Design and Evaluation of Rapidly Disintegrating Tablets of Racecadotril with Enhanced *in-vitro* Dissolution Achieved by Solid Dispersion Technique

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ABSTRACT

Racecadotril is an antidiarrheal drug which acts as a peripherally acting enkephalinase inhibitor. It is a solubility limited compound and thus the bioavailability can be improved by increasing its aqueous solubility. Solid dispersions of racecadotril were prepared using polymers β-cyclodextrin, poloxamer 188 (Lutrol F 68) and poloxamer 407 (Lutrol F127) in different proportions (1:1, 1:3, 1:5 and 1:10). Solvent evaporation method was employed using methanol as solvent. The solid dispersion complexes were also characterized using FT-IR, DSC and XRD. The optimized dispersions were formulated into rapid disintegrating tablets using Kollidon® CL-SF and sodium starch glycolate (SSG) as disintegrants with proportion of 2%, 3%, and 4%. The disintegration time, mean dissolution time (MDT), T_{50} and T_{90} of the formulated tablets were evaluated and compared with the marketed formulation. The pure drug showed aqueous solubility of 18.89 μg/ml while the solid dispersions with poloxamer 188 and poloxamer 407 in ratios 1:5 showed solubility of 70.75 μg/ml and 58.07 μg/ml. There was a 3 fold increase in drug solubility. The disintegration time of all the formulations were found to be less than 42 sec. Both Kollidon® CL-SF and SSG decreased the T_{50} and T_{90} values but Kollidon® CL-SF at a concentration of 4% was found to show the best results (T_{50} = 10.63 ± 0.17, T_{90} = 35.31 ± 0.57 and MDT = 13.85 ± 0.27 min). This was further compared with marketed formulation. The difference (f1) and similarity (f2) factors was found to be 89.91 and 21.11 respectively. The results suggest that the designed formulation is improved than the marketed formulation. The improved solubility, dissolution and drug release may be highly beneficial in improving the overall bioavailability of RDT.

Keywords: Racecadotril, Solid dispersion, Poloxamer 188, Poloxamer 407.

INTRODUCTION

Many patients, particularly children and the elderly population find it inconvenient to ingest conventional solid dosage forms such as tablets and capsules due to an impaired ability to swallow. This leads to patient non-compliance and potentially prolonged duration of treatment. Recent developments in the field of pharmaceutics have presented with viable dosage alternatives for paediatric, geriatric, bedridden, nauseous or non compliant patients. The development of orally fast disintegrating dosage forms that disperse or dissolve in the saliva and are swallowed without water aid in addressing the issue.[1] Besides improving the acceptability and compliance of patients, these dosage forms have been investigated for their potential to increase the bioavailability through the enhancement of the dissolution rate.[2] Additionally, pharmaceutical companies have another reason for the development of ODTs. At the end of the patent term of a drug, development of a new dosage form provides a life cycle extension of the product.[3]
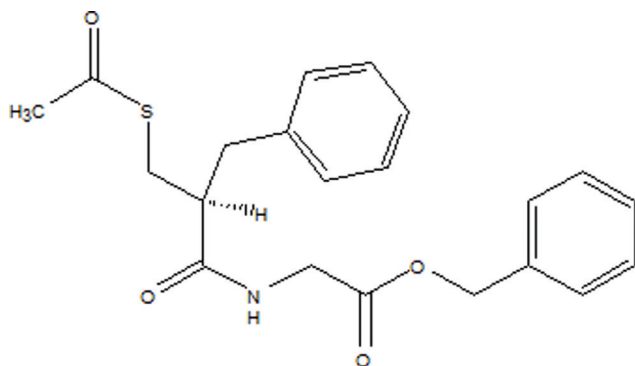
Figure 1: Structure of racecadotril.

Racecadotril (Fig. 1) is an antidiarrheal drug which acts as a peripherally acting enkephalinase inhibitor. Unlike other medications used to treat diarrhea, which reduce intestinal motility, racecadotril has an antisecretory effect and reduces the secretion of water and electrolytes into the intestine. RDT is a solubility limited compound and it is possible to improve its bioavailability by increasing its aqueous solubility.[4–5]

Practically there was no marketed drugs with less than 10 μg/ml solubility in 70's or 80's (0.01–0.1 mg/mL was considered low) but last few decades onward industry-wide increase in insoluble drug candidates. Now drug with solubilities of 0.1 μg/mL is not uncommon. Formulation Toolbox (advance technology) are invented to increase dissolution rate (improve wetting, disintegration time, surface area) and to increase dissolution extent (supersaturation).[6]

