RESEARCH ARTICLE

Formulation and Evaluation of Fenofibrate Dry Emulsion Tablets by Freeze Drying Method

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ABSTRACT

Fenofibrate (FF) is a lipid-lowering agent classified in the biopharmaceutics classification system (BCS) class II with lower solubility and higher permeability. This research work deals with developing FF containing liquid self-micro emulsifying drug delivery system (L-SMEDDS) and converting it into solid SMEDDS (S-SMEDDS) using a lyophilization technique followed by the manufacturing of tablets with enhanced solubility and dissolution rate. L-SMEDDS of FF were manufactured using Tween 80, oleic acid, and transcutol. With the help of the lyophilization technique, this L-SMEDDS was converted to S-SMEDDS using microcrystalline cellulose and finally, immediate-release tablets were developed using S-SMEDDS. The L-SMEDDS showed excellent stability due to zeta potential of -1.69 mV and a globule size of 250 µm. The lyophilized S-SMEDDS of FF showed nearly 58-fold solubility enhancement in distilled water in comparison to pure FF due to the formation of amorphous material confirmed in the X-ray diffraction (XRD) study. The F9 formulation showed 100% drug release within 40 minutes with enhanced dissolution properties compared to conventional tablets. The optimized formulation was robust and stable at the accelerated condition for 3 months. The current research work demonstrates lyophilization as a potential approach to convert the L-SMEDSS to a S-SMEDDS with an enhanced solubility and dissolution rate.

Keywords: Dissolution, Fenofibrate, Lyophilization, Microemulsion, Solubility.

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INTRODUCTION

Self-microemulsifying drug delivery system (SMEDDS) consists of oral solid or liquid dosage forms along with a combination of oil, surfactants, and co-surfactants.[1] Such dosage forms are applicable for poorly soluble drugs showing incomplete absorption.[2] After oral administration, it reaches the aqueous environment of the gastrointestinal tract (GIT) and forms a fine nano-emulsion (O/W). Due to gastric intestinal motility, it gives agitation to generate emulsion. Self-emulsifying drug delivery systems (SEDDS) shows enhancement in absorption and *in-vitro* dissolution rate of bio pharmaceutics classification system (BCS II) and IV drugs. This dosage form has benefits, including targeted drug delivery to the GIT and defense against the stomach's unfavorable environment. Conventional SMDDS are mostly formulated in liquid form.[3] Lipid-based drug carriers may affect bioavailability by improving the drug's solubilization in the GIT to minimize the variation in systemic exposures to a tractable level.[4] When a well-designed lipidic drug delivery is diluted with aqueous media, the drug can be transferred from the molecular dispersion it is presented in the formulation to the mixed micellar system.[4] Approximately 40% of newly found medications/investigational drugs have very less aqueous solubility and fall under BCS class II. (Highly permeable and low soluble). Due to their reduced bioavailability during the dissolution process, these weakly water-soluble drugs continue to provide a problem for current drug delivery research.[4, 5] The SEDDS are unsatisfactory due to their liquid form because of the issues with filling and the palatability of the oily liquid throughout the initial stages of development into a soft gelatin capsule. These issues are some of the things that made it difficult for technology-based products to be commercialised.[6] Several pharmaceutical dosage forms are available in soft gelatin capsules with liquid inside that contain medications, including cyclosporine A, ritonavir, and saquinavir.[7]

Fenofibrate (FF) is lipid lowering agent which is used in the treatment of hyperlipoproteinemias[8]. FF shows bioavailability problems due to poor water and physiological fluids solubility (Practically insoluble in water, BCS II drugs). The use of FF is limited in the pharmaceutical industry because of solubility issues.[8] Different approaches were tried to enhance FF's solubility and bioavailability profile by formulating

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SEDDS. Xiumin, Li *et al*., manufactured a SMEDDS of FF to improve the bioavailability.[9] Gamal Shazly *et al*., developed solid SEDDS of fenofibrate using an inorganic high-surface adsorption material to improve the dissolution properties.[10] Shah and Serajuddin developed solid SEDDS of FF and probucol using poloxamer 188 as a solidifier and emulsifier.[11]

