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Article

Enhancement of dissolution rate of racecadotril by liquisolid compact technology

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The current investigation was used to improve the rate of dissolution of an anti-diarrheal drug i.e., racecadotril (RT) at low pH conditions (i.e., in the stomach) by reducing the water secretion and electrolyte in to the intestine by liquisolid tablets. Different formulations (liquisolid) were prepared using Avicel PH 102 as a carrier. Aerosil 200 as a coating material and sodium starch glycolate used as a disintegrant. Polyethylene glycol 200 was used as a non-volatile vehicle to dissolve the drug. FTIR, DSC, XRD and dissolution studies were conducted to characterise liquisolid tablets. Characterisation studies indicated that no interactions between carrier and drug. Solid state characterization had shown a reduction in crystallinity that further supports increment in solubility and dissolution. The optimised formulation showed a significant increase in dissolution i.e., 99.54±0.62% in 30 min compared to directly compressible tablets (38.47±0.26%). The % dissolution efficiency of racecadotril liquisolid tablets 76.86% compared to marketed tablet (27.56%) and conventional direct compression tablet (17.11%). Significant reduction in mean dissolution time of racecadotril from liquisolid tablets (6.84 min) compared to direct compression tablet (44.57 min), indicating faster release of drug and faster onset of action. Formulation of liquisolid tablets could enhance solubility, dissolution and bioavailability of racecadotril.

Keywords: Avicel. Aerosil. Non-volatile vehicle. Liquisolid tablets. Dissolution.

INTRODUCTION

Poor solubility is the reason for inadequate bioavailability when absorption is dissolution rate limited (Wong, Kellaway, Murdan, 2006). The low rate of dissolution of poor water soluble drugs is still facing a fundamental problem in pharmaceutical industry. There are still so many newly discovered and beneficial drug substances still not reaching the public because of inadequate dissolution and low oral bioavailability (Spireas, Sadu, 1998). Various numbers of new techniques have been developed and reported to enhance dissolution rate and thereby the absorption of poor water soluble drugs. These methods include complexation (Jin *et al.*, 2012), self-emulsifying drug delivery systems (Gursoy, Benita, 2004), solid dispersions (Daravath, Tadikonda, Vemula, 2015), ball milling (Sonoda *et al.*, 2008), crystal engineering (Blagden *et al.*, 2007) and hot-melt extrusion (Luo *et al.*, 2012). These methods require highly sophisticated equipment, advanced method of preparation and also cost of the production is very high (Mie *et al.*, 2017).

The 'liquisolid compacts' concept is a new, novel and promising technology was developed to prepare liquid medication (i.e., drug in solution, suspension or liquid form) in to powders which are suitable for encapsulation or tableting from powdered solution technology (Tiong, Elkordy, 2009). This technique uses a non-volatile liquid vehicle by mixing with required amount of powder substrates containing a carrier and coating material that can produce readily compressible powder with non-adherent, dry and freely flowing properties (Javadzadeh *et al.*, 2005).

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Liquisolid compacts essentially have majorly two formulation components are, liquid medication and powder substrates. The powder substrates are consists of (i) carrier particles which are porous in nature and enhance compression (cellulose, lactose and starch) and (ii) coating particles which are highly adsorptive and very fine can improve flow property (Silica). The liquid formulation is initially absorbed by carrier powder particles and then the fine coating powder particles are adsorbed on to the carrier particles and allow freely flowing and readily compressible powder/liquid system (Spireas, Wang, Grover, 1999).

The oral bioavailability of drug from liquisolid tablets is enhanced may be because of increased wetting properties and surface area of drug particles for dissolution and consequently improve the drug release characteristics (Khaled, Asiri, El-Sayed, 2001).

This technology was successfully used for the variety of drugs in recent days are piroxicam (Javadzadeh *et al.*, 2007), fenofibrate (Karmarkar *et al.*, 2009), atorvastatin calcium (Gubbi SR, Jarag R, 2010), carbamazepine (Javadzadeh, Jafari, Nokhodchi, 2007), Telmisartan (Chella, Narra, Rama, 2014) and azithromycin dihydrate (Bhattacharya *et al.*, 2019).

In all age of group people commonly affecting illness is diarrhea. It is associated with excessive loss of water and electrolyte (Lindo, 2000). Racecadotril (RT) is an enkephalinase inhibitor used to treat acute diarrhea (Matheson, Noble, 2000). It has an antisecretory effect by reducing intestinal motility and there by reduces electrolyte and water secretion into the intestine (Cojocaru *et al.*, 2002). It also decreases the abdominal pain and also reduces the duration and frequency of acute diarrhea (Alam *et al.*, 2003; Primi *et al.*, 1999).

RT is comes under BCS class II drug with low bioavailability. About 1 hour is the time of peak plasma concentration of conventional RT tablets (Singh, Narayan, 2008). But it needs faster on set of action to prevent the excessive loss of fluid. Hence, an attempt has been made to develop a new RT dosage form to overcome this limitation.

In this present study, liquisolid tablets (LST) was prepared to enhance the rate of dissolution of poor water soluble racecadotril by promoting flow property, stability and absorption of RT that improves bioavailability and drug's acceptability.

