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FORMULATION AND EVALUATION OF ROSUVASTATIN SMEDDS FOR ENHANCEMENT OF GASTRO RETENTIVE ABSORPTION

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ABSTRACT

The objective of the present study was to develop self emulsifying drug delivery system of Rosuvastatin to improve solubility and dissolution rate of Rosuvastatin. Rosuvastatin is a BCS class II drug (poor solubility, good permeability) with low bioavailability (less than 5%). In present study Rosuvastatin self emulsifying drug delivery system was prepared with triacetin as oil, transcutol as surfactant and propylene glycol as co-surfactant. SMEDDS was characterized for stress study, *invitro* drug release, globule size, zeta potential, polydispersity index, transmission electron microscopy, *exvivo* permeation study and pharmacodynamic study. Improvement in antihyperlipidimic potential of SMEDDS as compared to plain drug can be attributed to improvement in solubility and drug dissolution rate of Rosuvastatin.

Keywords: Emulsification, solubility, particle size

INTRODUCTION

Various formulation approaches like salt formation, micronization, solid dispersion, complexation with cyclodextrins etc. can be used to improve solubility of BCS class II (low solubility and low permeability) drugs. However such techniques experience concrete difficulties and may not be applicable to all drugs **[1]**. In recent years

interest in lipid based drug delivery is increased to improve water solubility of drugs. Lipid based drug delivery consist of delivering drug in a system containing oil, surfactant and co-surfactant. Self emulsifying drug delivery system (SMDDS) consists of isotropic mixture of natural or synthetic oil with surfactant and co-surfactant. These systems spontaneously emulsify when exposed to GI fluids to form oil in water emulsion with droplet size in range of 20-200nm **[2]**.

Main advantages of these systems include improvement in oral bioavailability **[3]**, ease of manufacture and scale up **[4]**, reduction in inter-subject and intra-subject variability and food effects **[5]**, ability to deliver peptides **[6, 7]** minimal effect of lipid digestion system and increased drug loading capacity.

Rosuvastatin is a crystalline compound, practically insoluble in water and hence poorly absorbed from the GI tract **[8, 9]**. It is a potent and specific inhibitor of 3-hydroxy-3-methyl-glutaryl coenzyme A (HMG CoA) reductase **[22, 23]**, which catalyzes the reduction of HMG CoA to mevalonate. Thus, Rosuvastatin arrests a key step for cholesterol biosynthesis in the liver and is widely used in the treatment of hypercholesterolemia and dyslipidemia as an adjunct to diet. After oral administration, Rosuvastatin is metabolized to its β-dihydroxy acid form (Rosuvastatin acid) by the cytochrome-3A system in the liver, where it inhibits the rate-limiting step in cholesterol biosynthesis. This leads to up-regulation of low-density lipoprotein (LDL) receptors and an increase in catabolism of LDL cholesterol. Being a BCS Class II drug, it often shows dissolution rate-limited oral absorption and high variability in pharmacological effects. Therefore, improvement in its solubility and dissolution rate may lead to enhancement in bioavailability **[24]**.

MATERIAL AND METHODS:

Rosuvastatin was obtained a sample from Cipla Pvt ltd. Triacetin was purchased from sigma Aldrich Pvt. Ltd., Transcutol was procured as gift sample from Gattefosse India Pvt. Ltd. All other chemicals used were of AR grade and procured locally.

Solubility study of Rosuvastatin in various oils:

Primary screening of oils was carried out by qualitatively determining the potential oil to solubilise maximum amount of Rosuvastatin. One gram oil was placed in a glass vial and Rosuvastatin was incorporated in increment of 10mg. After each addition of drug mixture was cyclomixed to dissolve the drug. After few additions when oil was about to saturate with drug, mixture is warmed on boiling water bath to aid solution. Based on visual observation few promising oil which can solubilise more than 20mg per gram were

selected and evaluated further for quantitative estimation of solubility of Rosuvastatin.

Solubility of Rosuvastatin in selected oil was determined by adding excess of drug in 5gm of oil sample in a vial. Vial was placed on orbital shaker at RT for 24 hrs. After 24hr. sample is filtered and drug content in oil was determined by UV spectrophotometer at243nm.

Screening of surfactant:

Flask inversion method was used to identify ability of different surfactant to emulsify selected oily phase i.e triacetin. Emulsification efficiency was judged by measuring the number of flask inversion (FI) required to produce uniform emulsion and the transmittance value (%T) of the resultant emulsion.

In a glass vial 300mg of oil is mixed with 300mg of surfactant and mixed well using cyclo mixer and gentle heating on water bath. 50mg of oil and surfactant mixture is diluted to 50ml with double distilled water. Number of flask inversion required to produce uniform emulsion is counted and % transmittance is measured.