Solid SEDDS (S-SEDDS) at ambient temperature are semi-solid or solid and these are used to manufacture nanoparticles, powders, or more solid dose forms.[12] S-SEDDS combines the benefits of solid formulations, including improved stability, easy processing, lower manufacturing cost, and enhanced solubility and bioavailability.[13] S-SEDDS are formulated by liquid loading techniques. They may have the combined advantages of solid dosage form and liquid SDDS (improved solubility and bioavailability).[12]

So far, research on this topic is limited to developing compressible tablets containing fenofibrate drug. We have performed this research work to manufacture SMEDDS and then converted it into solid SMEDDS with the help of the lyophilization technique. This consideration of making solid SMEDDS has many advantages improving solubility, dissolution, and bioavailability enhancement of fenofibrate. A solid system enhances patient compliance and stability.

MATERIALS AND METHODS

Materials

Fenofibrate (FF) was obtained as a gift sample from Cipla, Mumbai India. Kolliphor RH 40, Cremophore RH 40, PEG 400, PEG 300, castor oil, oleic acid, etc., were purchased from BASF, Mumbai. Microcrystalline cellulose, CCS, talc and magnesium stearate were purchased from BASF Mumbai India.

Methods

FF Solubility Study

Excess amount of FF was dissolved separately into 5 mL of different oils (castor oil, oleic acid, virgin coconut oil, isopropyl myristate, soyabean oil), surfactant (tween 60, tween 80, span 80), co-surfactant (PEG 400, PEG 300, transcutol P, span 20), and vortexed it for 15 minutes followed by centrifugation at 12000 rpm for 20 minutes. The supernatant obtained was filtered through the membrane filter (MF-Millipore™ 0.45 µm) to remove the remaining insoluble drug. The supernatant was diluted with methanol and the absorbance of the supernatant was checked by UV analysis.[9]

Surfactant Emulsification Study

To select the surfactant, this study was performed. Oil and surfactant mixed at ratios from 1:9 to 9:1 with constant stirring to get a homogeneous mixture of the component. The distilled water was mixed with the oil and surfactant mixture before being visually inspected. As a result of the observation of the spontaneity of emulsification, the ratio of oil to surfactant was chosen.[9]

Co-surfactant Emulsification Study

This study was performed for the selection of oil: S-mix. The surfactant as well as co-surfactant were allowed to mix at varying concentrations (1:1, 1:2, 2:1). The water titration method was used to titrate the oil and S-mix combinations, and the endpoints at which emulsification was seen were reported. The quantity of water required to form the emulsion was noted.[9]

Pseudo-ternary Phase Diagram

The S-mix (surfactant and co-surfactant - 1:1, 1:2, 2:1) and oil ratios were fixed by the water titration method. The ternary phase diagram was plotted with three variables: oil, S-mix, and water, and the region with microemulsion was chosen.

Formulation and Optimization of L-SMEDDS

For the preparation of liquid SMEDDS 50 mg of FF was dissolved in oleic acid, Tween 80, and transcutol HP with a volume ratio of 43:28.5:28.5, respectively. The final mixture was stirred with a magnetic stirrer to get a clear solution. Further, the appearance of sign of turbidity or phase separation was examined.[4]

Characterization of Optimized Formulation of FF-loaded L-SMEDDS

pH and density

The pH of liquid SMEDDS was determined using calibrated pH meter (Lab India PICO^{+}). Density is mass per unit volume of L-SMEDDS. Density was measured by using a density measurement bottle

Viscosity

A Brookfield viscometer was utilized to determine the viscosity of SMEDDS. Spindle 7 was lowered perpendicularly into the sample after the formulation had been deposited in the sample container. The ideal speed was maintained for the spindle's rotation. At room temperature, the formulation's viscosity was measured with an angular velocity that was gradually increased from 0.5 to 20 rpm.

Zeta potential

Malvern zeta sizer ZS 90 was used to determine the zeta potential of the L-SMEDDS at a temperature of 25°C.

% Transmittance

UV spectroscopy identified the % transmittance of L-SMEDDS formulation by measuring the absorbances at 286 nm.

