

DEVELOPMENT AND IN-VIVO CHARACTERIZATION OF SMEDDS (SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM) FOR GEMFIBROZIL

RONAK N PATEL*, DHEERAJ TBAVISKAR, AMARJIT P RAJPUT

KVPS Institute of pharmaceutical education, Department of Pharmaceutics, Boradi. Tal Shirpur, Dist- Dhule, 425428 (MH)
Email: rnkpatel777@gmail.com*

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ABSTRACT

Objective: The intention of this study was to extend self-microemulsifying drug delivery system (SMEDDS) to improve the oral bioavailability of the defectively water-soluble drug, gemfibrozil and evaluating its *in vitro* and *in vivo* potential. The persuade of the oil, surfactant and co-surfactant types on the drug solubility and their proportion on forming competent and established SMEDDS were investigated in aspect.

Methods: Evaluation of microemulsification existence area through pseudoternary phase diagrams and *in vitro* dissolution test was investigated for release rate of gemfibrozil. SMEDDS formulations were tested for microemulsifying properties, and the consequential microemulsions were evaluated for clarity, precipitation, and particle size distribution. Based on result obtained from phase diagram and characteristics of resultant microemulsion, formulation development and screening was done.

Results: The optimized formulation for *in vitro* dissolution and pharmacodynamic studies was composed of Labrafac CM10 (31.5%), Cremophor EL (47.3%), and polyethylene glycol 400 (12.7%). As compared with the plain drug, SMEDDS formulation showed complete release in 14 minutes. In terms of lipid-lowering efficacy, comparative pharmacodynamic evaluation was investigated using a Triton-induced hypercholesterolemia model in rats. The SMEDDS formulation significantly decreased serum lipid levels in phases I and II of the Triton test, as compared with plain gemfibrozil. As per International Conference on Harmonization (ICH) guidelines the optimized formulation was then subjected to stability studies and was found to be stable over 12 months.

Conclusion: Thus, the study established that the SMEDDS formulation can be used as a possible alternative to traditional oral formulations of gemfibrozil to improve its bioavailability.

Keywords: Gemfibrozil, Pseudoternary phase diagrams, SMEDDS, Triton-induced hyperlipidemia.

INTRODUCTION

The oral route is the most physiologically favourable and easily accepted by patients. Therefore, it is essential to develop substitute oral routes of administration to improve the bioavailability of poorly water-soluble drugs, and additionally obtain more successful therapeutic effects. The use of self-microemulsifying drug delivery system (SMEDDS) is one of the most fascinating approaches to improving the solubility, dissolution and oral absorption for poorly water-soluble drugs [1-4].

Gemfibrozil (Fig. 1) is a lipid-regulating agent that has chemical, pharmacological, and clinical similarities to the fibrate drugs [5]. Gemfibrozil is a Biopharmaceutical Classification System (BCS) Class II drug with a high dose number. Thus, it can be assumed that the low oral bioavailability of gemfibrozil is due to its solubility and dissolution limitations [6]. Researchers have tried different methods (e.g., cyclodextrin complexation, micronization, solid dispersion) to overcome these restrictions [7-9]. Furthermore, it is reported that absorption of gemfibrozil is increased by ~35% when it is administered with food relatively than in a fasting state [5, 10].

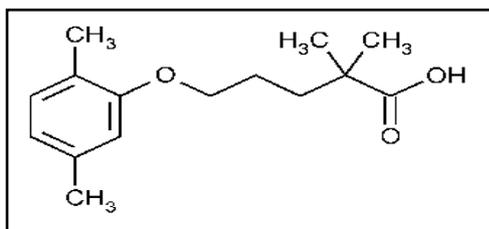


Fig. 1: Chemical structure of Gemfibrozil. [5, 10]

A commercially available SMEDDS preparation is Neoral® (cyclosporine A). Now, much more attention has been persistent on SMEDDS due to its exceptional effectiveness in delivering poorly water-soluble drugs and achieving an increase in bioavailability. SMEDDS are isotropic mixtures of oil, surfactant, co-surfactant, and

drug substance. Microemulsion can be generated rapidly upon gentle mixing with water or aqueous media. It is thought that the microemulsion is instinctively formed by the combined action of the specific pharmaceutical excipients with low free energy. The microemulsion droplets dispersed in the gastrointestinal tract provide large surface area and promote a rapid release of dissolved form of the drug substance and/or miscellaneous micelles containing drug substance, and they may be also liable for transporting the drug throughout the unstirred water layer to the gastrointestinal membrane for absorption. In addition to the enhanced dissolution of drugs by SMEDDS, another factor contributing to the increasing bioavailability is that lymphatic transportation is responsible for a portion of the entire drug uptake as well. The lipid composition of SMEDDS may be linked to facilitate the extent of lymphatic drug transport by stimulating lipoprotein configuration and intestinal lymphatic liquid flux [11, 12]. Over the past decades, SMEDDS have been comprehensively investigated to deliver various kinds of drugs [13-17]. Furthermore, SMEDDS offer various advantages such as decrease in inter and intra subject pharmacokinetic inconsistency, improvement in lymphatic transport and GI permeability and reversal of P-gp efflux, all of which help in recovering bioavailability of hydrophobic drugs [16, 18, 19].