Screening of Co-surfactant:

Mixtures of the co-surfactant, selected surfactant, and the selected oil were prepared and evaluated in similar fashion as described in the above section on surfactants

Construction of Pseudoternary phase diagram:

Pseudoternary phase diagram was constructed to determine optimum concentration of each excipient in system to produce fine, stable optimum SMEDDS formulation.

Surfactant mixture was prepared by mixing surfactant and co-surfactant in four different volume ratios (K_m = 1:1, 2:1, 3:1, and 1:2). Oil and surfactants was mixed thoroughly in a glass vial at 9 different weight ratios 9:1, 8:2, 7:3, 6:4, 5:5, 4:6, 3:7, 2:8, 1:9. The components in the vial are heated to 60- 70^0C on water bath and homogenized by cyclo mixing. The homogenized mixture of oil, surfactant and co- surfactant at each weight ratio were titrated with water by dropwise addition. After addition of each drop of water the system was homogenized by cyclomixing and the appearance to produce emulsion was examined by visual observation. The concentration of water at which turbidity-to-transparency or transparency-to-turbidity transition occurred was derived from weight measurement. The percent composition of each different incorporated phase at end point of titration was then calculated on weight basis and was used to plot pseudoternary phase diagram (separately for each four different K_m values) to determine the boundaries of microemulsion by using PCP disso v3

software. In total four different phase diagram were plotted to compare area of microemulsion existing region at different K_m values. Apexes of triangle represent the 100% w/w concentration of respective excipients. The coloured portions in ternary plots are the microemulsion region.

Optimization of SMEDDS of Rosuvastatin:

Keeping the ratio of surfactant: co-surfactant (1:1) constant various ratios of oil to S_{mix} were studied. The formulated systems were analysed for freeze thaw cycle, centrifugation and dispersibility studies.

Freeze thawing was performed to evaluate stability of formulation. In this study formulation was alternatively stored at freezing temperature i.e less than 5^0C and at room temperature for a period of 24hrs for 3 cycle. After visual observations formulations showing no sign of drug precipitation or phase separation were selected.

Robustness to dilution:

Robustness to dilution of optimized SMEDDS was checked in distilled water, 0.1N HCL and phosphate buffer pH 6.8 at 3 different dilution level 50,100 and 1000 times. Diluted solution was evaluated for appearance, % transmittance and drug precipitation.

Globule size, polydispersity index and zeta potential:

The SMEDDS, 50mg was diluted to 50ml with distilled water. The mean globule size, Polydispersity index (P.I.) and Zeta potential of the resulting microemulsion were determined by Malvern zeta sizer.

Transmission Electron Microscopy (TEM):

Transmission electron microscopy was employed to study the morphology of oil globules present in microemulsion. Prior to the analysis, the L-SMEDDS samples were diluted 1000fold with distilled water to form microemulsion, the resultant microemulsion was stained with 2% (w/v) phospho-tungstic acid for 30s and placed on 400-mesh copper grids with films for observations.

***In vitro* Drug release study:**

In vitro dissolution of plain Rosuvastatin powder (10mg) and optimized SMEDDS (equivalent to 10 mg of Rosuvastatin) filled in size 0 hard gelatin capsule was studied using IP apparatus II (Paddle) at 37 ± 2^0C and rotating speed of 100rpm using 900ml of 0.1N HCl with 0.5% SLS. During the study 5ml aliquot was withdrawn at each time point and replaced with same volume of fresh dissolution media. Samples were analyzed by UV visible spectrophotometer at λ_{max} of 239nm.

Drug content:

Accurately weighed SMEDDS equivalent to 10mg of Rosuvastatin was placed in 50mL volumetric flask and volume was

made up with methanol, followed by sonication in bath sonicator for 15-20min to extract and solublize the Rosuvastatin. The methonolic extract was filtered through Whatman filter paper and concentration was determined by inhouse developed and validated stability indicating HPLC method using Zorbax Eclipse® XDB- C18 column and acetonitrile (90) phosphate buffer pH 3.2(10) as mobile phase. Experiment was performed in triplicate.

***Ex-vivo* intestinal permeability study by everted sac technique:**

Ex vivo permeability of the formulation was checked through isolated duodenal part of the goat intestine. Goat intestine was procured from local slaughter house and continuously stored and aerated in Krebs ringer phosphate buffer pH 7.2. Tissue was thoroughly washed to remove mucus and lumen contents. Isolated segment of intestine was everted with the help of a glass rod. The everted sac was filled with 5 ml of Krebs ringer phosphate buffer pH 7.2 and both the ends were ligated with the help of silk thread. This gut sac was placed in 50 ml of either Rosuvastatin solution in Krebs ringer phosphate buffer pH 7.2 or Rosuvastatin SMEDDS in Krebs ringer phosphate buffer pH 7.2 with continuous aeration and constant temperature 37±0.5^{0}C. Mixing was performed with the help of magnetic stirrer at 50rpm. Post 60 min aliquot of drug sample was withdrawn from the serosal compartment and accurate volume was noted. Amount of Rosuvastatin permeated was determined by HPLC method as described earlier using suitable blank **[10, 11]**.

