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FORMULATION AND CHARACTERIZATION OF SOLID MICROEMULSION OF DARUNAVIR FOR ENHANCED SOLUBILITY AND DISSOLUTION

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ABSTRACT: The solid microemulsion of Darunavir, a promising antiretroviral drug, is attempted in the present work for enhancing the solubility and dissolution rate. For this purpose, solubility of Darunavir was determined in various oils, surfactant and cosurfactants. Pseudo-ternary phase diagrams were constructed to identify the microemulsion existing zone. The optimized formulation consisted of 65% of Capmul MCM, 20% of Cremophore RH 40: Transcutol P (1:1) and distilled water. The optimized microemulsion formulation was characterized for its refractive index, % transmittance, pH, viscosity, drug content and particle size. Particle size of the optimized microemulsion formulation was found to be 40.68 nm. Various adsorbents were incorporated in the optimized liquid microemulsion to get solid microemulsion. The solid microemulsion with aerosil 200 was optimized because of very low concentration (1:1) of aerosil was incorporated in microemulsion as compare to other adsorbent. The prepared solid microemulsion was subjected to characterization for angle of repose, bulk density, tapped density, Hausner's Ratio, Carr's index, drug content, *ex-vivo* drug release study and stability studies. The solid microemulsion with aerosil 200 showed excellent free flowing property and % compressibility. From *ex-vivo* drug release studies, the release of darunavir from solid microemulsion (74.96±1.42 %) was found to be higher than the pure drug (47.55±2.12%). The results of the present study concluded that the solid microemulsion of Darunavir can be a promising approach to increase solubility and dissolution of the drug to increase its absorption and bioavailability for oral drug delivery.

INTRODUCTION: Successful oral delivery of drugs has always remained a challenge to the drug delivery field, since approximately 40% of the new drug candidates have poor water solubility, and thus oral delivery is frequently associated with implications of low bioavailability. Many approaches have been meticulously explored to improve the oral bioavailability of such drugs including particle size reduction (micronization or nanosizing), complexation with cyclodextrins, salt formation, solubilization based on cosolvents, surfactants, etc. Of late lipid-based formulations have attracted great deal of attention to improve the oral bioavailability of poorly water soluble drugs.

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In fact, the most favoured approach is to incorporate lipophilic drugs into inert lipid vehicles such as oils, surfactant dispersions, microemulsions, self- emulsifying formulations, self microemulsifying formulations, and liposomes. This could lead to increased solubilization with concomitant modification of their pharmacokinetic profiles, leading to increase in therapeutic efficacy.[1]

Among all techniques microemulsion system has considerable potential to act as a drug delivery vehicle by incorporating a wide range of drug molecules Microemulsions have been widely studied to enhance the bioavailability of the poorly soluble drugs.. Interest in these versatile carriers is increasing and their applications have been diversified to various administration routes in addition to the conventional oral route. This can be attributed to their unique solubilization properties and thermodynamic stability which has drawn

attention for their use as novel vehicles for drug delivery.

Microemulsion has got advantage like excellent thermodynamic stability, high drug solubilization capacity, improved oral bioavailability and protection against enzymatic hydrolysis. The only problem with microemulsion is poor palatability due to the lipid content leading to the poor patient compliance. Moreover due to their water content, microemulsions cannot be encapsulated in soft gelatin or hard gelatin capsules.

All these problems may be overcome by formulating or converting microemulsion into another stable dosage form like conversion of microemulsion into powder or tablet by adsorbing onto the solid support i.e. adsorbent. Thus solid microemulsion technique is developing to modify the physicochemical and biopharmaceutical properties of drug having low solubility and high permeability.

Darunavir is a promising antiretroviral drug acting as a protease inhibitor used to treat HIV. It acts on the HIV aspartyl protease which the virus needs to cleave the HIV polyprotein into its functional fragments. Darunavir is classified under class II according to biopharmaceutical classification system. The drug shows pH dependent solubility. In aqueous media, darunavir exhibits very poor solubility (0.16-0.19 mg/l).

This poor solubility may cause poor dissolution and unpredicted bioavailability. Thus the objective of presented research work is formulation and characterization of solid microemulsion of poorly soluble drug, darunavir to enhance the solubility and dissolution for oral drug delivery.