The main objectives of the nearby study were to develop a SMEDDS formulation of gemfibrozil to improve its oral bioavailability.

MATERIALS AND METHODS

Chemicals and reagents

Gemfibrozil was received as a gift sample from Sun pharmaceutical industries Limited, Vadodara, India with a purity of 98.2%. Labrafac CM10, Maisine 35-1, Lauroglycol FCC, Labrafac M1944 CS, and Labrafac PG. Cremophor RH 40, Cremophor EL, and Solutol HS and Gelucire 50/13 were received from Colorcon Asia (Mumbai, India). Span 20, Cremophor EL, and PEG 400 were bought from Merck (Mumbai, India). Acetonitrile and methanol used in the present study were of high performance liquid chromatography (HPLC) grade. All other chemicals were reagent grade. Empty hard

gelatin capsule shells were generously donated by ACG Capsules (Mumbai).

Animals

Male Holtzman rats (weighing approximately 250±30 g) were used for the comparative lipid-lowering studies. The animals were maintained at a constant light (14L: 10D), temperature (24°C-25°C), and humidity (60%) and were supplied with food and water ad libitum. The animal requirement was approved by the Institute Animal Ethics Committee (IAEC), and all experiments were conducted as per the norms of the Committee for the Purpose of Supervision of Experiments on Animals, India.

Solubility studies

The solubility of gemfibrozil in various oils, surfactants, and cosurfactants was measured, correspondingly. An excess amount of gemfibrozil was added into each selected vehicle, and the mixture was constantly stirred for 72 h at 30 °C. After equilibrium was achieved, the mixture was centrifuged at 2500×g for 20 min, and the supernatant was filtered through a membrane filter. The concentration of gemfibrozil was determined by high-performance liquid chromatography (HPLC).

Pseudoternary phase diagrams

Construction of pseudoternary phase diagrams of oil, surfactant/cosurfactant (S/CoS), and water were developed using

the water titration technique. The mixtures of oil and S/CoS at certain weight ratios were diluted by water in a dropwise manner. For each one phase diagram at a precise ratio of S/CoS (ie, 1:1, 2:1, 3:1, and 5:1 wt/wt), a transparent and homogenous mixture of oil and S/CoS was produced by vortexing for 5 minutes. Then each mixture was titrated through water and visually observed for phase clarity and flowability. The amount 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. To determine the effect of drug addition on the microemulsion, phase diagrams were constructed in the presence of drug using drug-enriched oil as the hydrophobic element.

Preparation of SMEDDS formulations

A series of SMEDDS formulations were prepared using Cremophor EL and PEG 400 as the S/CoS mixture and Labrafac CM10 as the oil (Table 1). In all the formulations, the intensity of gemfibrozil was kept constant (ie, 8.5% wt/wt of the total formulation weight). Briefly, perfectly weighed gemfibrozil was placed in a glass vial, and oil, surfactant, and cosurfactant were added. Then the components were mixed by moderate stirring and vortex mixing and were heated at 40°C on a magnetic stirrer, until gemfibrozil was completely dissolved. The mixture was stored at room temperature until further utilize.

Table 1: Developed formulations with their compositions

Components (% wt/wt)	Batch							
	A	B	C	D	E	F	G	H
Gemfibrozil	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5
Labrafac CM10	27.5	28.5	29.5	30.5	31.5	30.5	31.5	31.5
Cremophor EL	48.25	47.50	46.75	46.00	45.25	46.71	46.67	46.30
PEG 400	15.75	15.50	15.25	15.00	14.75	14.29	14.33	13.70
S/CoS ratio	3:1	3:1	3:1	3:1	3:1	3.2:1	3.5:1	3.7:1

Freeze thawing

Freeze thawing was employed to evaluate the stability of formulations. The formulations were subjected to 3 to 4 freeze-thaw cycles, which included freezing at -4°C for 24 hours followed by thawing at 40°C for 24 hours. Centrifugation was performed at 3000 rpm for 5 minutes. The formulations were then observed for phase separation. Only formulations that were stable to phase separation were selected for further studies.

Emulsion droplet size analysis

One hundred microliters of every SMEDDS formulation was diluted to 250 mL in a beaker and lightly mixed by a glass rod. The consequential emulsion was then subjected to particle size analysis using Malvern Mastersizer with a particle size measurement range of 0.02 to 2000 µm. Particle size was calculated from the volume range distribution. All studies were repeated in triplicate, with excellent agreement being found between measurements.

Self-emulsification and precipitation assessment

Estimation of the self-emulsifying properties of SMEDDS formulations was performed by visual assessment as earlier reported. [15] In brief, altered compositions were categorized on speed of emulsification, transparency, and visible stability of the resultant emulsion. Visual evaluation was performed by dropwise accumulation of the concentrate (SMEDDS) into 250 mL of distilled water. This was prepared in a glass beaker at room temperature, and the contents were quietly stirred magnetically at ~100 rpm.

Precipitation was evaluated by visual assessment of the resultant emulsion after 24 hours. The formulations were then characterized as clear (transparent with bluish tinge), nonclear (turbid), stable (no precipitation at the end of 24 hours), or unstable (precipitation within 24 hours).