Accelerated stability study:

Physical and chemical stability of developed SMEDDS was assessed at 40±2°C/75±5% RH as per ICH guidelines. SMEDDS was filled in clear glass vial, sealed with rubber closure and secured with aluminum cap. Formulation was stored at aforementioned storage condition in stability chamber for 6 months. Required number of samples were removed on 0th, 30th, 60th, 90th and 180th day of stability study and analyzed. Stability samples were evaluated for physical appearance, drug content, self emulsification behavior and dissolution.

Pharmacodynamic Study:

The optimized formulation was selected for pharmacodynamic study. Adult male Wistar albino rats (250-300gm) were used in the study and were divided into three groups with six animals each. Animals were housed in controlled temperature environment. Rats were fasted overnight and were then injected intraperitonially with 350mg/kg Triton WR 1339. Animal dose was selected on the basis of body surface area. Vehicle (plain saline) was administered to control group, Rosuvastatin (0.9mg/kg) was administered to reference

group and SMEDDS equivalent (0.9mg/kg) was administered to test group. Oral administration was performed by oral intubation method by 18 gauge feeding needle. The volume fed was 1ml in all cases. Effect of lipid lowering was studied post 24hrs of administration by retro-orbital puncture. The serum sample was analyzed for total cholesterol, triglycerides, very low density lipoprotein (VLDL) and high density lipoprotein (HDL) level by invitro diagnostic kits (ERBA Pvt. Ltd. Mumbai). Low density lipoprotein levels were estimated using the Friedwal formula.

RESULTS

Solubility study of Rosuvastatin in various oils:

Primary screening of oil for solubility profile was aimed to identify few potential oil from pool of oils which can solubilise the target dose of Rosuvastatin (10mg). Based on primary screening one natural oil (clove oil) and three synthetic oil (Triacetin, captex 355, captex 200) were selected for quantitative estimation of Rosuvastatin solubility.

Solubility of Rosuvastatin in selected oil (mg/gm of oil) was as 27mg in clove oil, 55mg in triacetin, 11.5mg in captex 355 and 11mg in captex 200. Since triacetin can solublize maximum amount of Rosuvastatin itt was selected as the oil phase **(Figure 1)**.

Screening of surfactant:

Emulsification ability of various surfactants was studied to select the best surfactant from the pool of surfactants to spontaneously emulsify selected oil. Based on emulsification ability i.e. number of flask inversion required to produce microemulsion and % Transmittance, as shown in **Table 1** transcutol P was selected as the surfactant for the system.

Screening of Co-surfactant:

Various co-surfactants were screened to improve emulsification ability of transcutol to emulsify triacetin. Number of flask inversion required for formation of microemulsion and % transmittance was the basis for the screening of pool of co-surfactant. Since propylene glycol requires only 10 flask inversion and has 96% of transmittance, it is selected as co-surfactant for the triacetin and transcutol system **(Table 2)**.

Construction of Pseudoternary phase diagram:

From pseudoternary phase diagram it is observed that microemulsion existence area increased as the surfactant concentration is increased till 1:1 (K_m<1) it was observed that the microemulsion existence region goes on decreasing. It is also observed that increasing the Smix ratio increases viscosity of the system and hence flowability **(Figure 2)**. Hence surfactant to co-surfactant ratio of 1:1 is selected for further studies.

Optimization of SMEDDS of Rosuvastatin:

As listed in **Table 3**, all the batches passed freeze thaw cycling, centrifugation test and dispersibility test with % transmittance more than 97%, oil to S_{mix} 1:2 is selected as it contains least amount of surfactant and co-surfactant.

Robustness to dilution:

Physical integrity of microemulsion formed and drug solublization capacity after dilution of SMEDDS must be assessed and ensured as it gives an idea about its performance in vivo **[12]**. In view of this, SMEDDS were diluted with aqueous phases differing in pH. Optimized SMEDDS is robust in distilled water, 0.1N HCl and 6.8 pH phosphate buffer at all the three levels of dilution.

Globule size, polydispersity index and zeta potential:

The mean globule size obtained from optimized SMEDDS of Rosuvastatin was in the range of 10.64nm. The polydispersity index of SMEDDS was 0.324. These findings indicate that, the optimized Rosuvastatin SMEDDS produced fine microemulsion with a small mean size and a narrow particle size distribution. Zeta potential of globules was found to be -0.409 **(Figure 3)**.

