C8 | A | √ | √ | √ | + | Passed |
| | B | √ | √ | √ | + | Passed |
| | C | X | X | X | Xx | Failed |
| | D | √ | √ | √ | + | Passed |

Formulations III with 15% oil concentration

| Formulation code | Oil:S/CoS ratio | H/C | Cent. | Freeze | Disperse. | Inference |
|---|---|---|---|---|---|---|

| | | | | Thaw. | Grade | |
|---|---|---|---|---|---|---|
| C2 | A | X | X | X | Xx | Failed |
| | B | X | X | X | Xx | Failed |
| | C | X | X | X | Xx | Failed |
| | D | √ | √ | √ | + | Passed |
| C4 | A | √ | √ | √ | + | Passed |
| | B | √ | √ | √ | + | Passed |
| | C | √ | √ | √ | + | Passed |
| | D | √ | √ | √ | + | Passed |
| C7 | A | √ | √ | √ | + | Passed |
| | B | √ | √ | √ | + | Passed |
| | C | √ | √ | √ | + | Passed |
| | D | √ | √ | √ | + | Passed |
| C8 | A | √ | √ | √ | + | Passed |
| | B | √ | √ | √ | + | Passed |
| | C | √ | √ | √ | + | Passed |
| | D | √ | √ | √ | + | Passed |

Where; √- passed and X- Failed. Whereas, +- clear, xx- Slightly whitish and Xx- whitish. Heating cooling cycle (H/C), centrifugation (Cent.), freeze-thaw cycle (Freez. Tha.), Dispersibility test (Disperse.)

From the results of pseudoternary phase diagram, formulations C4 and C7 were further characterized for measurement of particle size and zeta potential.

Table 7: Particle size of the various SMEDDS formulations

| Formulation code | Average Particle size | |
|---|---|---|
| | Distilled Water | 0.02M buffer |
| C7 II D | 55.3 | 103.2 |
| C7II B | 9.55 | 23.9 |
| C4 II D | 218 | 458 |
| C4II B | 145 | 265 |
| C7 I D | 51.2 | 52.4 |
| C7 I B | 35.5 | 112 |
| C4I D | 220 | 242 |
| C4 I B | 101.5 | 91.5 |

Table 8: Particle size distribution of C7IIB in 0.02M buffer

| Parameter | Size (nm) |
|---|---|
| Di (90) | 23.9 |
| Di (50) | 12.2 |
| Di (10) | 7.8 |

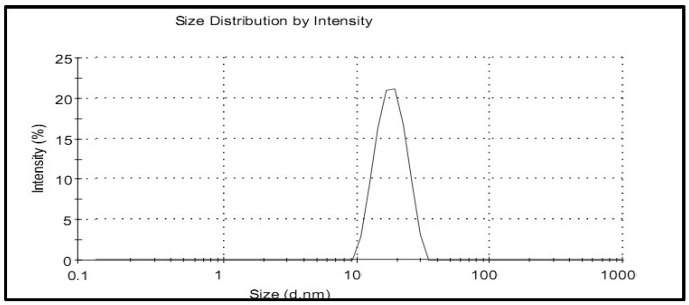



Figure 3: Particle size distribution of formulation C7IIB in 0.02M buffer

Table 9: Particle size distribution of C7IIB in water

| Parameter | Size (nm) |
|---|---|
| Di (90) | 9.1 |
| Di (50) | 8.52 |
| Di (10) | 6.25 |

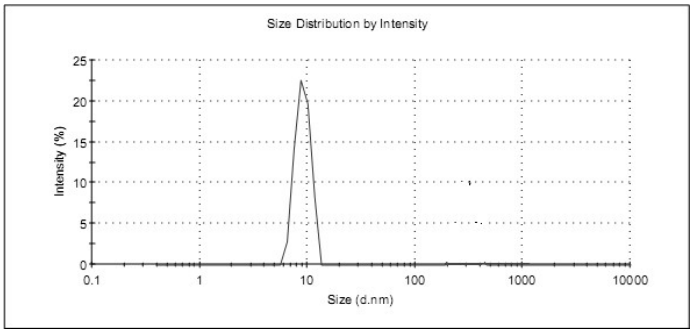



Figure 4: Particle size distribution of formulation C7IIB in Water

The zeta potential for various Dexlansoprazole SMEDDS formulations are as shown in table as follows;

Table 10: Zeta potential of the various SMEDDS formulations

| Formulation code | Zeta potential |
|---|---|
| C7II D | -16.9 |
| C7II B | -23.9 |
| C4II D | -14.4 |
| C4II B | -12.3 |
| C7I D | -19.1 |
| C7I B | -20.2 |
| C4I D | -12.6 |
| C4I B | -6.54 |

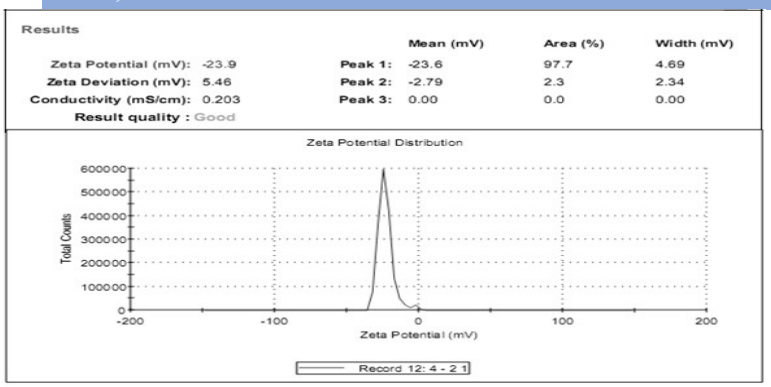



Figure 5: Zeta potential for formulation C7IIB

Formulation C7 has % transmittance value greater than 99%. These results indicate the high clarity of microemulsion. The results of %T are as shown in Table 11.