In vitro dissolution studies

The quantitative *in vitro* release test was performed in 900 mL of buffer pH 1.2 by USP Pharmacopeia XXIV dissolution apparatus II. The paddles were rotated at 100 rpm. The SMEDDS formulations were placed into hard gelatin capsules (0 sizes) and used for drug release studies; results were compared with those of plain gemfibrozil. During the release studies, a 5-mL sample of medium was taken out and subjected to drug analysis using HPLC. The removed volume was replaced each time with 5 mL of fresh medium. For determination of the *in vitro* dissolution of plain gemfibrozil, the medium was changed to buffer pH 1.2 containing cremophor EL (equal to the amount used in the formulation). Dissolution studies were also performed in other medium (buffer pH 4.5 and 7.2) to observe the effect of pH on drug release.

HPLC analysis

For the solubility, the loading content and the *in vitro* release studies, HPLC method was used for the analysis of Gemfibrozil. Samples were properly diluted by isopropyl alcohol and directly injected (20 µL) into the HPLC system without further treatment. Agilent HPLC system equipped with low pressure quaternary gradient pump along with photo diode array (PDA) detector and manual rheodyne sample injector has been used for the study of samples. The data was collected and processed using Ezichrom Elite software. A reverse phase C18 (250×4.5 mm) BDS column was used at room temperature with the chromatographic conditions were mobile phase acetonitrile:water (80:20% vol/vol); flow rate 1 mL/min; loop size 100 µL; detection at 289 nm; and retention time 7.5 ± 0.5 minutes.

Lipid-lowering studies

Male Holtzman rats (weighing 250 ± 30 gm) were used for the study. They were kept in air-conditioned rooms (24°C-25°C) with stable humidity. The rats were caged and allowed water and food ad

libitum prior they were distributed by weight into experimental groups. The rats fasted for the night and were then intraperitoneally injected with 250 mg/kg Triton WR 1339 (Tyloxapol, Sigma Chemical Co, St. Louis, MO) dissolved in 0.9 percent saline. Control groups of rats were given the vehicle (pure saline), and experimental groups were given plain gemfibrozil (9 mg/kg body weight) or the SMEDDS formulation (equivalent to 9 mg/kg gemfibrozil). Without anesthesia and by restraining rats by hand, the oral dosing was performed by intubation using an 18-gauge feeding needle (the volume to be fed was 1.0 mL in all cases). Blood samples were drawn at 0, 24 and 48 hours. Serum was removed by centrifugation at 10 000 g and used for biochemical investigation. Serum cholesterol and triglycerides were estimated in normal, control, and drug-treated groups by reported methods. [20]. Low-density lipoprotein (LDL) levels were estimated using the Friedwal formula. Statistical analysis of the collected data was performed by 1-way analysis of variance.

Stability studies

The SMEDDS formulations were put into empty hard gelatine capsules (size 0) and subjected to stability studies at 25°C/60% relative humidity (RH). Samples were charged in stability chambers with humidity and temperature control. They were withdrawn at specified intervals for investigation over a period of 6 months for intermediate and accelerated conditions and 12 months for long-term situation. Drug content of the capsules was analyzed using a previously developed and validated stability-indicating HPLC method.

RESULTS AND DISCUSSION

Solubility studies

The consideration for screening formulation of SMEDDS usually involves: the formulation composition should be simple, secure, and compatible; it should acquire good solubility; a large proficient self-microemulsification region which should be found in the pseudo-ternary phase diagram, and have competent droplet size following forming microemulsion [4, 21-23].

PEG indicates polyethylene glycol. [4, 21-23]

Appropriate vehicles should have good solubilizing capability of the drug substance, which is essential for composing a SMEDDS. The

results of solubility of gemfibrozil in several vehicles were shown in (Fig.2). The drug loading capability is the main factor when screening the oil phase. As seen from the (Fig.2), maisine 35-1 and labrafac CM10 showed the highest solubilisation capacity for gemfibrozil, followed by cremophor EL and PEG 400. Thus, for our study we selected maisine 35-1 and labrafac CM10 as oils and cremophor EL and PEG 400 as surfactant and cosurfactant, correspondingly.

Pseudoternary phase diagrams

Self-microemulsifying systems form fine oil-water emulsions with only mild agitation, upon their introduction into aqueous media. Surfactant and cosurfactant get preferentially adsorbed at the interface, falling the interfacial energy as well as provide a mechanical barrier to coalescence. The decrease in the free energy essential for the emulsion formation consequently improves the thermodynamic stability of the microemulsion formulation [24, 25]. Therefore, the assortment of oil and surfactant, and the mixing ratio of oil to S/CoS, play an significant role in the formation of the microemulsion. In the present study both Maisine 35-1 and Labrafac CM10 were tested for phase behaviour studies with cremophor EL and PEG 400 as the S/CoS mixture. As seen from the ternary plot (Fig. 3 and 4), Labrafac CM10 gave a wider microemulsion region than Maisine 35-1 at all S/CoS ratios. Thus, Labrafac CM10 was selected as the ideal vehicle for the optimized formulation. The microemulsion survival area increased as the S/CoS ratio increased. However, it was observed that increasing the surfactant proportion resulted in a loss of flowability. Thus, an S/CoS ratio between 3:1 and 4:1 was selected for the formulation study. PEG 400 is reported to be incompatible with hard gelatine capsules when used in elevated concentrations [26]. Thus, while optimizing the S/CoS ratio, we tried to keep the concentration of PEG 400 as low as possible (<15% wt/wt of whole formulation), as we had a final aim of putting the SMEDDS formulations into liquid-filled hard gelatin capsules. (Fig.5) shows phase diagrams in the presence of the drug. As seen from the (Figure 5), the inclusion of drug pointed the microemulsion existence area, because addition of the drug in the lipid phase led to development of the lipid phase and consequently a need for a higher S/CoS ratio for stabilization.