MATERIALS AND METHODS:

Darunavir was a gift sample from Mylan Laboratories Ltd, Hyderabad, India. Capmul MCM, Captex 200, Captex 300 and Captex 355 were gift samples from Abitec Corporation, WI, Cremophore RH 40, Cremophore EL was gift sample from BASF India Ltd. Mumbai, India. Transcutol P and Labrasol were gift samples from Gattefosse India Pvt. Ltd., Mumbai, India and Aerosil 200 was gift sample from Unijules, Nagpur, India. All the other chemicals were of the analytical grade.

Solubility study[2]:

The solubility of Darunavir (DRV) in various oils (Rice bran oil, Reconstituted Fish oil, Coconut oil, Soybean oil Capmul MCM, Captex 200,300, 355), surfactants (Cremophore EL, Cremophore RH40, Tween 80, Tween 20), and co-surfactants (PEG, Ethanol, Transcutol P) was determined by adding excess amount of DRV to 2 ml of each component placed in screw capped glass vial.

The ingredients were mixed using a magnetic stirrer and then kept on orbital shaker (Remi motors & RIS-24BL) for 72 h at temperature $37^0 \pm 2^0$ C. The samples were then centrifuged for 5 min at 37°C. The supernatant was pipetted out, diluted with methanol and analyzed by UV spectrophotometer (Shimadzu, Japan) at 263 nm for determining drug concentration.

The results are shown in Tables 1-3**.**

TABLE 1: SOLUBILITY OF DARUNAVIR IN VARIOUS OILS

Sr. No.	Oils	Solubility (mg/ml)
1	Rice bran oil	26.0 ± 0.20
2	Reconstituted Fish oil	68.0 ± 0.11
3	Coconut oil	14.0 ±0.3
4	Soybean oil	21.0 ± 0.28
5	Captex 200	34.0 ± 0.21
6.	Captex 300	9.0 ±0.3
7.	Captex 355	30. 0 ±0.2
8.	Capmul MCM	164.0 ± 0.15
9.	Labrafil 1944	54.0 ± 0.33

Data was expressed as mean ± S.D. (n=3)

TABLE 2: SOLUBILITY OF DARUNAVIR IN VARIOUS SURFACTANTS

Sr. No.	Surfactants	Solubility (mg/ml)
1	Tween 20	63.0 ± 2.0
2	Tween 80	174.0 ± 0.50
3	Cremophore RH 40	125.0 ± 0.38
4.	Cremophore EL	84.0 ±0.35

Data was expressed as mean ± S.D. (n=3)

TABLE 3: SOLUBILITY OF DARUNAVIR IN VARIOUS COSURFACTANTS

Sr. No.	Cosurfactants	Solubility (mg/ml)
1	Ethanol	12.0 ± 0.22
2	PEG 400	39.0 ± 0.17
3	Transcutol P	265.0 ± 0.03
4.	Capryol 90	152.0 ± 0.2

Data was expressed as mean ± S.D. (n=3)

Construction of pseudo-ternary phase diagrams[3]:

Pseudo-ternary phase diagrams were constructed to obtain the suitable components, and their concentration ranges that resulted in a large existence area of microemulsion, were preferred. In order to optimize the concentration of oil phase, surfactant and co-surfactant, different batches of varied concentration were prepared and titrated with distilled water till transparency persisted. Ternary phase diagram was prepared by using a constant ratio of surfactant to co-surfactant. Four ratios of surfactant (Cremophore RH 40) and co-surfactant (Transcutol P) were selected (1:1, 2:1, 3:1 and 4:1). The results are represented in **Fig.1**.

