

# Characterization of Thermal Fraction of Clarified Butter and its Applicability to Improve Bioavailability of Rosuvastatin

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## ABSTRACT

**Aim:** The present investigation shows confirmatory evidence for the complex formation of Rosuvastatin with a fraction of Clarified Butter. **Materials and Methods:** Fractions of Clarified Butter prepared according to thermal behavior at different temperatures (30°C, 40°C, 50°C). Rosuvastatin biform complex with Clarified Butter in the ratio (1:1) and (1:2) w/w were prepared. Physicochemical properties of all fractions of Clarified Butter was determined as per Indian Pharmacopoeia. The fractions were subject to Fourier-transform Infrared spectroscopy (FTIR), Differential Scanning Calorimeters (DSC) and *in-vitro* release studies (Simulated gastric fluid, pH 1.2 for 2 h and simulated intestinal fluid, pH 6.8 for 6 h). **Results:** Based on these investigations; the optimized ratio (1:1) w/w were further characterized for DSC and FTIR studies. Where Rosuvastatin exhibited a strong carbonyl band at 1543.05 cm<sup>-1</sup> all fractions showed the disappearance of strong carbonyl band at 1543.05 cm<sup>-1</sup>, spectra of biform complex shifted to higher frequency 1747.51 cm<sup>-1</sup> (13.29 % increase), that confirmed carboxylic and hydroxyl group of both saturated and unsaturated fatty acid present in Clarified Butter. From *in vitro* release study the highest percent release i.e. 99.23 ± 0.08% of Rosuvastatin was obtained from 1:1 biform complex. DSC thermogram revealed the formation of eutectic mixture by lowering the peak of pure Clarified Butter (67.4°C) to 58.10°C due to the formation of biform complex. **Conclusion:** Thus, Clarified Butter and its fraction illustrated enhanced bioavailability of Rosuvastatin.

**Key words:** Rosuvastatin, Clarified Butter, Peroxide value, Thermal oxidation, Bioavailability.

## INTRODUCTION

Clarified Butter is a material used in the cooking in South Asian country and well known in Indian tradition of medical practice "Ayurveda" for various purposes due to the versatile medicinal applications as well as adjuvant/vehicle properties.<sup>1</sup> Clarified Butter or their fractions enhance absorption characteristics of poor bioavailable pharmaceutical ingredients by entrapment into them.<sup>1-3</sup>

Rosuvastatin is a statin class of drug acts as a lipid-lowering agent used in the treatment

of pure hypercholesterolemia, mixed hyperlipidemia and hypertriglyceridemia. It is a competitive inhibitor of HMG-CoA reductase. Rosuvastatin works by reducing the total number of VLDL and LDL particles.<sup>4</sup> Moreover, its low bioavailability about 20% owes to its extensive extraction in the liver. Rosuvastatin is slightly soluble in water (7.8 mg/mL at 37°C) and has a pKa of 4.6.<sup>5,6</sup> The chemical structure of the Rosuvastatin is presented as Figure 1.

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The present investigation was envisaged with a hypothesis to improve the bioavailability of Rosuvastatin, which performed in two phases. In the first phase, the thermal fraction characterized for various parameters like shelf life determination by evaluating peroxide value, iodine number, saponification value, acid value, hydroxyl value, specific gravity and melting point. Whereas, in the second phase, the physical complex of Rosuvastatin with Clarified Butter was prepared in different ratios and characterized by DSC, FTIR like sophisticated analytical instruments. The present investigation is based on the study of effect of biform complex formation for the Rosuvastatin with the Clarified Butter and its effect over bioavailability.

## MATERIALS AND METHODS

### Materials

Rosuvastatin procured from Sigma-Aldrich Private Limited India. Clarified Butter was procured from Gau Vigyan Anusandhan Kendra, Deolapur, Nagpur, Maharashtra which is a research institution established by Maharashtra Government for enhancement of milk production and its quality. All the other chemicals used in the experiment were analytical grade.