MATERIAL AND METHODS

Material

Racecadotril (RT) was obtained exgratis by M/S Symed laboratory Limited (Hyderabad, India). Lactose, Aerosil 200, dicalcium phosphate (DCP), Sodium starch glycolate and Avicel PH102 were purchased from Sd Fine Chem Ltd. (Mumbai, India). Tween 80, Polyethylene glycol 200, Polyethylene glycol 400, Polyethylene glycol 600 and Propylene glycol were purchased from Qualikems Fine Chemicals Private Limited (Vadodara, India). Excipients, chemicals and reagents were used of analytical grade.

METHODS

Solubility studies:

Shake flask method was employed for carrying solubility studies of RT for selecting the non-volatile solvent (Daravath *et al.*, 2017). An amount of RT, more than saturation placed in a test tube having different concentrations of polyethylene glycol (PEG) 200, PEG 400, PEG 600, tween 80 and propylene glycol solution separately. The tubes were sonicated for 15 min and stirred continuously on an orbital shaker at room temperature for 48 h. After centrifugation, the supernatant of the suspensions was passed through 0.45 µm membrane filter and RT content was measured using Ultraviolet-Visible spectroscopy (UV-3200, Labindia, Mumbai, India) at 231 nm. The results were reported in Table I.

TABLE I - Solubility of racecadotril in different vehicles (mean±SD; n = 3)

Non-volatile vehicle	Solubility (mg/ml)
Polytethylene glycol 200	10.4 ± 0.73
Polytethylene glycol 400	8.6 ± 0.52
Polytethylene glycol 600	6.3 ± 0.64
Propylene Glycol	4.7 ± 0.26
Tween 80	3.6 ± 0.38

Calculation of excipient ratio and load factor

The required amount of carrier and coating material to retain the specific amounts of liquid medicament is depending on 'R' (excipient ratio), by maintaining free flow property and compression property of liquisolid tablets. The excipient ratio of a powder blend given by the equation (Spireas, Sadu, Grover, 1998).

$$R = \frac{Q}{q} - - - - - 1$$

Where 'q' is the amount of coating materials and 'Q' is the amount of carrier.

The liquisolid compacts with an appropriate flow rate and compressible properties can be formulated as a tablet, when the maximum liquid into carrier powder material should not exceed. This feature of liquid medicament is known as the liquid load factor (L_f). It was expressed by equation (Javadzadeh, Shariati, Movahhed, 2009).

$$L_f = \frac{W}{Q} - - - - - 2$$

Where 'Q' is amount of carrier material and 'W' is amount of the liquid.

The liquid load factor was calculated by adding increments amount of liquid (without drug) to 1 g of the carrier and mixed for 1 min. The addition of liquid to the carrier material was continued till free flowing powder/liquid admixtures were obtained.

Micromeritic properties of liquisolid blend

The flow properties of liquisolid blend was measured by determining angle of repose and Carr's compressibility index by equation given below (Daravath, Tadikonda, 2014):

$$\theta = Tan^{-1}\frac{H}{R} - - - - - 3$$

Where, 'θ' was angle of repose, radius was 'R' and height of pile was 'H'. Carr's index was measured by.

$$Carr's\ index = \frac{(\rho_p - \rho_b)}{\rho_p} X\ 100 \quad - - - - - 4$$

Where, 'ρ_p' was tapped density and 'ρ_b' was bulk density.

Formulation of liquisolid tablets

The liquisolid tablets of racecadotril (30 mg) formulated by dispersing in various non-volatile liquids (PEG 200, PEG 400, PEG 600, Tween 80 and propylene glycol) as per the procedure described in literature (Chella, Nalini, Rama, 2012). The drug solution was prepared by dissolving appropriate amount of racecadotril in a liquid vehicle. Then as per different excipient ratio (R), appropriate amount of the carrier (Avicel PH102, lactose or DCP) and coating materials (Aerosil 200) were added to liquid dispersion and mixed gently in the mortar without excessive trituration. Then add 10% of sodium starch glycolate (disintegrant) to powder blend and mixed thoroughly. Finally liquisolid tablets were compressed by using powder blend using rotary tablet press (Rimek Minipress, Karnavati Engineering Pvt. Ltd., Gujarat, India). Conventional directly compressible tablets were also manufactured in a similar method without a non-volatile vehicle (Table II).

TABLE II - Formulations of liquisolid tablets

Formulation code	Concentration of drug (%)	R	Load factor (Lf)	Avicel PH102 (mg)	Aerosil 200 (mg)	Total weight of tablet (mg)
F1	10	5	0.75	400	80	560
F2		10	0.55	550	55	695
F3		15	0.46	650	43.3	793.3
F4		20	0.38	780	39	929
F5	20	5	0.48	310	62	442
F6		10	0.39	380	38	498
F7		15	0.29	520	34.7	644.7
F8		20	0.24	620	31	751
F9	30	5	0.36	280	56	406
F10		10	0.29	350	35	455
F11		15	0.24	410	27.3	517.3
F12		20	0.22	460	23	563
F13	40	5	0.44	170	34	254
F14		10	0.38	200	20	270
F15		15	0.27	280	18.7	358.7
F16		20	0.18	420	21	521

R= Q/q (Excipient ratio); Q = weight of the carrier; q = weight of the coating material; Lf = W/Q (Liquid load factor); W = weight of the liquid medication; All formulations contain 10% sodium starch glycolate (disintegrating agent).

