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# Formulation and Evaluation of Self-Emulsifying Drug Delivery System of Orlistat

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## ABSTRACT

The objective of this study was to develop self-emulsifying drug delivery system (SEDDS) to enhance the solubility of the poorly water-soluble drug Orlistat. Orlistat is class II molecule according to BCS (Biopharmaceutical Classification System), having low solubility and low permeability. The rate and extent of absorption of class II compounds is highly dependent on the performance of the formulated product. These drugs can be successfully formulated for oral administration, but care needs to be taken with formulation design to ensure consistent bioavailability. Solubility of Orlistat was evaluated in various nonaqueous carriers that included oils, surfactants, and cosurfactants. Pseudoternary phase diagrams were constructed to identify the self-microemulsification region. Self microemulsifying formulations were prepared using mixtures of oils, surfactants, and cosurfactants in various proportions. The self microemulsification properties, droplet size and thermodynamic stability of these formulations were studied upon dilution with water. The optimized liquid SMEDDS formulation was converted into free flowing powder by adsorbing onto a solid carrier for encapsulation. The dissolution characteristics of solid intermediates of SMEDDS filled into hard gelatin capsules were investigated and compared with pure drug and commercial formulation. The results indicated that solid intermediates showed the rate and extent of drug dissolution for solid intermediates were significantly higher than commercial formulation. The results of the study demonstrated the potential use of SMEDDS as a means of improving solubility, dissolution and concomitantly the bioavailability.

**Keywords:** Lipid formulations, Particle size**,** SMEDDS, Solubility, Orlistat

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## INTRODUCTION

Dyslipidemia is a disorder of lipoprotein metabolism. Dyslipidemia is the elevation of plasma cholesterol, triglycerides, or both. It can also be manifested by the elevation of low-density lipoprotein (LDL), cholesterol and the decrease of high-density lipoprotein (HDL) cholesterol in the blood. Dyslipidemia is a primary risk factor that contributes to the development of atherosclerosis in the general population and in diabetic patients. Most people with high serum cholesterol also have elevated LDL because much of the serum cholesterol is transported in LDL. The concept therefore has emerged that LDL is the predominant atherogenic lipoprotein. The remarkable finding that LDL lowering therapy reduces the risk for subsequent coronary events even in patients with advanced atherosclerotic disease discloses a role for LDL in late stages of atherogenesis.[1]

Orlistat, [(1S)-1-[(2S, 3S)-3-hexyl-4-oxo-oxetan -2-y1] methyl] dodecyl] (2S)-2-formamido-4-methyl–9pentonate (figure 1) also known as tetrahydrolipstatin, is designed to treat obesity. It reduces the LDL concentration in the blood by inhibiting gastric and pancreatic lipases (the enzymes that break down triglycerides in the intestine).The primary effect of Orlistat is local lipase inhibition within the GI tract after an oral dose. When lipase activity is blocked, triglycerides from the diet are not hydrolyzed into absorbable free fatty acids and are excreted undigested instead, thereby reducing caloric intake.[2,3] A single dose of Orlistat will prevent approximately 30% of dietary fat from being absorbed, which indicates its effectiveness in controlling dyslipidemia. It also exhibits anti proliferative and antitumor properties in prostate and breast tissues. In a study conducted in an obese population over four years, the incidence of type-2 diabetes was reduced with Orlistat (6.2%) when compared with placebo.[4,5] Hence, Orlistat is an important drug in prophylactic management of obesity and for the management of type-2 diabetes. Orlistat has a short half-life (<2 h) and requires administration multiple times a day. The absorption window is restricted to the upper part of the gastrointestinal tract, which may lead to variability and non uniform absorption and makes the bioavailability unpredictable.[6]

According to recent patent reports, pharmaceutical compositions containing Orlistat have been formulated using various technological processes, such as extrusion and spheronization, micronization and other relatively time-consuming and demanding procedures (Shah, 1998). In contrast, formulations with Orlistat can also be produced by relatively simple and rapid methods such as blending and mixing with additives (Barbier et al., 2002). It has been included in film delivery systems (Myers et al., 2009) and soluble fibre tablets (Daggy and Mandel, 2003). The

problematic nature of Orlistat thus indicates the need for developing a novel drug delivery system that will be able to satisfy most of the formulation and pharmacodynamic requirements.[7]

In recent years, an area that is gaining popularity with formulation scientists is using lipid-based carriers to develop self-emulsifying drug delivery systems (SEDDS) to improve oral bioavailability of many lipophilic drugs. SMEDDS are isotropic and thermodynamically stable solutions consisting of an oil, surfactant, cosurfactant (CoS; or solubilizer) and drug mixtures that spontaneously forms oil in-water microemulsions when mixed with water under gentle stirring. The digestive motility of stomach and intestine provides the agitation required for self-emulsification in vivo. The advantages of these systems include not only improved drug solubilization but also enhanced release and absorption properties, due to the already dissolved form of drug in formulation and the resulting small droplet size thus providing a large interfacial surface area. The SEDDS formulation typically produce emulsions with a droplet size between 100 and 300 nm, while SMEDDS form transparent microemulsions with a droplet size that is less than 50 nm. The droplet size of the emulsion is a critical factor in self emulsification performance because it determines the rate and extent of drug release as well as absorption. When compared with emulsions, which are sensitive and metastable dispersed forms, SMEDDS are physically stable formulations that are relatively easy to manufacture. Thus, for lipophilic compounds that have dissolution-limited absorption, these systems offer a significant enhancement in the rate and extent of absorption and concomitantly providing more reproducible blood concentration time profiles.[8]

Being a class II drug it is poorly soluble, hence there is definite need for the enhancement of solubility of Orlistat by promising approach of SEDDS.