Table 11: % Transmittance for C7IIB formulation

| Period (months) | %T | |
|---|---|---|
| | 25˚C | 40˚C |
| 0 | 99.9 ± 0.2 | 99.9 ± 0.3 |
| 1 | 98.6 ± 0.5 | 99.5 ± 0.2 |
| 2 | 99.1 ± 0.3 | 98.3 ± 0.5 |
| 3 | 98.4 ± 0.6 | 94.4 ± 0.7 |

*Mean; n=2

The results show that formulations C3ID and C3IB does not pass the test as they have PDI more than 0.3 whereas remaining all formulations pass the test as they have PDI less than 0.3.

Table 12: Polydispersibility index of Dexlansoprazole SMEDDS formulations

| Formulation Code | PDI |
|---|---|
| C4 II D | 0.145 |
| C4II B | 0.085 |
| C7 II D | 0.256 |
| C7II B | 0.235 |

The dissolution profile for formulations C2IIB, C4IIB, C7IIB and C8IIB is as shown in the Figure 6. The formulation C7IIB showed highest release rate among all the liquid SMEDDS formulations i.e. 86.4% in 10 min which is highest among all batches.

Table 13: Comparison of In-vitro drug release of various liquid SMEDDS formulations

| Time (min) | C2IIB | C4IIB | C7IIB | C8IIB |
|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 |
| 10 | 42.4 | 67.2 | 86.4 | 52.4 |
| 20 | 55.2 | 78.3 | 93.1 | 67.4 |
| 30 | 770.4 | 92.4 | 95.2 | 74.8 |
| 60 | 81.8 | 97.1 | 97.6 | 83.2 |
| 75 | 92.9 | 98.4 | 98.9 | 95.1 |
| 120 | 95.4 | 99.1 | 99.9 | 98.3 |

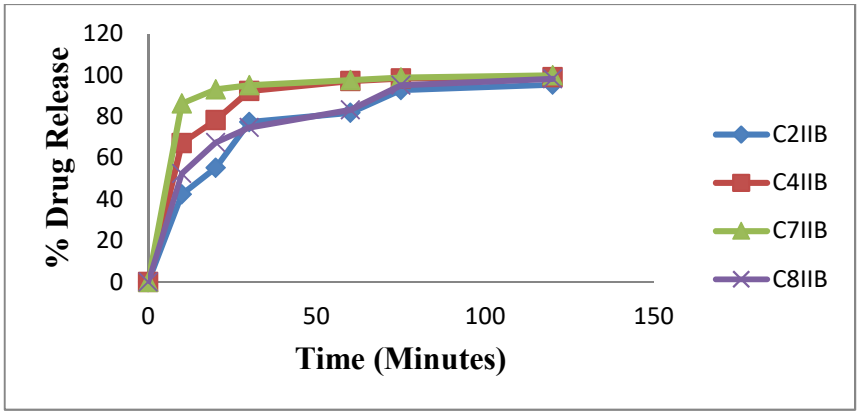



Figure 6: In-vitro diffusion study of various SMEDDS formulation

The comparison of in-vitro release of C7IIB, M and pure drug (S) are as shown in Figure 7.

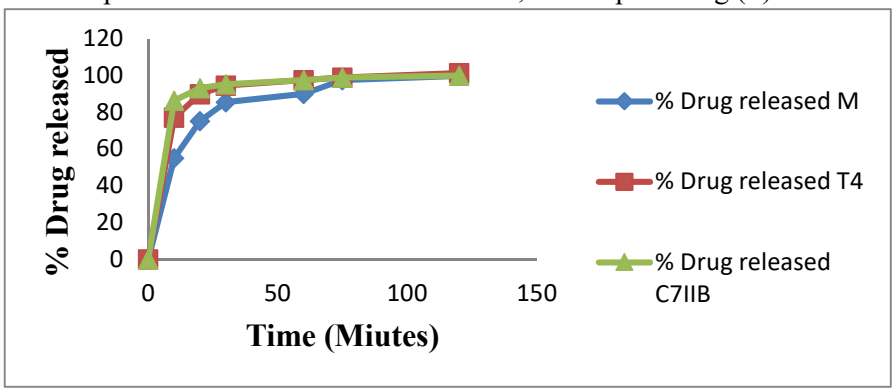



Figure 7: In-vitro diffusion study of C7IIB , M and S

Conclusion

Dexlansoprazole is a new-generation proton pump inhibitor (PPI) used for the management of symptoms associated with gastroesophageal reflux disease (GERD) and erosive esophagitis (damage to the esophagus from stomach acid), but its solubility, stability and oral bioavailability are poor. The objective of our investigation was to formulate a self microemulsifying drug delivery system (SMEDDS) of Dexlansoprazole using minimum surfactant concentration that could improve its solubility, stability and oral bioavailability. The composition of optimized formulation [C7IIB] consist of Capryol 90 as oil, Labrasol as surfactant and Captex 500 as cosurfactant , containing 30 mg of Dexlansoprazole showing drug release for liquid SMEDDS formulation (99.9%), droplet size (9.10 nm), Zeta potential (-23.9), viscosity (0. 9141 cP) and infinite dilution capability. In-vitro drug release of the C7IIB was highly significant ($p < 0.05$) as compared to marketed conventional tablet (M). From all above results it can be concluded that the proposed objective of the present research work of enhancing bioavailability of Dexlansoprazole, a low solubility Proton Pump Inhibitor drug, by improving solubility of drug was achieved successfully.

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