Transmission Electron Microscopy (TEM):

TEM images confirm the formation of spherical oil globules of nano size and globules were uniformly distributed. The results of TEM are in agreement to result obtained in particle size **(Figure 5)**.

***In vitro* Drug release study:**

Cumulative amount of drug release at the end of 2 hrs was 38.69% for plain Rosuvastatin and 86.56% for SMEDDS respectively **(Figure 6)**.

Drug Content:

The results obtained were in the range of 99.45% - 102.7% and it indicates that Rosuvastatin in dissolved the and homogenously distributed in self emulsifying drug delivery system **(Figure 7)**.

Ex vivo intestinal permeability study by everted sac technique:

Significant increase in permeability of Rosuvastatin was observed from SMEDDS as compared to plain Rosuvastatin. After 60min of study it was observed that, only 21.23% of Rosuvastatin was transported through intestinal lumen from Rosuvastatin solution, with relative permeability of 3.76µg/cm2**,** while 60.57% of Rosuvastatin was transported through intestinal lumen from microemulsion produce from SMEDDS, with nearly three folds improvement in relative permeability (10.69µg/cm2) formulation.

Accelerated stability study:

Data listed in **Table 4** indicate that formulation is stable.

***In vivo* Study:**

Serum lipid profiles of all the groups after 24 hr interval are presented in **Table 5**. A comparison among group was carried out by one way analysis of variance followed Dunnets test (n=6). $P < 0.05$ was considered significant. In case of Control (plain drug) % decrease in total cholesterol was 27.6% whereas for SMEDDS is 47.54%, % decrease in triglycerite level in case of control was 4.12% and SMEDDS it was 8.66%. % decrease in LDL level for control was 59.27% and for SMEDDS it was 30.86%. % decrease in VLDL level for control was 14.75% and for SMEDDS it was 23.31%. % increase in HDL level for control was 8.13% and for SMEDDS it was 16.24%. Thus results obtained indicate that test formulation (SMEDDS) has performed better than control group (Plain drug) which can be attributed to improved solubility and dissolution rate of the drug.

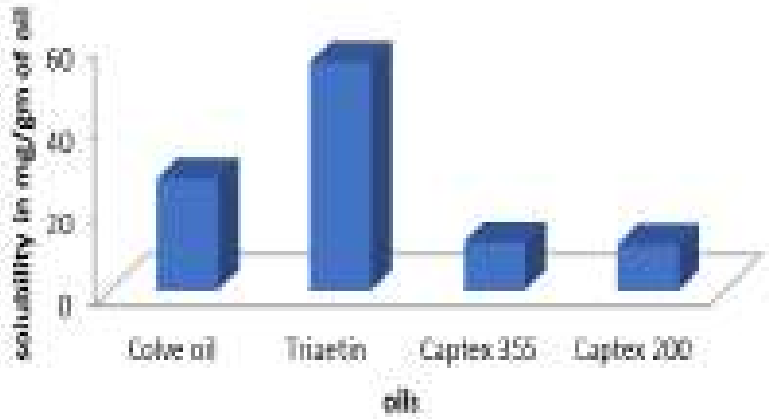

Figure 1: Solubility in selected oil

Table 1: Screening of surfactant

Oil + surfactant	No. of Flask inversion (FI)	% Transmittance	Appearance
Triacetin + Labrasol	15	83.47	Turbid
Triaetin + Lauroglyol fcc	15	76.36	Phase separation
Triaetin + Lauroglyol 90	15	90.54	Phase separation
Triaetin + Transutol P	15	93.49	Clear
Triaetin + Cremophor EL	15	92.41	Clear
Triaetin + Cremophor RH 40	15	92.22	Clear
Triacetin + Capmule MCM	15	76.52	Turbid
Triaetin + Capmule MCM C8	15	73.09	Turbid
Triacetin + Tween 80	15	92.37	Clear
Triaetin + Labrafil 1944	15	64.50	Turbid

Table 2: Screening of co-surfactant

Oil + Surfactant + Cosurfactant	No. of inversions to get clear solution	% Transmittance	Appearance
Triacetin + Transcutol P + Capmule MCM EP	50	73.35	Turbid
Triacetin + Trancutol P + Capmule MCM C8	50	75	Semi Transparent
Triacetin + Trancutol P+ Propylene glyol	10	96	Clear
Triacetin + Trancutol P + Laurogycol fcc	50	65.68	Turbid
Triacetin + Trancutol P + Lauroglyol 90	50	78.99	Phase separation
Triacetin + Trancutol P + Labrafil 1944	50	62.76	Turbid
Triacetin + Trancutol P + Labrafil 2125	50	69.97	Turbid