Evaluation of liquisolid tablets

Various evaluations test like friability, content uniformity, hardness and weight variation were determined as per the procedures specified in the literature (Tadikonda, Daravath, 2014). For drug content determination, twenty tablets were powdered. Required amount of blend (which is equal to 30 mg RT) taken in a flask and dissolved in pH 0.1 N hydrochloric acid with intermittent shaking for 4-5 h. The sample was filtered by membrane filter and RT content was analyzed at 231 nm. The time for disintegration was determined by introducing the tablet in to a USP disintegration apparatus (Electrolab India Private Limited, Mumbai, India) at 37±2 ^{0}C. The time taken for complete disintegration of tablet was noted.

In vitro dissolution and data treatment

In vitro dissolution studies of liquisolid tablets of RT, conventional directly compressible tablets and marketed tablets were performed using USP II paddle apparatus (UV3000$^+$, Lab India solutions, Mumbai, India) containing 0.1 N HCl (900 ml) at 37 ± 0.5 °C for 50 rotations per minute. 30 mg of RT was present in each formulation. Aliquot (5 ml) was removed at suitable time period and was replaced by equal amount of unused vehicle. Aliquot was passed through 0.45 µm membrane filters and contents were analyzed spectrometrically at 231 nm. Mean values were reported by performing the studies in triplicate.

Dissolution data treatment

Dissolution profiles were analysed and compared for various parameters like, cumulative percentage of drug release Q_{15} (in 15 min), percentage of drug release Q_{30} (in 30 min), MDT (mean dissolution time) and %DE (% dissolution efficiency) at 30 min as per the procedure described in the literature (Chella, Narra, Rama, 2014).

Characterization of liquisolid tablets

FTIR spectroscopy

FTIR spectrum of plain RT, physical mixture (directly compressible tablet) and liquisolid tablet (tablets were crushed) powderwere recorded on the FT-IR spectroscopy (IRTracer-100, Shimadzu, Japan) between 400 to 4000 cm^{-1} by potassium bromide pellet method (Chella *et al.*, 2016). The sample powder (5 mg) was blended with 100 mg of KBr. The mixture was compacted at a pressure of 12,000 psi under vacuum for 3 minutes.

Differential Scanning Calorimetry

Thermograms of RT, physical mixture and optimized LST formulation were recorded by using differential scanning calorimeter (DSC-60A, Shimadzu, Japan). Approximately 5-7 mg sample was heated in aluminium pan under the flow of nitrogen gas for a range of temperature of 0 to 400 ^{0}C at 5 ^{0}C/min rate.

X-ray powder diffraction

X-ray diffractometry (Siemens D5000, Texas, US) was used to record the X-ray diffractograms of the samples (pure RT, physical mixture and optimized LST) by scanning at 2θ range of 2^o to 50^o by exposing to Cu radiation at 30 mA current of 40 KV voltage under a wavelength of 1.540Å.

Stability Studies

Optimized LST formulation was stored for six months at 40±2 ^{0}C and 75±5% RH (relative humidity). Drug content and % assay were determined to study the effect of conditions of storage on formulations (Mathews, 1999). Similarity index (F2) was determined to find out the stability of tablets (Daravath, Swathi, Babu, 2017).

RESULTS AND DISCUSSIONS

Racecadotril is poorly water soluble with log P 3.3, a highly hydrophobic drug (Daravath, Kumari, 2021), makes it more ideal for the development of liquisolid tablet to enhance the solubility and rate of dissolution of drug. The current work was aimed to enhance the dissolution of racecadotril to improve the gastric absorption and there by the oral bioavailability by liquisolid technology.

Solubility Studies

Aqueous solubility of racecadotril was reported as 0.00176 mg/ml (Daravath, Kumari, 2021). The most important aspect in developing liquisolid compacts is the solubility of drug sample in a non-volatile vehicle system. The molecular dispersion of drug in to a non-volatile vehicle will contributes the solubility of the drug which will enhance the dissolution rate of drug. Mostly, water miscible and orally safe vehicles like, PEG 200, PEG 400, PEG 600, tween 80 and propylene glycol are used as the non-volatile liquid vehicles. The results of solubility data of racecadotril in various non-volatile solvents were reported in Table I. The solubility of racecadotril in PEG 200 is high (10.4 mg/ml). Hence, PEG 200 was selected as a non-volatile vehicle for the preparation of liquisolid formulations of racecadotril.

Formulation of Liquisolid compacts

The particles which are highly porous with high absorption properties and having large specific surface area were selected as carrier material such as cellulose, lactose and starch (Spireas, Wang, Grover, 1999).

The coating materials should be adsorb on to the surface of the carrier material and the powder's flow property has to be maintained (Tiong, Elkordy, 2009). A very fine and highly adsorptive silica powder is selected as coating material.