Self Micro-emulsifying time

It was evaluated by adding liquid SMEDDS into 6.8 phosphate buffer by stirring at 50 rpm using USP type II dissolution test apparatus (Lab India DS 8000) and the time of dispersion was recorded.[14]

Cloud Point Measurement:

L-SMEDDS was kept in a water bath and the temperature was allowed to raise gradually. The mixture was diluted at ratio of 1:250 with distilled water. The temperature at which clouds suddenly became visible was noted and considered as cloud point.[14]

Conductivity measurement

The conductivity of the liquid SMEDDS was evaluated by using a conductivity meter. A conductivity measurement test

Table 1: Tablet formulation batches of FF-loaded S-SMEDDS

Name of Ingredients	*Qty (mg/tablet)*								
	F1	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*	*F8*	*F9*
S-SMEDD eq. to 100 mg of FF	150	150	150	150	150	150	150	150	150
MCC	95	93.75	92.5	91.25	90	88.75	87.5	86.25	85
Croscarmellose sodium	1.25	2.5	3.75	5	6.25	7.5	8.75	10	11.25
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Mg stearate	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Total Weight	250	250	250	250	250	250	250	250	250

was performed to determine the micro-emulsions electro-conductivity nature, which identifies its nature such as o/w or w/o type of micro-emulsion.[14]

Centrifugation

Liquid SMEDDS formulation was introduced to centrifuge apparatus (Bio Lab BLD-165) to determine phase separation in the formulation by centrifugation method. Liquid SMEDDS were centrifuged at 3500 rpm for 30 minutes.

Formulation of S-SMEDDS from L-SMEDDS by Lyophilisation

Lyophilization is a form of freeze drying in which the water content present in the formulation is eliminated following freezing (primary drying) and then subjected to vacuum (secondary drying), enabling the frozen product to solidify by converting ice into solid without first going through the liquid phase. For the first three days of the primary drying process, the L- SMEDDS with 1% of trehalose as cryoprotectant was filled in glass vials and kept in a deep freezer at -40°C. SMEDDS were lyophilized for 72 hours using a lyophilizer (LABCONCO FreeZone 2.5). The dried powder so obtained was used for further characterization.[15]

Characterization of S-SMEDDS

Drug Content

FF content was determined by dissolving S-SMEDDS in methanol (100 mL). The resulting solution was filtered through syringe filter to get clear solution and analyzed at 286 nm using UV spectroscopy.

Scanning Electron Microscope

The morphological characteristics of the S-SMEDDS were observed by SEM at a distance of 8.6–8.7 mm. The SEM was used with a 1.0 kV accelerating voltage

X-Ray Diffraction

Philips PAN analytical expert Shimadzu XRD-7000 (Japan) was used to determine whether it was crystalline or amorphous in nature X-ray scattering measurements were carried out.

Differential Scanning Calorimeter Analysis

DSC study of pure FF and lyophilized S-SMEDDS of FF was performed using DSC (Hitachi 9020). Approximately 1–3 mg of FF and S-SMEDDS samples were placed on a heated aluminium pan at a nitrogen flow rate of 50 mL/min at a heating temperature of 10°C/min. Thermal analysis of data was then conducted with a DSC thermogram.

Saturation Solubility of Pure FF and S-SMEDDS of FF

The saturation solubility of the pure FF and S-SMEDDS of FF was determined in distilled water (DW). An excess amount of pure FF drug and S-SMEDDS of FF was added to 10 mL of DW and the solution was stirred for a period of 24 hours at the temperature of 37°C. The samples were withdrawn and filtered using a membrane filter to get a clear solution. The samples were analysed using UV spectroscopy at 286 nm. The saturation solubilities of the both pure FF and S-SMEDDS of FF were determined and compared.[16]

Angle of Repose

The powder material was poured through funnel to create a pile with a circular base to measure the angle of repose. The pile's height and the base's radius are measured for additional computations.

$\text{Tan}(\theta) = h/r$

Bulk Density (BD)

The BD of the lyophilized S-SMEDDS was estimated by pouring a predetermined weight sample in glass cylinder and volume occupied by the sample was noted down. The following formula was used to determine the BD

BD = Powder weight / Bulk volume

Tapped Density (TD)

Tapping the measuring cylinder prepared granules determined TD until constant volume is achieved. TD was determined by using formula.

TD= Powder weight / Tapped volume.