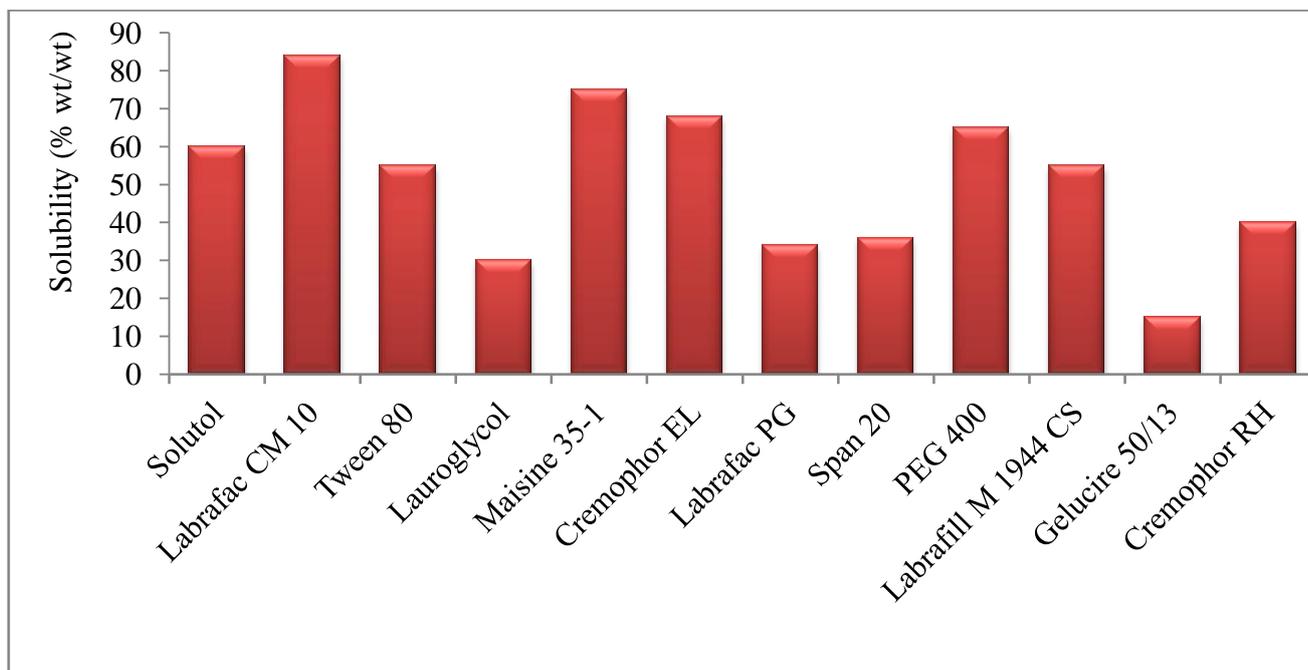


Fig. 2: Solubility of gemfibrozil in various components.