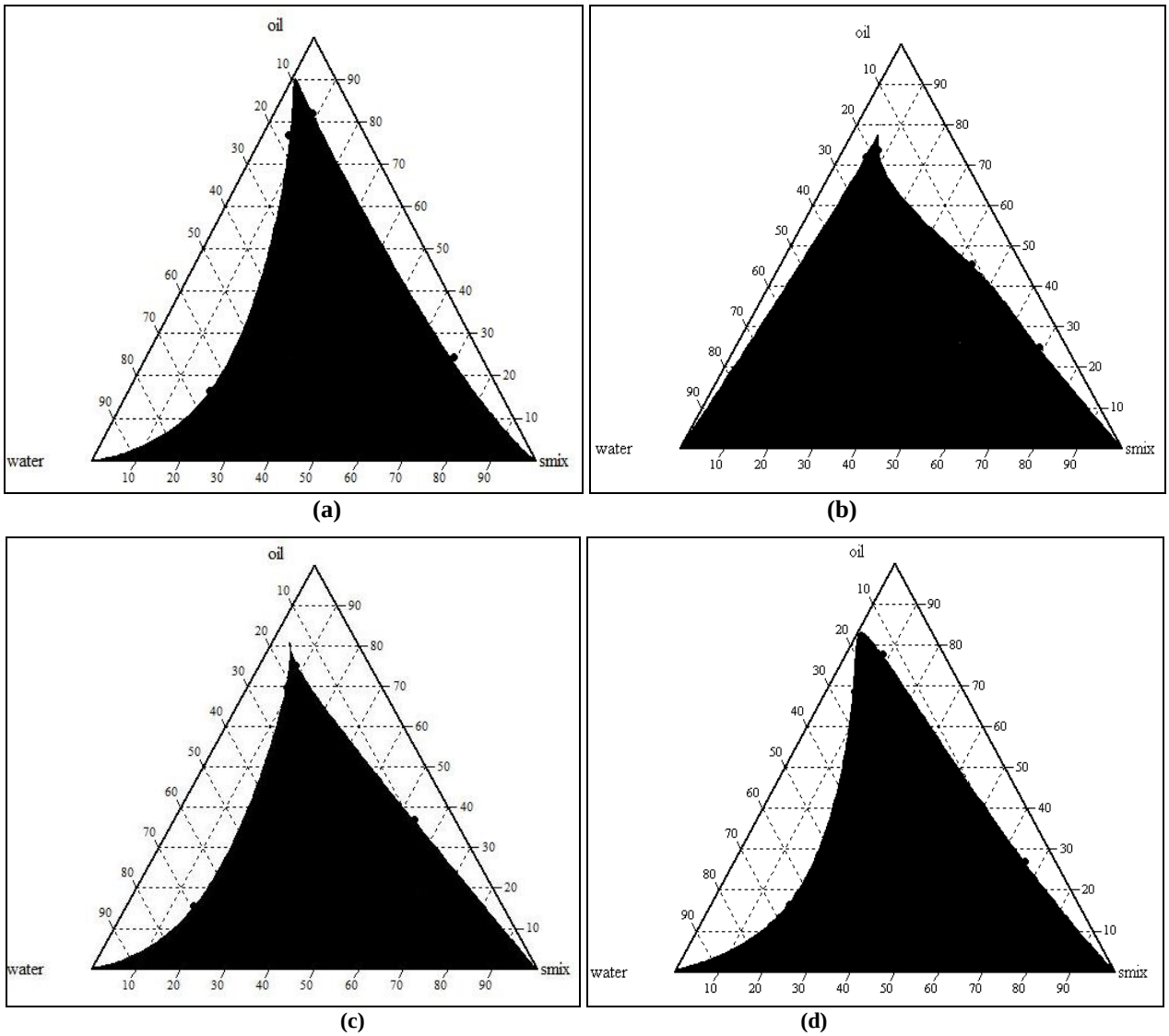

FIG. 1: PSEUDOTERNARY PHASE DIAGRAM OF MICROEMULSION COMPOSED OF CAMPUL MCM (OIL), WITH CREMOPHORE RH 40(SURFACTANT): TRANSCUTOL P(COSURFACTANT) (S:Cos), Water. (a) S: Cos 1:1 (b) S: Cos 2:1 (c) S: Cos 3:1 (d) S: Cos 4:1. THE SHADED AREA REPRESENTS MICROEMULSION REGION.

Preparation of microemulsion by water titration method [4]:

After the microemulsion regions in the phase diagrams were identified, the microemulsion formulations were selected at different component ratios as described in Table 1-3. In order to prepare the drug loaded microemulsions, the weighed amount of Darunavir was dissolved into mixture of oil and surfactant/cosurfactant mixture. Then this mixture was mixed thoroughly using magnetic stirrer until a homogenous dispersion was obtained. The mixture was titrated by adding water drop by drop with constant stirring till the microemulsion was obtained at ambient temperature. The results are depicted in **Table 4.**

TABLE 4: COMPOSITION OF MICROEMULSIONS

Sr. No.	Formulation code	Campul MCM %v/v	Cremophore RH 40% v/v	Transcutol P % v/v	Purified water %v/v	Observation
1	ME1	65	10	10	15	µE
2	ME2	50	10	10	30	µE
3	ME3	45	10	10	35	µE
4	ME4	40	10	10	40	µE
5	ME5	25	10	10	55	E
6	ME6	20	10	10	60	E
7	ME7	15	10	10	65	E
8	ME8	10	10	10	70	E

µE = Microemulsion, E = Emulsion

Characterization of microemulsion[5]:

The prepared darunavir microemulsions were inspected for transmittance and visual clarity, centrifugation, pH measurement, refractive index, viscosity.