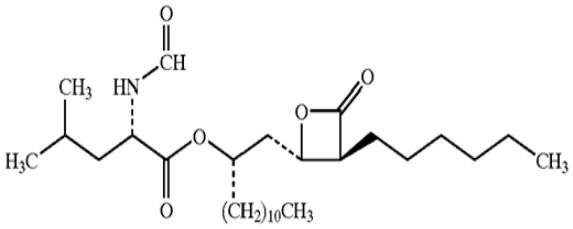


**Figure 1: Structure of Orlistat**

## MATERIALS AND METHODS:

The sample of Orlistat was procured from Cipla Ltd, Mumbai; Cremophor EL was obtained from BASF Chemical Corp., Mumbai. Captex 2OOP, Capmul MCM, Captex 355, Capmul PG 8 NF, Capmul 908 were obtained from Abitec Corp, USA. Tween 80, Span 80, Oleic acid, Magnesium aluminium silicate were obtained from Zim Research Lab, Nagpur.

**Determination of saturation solubility of Orlistat in different systems**

The solubility of Orlistat in each of various oil phases, surfactants, co surfactants and co solvents was determined by dissolving an excess amount of drug in 2 ml of each selected individual oils, surfactants and co surfactants contained in stoppered vials (5 ml capacity) separately. The liquids were mixed using a vortex mixer and the vials were then shaken using orbital shaker at 37°C±1°C for 72 h to reach equilibrium. The equilibrated samples were removed from the shaker and centrifuged (3000 rpm) for 15 min. The supernatants were taken out and filtered through a membrane. The concentration of Orlistat in various phases was determined by UV spectroscopy (Shimadzu 1800) at their respective $\lambda_{max}$.

**Construction of pseudo ternary phase diagram for identification of micro emulsion zone**

Based on the observations of solubility studies, components of emulsion viz oil phases, surfactants and co surfactants indicating highest solubility of Orlistat were selected. The surfactants and co-surfactants were blended together in 1:1, 2:1, 3:1, 4:1 proportions respectively. These blends of surfactants: co surfactants ($S_{mix}$) were mixed with oily phase by adding small amounts with constant stirring. The proportions of oil: $S_{mix}$ were varied as 9:1, 8:2, 7:1, 6:4, 5:5, 4:6, 3:7, 2:8 and 1:9. The resultant blends were titrated with distilled water taking care for proper stirring. Systems were allowed to reach equilibrium and the samples were checked visually for clarity. The pseudo ternary phase diagrams were constructed for each system of oil, surfactant, co surfactant. The point indicating the clear and isotropic mixtures were considered to be within the microemulsion region.

**Formulation of liquid SEDDS of Orlistat**

Liquid SEDDS were prepared by dispersing required quantity of Orlistat in appropriate quantity of co-surfactant. The mixture was homogenized and to it, accurately weighed quantity of oil: surfactant blends was added in small portion with stirring. The blends were mixed thoroughly using magnetic stirrer. The quantities of oil phase, surfactant and co-surfactant in appropriate portions were selected based on the result of solubility study and observing phase data of ternary diagram for each of the group A, B and C. The formulations were examined for signs of thermodynamic stability, turbidity or phase separation prior to self emulsification, percentage transmittance, drug content and particle size studies.[9]

**Preparation of solid SEDDS**

**Adsorption Method:**

The liquid SEDDS of Orlistat was adsorbed onto Neusilin US2 carrier at 1:1 ratio by physical mixing in a small mortar and pestle. The resulting solid SEDDS was uniformly homogenized to

ensure that the mixture was uniformly distributed. The damp mass was passed through sieve No.120 and was dried at ambient temperature.[10,11]

## CHARACTERIZATION OF SOLID-SEDDS

### Droplet size analysis

Solid SEDDS were diluted to 100 ml with distilled water. The droplet size distributions and polydispersibility index of the resultant microemulsions were determined using particle size analyzer (Malvern zetasizer 3000HS).[9]

### Zeta potential

The emulsion stability is directly related to the magnitude of the surface charge. The zeta potential of the diluted SMEDDS formulation was measured using a (Malvern Zetasizer 3000HS). The SMEDDS were diluted with a ratio of 1:20 v/v with distilled water and mixed for 1 min using a magnetic stirrer.[7]

### Drug content

The percent drug content of Orlistat in SEDDS was estimated by dissolving appropriate quantity of individual SEDDS equivalent to 100 mg in methanol. The samples were mixed thoroughly to dissolve the drug in methanol. The sample was sonicated using ultrasonicator for 15 min and analyzed using UV spectrophotometer and absorbance was recorded.[9]

### Drug release study *(in vitro)*

Apparatus type used was USP XXII type II (paddle), dissolution medium was 900 ml of 3% Sodium Lauryl Sulphate (SLS) and 0.5% sodium chloride w/v in distilled water at 37°C±0.5°C, speed of rotation of paddle was 75 rpm, volume of sample withdrawn was 10 ml, sampling interval was 30 min for 3h over entire duration of study. Required quantity of solid SEDDS (equivalent to 60 mg) and Orlistat (60 mg) was filled into hard gelatin capsules. The capsules were placed into a dissolution medium and the dissolution test was carried out. Aliquots were withdrawn at predetermined time intervals and equal volume of fresh dissolution medium was added. After each withdrawal sample was filtered through Whatman filter paper (No. 41) and analyzed spectrophotometrically[13] for cumulative percentage drug release. Marketed formulation of the drug was also studied for drug release.