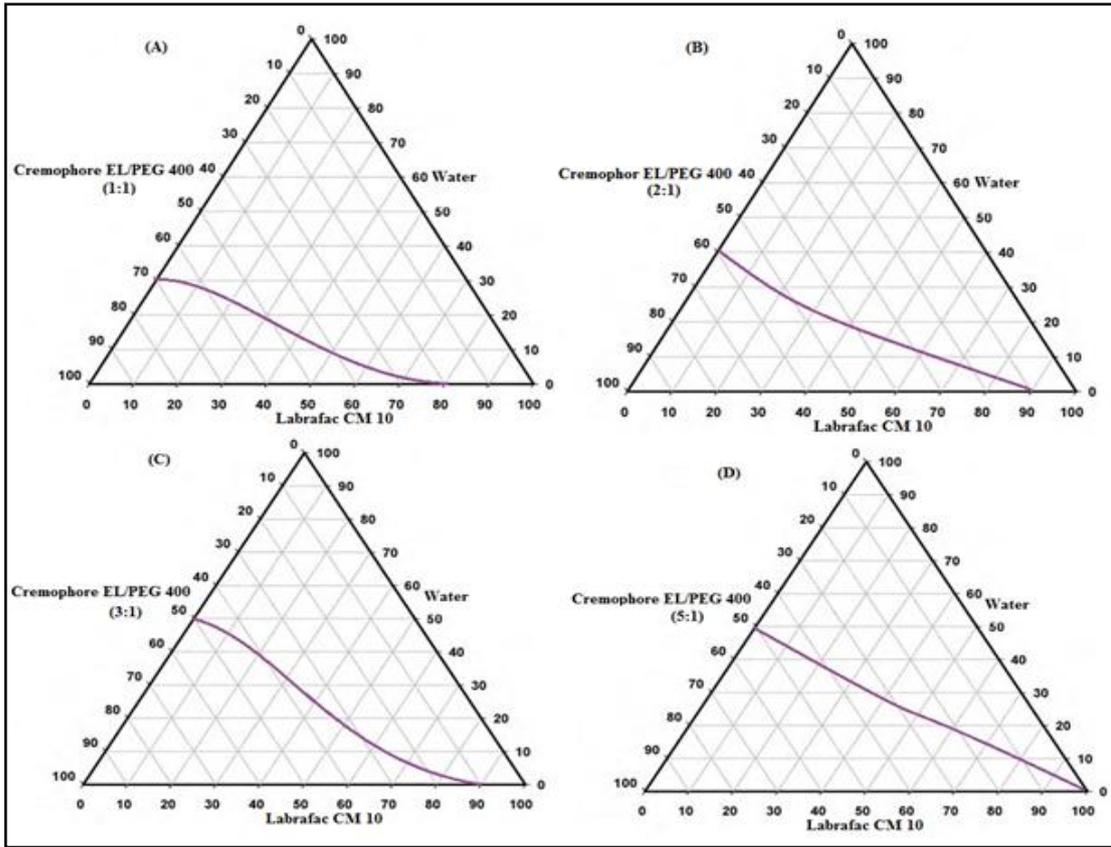


Fig. 3: Pseudoternary phase diagram of system.

S/CoS ratio of A is 1:1, B is 2:1, C is 3:1, and D is 5:1. [24, 25]

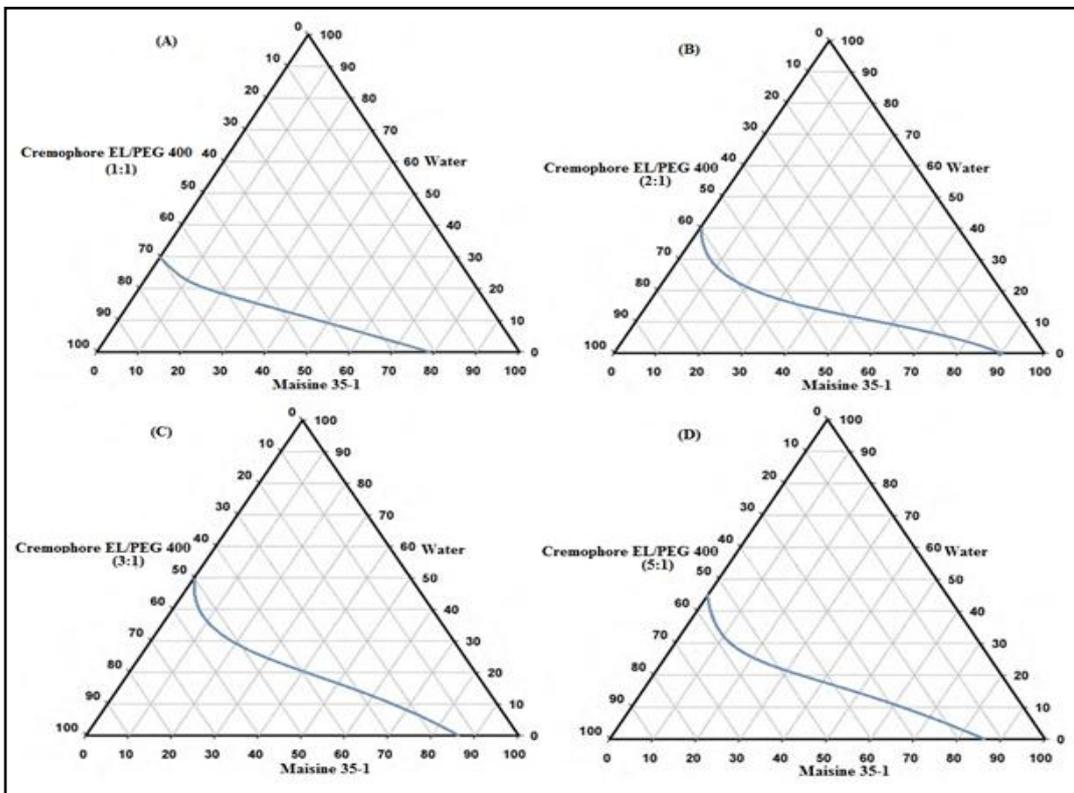


Fig. 4: Pseudoternary phase diagram of system.

S/CoS ratio of A is 1:1, B is 2:1, C is 3:1, and D is 5:1. [24, 25]