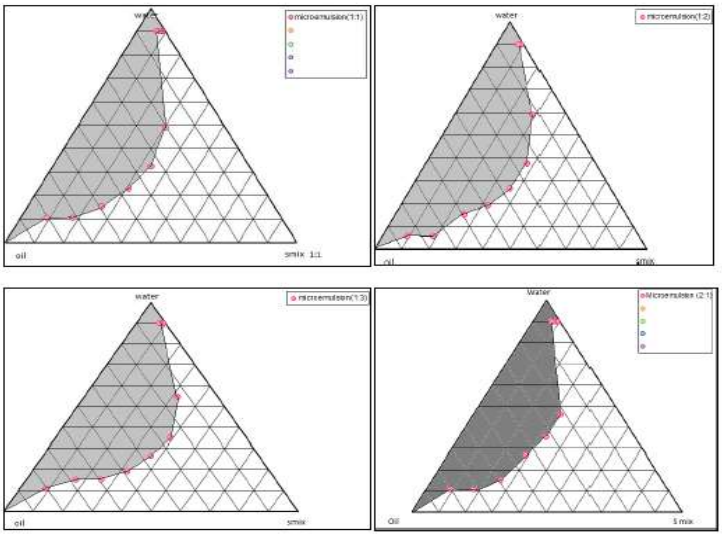

Figure 2: Pseudoternary phase diagram

Table 3: Optimization of SMEDDS

Test and parameter	S1	S2	S3	S4	S5	S6
Ratio Oil: Smix	1:2	1:2.5	1:3	1:3.5	1:4	1:5
Freeze thaw cycle						
1 cycle						
Phase separation	Stable	Stable	Stable	Stable	Stable	Stable
Drug precipitation	Stable	Stable	Stable	Stable	Stable	Stable
2 cycle						
Phase separation	Stable	Stable	Stable	Stable	Stable	Stable
Drug precipitation	Stable	Stable	Stable	Stable	Stable	Stable
3 cycle						
Phase separation	Stable	Stable	Stable	Stable	Stable	Stable
Drug precipitation	Stable	Stable	Stable	Stable	Stable	Stable
Centrifugation test						
Phase separation	Stable	Stable	Stable	Stable	Stable	Stable
Drug precipitation	Stable	Stable	Stable	Stable	Stable	Stable
Dispersibility Test	Good	Good	Good	Good	Good	Good
% Transmittance	97.11	97.5	98.48	98.67	99.76	99.87

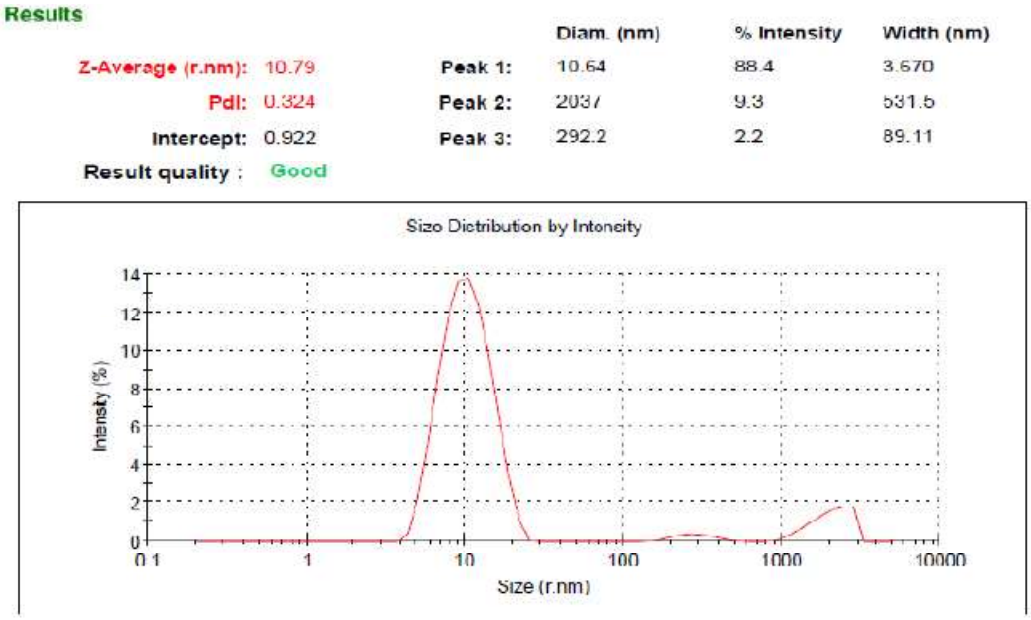

Figure 3: Particle size analysis of optimized batch

Results

		Mean (mV)	Area (%)	Width (mV)
Zeta Potential (mV): 2.14	Peak 1:	-0.409	94.3	4.37
Zeta Deviation (mV): 11.3	Peak 2:	44.8	5.7	2.27
Conductivity (mS/cm): 0.268	Peak 3:	0.00	0.0	0.00