Many methods are available to improve the solubility characteristics of poorly soluble agents which include salt formation, micronization, nanosuspension, addition of solvent or surface active agents, self emulsifying systems, creation of nano-crystals, modification of the crystal habits, eutectic mixtures, solid dispersions, micro emulsions, cyclodextrin inclusion and lipid based delivery systems etc. Solid dispersions are one of the most promising strategies to improve the oral bioavailability of poorly water soluble drugs. Solid dispersion (SD) is one of such methods and involves a dispersion of one or more active ingredients in an inert carrier or matrix in solid state prepared by melting, dissolution in solvent or melting-solvent method. The formulation of drugs having low aqueous solubility using solid dispersion technology has been an active area of research since 1960. Among the various approaches to improve solubility, the solid dispersion (SD) technique has often proved to be the most successful in improving the dissolution and bioavailability of poorly soluble drugs because it is simple, economic, and advantageous. The term solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. The matrix can be either crystalline or amorphous. Once the solid dispersion gets exposed to aqueous media, the carrier gets dissolved and the drug gets released as very fine colloidal particles. By reducing drug particle size to the absolute minimum, and hence improving drug wettability, the dissolution rate and the bioavailability of poorly water-soluble drugs are expected to improve significantly. The dispersions are usually presented as amorphous products, mainly obtained by melting and solvent evaporation techniques.[7–8] Now-a-days, surfactants have been included to stabilize the formulations, thus avoiding drug re-crystallization and potentiating their solubility. Solid dispersions have been prepared using various hydrophillic agents like poloxamer[9], polyethylene glycol[10] and polyvinyl pyrollidone.[11] Poloxamers are non-ionic poly ethylene oxide (PEO) - poly propylene oxide (PPO) copolymers used in pharmaceutical formulations as surfactants, emulsifying agents, solubilizing agents, dispersing agents, and in-vivo absorbance enhancers.[11] Two of the important surface-active carriers are Gelucire 44/14 and Vitamin E R-alpha-tocopheryl polyethylene glycol 1000 succinate (TPGS). Gelucire 44/14 (Gattefosse Corp, Gennevilliers, France) has commonly been used in solid dispersion for the bioavailability enhancement of drugs.[12]

In the present investigation, rapid disintegrating tablets of Racecadotril were proposed. The solubility limited drug was first converted to a solid dispersion for solubility enhancement, and then formulated as a rapid disintegrating tablet. The formulated tablet was evaluated for various parameters.

MATERIALS AND METHODS

Racecadotril and Sodium Starch Glycolate were obtained as gift samples from Dr. Reddy's Labortories (Hyderabad, India). Poloxamer and Kollidon® CL-SF were obtained as gift samples from BASF (Bangalore, India). β-cyclodextrin was obtained as a gift sample from Torrent Pharmaceuticals (Ahmedabad, India). The following materials were procured and used as received, Sucrose (Fischer Scientific, Mumbai), PVP K-30 (Sisco Research Laboratories, Mumbai), Saccharin sodium (Yarrow Chem Products, Mumbai), Vanillin (Spectrochem Pvt.Ltd., Mumbai), Magnesium Stearate (Central Drug House, New Delhi), Talc (Central Drug House, New Delhi) and Methanol (Merck Laboratories,). All other reagents and solvents used were of analytical grade.

Solubility study

Shake flask method was employed for the solubility measurements, performed in triplicates. Excess amounts of RDT was added to pH 1.2 (0.1N HCl)

buffer, pH 4.5 acetate buffer and pH 6.8 phosphate buffer at 25 ± 0.5°C in tarson tubes. The solutions were vortexed for 2 mins and placed on orbital shaker at 100 rpm and 27°C for 24 hrs. After equilibrium was reached, the solution was filtered through whatman filter paper (#41) and the concentration of drug was determined spectrophotometrically at 232 nm (Shimadzu, Japan).

Preparation of solid dispersion

The method employed for the preparation of the solid dispersions was solvent evaporation method using methanol as the solvent. The main advantage of this method is that the thermal decomposition of drug/polymers can be prevented because of the relatively low temperatures required for the evaporation of organic solvents. Twelve solid dispersions were prepared with varying ratios of three polymers. The polymers employed were β-cyclodextrin, poloxamer 188 (Lutrol F 68) and poloxamer 407 (Lutrol F127) in various proportions (1:1, 1:3, 1:5 and 1:10) as shown in Table 1. The physical mixture of the drug and carrier were dissolved in methanol, the common solvent, and evaporated to obtain a solvent free solid residual film. The film was further dried to constant weight (about 24 hrs) and sifted through 50 mesh sieve to get a fine solid dispersion of the drug.

Solid dispersion characterization

Phase solubility studies

Shake flask method was employed for phase solubility studies which was performed in triplicates. Excess amounts of RDT and the prepared solid dispersions were added into tarson tubes filled with 10 ml of water and vortexed for 2 mins. The tubes were then placed

on orbital shaker at 100 rpm and 27°C for 24 hrs. The samples were filtered through a whatman filter paper (#41) and analysed using UV-Visible Spectrophotometer (Shimadzu, Japan) at a wavelength maximum (λ max) of 232 nm.