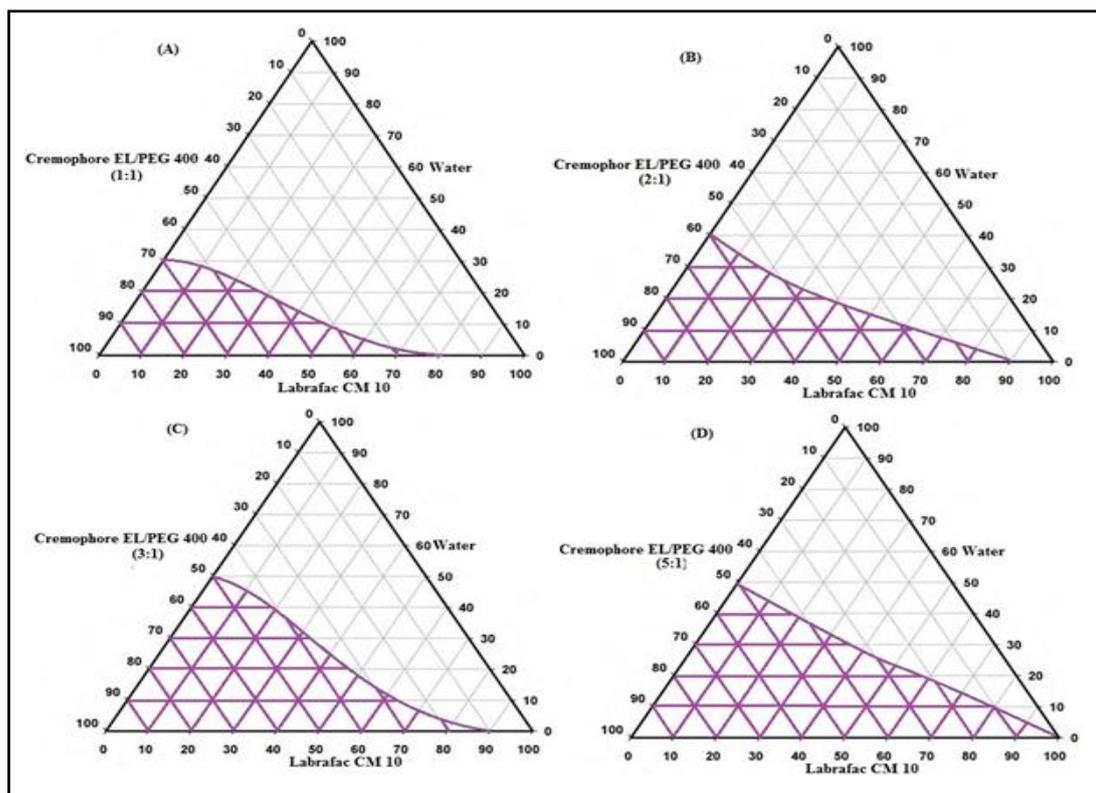


Fig. 5: Pseudoternary phase diagram of system with the following components:

oil = drug-enriched labrafac CM10, surfactant = cremophor EL, and cosurfactant = PEG 400.

S/CoS ratio of A is 1:1, B is 2:1, C is 3:1, and D is 5:1.[24, 25]

Droplet size analysis

The droplet size distribution of different formulations is given in (Table 2). An increase in the proportion of the oil phase (Labrafac CM10) resulted in a relative increase in particle size, because of the simultaneous decrease in the S/CoS ratio. Increase the S/CoS ratio led to a decrease in mean droplet size. Batch H, with the maximum proportion of surfactant (47.3% wt/wt cremophor EL) at a fixed amount of oil (31.5% wt/wt), had the smallest mean particle diameter. This could be attributed to an increased surfactant ratio relative to cosurfactant. It is recognized that the addition of surfactants to the microemulsion systems causes the interfacial film to stabilize and condense, while the addition of cosurfactant causes the film to expand; thus, the relative proportion of surfactant to cosurfactant has different effects on the droplet size [1,27].

Self-emulsification and precipitation studies

The results of self-emulsification and precipitation studies are specified in (Table 2). It was seen that an increase in the ratio of

Labrafac CM10 in the composition resulted in decreasing self-emulsification time up to a concentration of 31.5% wt/wt, beyond which it resulted in generation of non clear dispersion. The reduction in self-emulsification time can be assumed to be due to the relative decrease in surfactant concentration, leading to decreased viscosity of the formulation. The S/CoS ratio of 3:1 was kept stable for the initial formulation study. However, it was found that the resultant dispersion showed precipitation and thus was not stable, because of the existence of PEG 400. PEG 400 can be assumed to act as a cosolvent for gemfibrozil (as seen from solubility studies), and thus it increases the solubilisation capability of the vehicle (Labrafac CM10). However, when the pre concentrate (SMEDDS) is dispersed in water, PEG400, being water-soluble, is anticipated to enter the water phase and reorganize mainly between the water phase and the emulsion-water interface, resulting in a loss of solvent ability of the vehicle. A similar surveillance was reported for a composition containing ethanol as the cosolvent [28, 29]. Thus, the difficulty of precipitation was solved by increasing the surfactant ratio (S/CoS 3.7:1) in the system.