Carr's Index (CI)

The CI of the powder material was determined by using the following formula

CI = TD – BD / TD

Hausner's Ratio (HR)

HR of the powder material was determined by using the following formula

HR = TD / BD

Formulation of Tablets from Solid SMEDDS

The tablets were manufactured by direct compression of the excipients. All excipients were weighed properly as per the batch quantity. Lyophilised S-SMEDDS equivalent to 100 mg of FF was properly mixed with other ingredients (MCC and CCS) in a polybag. Magnesium stearate and talc were passed through sieve no.60, added to blend

containing FF, and blended properly for 5–10 minutes. The lubricated blend was compressed using 8 mm punch on Cadmach 16-station tablet compression machine. The formula of all batches is represented in Table 1.

Characterization of Tablets[17]

Thickness

For the determination of diameter and thickness digital vernier caliper was used. This was done by selecting 10 tablets randomly from each batch and thickness was measured in mm.

Hardness

The hardness of the tablets was measured on randomly selected ten tablets using the Stokes Monsanto hardness tester. The average, as well as the standard deviation, was calculated.

Friability

For this test, 20 tablets were chosen at random from individual batches, and the test was run for 100 rotations on an automatic friabilator. The weight of dedusted tablets was recorded and friability was determined and calculated as the mean of three determinations. The tablets with less than 1 % weight loss were usually deemed suitable**.**

Content uniformity

A content uniformity test was conducted according to USP protocol on 10 tablets randomly selected from each batch. These tablets were subjected to crushing and kept in a buffer having pH 1.2 for 24 hours to equilibrate. Filtration was done through a 0.45 µm filter followed by appropriate dilution to estimate FF by using UV spectroscopy

Weight Variation

The official procedure was used to calculate the weight variation of each batch. randomly, 20 tablets were chosen and their weights were measured accurately in mg. The mean, as well as standard deviations, were determined.

Disintegration Test

The DT of the manufactured tablets was carried out in disintegration test apparatus containing 900 mL of DW (37 ± 0.5°C). The disintegration time was noted when no visible residue of the tablet left in the DT apparatus. The time was noted in seconds.

In-vitro Dissolution Studies

USP Type II dissolution test apparatus was used to determine the drug release in 900 mL pH 6.8 PBS buffer (37 ± 0.5°C; 25 rpm). The samples (5 mL) were withdrawn at a predetermined time interval and the same volume of buffer was added to maintain the sink condition. The samples were analyzed using UV spectrophotometer at 286 nm wavelength and drug release was determined at each time point.

Stability Studies

The F9 formulation was loaded for accelerated stability study based on their acceptable disintegration time, hardness, thickness, weight variation, dissolution, and content uniformity. For the selected formulation, the formulation was loaded at 40ºC/75%RH for 3 months. After every month, the samples were analyzed results were noted down.