Preliminary studies are conducted with different excipients for the selection of coating and carrier material. The specific surface area (SSA) of avicel is 1.18 m^2/g (Javadzadeh, Shariati, Movahhed, 2009) which is more than other carriers like 0.6 m^2/g for starch, 0.37 m^2/g for sorbitol and 0.35 m^2/g for lactose (Nokhodchi, Hentzschel, Leopold, 2011). Since, Avicel has absorbed more amount of liquid medicament by retaining the flow property of the powder mixture; it is selected as carrier material. Aerosil 200 is amorphous anhydrous colloidal silicon dioxide having a very high specific surface area of 200 m^2/g. Highly absorptive particles of aerosil cover the wet carrier particles and convert a dry powder by adsorbing excess liquid to ensure good flowability of the blend. This results in improved free-flow properties of the formulation. Hence, Aerosil 200 and Avicel PH102 and were selected as coat and carrier materials.

Racecadotril liquisolid tablets using PEG 200 as vehicle with various excipient ratios (R) were prepared (Table II) from the liquid load factors which determine the appropriate amount of the carrier to bind the liquid medicament. The liquisolid compacts prepared by increasing *R* values. As the R value increases, $L_f$values decreases. Various concentrations (10%, 20%, 30% and 40%) of racecadotril solutions were used to prepare liquisolid compacts. As the concentration of drug increases, the liquid load factor was decreases and also the amount of carrier material required is decreases. As the R value increases, the amount of the carrier material used to bind liquid medicament also increases.

Flow Properties of liquisolid compacts

The angle of repose characterizes the cohesion of the particles or internal friction of the particles. Cohesive powders will have higher angle of repose and non-cohesive powders will have lower angle of repose. The formulations F1 – F7, F9 – F10, F13, F14 and F15 having L_f value greater than 0.25, showed poor flow property (Javadzadeh, Jafari, Nokhodchi, 2007). The flow property of these powder compacts is decreases may due to increasing the moisture content of carrier materials. The angle of repose of plain racecadotril drug was 43.82° indicates poor flow property (Table III). But the liquisolid compacts F8, F11, F12, and F16 exhibits good flow properties as the angle of repose values less than 30°. The carr's index values of F8, F11 and F16 were of 18.27, 18.36 and 20.15 respectively, and they having fair flow properties. F12 having carr's index value of 13.87 indicates excellent flow property. The optimum R value required to get maximum flowability of optimized formulation (F12) is 20 (Spireas, Sadu, 1998; Tayel, Soliman, Louis, 2008). These formulations were considered for further analysis.

TABLE III - Flow properties of racecadotril liquisolid tablet formulations (Mean ± SD, n=3)

Formulation	Angle of Repose (°)	Carr's Index (%)
F8	28.41±0.68	18.27
F11	29.73±0.24	18.36
F12	27.53±0.62	13.87
F16	28.81±0.47	20.15
Plain drug	43.82±0.39	30.32

Evaluation of liquisolid tablets

Various evaluations test like friability, disintegration time, hardness and content uniformity were determined and showed in Table IV. Average weight of the liquisolid tablets F8, F11, F12 and F16 was found to 751 mg, 517.3 mg, 563 mg and 521 mg respectively. The differences in the weight of the liquisolid tablets were observed due to differences in excipient ratio and liquid load factor. This difference in weight also depends on the solubility of racecadotril in non-volatile vehicles and it also affects the dissolution rate. Higher the solubility of drug in the non-volatile vehicle, lower the quantity of carrier and coating material and there by the weight of the tablet is low (Elkordy, Tan, Essa, 2013; Saeedi *et al.*, 2011). Hence, the optimized formulation F12 has lower weight compared with other tablets but slightly more than F11.

The hardness was found to be 4.1±0.47 kg/cm^2, disintegration time was found to be 186±09 sec and friability was found to be 0.32% and drug content was found to be 99.42±1.46% for formulation F12. All evaluation tests of liquisolid tablets were within pharmacopoeia limits.

TABLE IV - Evaluation of racecadotril liquisolid tablets (Mean ± S.D.)

Formulation code	Friability (%)	Hardness (Kg/cm^2)	Disintegration time (sec)	Drug content (%)
F8	0.42	3.0±0.52	156±13	92.38±1.38
F11	0.35	3.5±0.26	173±16	94.15±1.28
F12	0.32	4.1±0.47	186±09	99.42±1.46
F16	0.43	4.3±0.63	212±15	98.63±2.53
Marketed tablets	0.39	3.4±0.39	197±15	98.52±1.81
Direct compressible tablets	0.46	4.5±0.15	316±12	97.82±1.72

In vitro dissolution studies

Release patterns of racecadotril from various formulations like liquisolid tablets, conventional direct compression tablets and marketed tablets are shown in Figure 1. The optimized formulation F12 showed highest drug release compared to other formulations. Formulation F12 reached 99.54±0.62% within 30 min, while the conventional directly compression tablets and marketed tablets were releases 38.47±0.26% and 51.27±0.1.54% respectively in 30 min.

The drug concentration in liquid medication also has great impact on the dissolution of drug. The drug dissolution is increased with increase in drug concentration up to 30%. As drug concentration further increased to 40%, drug dissolution is decreased; it may be due to the saturation of the drug in liquid solvent and also due to conversion of drug from solution form to suspension in liquid vehicle.