### Collection of Clarified Butter and its fractionation

For thermal fractionation, the Biological Oxygen Demand (BOD) incubator was used for better-precised control of temperature and to maintain a constant level of condition with minimum fluctuation. 100 g of Clarified Butter was taken in the glass tube and placed inside BOD incubator. The operation time of BOD incubator was set for 24 h at 30°C. After 24 h only a melted fraction of Clarified Butter was collected. The procedure was repeated using fresh Clarified Butter at temperature 40°C, 50°C and 120°C. Fractions were stored at room temperature until further experimentation.

### Preparation of biform complex of thermal fractionated Clarified Butter fraction with Rosuvastatin

A particular laboratory fabricated instrument equipped with a thermocouple inbuilt three-sided, double jacket water circulated hot plate system used with minimum temperature variation  $\pm 0.5^\circ\text{C}$ . A definite proportion of the 30°C separated fraction of Clarified Butter was taken on the incubation tube and transferred it into a house fabricated thermal system. An equal proportion of the drug was mixed with the Clarified Butter fraction to get 1:1 w/w biform complex. Mixing was done using a sonicator

to get a uniform and homogeneous mixture along with stirring. The similar procedure was followed to obtain 1:2 w/w clarified butter and drug ratio. Similar steps were repeated with 40°C and 50°C separated fractions to obtain; 1:1 and 1:2 w/w drug Clarified Butter mixtures.

### Analysis of physicochemical parameters

Physicochemical parameter were evaluated by using Peroxide values, Iodine value, Saponification values, Acid value, Specific gravity, Melting range, Ester values and Hydroxyl value.<sup>7-9</sup>

### Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectra of Clarified Butter, thermal fractions, drug and their biform complex were subjected to study by using FTIR 4000 Series (JASCO) and spectra recorded from 500-3500  $\text{cm}^{-1}$ .<sup>10,11</sup>

### In-vitro Release Study

*In-vitro* release study performed for all six prepared biform complexes of Rosuvastatin with Clarified Butter fractions. The test was performed using eight stations dissolution test apparatus USP-1 (Electro lab India), with Simulated Gastric Fluid (SGF) pH 1.2 without pepsin for first 2 h and followed by 6 h in Simulated Intestinal Fluid (SIF) pH 6.8 phosphate buffer. The temperature of the media maintained at  $37^\circ\text{C} \pm 0.5^\circ\text{C}$  at a stirring rate of 50 RPM. Drug analysis was performed using UV spectrophotometer (UV-1800, Shimadzu, Japan) equipped with UV probe software. Absorbance maxima of Rosuvastatin in simulated gastric fluid and simulated intestinal fluid was measured at 244nm and 250nm, respectively.<sup>12</sup>

### Drug release kinetic model

The release kinetic of Rosuvastatin biform complex was carried out. The percentage release data were tested for the Zero order, First order, Higuchi, Korsmeyer- Peppas model, Hixson- Crowell.

### Drug content

The percentage drug content of drug Clarified Butter biform complex in various ratios was determined by UV spectrophotometer. An equivalent to about 100mg of Rosuvastatin biform complex dissolved in 10 ml of alcohol using the magnetic stirrer (Remi India). To the resultant solution, simulated gastric fluid/simulated intestinal fluid added and the volume was made up to 100 ml. It was then filtered through Whatman filter

paper no. 42 and after required dilutions the absorbance recorded at 244 nm.<sup>13</sup>

### Differential Scanning Calorimetry (DSC)

Differential scanning calorimetry (DSC) analysis of drugs, Clarified Butter fraction and the biform complex was performed using a Mettler STAR SW9.00 system. The transition Temperature ( $T_m$ ) was measured in triplicate in aluminum crucibles at a heating rate of 10°C/min within a temperature range of 0 to 300°C. Sample weights were taken approximately to be  $20 \pm 5$  mg. The temperature modulation amplitude kept in between  $0.01 \pm 10^\circ\text{C}$ .<sup>14</sup>

### Statistical analysis

The *t*-test performed on all collected mean data obtained from physiological evaluation as well as release studies and significance accepted at  $p \leq 0.05$ . All the data expressed as a mean  $\pm$  SD. The sample size was  $n=3$  in physical characterization and *t*-test were performed. All the statistical analyses performed with GraphPad Prism 6 Demo software.