1. Transmittance and visual clarity:

The droplets of the microemulsions being smaller than ¼th the wavelength of visible light, permit white light to pass through the dispersed system making it transparent or translucent. The microemulsion systems were inspected for optical transparency and homogeneity by usual observation against strong light. The system was also checked for the presence of undissolved drug or other solid ingredient. The results are shown in **Table 6**.

2. Centrifugation:

Physical stability of the microemulsions was studied by centrifugation at 3,000 rpm for 2 hours. After centrifugation the samples were observed for clarity and any phase separation or precipitation. The results are shown in **Table 6**.

3. pH measurement:

The pH measurement of the microemulsions was determined by using a pH meter which was calibrated before use with standard buffer solutions at pH 4 and 7. The results are shown in **Table 6**.

4. Refractive index:

The refractive index of medicated formulation was determined using an Abbe refractometer. The results are shown in **Table 6**.

5. Viscosity:

The viscosity of the prepared microemulsions was measured using Brookfield viscometer using spindle no. S 64, at 100 rpm. Experiments were carried out in triplicate for each sample and the results are presented as an average ± standard deviation in **Table 6**.

6. Drug content:

The microemulsion formulation was analyzed for drug content by U.V. spectrophotometer at 263nm. The results are shown in **Table 6.**

7. Particle size Analysis:

Mean globule size of the optimized microemulsion was determined by photon cross-correlation spectroscopy. Microemulsion was placed in transparent polystyrene cuvette (path length = 1 cm) which was placed in thermostatic sample chamber maintained at 25°C. Sample temperature was set at 25°C and 3 runs of 60s were performed. Detection was carried out at a scattering angle of 90°. From the resulting correlation curves, a 2nd order analysis was performed to calculate the mean globule size and standard deviation. The results are represented in **Fig.2.**

8. *Ex-vivo* drug permeation study[6]:

To check the drug release pattern through intestine, small portion of small intestine was isolated and used for the study. The tissue was thoroughly washed with pH 7.4 phosphate-buffered saline to remove any mucous and lumen contents. The microemulsion of Darunavir (ME 1 ME 2, ME 3 and ME 4) 5.0 ml (equivalent to 60 mg darunavir) was diluted up to 10 ml with distilled water and mixed for 1 minute. The resultant sample (6.0 mg/ml) of microemulsion of darunavir was injected into the lumen of the small intestine tissue using a syringe, and the two sides of the intestine were tightly closed with the help of a thread. The tissue was placed in a beaker filled with 30 ml of pH 5.5

phosphate-buffer with constant stirring at 37°C. The two ends of tissues were fixed horizontally on to a beaker with the help of a thread. Aliquots of 5 ml were withdrawn at 1 hour time interval till 7 hours and suitably diluted further. The absorbance was measured using a UV-Visible spectrophotometer at a wavelength of 263 nm. The amount of drug permeated (%) was calculated against time and plotted on a graph.

Preparation of Solid microemulsion[7]:

The microemulsion was optimized on the basis of the transparency, drug content, particle size and drug permeated (%). The optimized microemulsion was composed of Campul MCM (65%), (1:1) Cremophore RH 40: Transcutol P (20%) and distilled water. After the formulation and evaluation of microemulsion the task ahead was to bring it into solid dosage form. The solid microemulsion dosage form was prepared by adsorbing the liquid microemulsion onto a particulate solid material so as to provide the adsorbent in the form of a powder. To convert liquid microemulsion into solid, five adsorbing agents were used. They were bentonite, aerosol 200, aluminium hydroxide, magnesium hydroxide and magnesium oxide. The solid microemulsions were prepared by adsorption of microemulsion onto adsorbent. The results are depicted in **Table 5**.

TABLE 5: COMPOSITION OF SOLID MICROEMULSION

Sr. No.	Formulation code	Different Adsorbent	Concentration in % w/w
1	SME 1	Bentonite	1:11
2	SME 2	Aerosil 200	1:1
3	SME 3	Aluminium hydroxide	1:3
4	SME 4	Magnesium hydroxide	1:6
5	SME 5	Magnesium oxide	1:7

Characterization of Solid Microemulsion[8]:

The prepared solid microemulsion were characterized by angle of repose, bulk density, tapped density, Carr's index, Hausner's ratio, drug content, *ex-vivo* drug release study and stability studies.