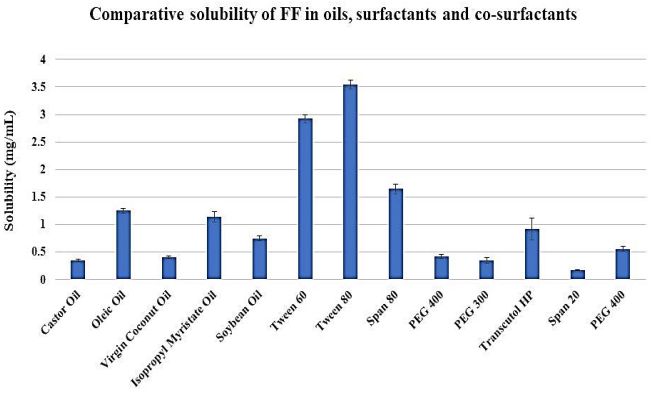

Figure 1: Comparative solubility of FF in oils, surfactants, and co-surfactants

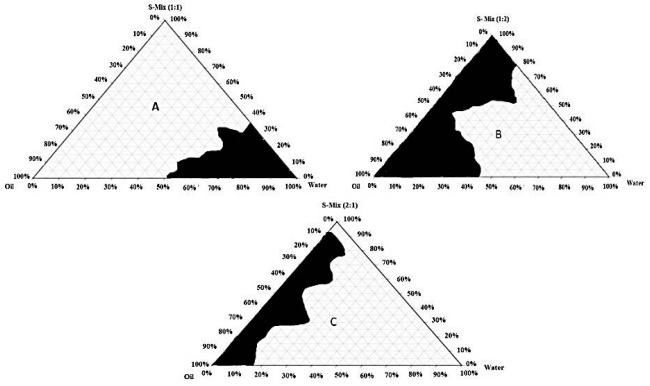

Figure 2: Pseudoternary Phase Diagram A) S-Mix (1:1), B) S-Mix (1:2), C) S-Mix (2:1)

RESULTS AND DISCUSSION

Solubility Study of FF

Among all the oils tested, oleic oil showed the highest solubility of 1.25 ± 0.32 mg/mL. In the case of surfactants, the FF exhibited the highest solubility in tween 80 (3.54 ± 0.43) while among co-surfactants, transcutol HP showed the highest solubility of 0.92 ± 0.15 mg/mL. The comparative solubility of FF in different oils, surfactants, and co-surfactants is represented in Figure 1**.**

Through pseudo ternary phase diagram, it was found that an s-mix with a 1:1 ratio of the concentration of surfactant and co-surfactant gives an appropriate region of the o/w type of microemulsion. Figure 2 represents the phase diagram where A) S-Mix (1:1) B) S-mix (1:2), and C) S-mix (2:1).

Physicochemical Characterization of L-SMEDDS

The pH of liquid FF SMEDDS was found to be 7.8 and had a viscosity of 420 cps while density of 0.719 g/mL was observed. The value of zeta potential of liquid SMEDDS of FF was found to be -1.69 mV, indicating good quality and stability of microemulsion and rapid emulsification of microemulsion. The ideal range of zeta potential as per official documents ranges

Table 2: % Drug content of SMEDDS Formulation

Sr. No.	*Drug Content (%w/w)*
1	100.37 ± 0.86
2	99.67 ± 2.61
3	98.63 ± 1.85
4	101.53 ± 2.00

between -30 to +30 mV.[18] The globule size of the microemulsion was found to be 250 microns. The %T value was found to be nearly 92% which indicates good transparency. It was found that the time required for emulsification of liquid FF SMEDDS was 1.34 ± 0.12 minutes. The cloud point was found to be 66.9°C indicating excellent stability of the formulation at room temperature. The conductivity of SMEDDS formulation was reported 23.3 ± 0.01 µS/cm indicating that formulation is o/w type microemulsion. It was concluded that no phase separation was observed in the formulation during the centrifugation test. Overall, the developed L-SMEDDS was found to have desirable physicochemical properties.

Characterization of S-SMEDDS

Drug Content

Results that adhere to the range of 95–110% w/w of FF in SMEDDS formulation are listed in Table 2.

SEM

SEM technique confirmed the surface structure and morphology of the FF and formulated FF loaded SMEDDS. Optimized fenofibrate loaded SMEDDS as the photograph showed particles on the surface were smooth and rod in size**.** Figure 3 shows an SEM image of FF API and FF-loaded SMEDDS.

XRD

To determine the crystalline or amorphous nature of the pure FF and lyophilized S-SMEDDS XRD study was performed. Pure FF exhibited sharp and high-intensity peaks at a diffraction angle (2θ) at 14.3°, 16.1°, 22.2°, 30.5°, and 35.3° confirming the crystalline nature. The XRD diffractogram of lyophilized S-SMEDDS showed reduced peak intensities at different diffraction angle, suggesting the amorphous characteristics. The considerable improvement in the dissolution rates and therefore the bioavailability by FF SMEDDS formulation can be attributed to this marked decrease in peak intensities. Figures 4 show the XRD diffractograms of pure FF and S-SMEDDS of FF.

DSC

The thermal analysis of pure FF exhibited a sharp endothermic peak at 80.9°C correlating to the melting point of FF (Figure 5A). The freeze-dried S-SMEDDS of FF reveal an endothermic peak at 190.7°C (Figure 5B). The slight change in the endothermic peak demonstrated the proper encapsulation of FF in SMEDDS.