Result quality : Good

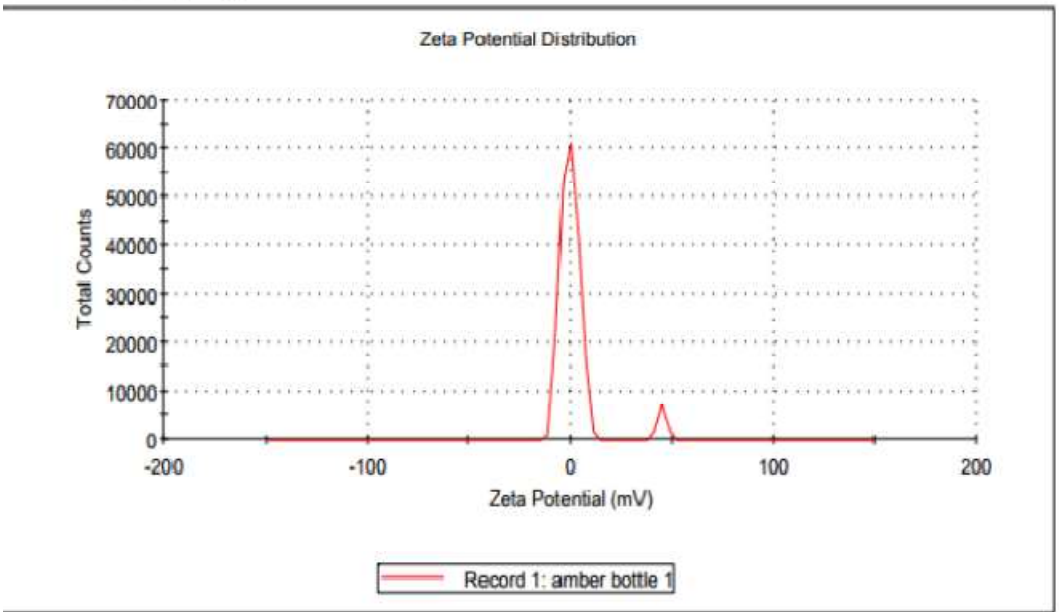

Figure 4: Zeta potential of optimized batch

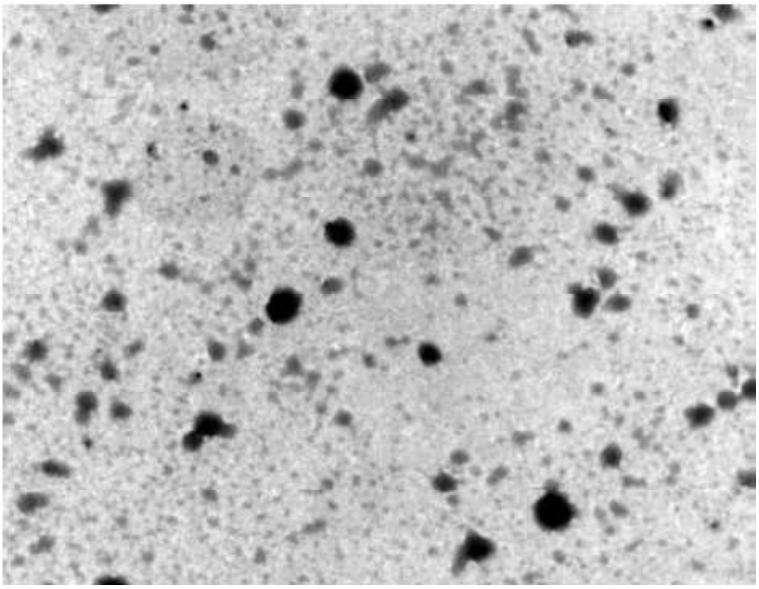

Figure 5: TEM of optimized batch

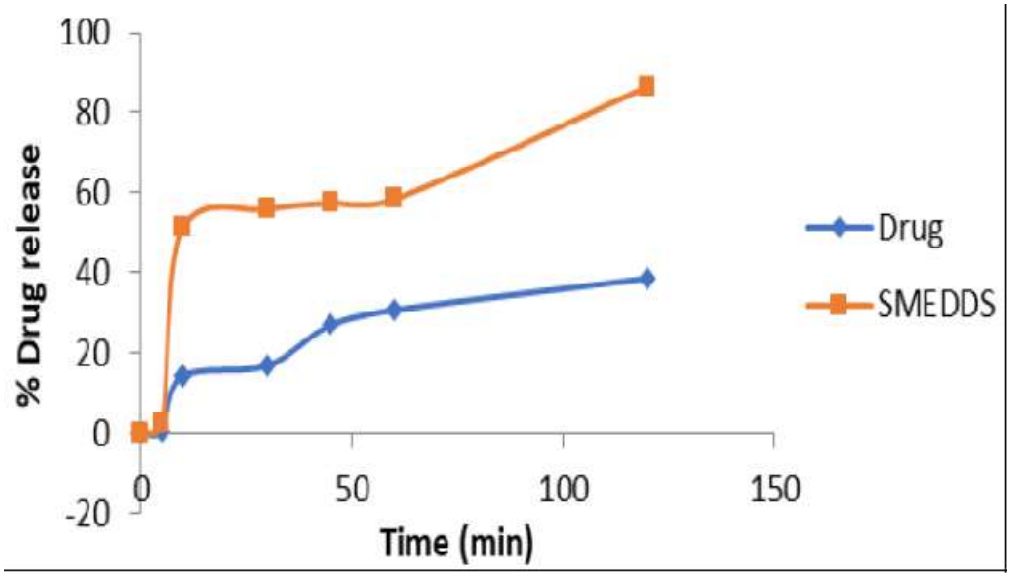

Figure 6: Dissolution profile of SMEDDS and plain drug

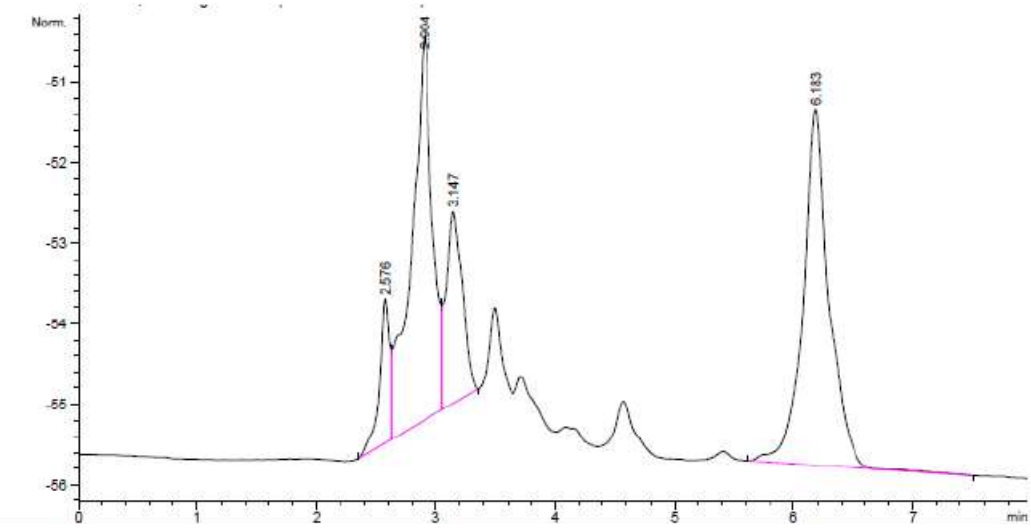

Figure 7: Chromatogram of Rosuvastatin

Table 4: Stability study data of optimized batch

Parameters assessed	Duration				
	0th day	30th day	60th day	90th day	180th day
Physical appearance	Colorless, Clear and Isotropic	Colorless, Clear and Isotropic	Colorless, Clear and Isotropic	Colorless, Clear and Isotropic	Colorless, Clear and Isotropic
Drug content (%)*	102.7	102.3	100.4	101.6	100.1
No. of flask inversion	10	10	10	10	10
Appearance in distilled water	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
% transmittance in distilled water*	97.3	96.9	96.5	96.1	96.8
Dissolution at the end of 2hrs #	87.01%	86.96%	86.91%	86.78%	86.75%

*** Value expressed as mean n=3**
 # Value expressed as mean n=6

Table 5: Lipid lowering profile for *In vivo* Bioavailability study in rats

Parameters	Control (mg/dl)	Plain drug (mg/dl)	% response	Microemulsion (mg/dl)	% response
Total cholesterol	256.01±1.86	185.34±1.09	72.39	134.29±0.37	52.45
Triglycerite	428.03±2.12	410.38±2.03	95.87	391±0.07	91.34
LDL	125.44±3.12	51.09±2.07	40.72	35.32±0.08	63.13
VLDL	28.26±1.03	24.09±3.01	85.24	21.67±1.32	76.68
HDL	62.9± 2.01	68.02±1.5	108.13	73.12±0.9	116.24

DISCUSSION

Solubility study of Rosuvastatin in various oils:

For any stable self- emulsifying drug delivery system solubility of drug in oil is very important and crucial factor. Higher solubility of drug in oil is important to avoid the precipitation of drug on dilution in vivo. Higher the solubility potential of oil phase higher the drug loading capacity of the optimized formulation **(Pouton 2000)**.