### Drug release (*ex – vivo*)

Drug release study was performed on rat ileum in dissolution apparatus equilibrated at 37°C±0.5°C. One end of rat ileum was tied and SMEDDS corresponding to 60 mg was put into it followed by tying up of the other end., the ileum was dipped into the dissolution media (combination of 3% SLS and 0.5% Sodium chloride (w/v) solution in distilled water) in the

dissolution vessel and the dissolution study was performed at 50 rpm and 37°C±0.5°C. Samples were withdrawn at predetermined intervals which were further analyzed for studies at the maximum wavelength of 208 nm on UV-spectrophotometer. The above procedure was performed for the pure drug and the marketed formulation.[14]

**Differential scanning calorimetry**

The physical state of Orlistat in solid SEDDS was characterized by differential scanning calorimetry. The sample was placed in standard Aluminium pan and dry nitrogen was used as effluent gas. The sample was scanned at the speed of $10^0$C/ min at a heat flow from $0^0$C to $180^0$C. Differential scanning calorimetry was performed using differential scanning calorimeter (DSC 60, Shimadzu) to study the thermal behaviour of prepared optimized formulation.[10]

**Scanning electron microscopy**

The surface morphology of solid SEDDS of Orlistat was determined using analytical electron microscope (JEOL-ASM, 6360 A). The sample was lightly sprinkled on double adhesive tape stuck on Aluminium stub. The stubs were then coated with platinum to a thickness of above $10^o$A under an Argon atmosphere using a Gold sputter module under a high vacuum evaporator and the stub containing coated sample was placed in scanning electron microscope chamber.[10]

**Infrared spectroscopy**

Solid SEDDS of Orlistat (1-2 mg) was mixed with small quantity of Potassium bromide and transparent disc was prepared. The baseline correction of infrared spectrophotometer (Shimadzu 1800) was carried out using dried Potassium bromide disc and then the spectrum of dried mixture of drug and potassium bromide was recorded by placing the compressed disc in the light path.[1]

**X- ray diffraction**

The physical state of drug Orlistat and its solid SEDDS was characterized by X ray powder scattering (XRD) measurements using X ray diffractometer (Philips). The measurements were performed at room temperature using monochromatic CuKα-radiation at 40 mA and at 40 kV over a 2Θ range of 7° to 80° with a continuous scanning speed of 4°/min. The analyzed sample was compactly packed in the cavity of an Aluminum sample holder using a glass slide.[8]

## RESULTS AND DISCUSSION:

**Saturation solubility evaluation of Orlistat**

Amongst the individual oil phases the saturation solubility of Orlistat in Oleic acid was far superior as compared to other oils and esters (figure 2).

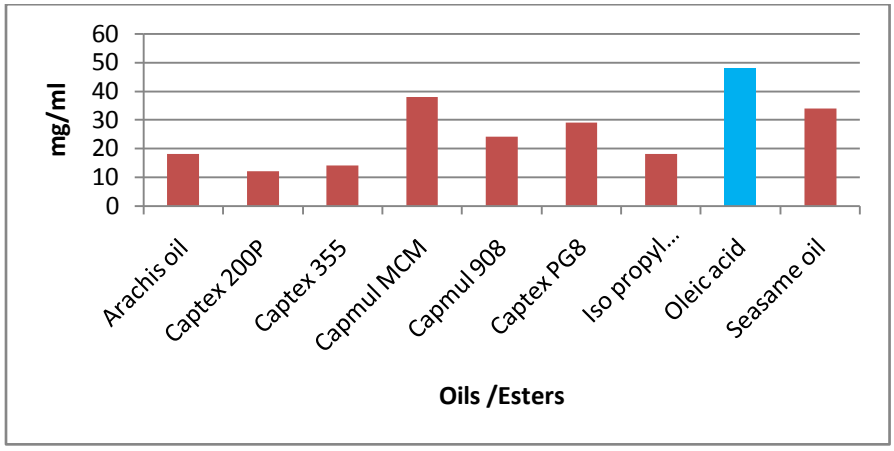


**Figure 2: Saturation solubility of Orlistat in different excipients oils/esters**

Amongst the surfactants the saturation solubility of Orlistat in Cremophor EL was far superior followed by Tween 80 and Span 80 (figure 3).