This improvement of dissolution from liquisolid tablets may be due to increased particle surface area and enhancement in wetting property by reducing the interfacial tension of drug particles (Javadzadeh *et al.*, 2007; Elkordy, Tan, Essa, 2013; Fahmy, Kassem, 2008; Suliman, Anderson, Elkordy, 2014).

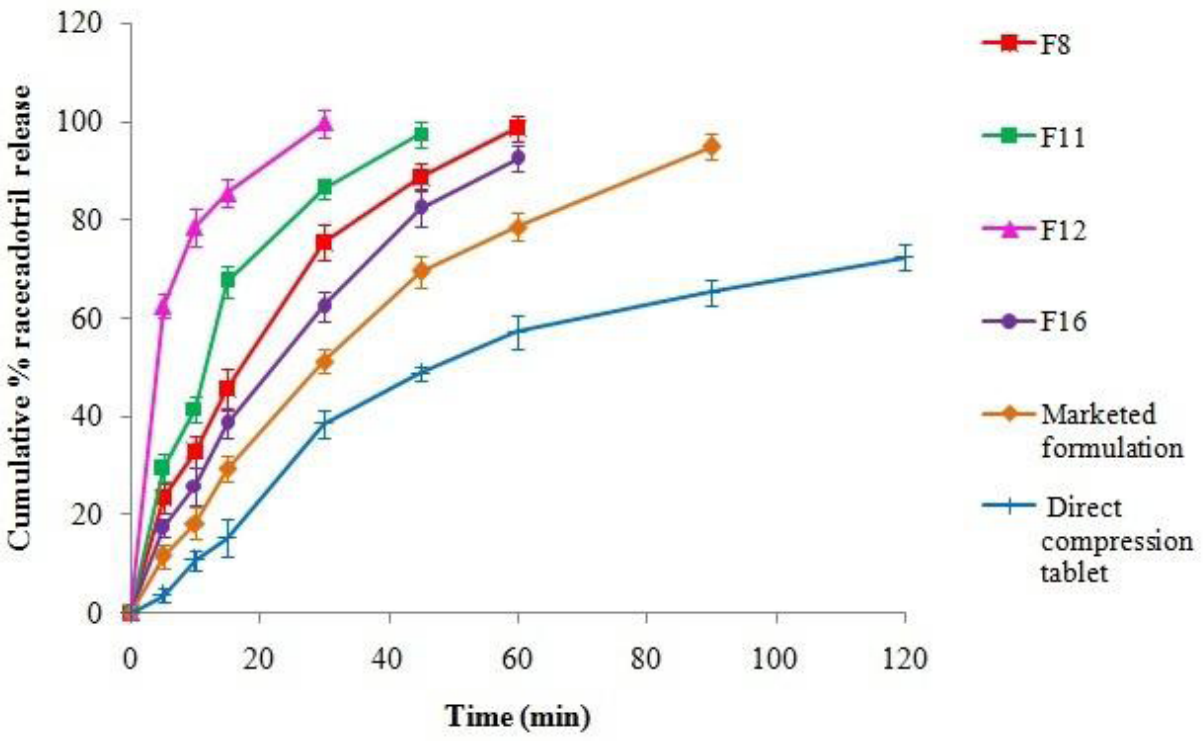

FIGURE 1 - Comparison of release of RT from liquisolid tablets, conventional direct compression tablets and marketed tablets (n=6).

DISSOLUTION DATA TREATMENT

The dissolution data was analysed further for %DE and MDT. The results (Table V) showed significant improvement in %DE of racecadotril liquisolid tablets 76.86 (F12 formulation) compared to marketed tablet (27.56) and conventional direct compression tablet (17.11). Significant reduction in MDT of racecadotril from F12 (6.84min) was observed compared to all other formulations indicating faster release of drug and faster onset of action.

TABLE V - Dissolution parameters of racecadotril formulations (Mean ± SD, n=3)

Formulation	Q_{15} (%)	Q_{30} (%)	$\%DE_{30}$	MDT (min)
F8	45.63±0.63	75.29±0.47	43.39	20.11
F11	67.46±1.37	86.32±1.58	55.91	13.65
F12	85.43±0.17	99.54±0.62	76.86	6.84
F16	38.52±1.75	62.37±1.93	35.62	22.52
Marketed formulation	29.35±1.82	51.27±0.1.54	27.56	32.55
Direct compression tablet	15.28±0.48	38.47±0.26	17.11	44.57

Q_{15}: Percentage of drug release in 15 min; Q_{30}: Percentage of drug release in 30 min; $\%DE_{30}$: Percentage dissolution efficiency in 30 min; MDT: Mean dissolution time.

Characterization of liquisolid tablet

FTIR spectra of F12 liquisolid tablet was compared with plain drug and directly compressible tablet physical mixture (Figure 2). FTIR spectra of RT is characterized by N-H amide stretch (3290.67 cm^{-1}), C=O ester group of stretch (1770.71 cm^{-1}), C=C aromatic group of stretch (1558.45 cm^{-1}) and C-S stretching (1280.78 cm^{-1}). Directly compressible tablet physical mixture also exhibits similar types of peaks. Absence of extra new peaks, presence of all drug peaks in F12 suggests interaction is absent between drug and carrier and coating material. Similar types of results were obtained by Daravath *et al.*, 2017.