## RESULTS AND DISCUSSION

### Physico-chemical analysis of Clarified Butter and their fractions

Clarified Butter is contains a variety of both saturated and unsaturated fatty acids. These fatty acids are used as pharmaceutical excipient for various formulations.<sup>15</sup> In the present investigation a Clarified Butter is subjected to thermal fractionation because as per another researcher Mehta *et al.* 2013 all the fatty acid of clarified butter shows different melting points.<sup>16</sup> We found a color variation in collected fractions of clarified butter, which giving a primarily idea about variation in chemical composition. The colors of each fraction were reported in (Table 1). A clear color variation was found in all five samples (Justified with result found by Mehta *et al.* 2013). Increment of fractionation temperature, found lighting of color from creamy yellow to transparent yellow for fraction separated at 30°C and 50°C, respectively. Fraction separated 120°C was tend to light brown due to the accumulation of non-volatile decomposition products, such as oxidized triacylglycerols and free fatty acid.<sup>17,18</sup> When overheat the Clarified Butter, some of fatty acid might be burned and convert into small coloring particles. The color change in the most of fats and oils in ambient storage condition is due to the involvement of the Amino acids. Most strong coloring amino acid is methionine (Met) while glutamine (Glu) was the least.<sup>19</sup> The protein content of clarified

butter is very low, so the color change obtained in all thermal fractions indicate the presence of different fatty acids, separated by thermal treatment. The Clarified Butter contains small, medium and long chain saturated fatty acids which shows different melting point.<sup>16</sup>

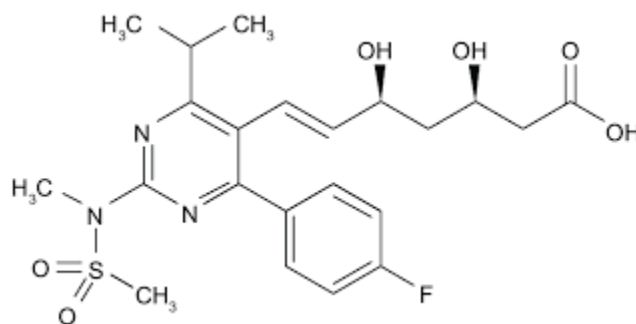
The conclusion was also supported by specific gravity test. It was increased toward oxidation. The specific gravity of Clarified Butters was found  $0.889 \pm 0.147$  g/cc, which was lower than thermal fraction of Clarified Butter. The specific gravity of all four fractions was founded in increasing order with increasing the temperature. The values were reported in the Table 1. A clear conclusion drawn that the extent of oxidation may enhance the specific gravity of clarified butter.<sup>20</sup>

The physicochemical properties of Clarified Butter and its thermal fractions summarized the Table 1. All the measured parameter of Clarified Butter and its thermal fractions passes the standards and limit given in Ayurvedic Pharmacopoeia and Indian Pharmacopoeia respectively.<sup>21,22</sup>

Untreated Clarified Butter had higher acidic values, which was decreased with heating, followed by a gradual increment till 50°C, whereas the melting range and peroxide values increased, which were consistent with reported findings.<sup>23</sup> Saponification values increases with increasing fractional temperature. After formulating the drug Clarified Butter biform complex, the acidic values decreased which probably indicates about involvement of  $\text{H}^+$  ions in complexation, followed by the reduction in iodine values, due the saturation of fatty acid of clarified butter at the same time.<sup>20</sup> The thermal treatment, oxidized the fatty acid and lead to saturation of carbon chain with by lebrated  $\text{H}^+$  ion.<sup>24,25</sup>