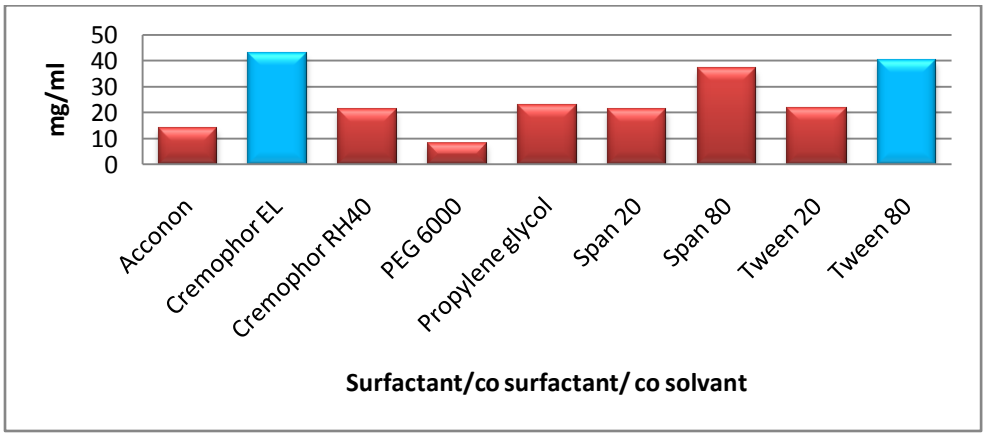


**Figure 3: Solubility in Surfactants /Co surfactants/Co solvents**

Solubility in different combination of oils/surfactants in 1:1 ratio was found to be highest in Oleic acid- Cremophor EL combination followed by Oleic acid– Tween 80 (figure 4).

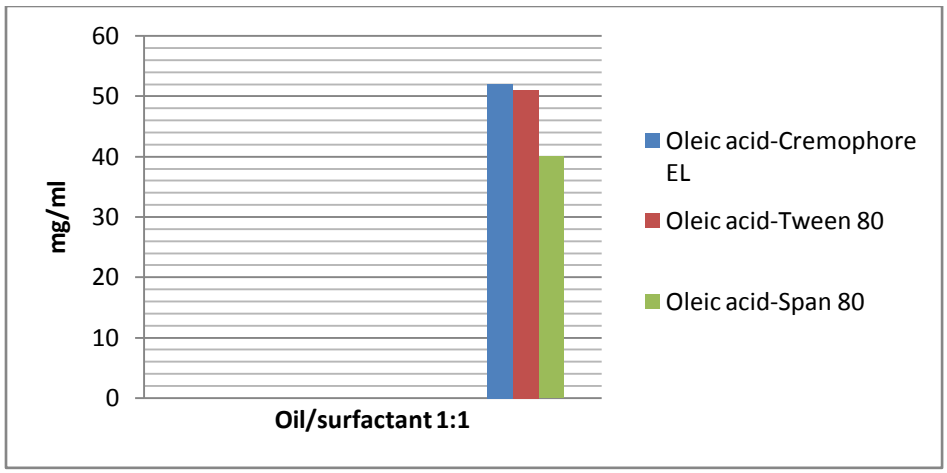


**Figure 4: Solubility in combination of oils/surfactant**

From the solubility studies the combinations of components of SMEDDS were selected (table 1)

**Table 1: Selected combination of components of SEDDS**

| Sr. No. | Oil | Surfactant | Co surfactant |
|---|---|---|---|
| 1 | Oleic Acid (60% w/w) | Cremophor EL (26.66 % w/w) | Tween 80 (13.33 % w/w) |

**Pseudo ternary phase diagrams with varying proportion of $S_{mix}$ with oils**

The SEDDS has an important characteristic of drug precipitation on dilution with water due to loss of solvent capacity. Selection of oil and surfactant and the mixing ratio of oil and other components play an important role in the formation of SEDDS. Therefore the phase behavior of each SEDDS needs to be carefully studied using the phase diagram as a guide (Figure 5). The microemulsion phase was identified as the area where clear and transparent formulations were obtained on dilutions based on visual inspection of samples. Phase diagram also helped to establish the study of micro emulsifying capacity and effect of drug on phase structure. The prototype formula compositions were selected within the microemulsion region of phase diagrams.[15]

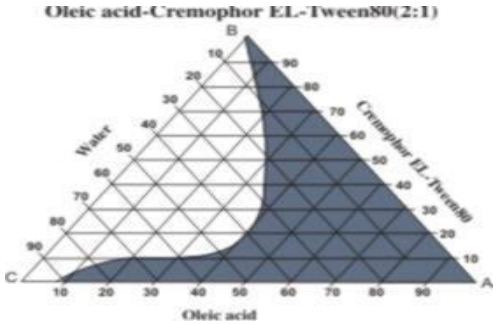


**Figure 5: Ternary diagram for Oleic acid /Cremophor EL: Tween 80(2:1) water system**

**Characterization of liquid SEDDS**

In SMEDDS, the primary means of self-emulsification assessment is visual evaluation. The efficiency of self-emulsification could be estimated by determining the rate of emulsification and droplet size distribution. The droplet size of the emulsion is a crucial factor in self-emulsification performance because it determines the rate and extent of drug release as well as absorption.[3] The selected combination of SEDDS (Oleic acid 60% w/w, Cremophor EL 26.66 % w/w and Tween 80 13.33% w/w) passed thermodynamic stability test, had self emulsification property, high transmittance, high drug content and particle size was below 100 nm.

**Formulation of solid SMEDDS:**

The solid SMEDDS (F4S) were prepared as per the procedure and free flowing powder was obtained and its various parameters were evaluated.