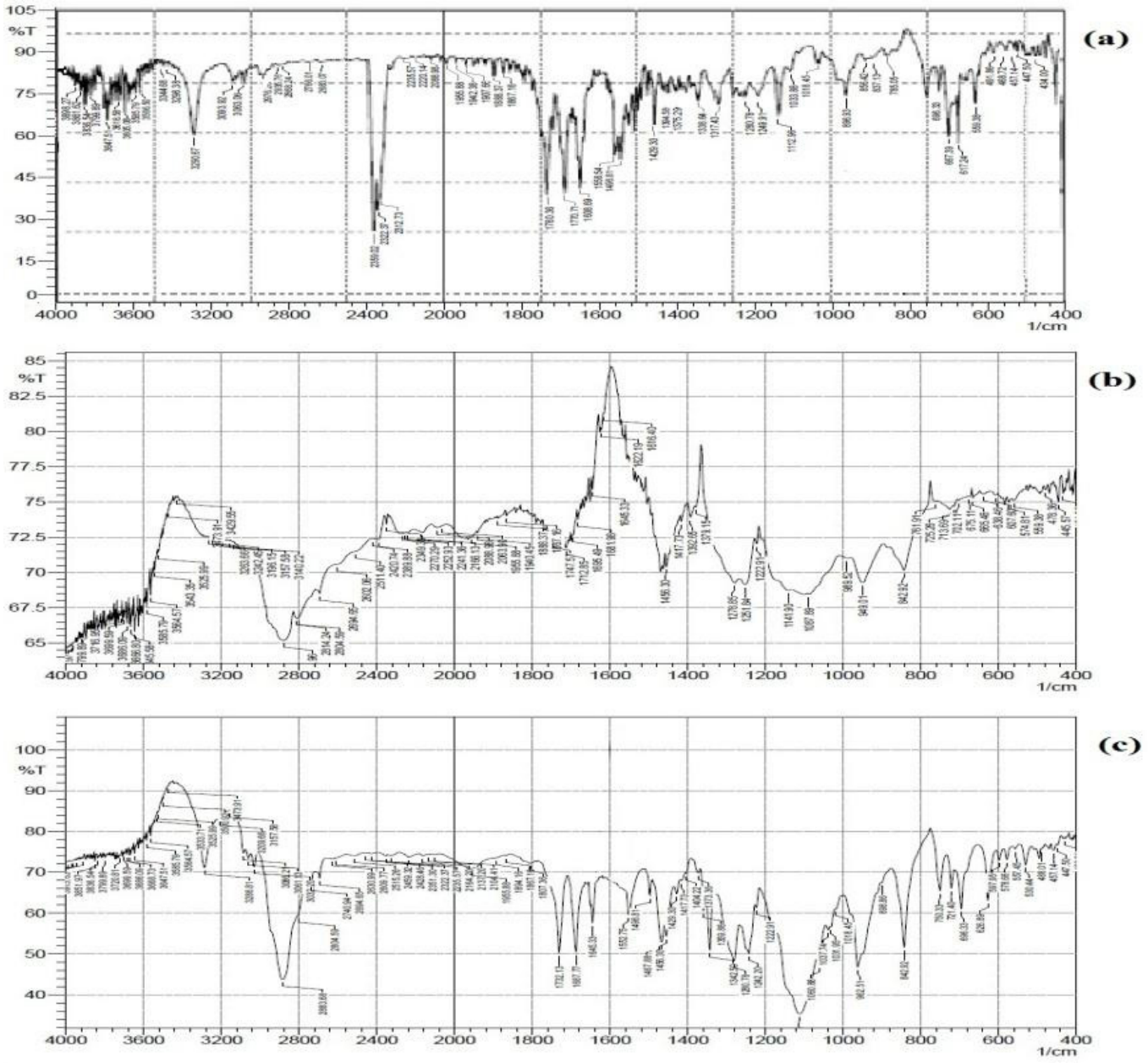

FIGURE 2 - Fourier transform infrared spectrum of a) RT b) conventional direct compression physical mixture c) optimized F12 liquisolid tablet.

DSC thermograms of RT showed endothermic sharp peak at 81.76 °C (Figure 3; a). In directly compressible tablet physical mixture (Figure 3; c) showed two broad endothermic peaks at 81.9 and 265.4 °C corresponding to the melting points of racecadotril and carrier. It indicates the drug is incorporated in the carrier but the drug is not molecularly dispersed. However, the F12 (Figure 3; d), the peak was broadened at 82.9 °C, indicates molecular dispersion of drug in the carrier and may be converted into an amorphous form. That could support the dissolution enhancement of the drug. Similar results were reported by Chella *et al.*, 2016.