### Drug content

Maximum drug content found at 30°C fraction in 1:1 drug Clarified Butter biform complex ( $98.55\% \pm 0.21$ ) in simulated gastric fluid and simulated intestinal fluid



**Figure 1: Rosuvastatin has structural similarities with most other synthetic statins, but unlike other statins, rosuvastatin contains sulfonyl functional group.**

**Table 1: Physicochemical Parameters of Clarified Butter and its fraction.**

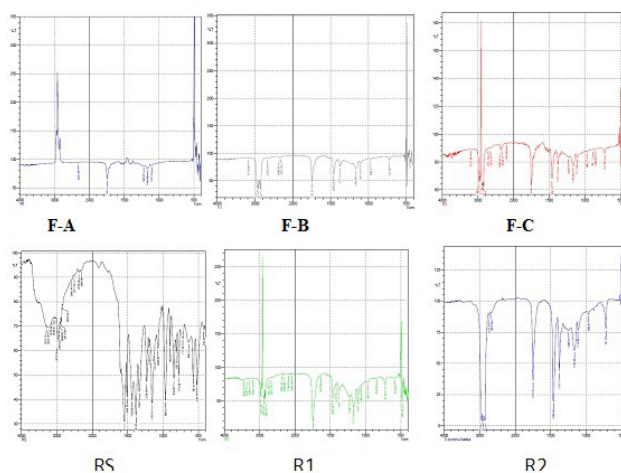
S. No	Physicochemical Parameters of Clarified Butter	Clarified Butter and its fraction (Fractionation based on temperature)				
		Clarified Butter (At room temp) (Mean $\pm$ S.D.)	Fraction 1 (at 30°C) (Mean $\pm$ S.D.)	Fraction 2 (at 40°C) (Mean $\pm$ S.D.)	Fraction 3 (at 50°C) (Mean $\pm$ S.D.)	Oxidized Clarified Butter (120°C) (Mean $\pm$ S.D.)
1	Color	Creamy yellow	Creamy yellow	Slightly Transparent yellow	Transparent Yellow	Light brownish
2	Specific gravity (g/cc)	0.889 $\pm$ 0.147	0.894 $\pm$ 0.119	0.911 $\pm$ 0.078	0.980 $\pm$ 0.185	1.111 $\pm$ 0.121
3	Melting range (°C)	37.1 – 37.6	30.1 – 31.2	37.2 – 38.1	38.4 – 39.3	41.3 – 42.2
4	Acid value	0.367 $\pm$ 0.078	0.266 $\pm$ 0.086	0.277 $\pm$ 0.043	0.297 $\pm$ 0.041	0.496 $\pm$ 0.018
5	Ester value	234.21 $\pm$ 0.995	233.03 $\pm$ 0.900	232.27 $\pm$ 0.603	232.37 $\pm$ 0.549	230.73 $\pm$ 0.573
6	Hydroxyl value	16.266 $\pm$ 0.152	16.210 $\pm$ 0.066	16.231 $\pm$ 0.099	16.150 $\pm$ 0.051	16.228 $\pm$ 0.100
7	Iodine value	29.336 $\pm$ 0.499	31.003 $\pm$ 0.655	30.456 $\pm$ 0.274	8.123 $\pm$ 0.505	4.490 $\pm$ 0.308
8	Peroxide value	4.55 $\pm$ 0.360	4.82 $\pm$ 0.110	6.82 $\pm$ 0.110	7.49 $\pm$ 0.599	8.49 $\pm$ 0.670
9	Saponification value	215.23 $\pm$ 0.11	215.33 $\pm$ 0.16	215.5 $\pm$ 0.360	218.16 $\pm$ 0.30	220.73 $\pm$ 0.21
10	Solidification temperature (°C)	22.1-23.3	19.2-19.8	18.4 -18.1	18.2- 17.3	17.0 – 16.1

\*Represent mean  $\pm$  S.D. (n=3)**Table 2: Percent drug content of Rosuvastatin from biform complex.**