**CHARACTERISATION OF SOLID SMEDDS**

**Droplet size analysis**

Droplet size distribution following self-microemulsification is a critical factor to evaluate a self-microemulsion system. Droplet size is thought to have an effect on drug absorption as has been illustrated in several papers. The smaller the droplet size, the larger the interfacial surface area will be provided for drug absorption.[16]

The mean globule size of the reconstituted microemulsion seems to be less effected by the method of conversion of liquid to solid. The size of F4S was found to be below range of 100 nm which indicated that formulation F4S was SMEDDS (table 2 and figure.6).

**Table 2: Droplet size analysis of F4S**

| Sr. No. | Formulation code | Globule size (nm) | Polydispersibility index | Zeta potential |
|---|---|---|---|---|
| 1 | F4S | 25.43 | 6.57 | -20 |

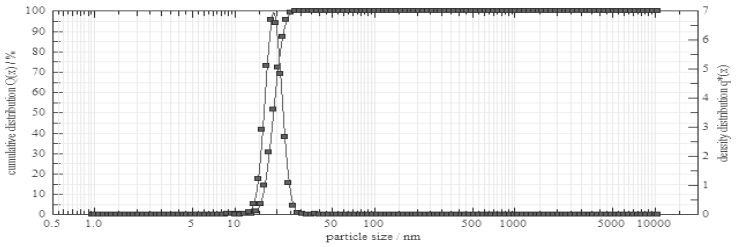


**Figure 6: Droplet size analysis of F4S**

**Zeta potential**

The magnitude of the zeta potential gives an indication of the potential stability of the colloidal system. If all the particles have a large negative or positive zeta potential they will repel each other and there is dispersion stability. If the particles have low zeta potential values then there is no force to prevent the particles coming together and there is dispersion instability. A dividing line between stable and unstable aqueous dispersions is generally taken at either +30 or -30 mV. Particles with zeta potentials more positive than +30 mV are normally considered stable. Particles with zeta potentials more negative than -30mV are normally considered stable. Zeta potential of the system negative (-) mV, which indicated the droplets of microemulsion having negative charge, which is closer to range ie -20mV (Figure 7 and table 2).[17]

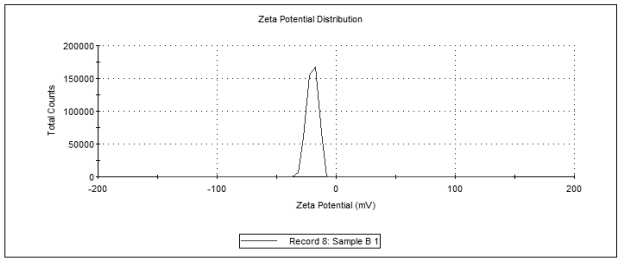


**Figure 7: Zeta potential of formulation F4S**

**Drug content**

The drug content in reconstituted solid SMEDDS of Orlistat was almost identical with those obtained in liquid SMEDDS so there is no change of percentage drug content after conversion of liquid to solid SMEDDS (table.3).

**Table 3: Drug content of F4S**

| Sr. No. | Formulation code | Percentage drug content |
|---|---|---|
| 1. | F4S | 98±0.04% |

**Drug release [*in vitro*]**

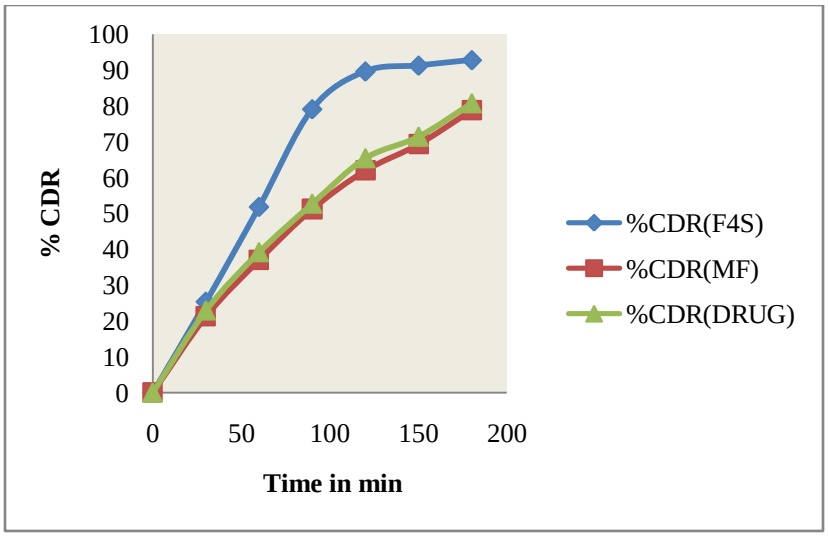


**Figure 8: Cumulative drug release of F4S, marketed formulation (MF) and pure drug**

**Table 4: Cumulative drug release of F4S, marketed formulation (MF) and pure drug**

| Sr. No. | Time (min) | %CDR (F4S) | %CDR (MF) | %CDR (Drug) |
|---|---|---|---|---|
| 1 | 0 | 0 | 0 | 0 |
| 2 | 30 | 25.31±0.75 | 21.27±0.72 | 22.92±0.45 |
| 3 | 60 | 51.82±0.36 | 37.01±0.33 | 39.21±0.23 |
| 4 | 90 | 79.13±0.40 | 51.22±0.74 | 52.77±0.61 |
| 5 | 120 | 89.68±0.69 | 62.01±0.40 | 65.47±0.42 |
| 6 | 150 | 91.31±0.74 | 69.32±0.21 | 71.49±0.95 |
| 7 | 180 | 92.84±0.63 | 78.82±0.74 | 80.83±0.15 |

Mean ± S.D, n = 3)

The *in vitro* studies were performed to compare the enhancement of solubility of Orlistat with respect to marketed and pure drug. It served as a quantitative tool to differentiate between the self micro emulsification efficiency of SMEDDS after dissolution of capsule shell.