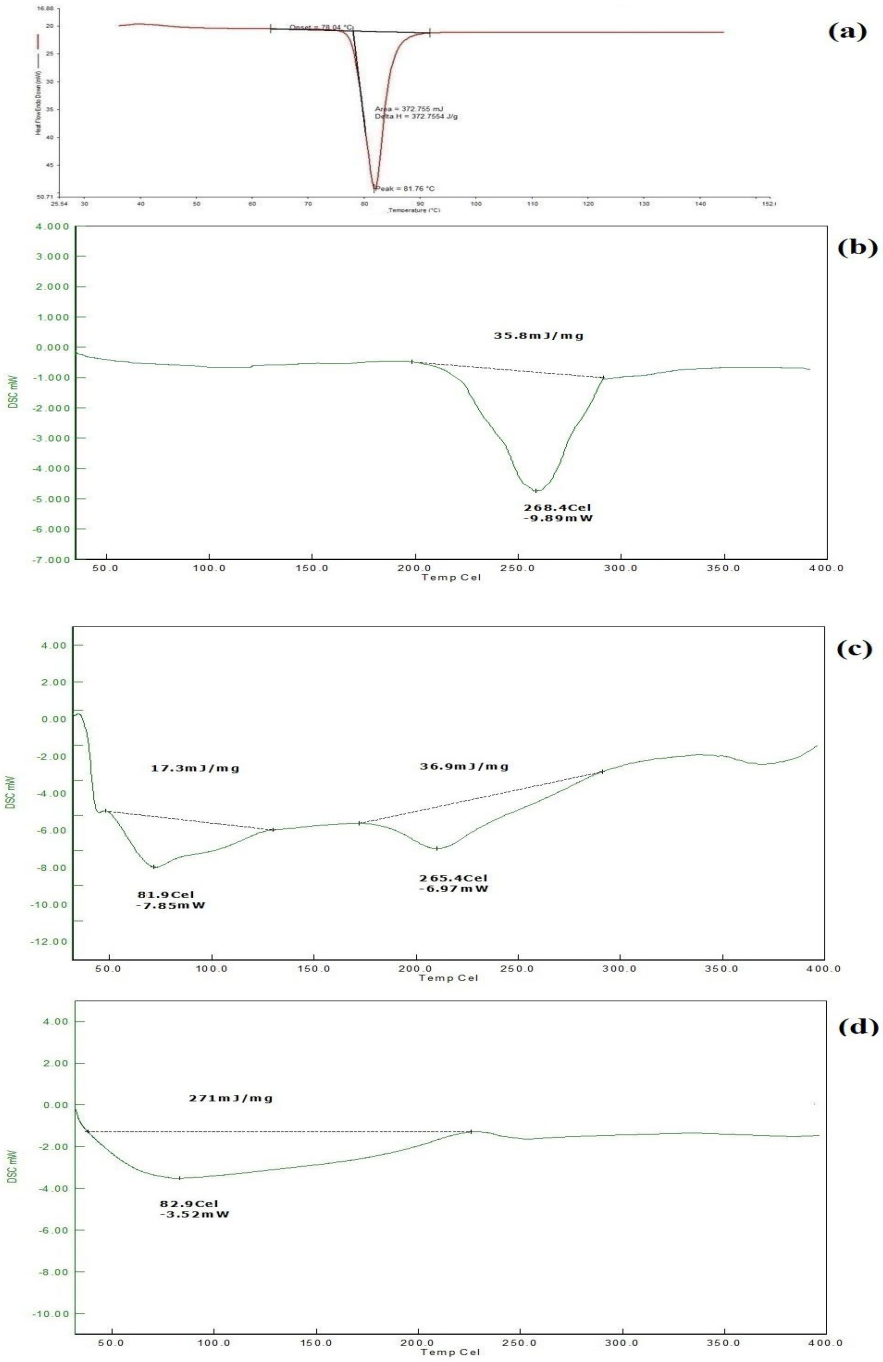

FIGURE 3 - Differential scanning colorimeter thermograms of a) RT b) carrier c) conventional direct compression physical mixture d) optimized F12 liquisolid tablet.

Figure 4 showed the X-ray diffractogram of plain RT, directly compressible tablet physical mixture and F12 formulation. The pattern of X-ray diffraction of RT at 2θ angles of diffraction i.e., 4°, 9°, 13°, 17°, 18° and 20° (Figure 4a). The directly compressible tablet mixture (Figure 4b) shows some intense peaks; indicate that drug completely may not undergone solid state transition. The peak intensity was decreased or disappeared in F12 formulation (Figure 4c) indicates reduction in crystalline to amorphous drug form. Similar types of results were observed by reduction in the crystallinity of tadalafil has increase the rate of dissolution (Lu *et al.*, 2017).