1. Angle of repose:

The fixed funnel and free standing cone method was employed. A funnel that is secured with its tip at a given height, h, which was kept 2 cm above graph paper that is placed on a flat horizontal surface. With r being the radius of base of conical pile, angle of repose can be determined by following equation:

$$\Theta = \tan^{-1}(h/r)$$

Where, Θ is the angle of repose,

h is height of pile,

r is radius of base of the pile.

The results are shown in **Table 7**.

2. Bulk density:

The solid microemulsion was introduced into the 10 ml graduated cylinder. The volume occupied by the SME was recorded. Bulk density was calculated using following formula:

Bulk density = Mass of powder/Bulk volume

It is calculated in g/ml. The results are shown in **Table 7.**

3. Tapped Density:

Solid microemulsion (2 gm) was poured through a glass funnel into 10 ml of graduated cylinder. The cylinder was tapped gently from the height of 2 inches until a constant weight was obtained. The volume occupied by the solid microemulsion after tabbing was recorded and tapped density was calculated using following formula:

Tapped density = Mass of powder/Tapped volume

The results are shown in **Table 7**.

4. Carr's index:

Carr's index can be determined by the following equation,

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

The results are shown in **Table 7.**

5. Hausner's ratio:

Hausner's ratio can be determined by the following equation,

Hausner's ratio = Tapped Density / Bulk Density

The results are shown in **Table 7**.

6. Drug content: The drug content was calculated by dissolving solid microemulsion equivalent to 60

mg of Darunavir was transferred to 100 ml volumetric flask and dissolved in minimum amount of methanol and the volume was made up to 100 ml with phosphate buffer (pH 5.5) and then the solution was filter through 0.45-µm membrane filter paper and assayed for drug content using UV spectrophotometer at 263 nm. The results are shown in **Table 7.**

7. *Ex-vivo* drug permeation study:

To check the drug release pattern through intestine, small portion of small intestine was isolated and used for the study. The tissue was thoroughly washed with pH 7.4 phosphate-buffered saline to remove any mucous and lumen contents. The solid microemulsion of Darunavir, 3.28g, (equivalent to 60 mg darunavir) and pure drug darunavir (60 mg) were diluted up to 10 ml with distilled water and mixed for 1 minute. The resultant samples (6.0 mg/ml) of solid microemulsion of darunavir and pure drug darunavir (60 mg) were injected into the lumen of the small intestine tissue using a syringe, and the two sides of the intestine were tightly closed with the help of a thread. The tissue was placed in a beaker filled with 30 ml of pH 5.5 phosphate-buffer with constant stirring at 37°C. The two ends of tissues were fixed horizontally on to a beaker with the help of a thread. Aliquots of 5 ml were withdrawn at 1 hour time interval till 7 hours and suitably diluted further. The absorbance was measured using a UV-Visible spectrophotometer at a wavelength of 263 nm. The amount of drug permeated (%) was calculated against time and plotted on a graph. The results are shown in **Fig.3**.

8. Stability studies:

To assess the stability of drug and formulation, stability studies were done as per ICH guidelines. The formulated solid microemulsion were wrapped in aluminium foil and stored at 45 ± 0.5ºC for period of one month. After an interval of 15 days the solid microemulsion were tested for physical appearance, angle of repose, bulk density, tapped density, Carr's index, Hausner's ratio, drug content. The results are shown in **Table 8.**

RESULT AND DISCUSSION:

Solubility Study: The solubility of darunavir in various vehicles is shown in **Table 1 to 3**. The components and their concentration ranges can be obtained by the construction of a pseudo-ternary phase diagram. The drug loading capability is the main factor when screening the oil phase. Darunavir has the highest solubility in Capmul MCM as shown in **Table 1** and was, therefore selected as an oil phase in the present study. On the basis of the solubility profile as shown in **Table 2** and 3, Cremophore RH 40 was considered as a surfactant and Transcutol P as a co- surfactant.