The formulation F4S was released almost the 90% drug within 180 min as compared to marketed formulation and pure drug and hence it possessed maximum microemulsion efficiency and maximum release than marketed formulation and pure drug (Figure 8 and table 4). Thus, the selected

formulation F4S indicated considerable enhancement of solubility of Orlistat as compared to pure drug.

**Drug release [*ex-vivo*]**

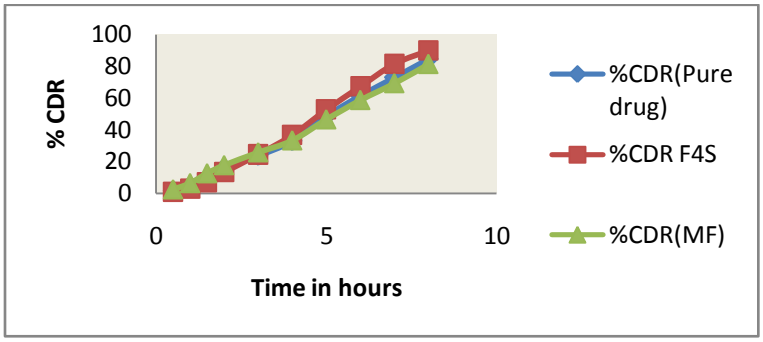


**Figure 9: Cumulative drug release (*ex vivo)* of F4S, marketed formulation and pure drug.**

**Table 5: Cumulative drug release (*ex vivo)* of F4S, marketed formulation and pure drug**

| Sr. No. | Time in h | % CDR(Pure drug) | % CDR F4S | % CDR(MF) |
|---|---|---|---|---|
| 1 | 0 | 0 | 0 | 0 |
| 2 | 0.5 | 1.69±0.80 | 0.74±0.34 | 2.40±0.32 |
| 3 | 1 | 4.53±0.84 | 2.68±0.50 | 6.34±0.21 |
| 4 | 1.5 | 9.45±1.04 | 6.79±0.59 | 12.55±0.39 |
| 5 | 2 | 15.77±0.59 | 13.17±0.61 | 17.67±0.28 |
| 6 | 3 | 23.65±1.03 | 24.33±0.78 | 25.77±0.96 |
| 7 | 4 | 32.98±0.26 | 36.27±1.05 | 33.32±0.86 |
| 8 | 5 | 48.66±0.47 | 52.61±0.82 | 46.58±0.43 |
| 9 | 6 | 61.41±0.34 | 67.34±0.78 | 58.78±0.91 |
| 10 | 7 | 72.94±0.55 | 81.66±0.33 | 69.41±1.16 |
| 11 | 8 | 84.59±0.61 | 89.97±1.02 | 81.52±0.28 |

(Mean ± S.D, n = 3)

In *ex-vivo* drug release study of F4S, marketed formulation (MF) and pure drug in combination of 3% SLS and 0.5% w/v Sodium chloride solution in distilled water, the drug diffused at a faster rate from the microemulsion system (F4S) as compared to the plain drug and marketed formulation (figure 9 and table 5) due to smaller particle size of micro emulsion and enhanced solubility of drug.

In the self-emulsifying systems, the free energy required to form an emulsion was very low, thereby allowing spontaneous formation of an interface between the oil droplets and water. It is suggested that the oil/surfactant/cosurfactant and water phases effectively swell, decrease the oil droplet size and eventually increase the release rate.

**Differential scanning calorimetry**

Differential scanning calorigraph of pure Orlistat represented sharp endothermic peak at 44°C (figure 10 {A}) and FS4 SMEDDS (figure 10 {B}) represented no such peak which indicated

change in melting behavior of drug and inhibition of crystallization thus, it can be confirmed that drug was solubilised into excipients of SMEDDS.