Saturation Solubility of Pure FF and S-SMEDDS of FF

The use of FF is restricted due to lesser aqueous solubility and it belongs to BCS class II and has bioavailability issues. In our

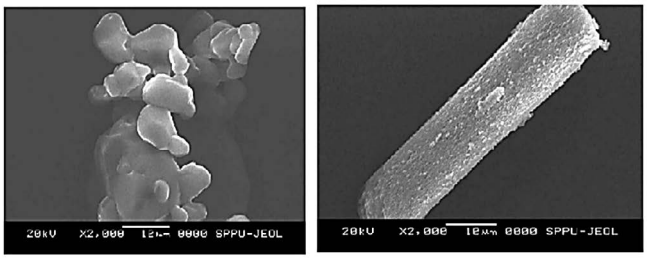

Figure 3: SEM image of Fenofibrate API and Fenofibrate loaded SEMDDS

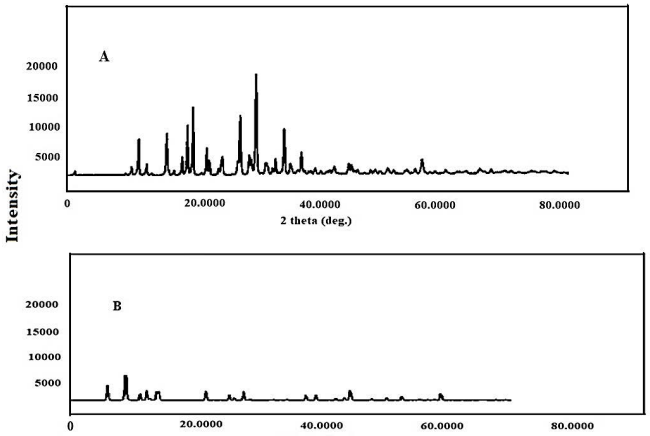

Figure 4: X-RD graph for pure FF (A) and S-SMEDDS of FF (B)

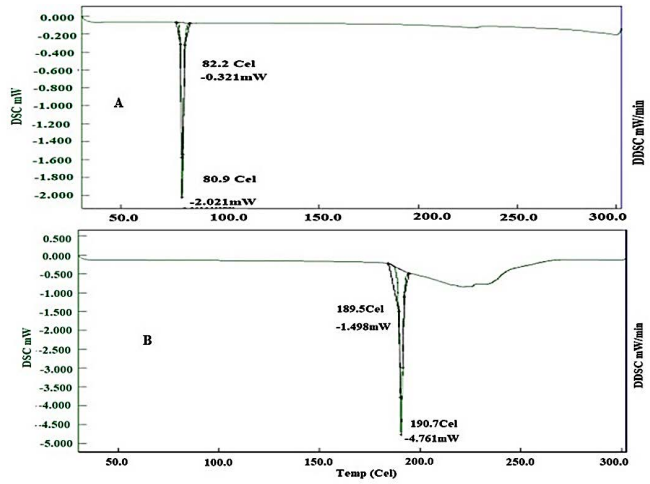

Figure 5: DSC thermogram of pure FF (A) and FF-loaded S-SMEDDS (B)

experiment, the saturation solubility of the FF in distilled water was found to be 0.707 µg/mL while freeze-dried S-SMEDDS of FF had shown tremendous enhancement in saturation solubility (4.5 µg/mL). Nearly 58-fold enhancement in the solubility of FF was observed with freeze-dried S-SMEDDS. The comparative solubility profiles of pure FF and freeze-dried S-SMEDDS are presented in Figure 6**.** This solubility enhancement was due to the formation of amorphous powder of the freeze-dried S-SMEDDS of FF.[19]