Pseudo-ternary phase diagrams:

Pseudo-ternary phase diagrams of the systems containing Capmul MCM as an oil phase, Cremophore RH 40 as a surfactant, Transcutol P as a co-surfactant and distilled water were constructed at the surfactant /co-surfactant ratio of 1:1, 2:1, 3:1 and 4:1 (w/w) to determine the existence of microemulsion region as shown in **Fig. 1**. The phase study revealed that the obtained microemulsion regions at surfactant/ co-surfactant ratios of 1:1was maximum where as for 2:1, 3:1 and 4:1 was almost similar. Thus the S/Cos ratio of 1:1 was taken for formulation of microemulsion.

Characterization of microemulsion:

The formulated microemulsions were characterized for pH, refractive index, centrifugation, transparency/translucency, viscosity, drug content, particle size analysis.

1. Transparency:

All the microemulsions were transparent and appeared like a homogenous single-phase liquid, when observed for visual clarity against strong light. No traces of undissolved drug or other solid ingredient were found in all the formulations. This indicated that the drug was completely soluble in the system.

2. Centrifugation:

None of the microemulsion systems showed signs of phase separation on centrifugation at 3000 rpm for 2 hours. This result provided a rapid and full proof identification of the system as microemulsion.

3. pH Measurement: The pH of microemulsion was found to be in the range of 6.40±0.2 to

6.60±0.2. The range is suitable for oral administration.

4. Refractive index:
The refractive index was in the range of 1.386±0.01 to 1.412±0.02. The values of the refractive index of microemulsion showed that the systems were transparent concluding very small particle size of the system.

5. Viscosity: The viscosity of the microemulsion was ranged between 84±2.00cp to101±3.00cp. The viscosity values indicated the o/w nature of microemulsions.

6. Drug content:
The drug content of microemulsion formulation was determined. The drug content of ME1, ME2, ME3 and ME4 was found to be 99.42, 98.18, 96.23 and 95.10 respectively. The formulation ME1 was showing good % transmittance, refractive index, viscosity, pH, drug content. Thus ME1 was optimized for further study.

TABLE 6: PHYSICOCHEMICAL CHARACTERISTICS OF MICROEMULSIONS

Sr. No.	Formulations	ME 1	ME 2	ME 3	ME 4
1	pH	6.50 ± 0.02	6.40 ±0.02	6.40 ±0.01	6.60 ±0.02
2	Refractive index	1.3820 ±0.01	1.3860±0.02	1.3964±0.01	1.4120±0.02
3	Centrifugation	No phase separation	No phase separation	No phase separation	No phase separation
4	% Transmittance	98.0 ± 1.01	96.0 ± 1.03	95.5 ± 1.02	95.0 ± 1.03
5	Viscosity at 100 rpm(cps)	101 ± 3.00	90 ± 1.00	88 ± 1.00	84± 2.00
6	Drug content	99.42	98.18	96.23	95.10

Data was expressed as mean ± S.D. (n=3)

7. Particle size Analysis:
The particle size of the optimized microemulsion was determined by photon cross-correlation spectroscopy. The particle size of darunavir microemulsion was found to be 40.68 nm. The particle size was within the range indicating the microemulsion of very low globule size. The results are represented in **Fig. 2**.