Screening of surfactant:

The criteria to select surfactant and co-surfactant to produce optimized SMEDDS formulations should be their efficiency to spontaneously emulsify the selected oil rather than solublising the active **[25]**. Hence it's crucial to select the proper surfactants and co-surfactants which could emulsify the selected oily phases.

Screening of co-surfactant:

Addition of a co-surfactant to the surfactant containing formulation lowers the interfacial tension, fluidizes the hydrocarbon region of the interfacial film and decreases the bending stress of interface which improves the dispersibility and drug absorption from the formulation (Porter et al 2008, Eccleston GM microemulsion encyclopedia of pharmaceutical technology, VOL 9, new York, Marcel Dekker 1992, 375-42)

Construction of Pseudoternary phase diagram:

Self microemulsifying system form fine oil- water emulsion with gentle agitation, upon introduction in aqueous media. Surfactant and co-surfactant preferentially adsorbed at their interface reducing the interfacial energy as well as providing a mechanical barrier to coalescence. The decrease in the free energy required for the emulsion formation consequently improves the thermodynamic stability of the microemulsion formulation. (Finofibrate Vaivia). Therefore selection oil, surfactant and mixing ratio of oil to surfactant: co-surfactant (K_m) play an important role in the formation of the microemulsion. Physical integrity of microemulsion formed and drug solublization capacity after dilution of SMEDDS must be assessed and ensured as it gives an idea about its performance in vivo.

Optimization of SMEDDS of Rosuvastatin:

SMEDDS are thermodynamically stable systems and are formed at a particular concentration of oil, surfactant and Co surfactant, with no phase separation, creaming or cracking. It is the thermo stability which differentiates nano-or microemulsion from emulsions that have kinetic stability and will eventually shows phase separation **[13, 14]**. Thus, the selected formulations were subjected to different thermodynamic stress tests; freeze thaw cycle followed by centrifugation. Those formulations, which survived in thermodynamic stress tests, were evaluated further for their robustness to dilution study.

Globule size, polydispersity index and zeta potential:

The globule size of the emulsion is a crucial factor for self-emulsification performance because it determines the rate and extent of drug release as well as drug absorption. Also, it has been reported that the smaller globule size of the emulsion droplets may lead to more rapid absorption and improve the bioavailability **[15, 16, 17]**. Result obtained indicate that SMEDDS will form uniform microemulsion in biological fluid and will be stable till it gets absorbed **[18, 19]**.

***Ex vivo* intestinal permeability study by everted sac technique:**

This improvement in permeability of Rosuvastatin from SMEDDS was attributed by many reasons mainly the uniformly dispersed globules with nano size in which Rosuvastatin is present in the dissolved state, these fine globule size increases the surface area facilitates the permeability of drug **[19]**.

Stability study:

Physical characteristics and Dissolution remained unchanged after 6 months of accelerated conditions suggesting that SMEDDS of Rosuvastatin is stable. Furthermore there was no sign of phase separation or drug precipitation. Thus stability study confirms the stability of developed formulation.

***In vivo* Study:**

In vivo study was carried to compare pharmacodynamic potential of the developed SMEDDS formulation and plain Rosuvastatin using a Triton induced hyperlipidemia model. Triton is a non ionic surfactant that induces hyperlipidemia by inhibiting peripheral lipoprotein lipase enzyme which is responsible for removing lipid form the body **[20, 21]**. Administration of triton leads to transient increase in lipid levels which reach a peak at 18-24hrs after administration and start to decline following day. The mechanism of action of Rosuvastatin is inhibition of hydroxymethyl glutaryl Co-enzyme A reductase (HMG COA reductase), a rate limiting enzyme is cholesterol synthesis. The higher lipid lowering activity can be

explained by the fact that SMEDDS formulation resulted in complete dissolution of Rosuvastatin and therefore higher bioavailability. The above difference in pharmacodynamic activity and results from *invitro* dissolution and *ex vivo* permeation study suggested improvement in oral bioavailability as compared to plain Rosuvastatin.

CONCLUSION

In conclusion SMEDDS of Rosuvastatin prepared by phase titration method showed significantly higher *invitro* drug dissolution rate. In vivo antihyperlipidemic study on rats showed a higher percent drug inhibition of total cholesterol, triglycerite VLDL, LDL and higher percent increase in HDL levels. This can be explained by improvement in bioavailability by enhancement in rate and extent of drug release. Thus Developed formulation can be used as a possible alternative to traditional oral formulation of Rosuvastatin to improve its bioavailability.

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CONFLICT OF INTEREST

None

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