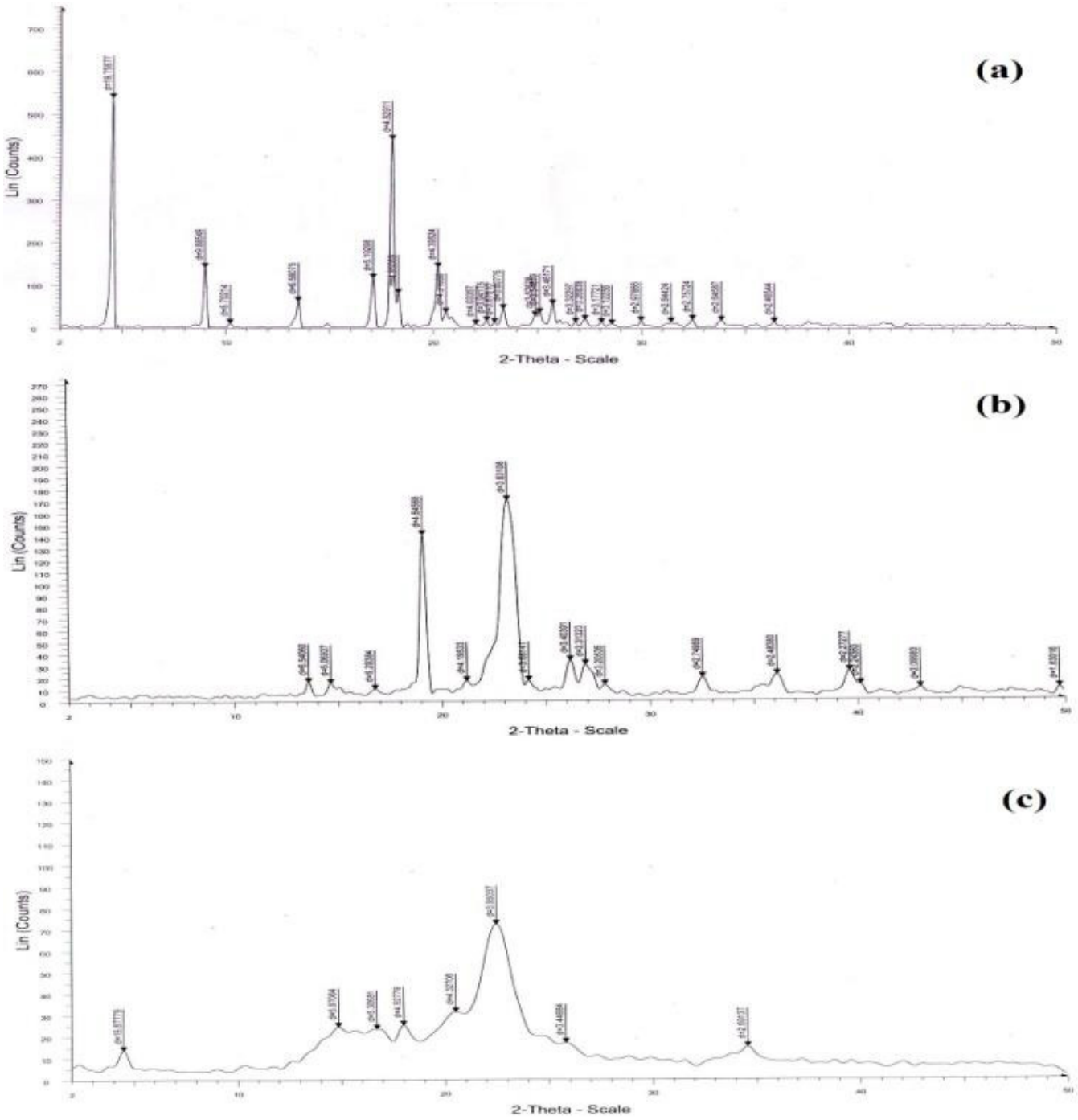

FIGURE 4 - X-ray diffraction patterns of a) RT b) Direct compression physical mixture c) optimized F12 liquisolid tablet.

Stability studies

F12 formulation was studied for stability according to ICH and stored for six months. No significant differences (Table VI) in drug release and drug content were observed between before and after storage formulations indicating the formulations were stable for six months.

TABLE VI - Stability studies of F12 optimized formulation (n=3)

Time (min)	Cumulative % racecadotril release (Mean ± S.D)					Similarity Factor (F2)
	Before storage	After 1 months of storage	After 2 months of storage	After 3 months of storage	After 6 months of storage	
5	62.54±1.37	61.53±1.74	59.62±1.48	59.17±1.63	58.74±1.82	68.55
10	78.45±1.52	76.53±1.26	74.12±1.78	73.62±0.84	72.38±1.57	
15	85.43±1.28	84.94±0.14	83.52±1.34	82.48±1.38	81.97±0.73	
30	99.54±0.62	99.38±0.82	98.15±0.25	97.84±0.72	97.26±0.64	
% Assay	99.73±1.64	99.22±1.64	98.72±1.39	98.25±1.26	97.35±1.57	-

CONCLUSION

An effort was made to prepare liquisolid tablets of racecadotril using polyethylene glycols 200 as non-volatile vehicle, Avicel PH102 as carrier and Aerosil 200 as coating material, showed the faster drug release with improved flowable and compressible characteristics. The presence of PEG 200 as non-volatile vehicle showed significant enhancement in solubility and rate of dissolution of poor water soluble racecadotril. The improvement of dissolution rate from liquisolid formulation may be due to increased in surface area and enhancement in wetting by reducing the interfacial tension of drug particles. FTIR studies showed that interactions were not observed between drug and other excipients. DSC and XRD studies indicate molecular dispersion of drug in carrier and reduction in crystalline to amorphous drug form. The use of liquisolid tablets is a promising method to promote the flow property, compressibility, stability and dissolution that improves oral bioavailability of racecadotril. Thus, liquisolid technology makes feasible for commercial production in large scale.

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CONFLICT OF INTEREST

The authors report no conflicts of interest.

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