Sr. no	Biform complex w/w proportion	Drug content* %	
		SGF	SIF
1	FA-1:1	98.55 $\pm$ 0.21	98.45 $\pm$ 0.24
2	FA-1:2	96.29 $\pm$ 0.23	96.18 $\pm$ 0.24
3	FB-1:1	96.67 $\pm$ 0.17	97.26 $\pm$ 0.13
4	FB-1:2	94.25 $\pm$ 0.27	94.33 $\pm$ 0.16
5	FC-1:1	95.48 $\pm$ 0.21	95.12 $\pm$ 0.20
6	FC-1:2	93.46 $\pm$ 0.10	93.24 $\pm$ 0.25

\*Represents mean  $\pm$  S. D. (n=3).

(98.45 $\pm$ 0.24). Drug content finding is reported in the Table 2. All fractions of 1:1 drug Clarified Butter complexes entrapped higher drug content as compared to 1:2 w/w drug Clarified Butter complexes. These observations indicate better entrapment capacity of formed biform complex by holding or binding tendency of Clarified Butter with Rosuvastatin drug molecules. Drug content was almost similar in both simulated gastric fluid and simulated intestinal fluid indicating a better release in both GI fluids. The drug content in Clarified Butter fractions of 50°C was less as compared to 30°C this may be due to decreased iodine values, increased saturation, as well increased melting point of Clarified Butter at higher temperatures, which probably lead to poor complexation of drug molecules. In other words, intermolecular interactions between drug and Clarified Butter were less at higher temperatures, as Clarified Butter unsaturation decreases.



**Figure 2: FT-IR Spectra of (F-A) Clarified Butter Fraction at 30°C, (F-B) Clarified Butter Fraction at 40°C, (F-C) Clarified Butter Fraction of 50°C, Rosuvastatin, (R1) biform complex of Rosuvastatin with thermal fraction of Clarified Butter in (1:1) w/w, (R2) biform complex of Rosuvastatin with thermal fraction of Clarified Butter in (1:2)w/w.**

### Fourier Transform Infrared Spectroscopy

In the IR spectrum of Rosuvastatin Figure 2, a broad region of the band saw between 3600-3200  $\text{cm}^{-1}$  that was an indication of presence hydroxyl group. The presence of characteristic carbonyl stretched peak at 1654  $\text{cm}^{-1}$  confirmed the hydroxyl peak come from carboxylic group with an overlapping hydroxyl group in the region of 3600-3200  $\text{cm}^{-1}$ . Adjacent to this band a sharp peak at 2939  $\text{cm}^{-1}$  seen this is specific for olefinic C-H of the heptanoic side chain. A peak for bending vibrations of methyl C-H was present at 1438  $\text{cm}^{-1}$ .

Peaks for distinguished sulfoxide group of the drug were confirmed by the presence of asymmetric and symmetric strong stretching vibrations at  $1334\text{ cm}^{-1}$  and  $1153\text{ cm}^{-1}$  respectively. The peak at  $1230\text{ cm}^{-1}$  followed the C-F stretch of aromatic ring present in the compound. In fatty acids, the presence of bands at  $3000\text{--}2500\text{ cm}^{-1}$  and at  $1708\text{ cm}^{-1}$  and a few additional bands at  $1431\text{ cm}^{-1}$ ,  $1300\text{ cm}^{-1}$  and  $938\text{ cm}^{-1}$  may be attributed to a carboxylic acid dimer.