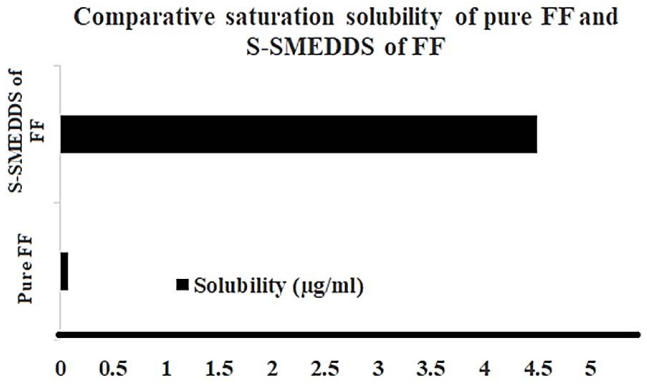

Figure 6: Saturation solubility of the pure FF and FF-loaded S-SMEDDS

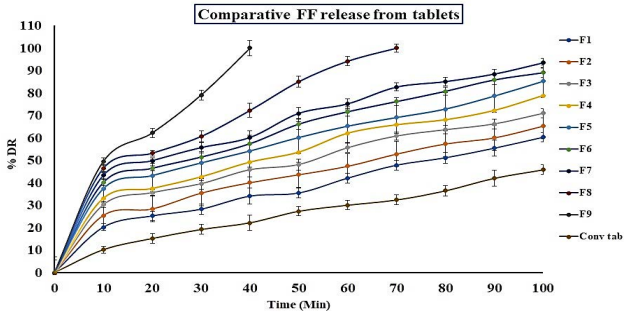

Figure 7: Comparative cumulative % drug release from tablets manufactured with S-SMEDDS of lyophilization and conventional tablet

Flow Properties of Freeze-dried S-SMEDDS

The flow properties of the powder play a very important role during pharmaceutical product development. Excellent flow properties are highly desirable for manufacturing solid oral dosage forms. The BD of the S-SMEDDS was found to be 0.445 g/mL while TD was 0.821 g/mL. The angle of repose was 240 while CI was 8 (< 10); hence, the granules had excellent flow properties. The HR was found to be 1.05 (1.00–1.11); hence, the granules have excellent flow properties.[20] The flow properties of the freeze-dried S-SMEDDS powder were excellent, and such powder materials could be used in manufacturing tablet dosage form.

Evaluation of Tablets containing S-SMEDDS of FF

Various physio chemical parameters are presented in Table 3. The thickness ranged from 2.1 ± 0.07 to 3.2 ± 0.06 mm while hardness was found between 49 ± 0.15 to 62 ± 0.24 N. The friability in all batches was also found to be within an acceptable range (should not be more than 1%). The friability ranged between 0.46 ± 0.38 to 0.75 ± 0.11%. The tablets showed excellent weight uniformity, lying between 0.65 ± 0.11 to 0.77 ± 0.20 %. The average weight of tablets did not deviate more than 5% w/w and none of the tablets deviated by 10% w/w of average weight, indicating compliance with the weight variation test. No wide variation (95.11 ± 1.5 to 99.08 ± 0.24) was observed for FF content in all the batches it was due to the uniformity of the weights of the tablets. The DT of the tablets was found to be dependent on the concentration of the CCS and it ranged between 62 to 150 seconds. All physical parameters were found to be within an acceptable range.

In-vitro Dissolution Study

The compressed tablets were evaluated for dissolution studies in pH 6.8 PBS buffer. To understand the effect of freeze-dried S-SMEDDS, a conventional tablet without freeze-dried S-SMEDDS was also formulated, and in vitro dissolution test was performed. It has been observed that the tablets containing freeze-dried S-SMEDDS showed a rapid release of FF in comparison to a conventional tablet. Among all the batches tested, the F9 formulation showed very excellent immediate release characteristics with 100% FF release within 40 minutes.

The presence of both CCS and S-SMEDDS of FF contributed to the fast disintegration and dissolution profile. The rapid bursting of the tablet was observed during dissolution due to the presence of CCS. In addition, the tablet's S-SMEDDS component also played a very important role in solubilizing the FF in pH 6.8 PBS buffer. Increased solubility caused FF to release more quickly in the buffer. Table 4 and Figure 7 show the comparative dissolution profile from all batches.