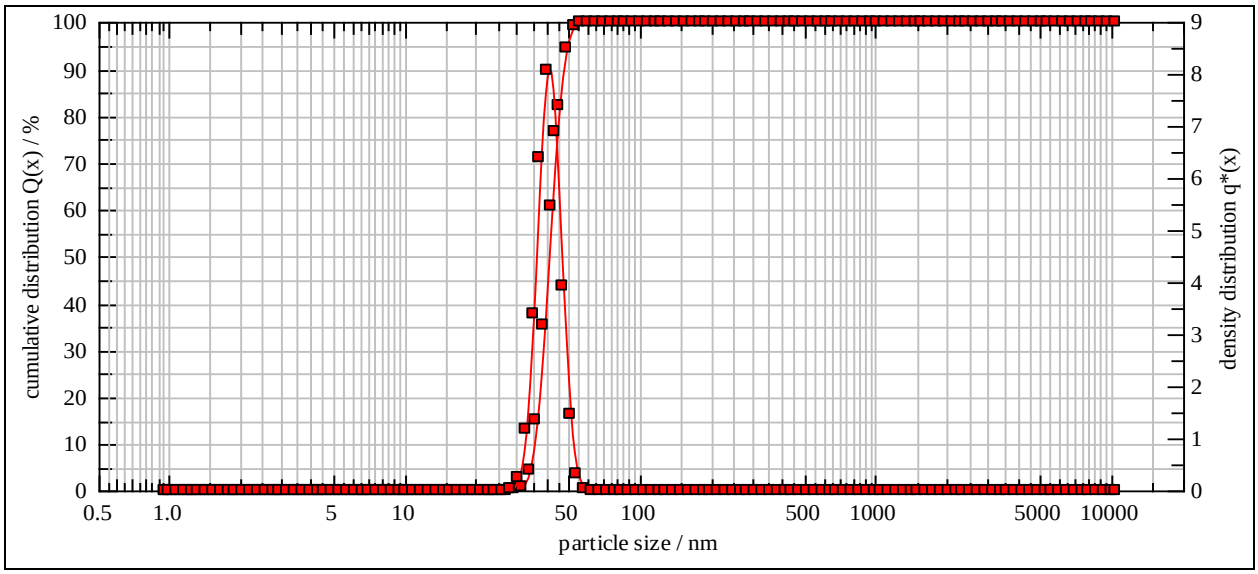

FIG.2: PARTICLE SIZE ANALYSIS OF DARUNAVIR MICROEMULSION

***8. Ex-vivo* Drug Permeation study:**
To understand the characteristics of drug permeation, *ex vivo* intestinal tissue permeation study was carried out across the small intestine of male Sprague-Dawley rats[6].The *ex-vivo* intestinal drug permeation from the microemulsions (ME 1 to ME 4) is shown in **Fig. 3**. The results revealed that formulation ME 1 permeated higher percentage of the drug as compared to ME2, ME3 and ME4. The higher permeation may be due to the higher amount of the oil phase incorporated in ME 1 which is reponsible for enhanced solubility of the drug and permeation.

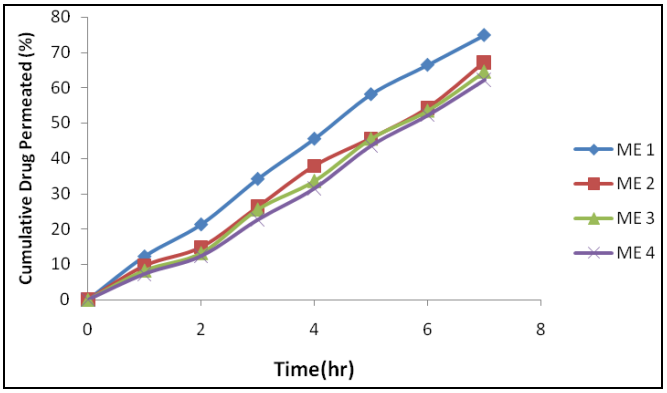

FIG.3: *EX VIVO* INTESTINAL PERMEATION PROFILE OF DARUNAVIR MICROEMULSIONS

Preparation of Solid Microemulsion:

The solid microemulsion of darunavir was prepared in a view to convert the liquid microemulsion in solid dosage form with improved palatability. Adsorption with aerosil 200 (SME 2) was optimized as liquid to solid conversion was effective at very concentration amongst all other adsorbents.

Characterization of solid microemulsion:

The optimized solid microemulsion (SME 2) was subjected to characterization for angle of repose, bulk density, tapped density, Carr's index, Hausner's Ratio, drug content, *ex-vivo* drug release study and stability studies. The results are revealed in Table 7.

1. Angle of Repose:

The angle of repose was found to be 28.88°±0.8°.

2. Bulk density:

The bulk density was found to be 0.415 ±.004 g/cm³.

3. Tapped density:

The tapped density was found to be 0.512 ±0.02 g/cm³.

4. Hausner's Ratio:

The Hausner's ratio was found to be 1.23± 0.03.

5. Carr's index:

The Carr's index was found to be 18.94 ± 0.6 %.

6. Drug content uniformity:

The percentage drug content of SME 2 was found to be 98.56±0.32 %. The solid microemulsion was found to be uniform in drug content.