The FT-IR spectrum of biform complex did not record any significant changes in terms of absence or presence and shifting of characteristic bands of either drug or fatty acid, however, changes in the shape and decrease in intensity of carboxylic acid bands of fatty acid and -NH stretching band ( $2839\text{ cm}^{-1}$ ) of Rosuvastatin observed. The ability of the Clarified Butter to form a biform complex with Rosuvastatin depends on the configurational nature of unsaturated fatty acids present in Clarified Butter (composed of saturated and unsaturated fatty acids), electrostatic interactions between the Clarified Butter and Rosuvastatin.<sup>26</sup>

Comparative spectral analysis revealed a mild shift in the absorption peaks of the drug in a biform complex as compared to the pure drug. The drug fatty acid biform complex showed an increase in the intensity of a peak in the region  $3100\text{ cm}^{-1}$  to  $3500\text{ cm}^{-1}$  probably indicates the interaction between the NH group of Rosuvastatin and OH group of fatty acid. It can be attributed to the formation of weak intermolecular hydrogen bonding interactions between the two functional groups, leading eventually to the shift in peak area and ratifying the formation of drug fatty acid biform complex. However, other signature peaks of the drug remained intact construing no significant change in the biform complex.<sup>27</sup>

### Percentage Release of Rosuvastatin

A drug release study of the Rosuvastatin Clarified Butter biform complex was performed in dissolution test

apparatus. Data is presented in the Table 3 and Figure 4. CB Biform complex FA 1:1 fraction at  $30^\circ\text{C}$  exhibited highest drug release in 8 hrs. Obtain data confirming the efficacy, integrity and entrapment of Rosuvastatin in biform complex. The order of percent cumulative Rosuvastatin release was FA1:1>FA1:2>FB 1:1>FC 1:1> FB1:2 > FC1:2.

### Release kinetics studies

For the linearity correlation coefficient ( $R^2$ ) value was also determined for Zero order, First order, Higuchi, Korsmeyer- Peppas model, Hixson- Crowell (Table 4). The result of release kinetic model was found that the rosuvastatin biform complex shows the highest  $R^2$  value (0.985) at ratio (1:1) w/w and it follows zero order kinetics. The result of kinetic studies was indicates the tendency of the drug release from Rosuvastatin biform complex (1:1) w/w.

### Differential Scanning Calorimetry (DSC)

The thermal behavior of biform complex was studied using DSC in order to confirm the formation of biform complexes. The DSC thermogram of Rosuvastatin, Clarified Butter  $30^\circ\text{C}$  fraction and biform complexes prepared with Rosuvastatin with Clarified Butter  $30^\circ\text{C}$  fraction (1:1) w/w shown as Figure 3(a), Figure 3(b) and Figure 3(c). The DSC thermogram of Rosuvastatin showed that a broad endothermic peak observed at  $132.01^\circ\text{C}$ . A sharp endothermic peak for Clarified Butter fraction ( $30^\circ\text{C}$ ) was observed at  $65.6^\circ\text{C}$  and two sharp endothermic peaks for a biform complex were observed at  $201.7^\circ\text{C}$  and  $211.9^\circ\text{C}$ . Two another broader endothermic peak also obtained at  $120.9^\circ\text{C}$  and  $136.8^\circ\text{C}$ . The thermogram exhibits that little change in melting isotherm of Rosuvastatin, indicating no significant interaction between drugs and the fraction of Clarified Butter.

**Table 3: Cumulative % Rosuvastatin release of various biform complexes.**

Time (h)	Cumulative % Rosuvastatin Release					
	F-A 1:1	F-A 1:2	F-B 1:1	F-B 1:2	F-C 1:1	F-C 1:2
1	6.77±0.04	5.23±0.10	5.63±0.10	4.34±0.20	6.23±0.16	4.19±0.07
2	18.7±0.11	15.19±0.03	13.23±0.13	14.62±0.03	15.14±0.09	15.11±0.12
3	41.34±0.19	43.38±0.04	45.52±0.31	42.25±0.10	45.11±0.29	38.14±0.20
4	54.42±0.01	61.58±0.13	54.45±0.28	49.95±0.05	54.14±0.03	48.43±0.12
5	71.32±0.16	71.28±0.07	67.57±0.18	65.64±0.20	63.12±0.015	62.39±0.23
6	86.45±0.19	84.35±0.19	80.63±0.23	78.52±0.17	79.39±0.22	74.54±0.14
7	96.45±0.05	94.36±0.08	88.73±0.18	88.63±0.24	86.13±0.19	81.29±0.28
8	99.23±0.08	97.37±0.11	95.53±0.31	91.53±0.30	92.13±0.015	89.28±0.40

\*Represents mean ± S. D. (n=3).