Table 2: Evaluation parameters of various formulations

Formulations	Particle Size Distribution(μm)			Time (secs)	Clarity	Precipitation
	D (0.1)	D (0.5)	D (0.9)			
A	0.113	0.156	0.209	98 \pm 5	Clear	Unstable
B	0.124	0.167	0.217	78 \pm 3	Clear	Unstable
C	0.128	0.175	0.226	67 \pm 2	Clear	Unstable
D	0.133	0.180	0.249	51 \pm 3	Clear	Unstable
E	0.159	0.201	0.357	55 \pm 4	Nonclear	-----
F	0.131	0.179	0.242	52 \pm 1	Clear	Unstable
G	0.129	0.171	0.239	59 \pm 4	Clear	Unstable
H	0.119	0.161	0.229	58 \pm 2	Clear	Stable

In Vitro Dissolution Studies

Drug release from the SMEDDS formulation Batch H (Fig. 6-B) was established to be significantly higher as compared with that of plain gemfibrozil (Fig. 6-A). It could be suggested that the SMEDDS formulation resulted in spontaneous formation of a microemulsion with a small droplet size, which permitted a faster rate of drug release into the aqueous phase, much faster than that of plain gemfibrozil. Thus, this better availability of dissolved gemfibrozil from the SMEDDS formulation could lead to higher absorption and higher oral bioavailability. It was also seen that changes in the dissolution medium (buffer pH 1.2, 4.5, and 7.2) had no effect on the drug release from either plain gemfibrozil or the SMEDDS formulation (Fig. 6-A & B). This study can be explained by the fact that gemfibrozil has no ionizable group and thus its solubility and dissolution is not depend on pH.

Lipid lowering studies

The study was performed to estimate the pharmacodynamic potential of a developed formulation (Batch H) against plain gemfibrozil by a Triton-induced hyperlipidemia model. Triton is a non-ionic surfactant that induces hyperlipidemia through inhibiting peripheral lipoprotein lipase enzymes liable for removal of lipid

particles from body [24].The administration of triton promotes to brief elevation of lipid levels, which reach a peak at 18 to 24 hours following administration (phase I) and start to lower again the after day (phase II)[30, 31]. This experimental model has been earlier used for screening the activity of the antilipidemic mediator bezafibrate [32].Thus, for our current study this method was used to estimate the lipid-lowering activity of the developed formulation. The defined mechanism by which gemfibrozil exerts its hypolipidemic effect has not been clearly established. It was observed that gemfibrozil and its formulation were found to influence the serum lipid level in both phase I and phase II.(Fig. 7-A) shown the effect of treatments on serum lipid levels in phase I (24 hours). Gemfibrozil produced a reduce in serum cholesterol (53.50% inhibition), triglyceride (60.21% inhibition),and LDL (55.51% inhibition). The SMEDDS formulation, as expected, performed better than gemfibrozil, resulting in a significant reduction of serum cholesterol(91.39% inhibition), triglycerides (91.13% inhibition), and LDL levels (91.22% inhibition).It has been noted that there is a usual tapering in cholesterol and triglyceride values in phase II of the Triton test. However, this normal clearance of serum lipid in phase II of the Triton test can also be triggered by the existence of a drug in the circulation [26]. Gemfibrozil is known to have a longer stay in the blood circulation, as it has a biological half-life of 20 hours[33].

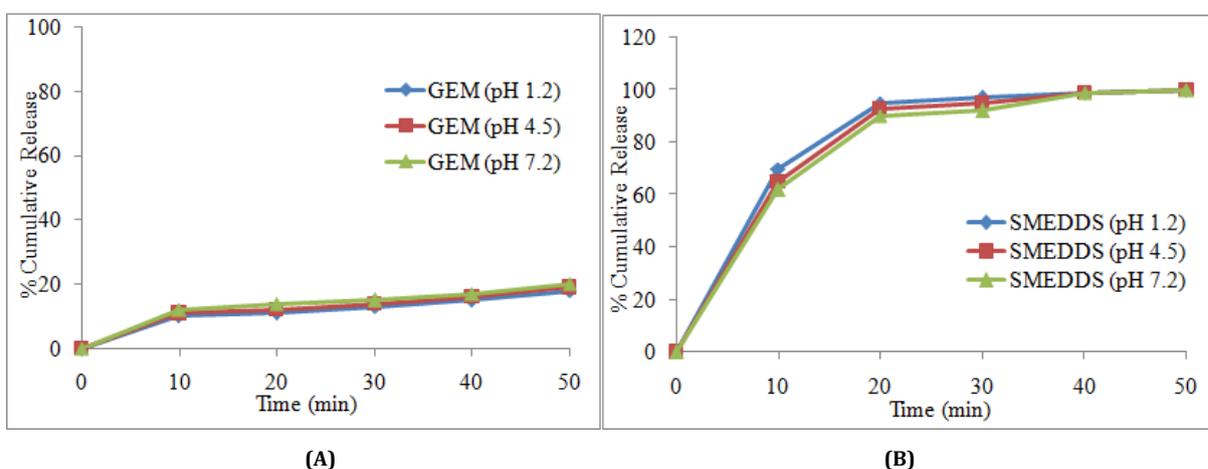


Fig. 6: Results of drug release from (A) plain Gemfibrozil and (B) SMEDDS formulation in different dissolution media; n = 6 and range of variability = 1% to 3%. GEM indicates plain Gemfibrozil;SMEDDS indicates self-microemulsifying drug delivery system.