Stability Study

The optimized tablet formulation (F9) was studied for the accelerated stability (40ºC/75%RH) study for 3 months. All physicochemical parameters tested at each time point did not

Table 3: Physicho chemical characterization of tablets

Formulation	*Thickness (mm)*	*Hardness (N)*	*Uniformity of weight (%)*	*Friability %*	*Total FF content*	*DT (Sec)*
F1	2.5 ± 0.09	60 ± 0.51	0.77 ± 0.20	0.65 ± 0.12	96.08 ± 0.29	150
F2	3.1 ± 0.04	49 ± 0.15	0.75 ± 0.32	0.66 ± 0.21	95.11 ± 1.5	145
F3	3.2 ± 0.06	62 ± 0.24	0.69 ± 0.24	0.59 ± 0.11	98.4 ± 0.24	133
F4	2.9 ± 0.04	55 ± 0.27	0.71 ± 0.21	0.65 ± 0.27	96.11 ± 0.56	121
F5	3.0 ± 0.10	58 ± 0.12	0.65 ± 0.11	0.70 ± 0.45	98.37 ± 1.5	115
F6	2.8 ± 0.04	50 ± 0.21	0.72 ± 0.25	0.75 ± 0.11	95.21 ± 1.9	100
F7	2.6 ± 0.03	52 ± 0.47	0.69 ± 0.25	0.49 ± 0.47	96.77 ± 0.24	91
F8	2.7 ± 0.04	51 ± 0.27	0.73 ± 0.11	0.52 ± 0.46	97.11 ± 0.27	81
F9	2.1 ± 0.07	62 ± 0.24	0.75 ± 0.14	0.46 ± 0.38	99.08 ± 0.24	62

Table 4: Observations of *in-vitro* dissolution studies

Time (min)	*Batch*									
	F1	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*	*F8*	*F9*	*Conv tab*
0	0	0	0	0	0	0	0	0	0	0
10	20.25	25.51	30.24	33.11	37.42	40.16	43.34	46.46	49.51	10.25
20	25.3	28.42	35.67	37.51	43.26	46.51	49.9	53.21	62.23	15.24
30	28.29	35.46	39.65	42.67	48.9	51.51	55.71	60.67	79.11	19.27
40	34.11	40.11	45.87	49.26	54.2	57.47	60.21	72.26	100	22.25
50	35.51	43.67	48.21	53.71	60.2	66.2	70.97	85.11		27.41
60	42.11	47.45	55.67	62.11	65.26	71.71	75.2	94.2		30.12
70	47.9	52.89	60.9	65.89	69.11	76.24	82.67	100		32.45
80	51.18	57.41	63.71	68.12	72.87	80.82	85.11			36.52
90	55.46	60.11	66.29	72.27	78.65	85.9	88.46			42.11
100	60.31	65.34	71	78.9	85.23	89.11	93.45			45.9

Table 5: Stability studies of Dry emulsion tablet (F9 formulation) stored at 40ºC/75%RH

Sr. no.	*Parameters (F9)*	*40ºC/75%RH*			
		Initial	*1M*	*2M*	*3M*
1	Disintegration time in water (sec)	62	65	63	69
2	Hardness(N)	62 ± 0.24	59 ± 0.37	65 ± 0.11	64 ± 0.71
3	Thickness (mm)	2.1 ± 0.07	2.2 ± 0.04	2.2 ± 0.07	2.1 ± 0.05
4	Weight variation (%)	0.75 ± 0.14	0.73 ± 0.24	0.74 ± 0.43	0.75 ± 0.21
5	Assay (%)	99.08 ± 0.24	99.6 ± 0.50	99.047 ± 0.51	98.5 ± 0.51
6	DR at 40 min (%)	100	99.0	98.5	99.0

show any significant changes with initial parameters. The formulation was found robust and stable over 3 months. The comparative stability study results are presented in Table 5.

CONCLUSION

The current research work confirmed the successful development of tablets containing dry emulsion with enhanced solubility and dissolution of FF. The conversion of L-SMEDDS to S-SMEDDS using the lyophilization technique was a potential alternative approach to form amorphous powder with enhanced solubility and dissolution profiles. The S-SMEDDS showed a 58-fold enhancement in solubility in comparison to pure FF. The tablets manufactured with lyophilized S-SMEDDS of FF showed an immediate release profile as compared to conventional tablets. The optimized formulation exhibited excellent stability and for 3 months. The present study demonstrates lyophilization as a potential approach to convert the L- SMEDSS to a solid form with an enhanced solubility and dissolution rate.

Conflict of interest

Authors do not report any conflict of interest with respect to this research work

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