Table 4: Drug release kinetic of various Rosuvastatin biform complexes.						
Release Model	F-A 1:1	F-A 1:2	F-B 1:1	F-B 1:2	F-C 1:1	F-C 1:2
	$R^2$	$R^2$	$R^2$	$R^2$	$R^2$	$R^2$
Zero Order	0.985	0.955	0.959	0.967	0.959	0.976
First Order	0.868	0.936	0.940	0.966	0.965	0.973
Higuchi Release	0.986	0.980	0.979	0.984	0.980	0.990
Korsmeyer- Peppas model	0.978	0.956	0.951	0.882	0.890	0.886
Hixson Crowell Model	0.900	0.859	0.863	0.869	0.866	0.877

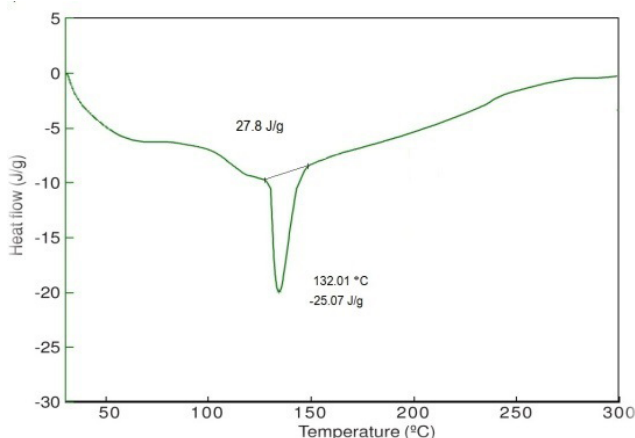


Figure 3(a): DSC thermogram of pure Rosuvastatin drug: A sharp endothermic peak obtained.

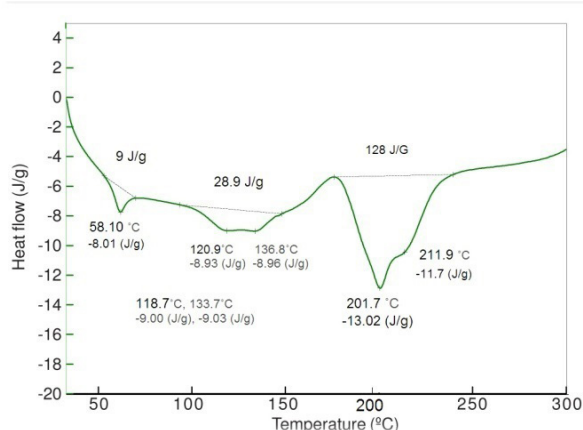


Figure 3(c): DSC thermogram of biform complex of Rosuvastatin with Fraction of Clarified Butter at 30°C in 1:1 w/w Proportion: Two broader endothermic peaks obtained

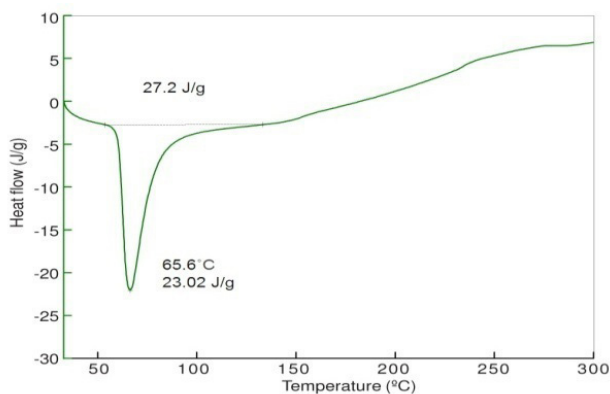


Figure 3(b): DSC thermogram of fraction F-A of Clarified Butter at 30°C: A sharp endothermic peak obtained.