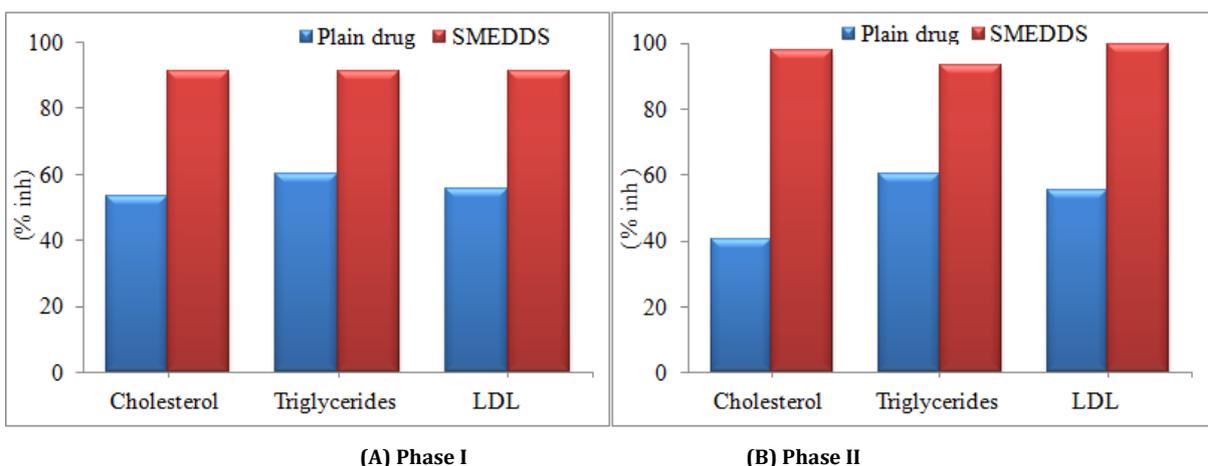


Fig. 7: Effect of Treatment on Serum Lipids in (A) Phase I and (B) Phase II of Triton Test.

LDL indicates low-density lipoprotein

SMEDDS indicates self-microemulsifying drug delivery system

We furthermore evaluated the effect of gemfibrozil and the SMEDDS formulation in phase II of the Triton test. As seen from (Fig. 7-B),

plain gemfibrozil lowered cholesterol(40.54% inhibition), triglyceride (60.24% inhibition), and LDL(55.40% inhibition). The SMEDDS formulation resulted in a greater reduction of cholesterol (97.84% inhibition), triglyceride(93.46% inhibition), and LDL (99.5% inhibition)Thus, the higher lipid-lowering activity of the

SMEDDS formulation in both phase I and phase II of the triton test can be explained by the fact that the SMEDDS formulation resulted in absolute dissolution of gemfibrozil, which could have increased absorption and thereby led to a higher plasma drug concentration (higher bioavailability). The above difference in pharmacodynamic activity and the results from *in vitro* dissolution studies thus suggest that the SMEDDS formulation resulted in higher oral bioavailability due to higher solubilization of gemfibrozil from the SMEDDS formulation as compared with plain gem fibrozil.

Stability Studies

Generally, SMEDDS formulations are put into hard gelatine capsules as the final dosage form. However, liquid-filled hard gelatin capsules are susceptible to leakage, and the entire system has a very limited shelf life due to its liquid characteristics and the opportunity of precipitation of the drug from the system. Thus, the developed formulation was subjected to stability studies to estimate its stability

and the integrity of the dosage form. (Table 3) gives the results of the evaluation test conducted on stability samples. The formulation was found to be stable for 6 months at intermediate and accelerated conditions and 12 months at long-term conditions. There was no considerable change in the drug content, drug release (t_{90}), or particle size of the resultant emulsion. It was also seen that the formulation was compatible with the hard gelatin capsule shells, as there was no sign of capsule shell deformation. There were also no significant changes in the appearance, disintegration time, or microemulsifying property. Additionally, the formulation was found to show no phase separation, drug precipitation, or capsule leaks. Thus, these studies confirmed the stability of the developed formulation and its compatibility with hard gelatin capsules. In practice, the key difference between emulsions and microemulsions are that the former, whilst they may exhibit excellent kinetic stability, are fundamentally thermodynamically unstable and will eventually phase separate. [34]

Table 3: Evaluation Data of SMEDDS Formulation Subjected to Stability Studies (n = 10)*

Evaluation Data	Sampling Point				
	0 Days	3 Months	6 Months	9 Months	12 Month
Weight Variation (mg)	623 ± 4	632 ± 4	630 ± 5	633 ± 4	636 ± 2
Disintegration Time (min)	3.8 ± 1.1	4.1 ± 0.9	4.5 ± 1.3	4.0 ± 0.5	4.1 ± 1.2
% Drug Content	100.5 ± 0.7	98.9 ± 2.7	97.8 ± 3.1	96.7 ± 3.7	94.6 ± 0.8
Particle Size D (0.9 µm)	0.250	0.246	0.261	0.240	0.250
t ₉₀ % (min)	<15	<15	<15	<15	<15

CONCLUSIONS

An optimized SMEDDS formulation consisting of Labrafac CM10 (31.5% wt/wt), Cremophor EL (46.13% wt/wt), PEG 400 (13.7% wt/wt), and gemfibrozil (8.5% wt/wt) was successfully developed with an increased dissolution rate, solubility, and bioavailability of a poorly water-soluble drug, gemfibrozil. The developed formulation showed advanced pharmacodynamic potential as compared with plain gemfibrozil. Results from stability studies established the stability of the developed formulation. Thus, our study confirmed that the SMEDDS formulation can be used as a possible alternative to traditional oral formulations of gemfibrozil to improve its bioavailability.

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