TABLE 7: PHYSICOCHEMICAL CHARACTERISTICS OF DARUNAVIR SOLID MICROEMULSION

Sr. No.	Parameters	SME 2
1	Angle of repose	28.88°±0.8°
2	Bulk density	0.415±.004 g/cm³
3	Tapped density	0.512±0.02 g/cm³
4	Hausner's ratio	1.23±0.03
5	Carr's index	18.94±0.6 %
6	Drug content (%w/w)	98.56±0.32 %

Data was expressed as mean ±S.D. (n=3)

9. *Ex-vivo* drug permeation studies:

Ex-vivo drug permeation studies were carried out to compare the permeation pattern from darunavir solid microemulsion and the pure drug. The outcomes are depicted in **Fig. 4.** The release of Darunavir from solid microemulsion prepared from aerosil 200 (74.96±1.42 %) was found to be higher than the pure drug (47.55±2.12%). This may be due to the fact that in the microemulsion system, the solubility of Darunavir might have increased due to oil phase and surfactant.

The mechanism reported to improve the oral absorption of lipophilic drugs when incorporated into solid microemulsion includes, increasing membrane fluidity, opening of tight cellular junctions, inhibiting P-gp and/or CYP450 by surfactants and stimulating lipoprotein/chylomicron production by lipid. The better permeation observed with the developed solid microemulsion formulation might be due to the oil and surfactant content that could have made the intestinal wall more permeable by partial disruption of membrane. The surfactant-induced membrane fluidity and inhibition of P-gp might play an important role in the permeability change and the increase of drug absorption in the gastrointestinal tract.[9]

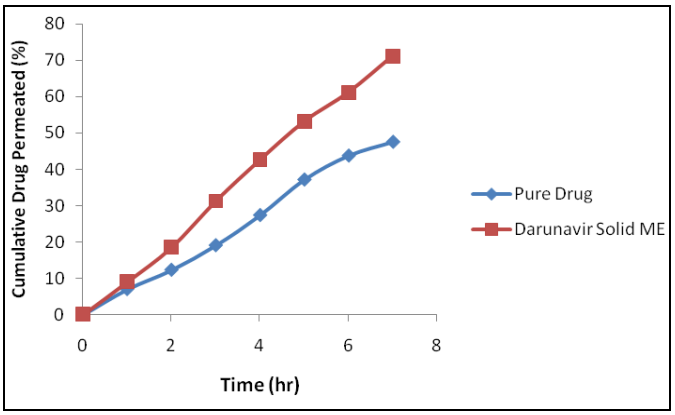

FIG. 4: *EX VIVO* INTESTINAL PERMEATION PROFILE OF DARUNAVIR SOLID MICROEMULSION AND PURE DRUG

8. Stability studies:

The result of stability studies shown that there were no significant changes in the angle of repose, bulk density, tapped density, Hausner's ratio, Carr's index, drug content of solid microemulsion after storing at a temperature of 40ºC ± 2ºC / 75% ± 5% relative humidity for one months. These results indicated that drug remain stable after incorporating in the solid microemulsion containing aerosol 200 as an adsorbent.

TABLE 8: STABILITY STUDIES OF OPTIMIZED SOLID MICROEMULSION OF DARUNAVIR

Formulation	SME 2		
Periods (days)	**0**	**15**	**30**
Physical appearance	No change	No change	No change
Angle of repose	28.88°±0.5°	28.86°±0.8°	28.84°±0.5°
Bulk density	0.415±.004 g/cm³	0.413±.005 g/cm³	0.414±.004 g/cm³
Tapped density	0.512±0.02 g/cm³	0.510±0.03 g/cm³	0.511±0.02 g/cm³
Hausner's ratio	1.23±0.03	1.234±0.03	1.23±0.02
Carr's index	18.94±0.6 %	19.01±0.4 %	18.98±0.6 %
% Drug content	98.56±0.32 %	98.32±0.24 %	98.46±0.28 %

Data were expressed as mean ± S.D (n=3).

CONCLUSION: A solid microemulsion containing poorly water-soluble drug, Darunavir, was formulated for oral administration. The components and their ratio ranges for the formulation of microemulsion were obtained by solubility study, pseudo-ternary phase diagram. The optimum formulation of the microemulsion consisted of 65 % of Capmul MCM as oil, 10 % of Cremophore RH 40 as surfactant, 10 % of Transcutol P as co- surfactant and distilled water which had sufficient drug loading and forming droplet size in the range of microemulsion. The study indicated that the developed darunavir solid microemulsion formulation showed greater intestinal permeability than the drug suspension. The present study focused on the potential of using solid microemulsion as an efficient strategy for the oral delivery of hydrophobic darunavir. Since nearly 40% of drugs are hydrophobic, solid microemulsion can be a promising formulation approach for enhancing solubility and dissolution thus improving oral bioavailability of drugs with poor aqueous solubility. [10-15]

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