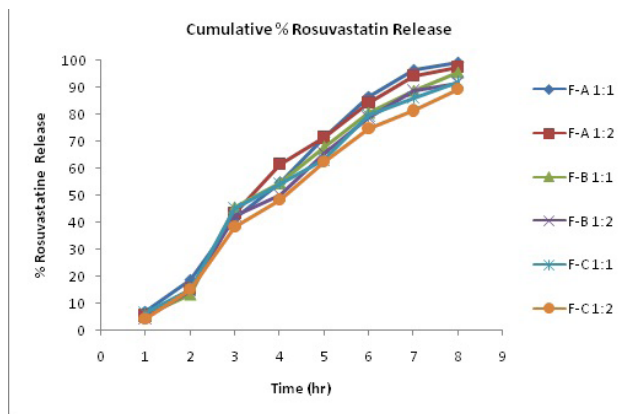


Figure 4: Percent Rosuvastatin release from biform complex: the highest release is obtained with 30°C fraction 1:1 w/w complex.

In thermogram of biform complex the intensity of drug peak reduced and shifted to lower band of temperatures ranging from 120.9°C to 136.8°C. This reduction is probably due to formation of biform complex.<sup>28</sup> These two lower and higher temperature bands probably indicate weak and robust bonds respectively, between Rosuvastatin-Clarified Butter drug.

These weak bonds may be the intermediates, in the formation of strong bond products during complexation.

### CONCLUSION

The present work confirmed the enhancement of the bioavailability of Rosuvastatin by formation of biform complex structure with Clarified Butter. The biform

complex formation was verified by FTIR and DSC studies. The research work indicated a promising approach to enhance bioavailability of drugs through complexation with Clarified Butter and later also can be used as an adjuvant for various formulations. Also, the present work based on the use of natural resources that is safe and can replace other synthetic adjuvant used for a similar application.

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## CONFLICT OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

## ABBREVIATIONS

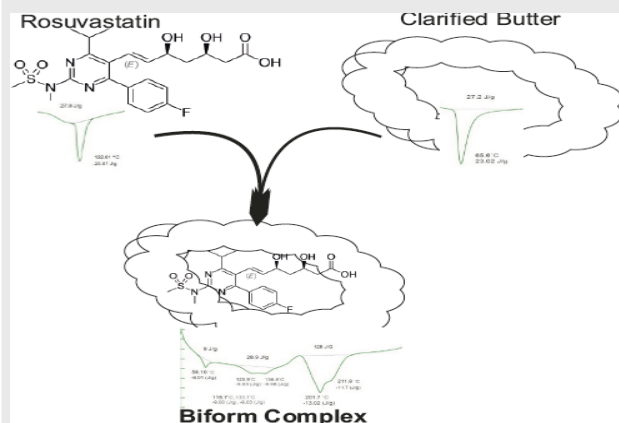
**CB:** Clarified Butter; **DSC:** Differential Scanning Calorimetry; **IR:** Fourier Transform Infrared Spectroscopy; **UV:** Ultraviolet; **F-A:** Clarified Butter Fraction at 30°C; **F-B:** Clarified Butter Fraction at 40°C; **F-C:** Clarified Butter Fraction of 50°C; **R1:** Biform complex of Rosuvastatin with thermal fraction of Clarified Butter in (1:1)w/w; **R2:** Biform complex of Rosuvastatin with thermal fraction of Clarified Butter in (1:2)w/w.

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### PICTORIAL ABSTRACT



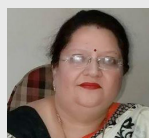
### SUMMARY

Rosuvastatin forms eutectic biform complex with Clarified Butter which was confirmed by FTIR and DSC studies. The highest drug release obtained with biform complex made with 30°C thermal fractionated Clarified Butter 1:1 w/w drug complex. This might be due to the entrapment of Rosuvastatin into the lipoidal core of fatty acid chain of Clarified Butter.

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