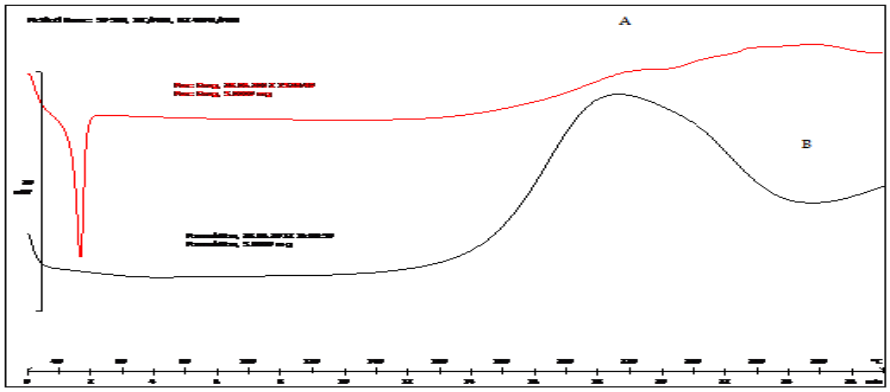


**Figure 10:Differential scanning calorigraph: (A) Drug Orlistat (B) SMEDDS of Orlistat (F4S)**

**Scanning electron microscopy**

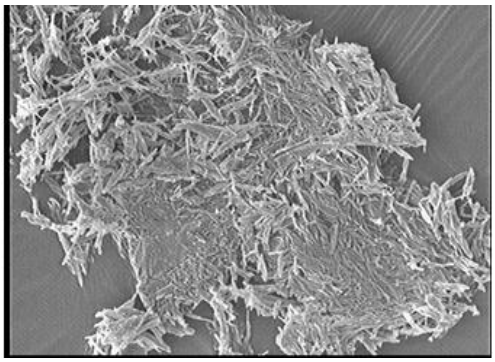

**Figure 11 (A): SEM of Orlistat**

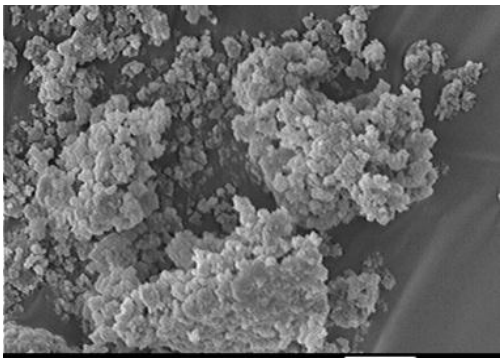

**Figure 11 (B): SEM of Orlistat SMEDDS (F4S)**

Scanning electron microscopy was carried out for comparison of surface of pure drug of Orlistat and with the loaded solid SMEDDS. Pure Orlistat appeared under the scanning electron microscope as needle shaped crystals (figure 11 A) having rough surfaces. However, the photomicrograph of (figure 11 B) it's solid SMEDDS indicated the uniform surface. This suggested that the entire drug was diffused in the adsorbent, distributed uniformly in the carrier mass and represented well-separated particles with no much agglomeration. Micrographs of solid SMEDDS exhibited liquid SMEDDS adsorbed onto the surface of Neusilin US2 particles. Since the formulation process involved facilitating adsorption, partially covered Neusilin US2 was also visible in the field of vision.

**Infrared spectroscopy**

Pure Orlistat shows major peak at 1708, 2920, 887.7 and 1521.79 $(cm)^{-1}$ (figure 12 A) and IR spectra of SMEDDS of F4S revealed no considerable change in major peaks when compared to

IR of pure drug which proved that there was no interaction between drug and excipients (figure 12 B and table 6).

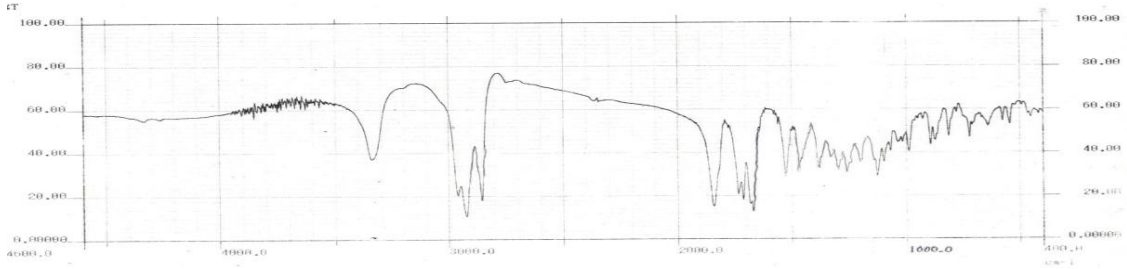

**Figure 12 (A): Infrared spectrum of Orlistat**

**Figure 12 (B): Infrared spectrum of SMEDDS of Orlistat (F4S)**

**Table 6: Interpretation of IR spectrum of SMEDDS of Orlistat (F4S)**

| Sr. No. | Wave number $(cm)^{-1}$ | Group | Stretching / Deformation |
|---|---|---|---|
| 1 | 1708 | C=O | Stretching |
| 2 | 2920 | C-H | Stretching in $CH_3$ |
| 3 | 887.7 | C-H | Deforming |
| 4 | 1521.7 | C=C | Aromatic stretching |

**X-ray diffraction**

X-ray diffraction pattern of SMEDDS of Orlistat (F4S) verified the physical state of the drug in the solid SMEDDS. Pure Orlistat drug represented sharp peak which indicated it was highly crystalline in nature (figure 13 A) whereas F4S formulation was not indicating significant crystalline peaks, which confirmed the molecularly dispersed state of Orlistat in the formulation and effective solubilisation of drug (figure 13 B).

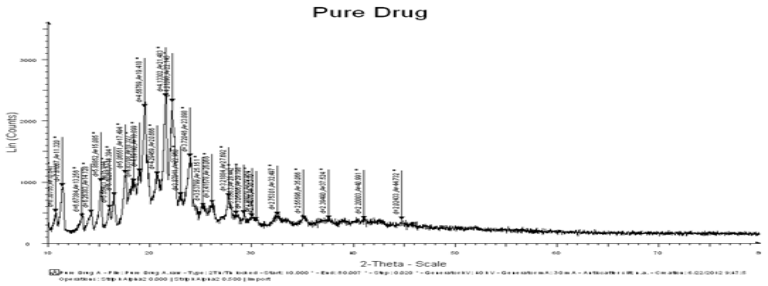


**Figure 13(A): X-ray diffraction pattern of pure Orlistat**

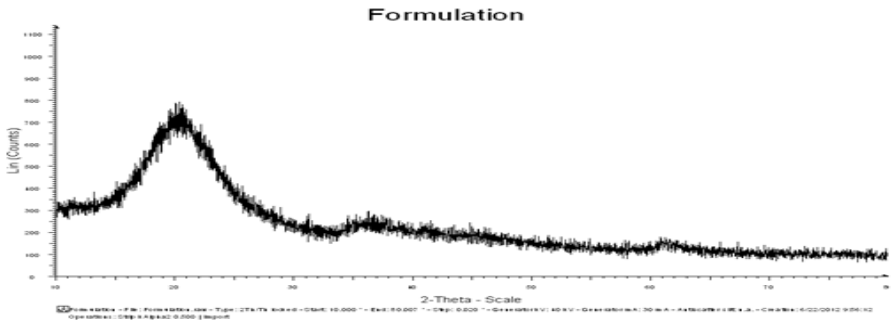


**Figure 13 (B): X-ray diffraction pattern of SMEDDS of Orlistat (F4S)**

## CONCLUSION

A SMEDDS containing poorly water-soluble drug, Orlistat, was formulated for oral application. The components and their ratio ranges for the formulation of SMEDDS were obtained by solubility study, pseudo-ternary phase diagram construction and droplet size analysis. The optimized formulation of the SMEDDS consisted of Oleic acid 60% w/w, Cremophor EL 26.66 % w/w and Tween 80 13.33 % w/w) which had sufficient drug loading, rapid self-microemulsification in aqueous media, and forming droplet size in the range of microemulsion. The formulation of SMEDDS showed greater extent of release than pure drug and marketed formulation. These results suggested the potential use of SMEDDS for oral administration of Orlistat.

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## REFERENCES

1. Sateesha SB. et al. Gastroretentive Orlistat Microspheres: Formulation, Characterization and *In Vitro* Evaluation, Dissolution Techno 2011
2. Tsutsumi K. Lipoprotein Lipase and Atherosclerosis. Curr Vasc Pharmacol 2003; 1:11–17.
3. Al-Suwailem K, Al-Tamimi S, Al-Omar MA, Al-Suhibani MS. Safety and mechanism of action of Orlistat (tetrahydrolipstatin) as the first local antiobesity drug, J Appl Sci Res 2006; 2 (4): 205–08.
4. Drew BS, Dixon AF, Dixon JB. Obesity management: Update on Orlistat Vasc Health Risk Manag 2007; 3(6):817–21.

5. Anderson JW, Kendall CW, Jenkins DJ. Importance of weight management in type 2 diabetes: review with meta-analysis of clinical studies, J Am Coll Nutr 2003; 22 (5): 331–39.
6. Kazmi SA, Khan M, Mashori GR, Saleem A, Akhtar N, Jahangeer A. Influence of Sibutramine, Orlistat and Ispaghula in reducing body weight and total Body fat content in obese individuals, J Ayub Med Coll Abbottabad 2009;21 (2): 45–48.
7. Dolenc A. Nanosized particles of Orlistat with enhanced *in vitro* dissolution rate and lipase inhibition, Int J Pharm 2010: 149–55.
8. Nekkanti V. et al. Solid Self-Microemulsifying Formulation for Candesartan Cilexetil, AAPS PharmSciTech, 2010; 11(1):9-16.
9. Dange M, Madan J. Emulsion based drug delivery system, Ind J Novel Drug delivery 2011; 3(1):2-8.
10. Bandivadikar MM.et al. Preparation and characterization of solid SMEDDS by adsorbent technique to improve dissolution profile of poorly aqueous soluble drug Ramipril, IJPR 2011; 2 (6): 85-90.
11. Venkatesan N. Liquid filled nanoparticles as a drug delivery tool for protein therapeutics, Biomaterials, 2005; 2: 7154-63.
12. Singh AJ. et al. Oral Bioavailability Enhancement of Exemestane from Self-Microemulsifying Drug Delivery System (SMEDDS) 2009. AAPS PharmSciTech, 2009; 10(3):906-16.
13. Kumar .et al. Estimation of Orlistat by UV Spectrophotometric Method, IJPSR 2011; 2(9): 2469-71.
14. Mandal S.et al. Brain targeting of Fluranazine hydrochloride by solid lipid nano particals for prophylaxis of migraine. IRJP 2011:2(9):99-102.
15. Sckick MJ. Textbook on Non ionic surfactants, Marcel Dekker, New York 1997. Vol 19.
16. Ping Z, Ying L, Nianping F. Preparation and evaluation of self-microemulsifying drug delivery system of Oridonin, Int J Pharm 2008; 355: 269–76.
17. Gupta AK, Mishra DK and Mahajan SC. Preparation and in-vitro evaluation of self emulsifying drug delivery system of antihypertensive drug Valsartan, Int J Pharm Sci 2011; 2(3): 633-39.