Differential scanning calorimetry study

Differential scanning calorimetry (DSC) thermograms of RDT, poloxamer and their solid dispersion formulations were performed on a Differential Scanning Calorimeter (DSC-60, SHIMADZU) provided with a thermal analyzer. Nitrogen gas flowed at 40 ml/min to create the inert atmosphere required to prevent any oxidation reaction in the sample holder. The equipment was calibrated for baseline and temperature with indium metal. Accurately weighed samples (5 mg) were hermetically sealed in aluminum pans and run from 20°C–150°C at a scanning rate of 10°C/min.

Fourier transform infrared spectroscopy

FTIR (Fourier transform infrared spectroscopy) spectra of pure components and their solid dispersion formulations were performed by FTIR instrument (SHIMADZU, Japan). The samples were previously ground and mixed thoroughly with potassium bromide in the ratio 1:5. The scanning range was 4000 to 400 cm^{-1}. 'IR solutions' software was used to capture and analyze the spectra.

Powder X-ray diffraction (XRD)

Powder X-ray diffraction patterns were recorded using a powder X-ray diffractometer (Rigaku, model: MiniFlex 600, Japan) under the following conditions: target Cu; filter Ni; voltage 40 kV; current 300 mA; receiving slit 0.15 millimeters. The data were collected in the continuous scan mode using a step size of 0.02° at 2θ/s. The scanned range was 3–50°.

Tablet compression of solid dispersion

The prepared solid dispersion was formulated into rapid disintegrating tablets by using wet granulation technique. The composition of tablet formulations (Table 2) consisted of solid dispersion (60 mg i.e, equivalent to 10 mg of RDT), sucrose as diluent (90 mg intra-granular and 90 mg extra-granular), sodium starch glycolate/Kollidon® CL-SF as the super disintegrant (12 mg), saccharin as a sweetener (8 mg), vanillin as a flavouring agent (10 mg), magnesium stearate (10 mg) and talc (10 mg) as glidant and lubricant respectively. To overcome the bitter taste of the drug, saccharin was added as a sweetner and sucrose selected as the diluent. All the formulation components other than the flavoring agent, glidant and lubricant were accurately weighed passed through a #40 sieve and blended appropriately.

S. No	Polymer	Drug:Polymer Ratio	Solubility (µg/ml) ± S.D
Table 1: Various Solid Dispersion and Their Phase Solubility			
1.	β-cyclodextrin	1:1	55.68 ± 1.71
		1:3	57.41 ± 0.49
		1:5	61.02 ± 1.64
		1:10	61.55 ± 1.03
2.	Poloxamer 188 (Lutrol F 68)	1:1	57.84 ± 1.42
		1:3	141.6 ± 1.06
		1:5	211.67 ± 0.52
		1:10	157.72 ± 0.72
3.	Poloxamer 407 (Lutrol F127)	1:1	66.75 ± 1.88
		1:3	120.23 ± 0.88
		1:5	174.15 ± 1.00
		1:10	142.82 ± 1.26
4.	Pure Drug without polymer	-	55.90 ± 1.25

Table 2: Formulation Composition of Rapid Disintegrating Tablets

Ingredients	F1	F2	F3	F4	F5	F6
Soild Dispersion of Racecadotril (1:5)	60	60	60	60	60	60
Sucrose	180	180	180	180	180	180
Kollidon® CL-SF	6 (2%)	9 (3%)	12 (4%)	–	–	–
Sodium starch glycolate	–	–	–	6 (2%)	9 (3%)	12 (4%)
PVP K-30	10	10	10	10	10	10
Saccharin	8	8	8	8	8	8
Vanillin	10	10	10	10	10	10
Magnesium Stearate	10	10	10	10	10	10
Talc	10	10	10	10	10	10

all the quantities were taken in mg.

The blend was granulated using PVP K-30 in isopropyl alcohol (1%, w/v) as the binder, dried in an oven at 50ºC for 2 hrs and passed through #20 sieve. Sucrose, vanillin, Magnesium stearate and talc were passed through #40 sieve, added to the granules and blended appropriately. The tablets (300 mg) were compressed by using Rimek Mini Press-1, 10-station tabletting machine and 10 mm flat die and punch set. The formulated tablets were assessed for various quality control tests.

Weight variation

Twenty tablets were selected in a random manner for performing the weight variation test. The tablets were weighed individually and as a whole. The average tablet weight was calculated and compared with the individual tablet weights.

Hardness

The hardness of tablets was measured by Monsanto hardness tester. The hardness (kg/cm²) of ten tablets was measured and the average hardness was calculated.

Friability

The friability of tablets was determined using Thermonik friabilator. Tablets equivalent to a weight of 6.5 g (22 tablets) were taken and tested for calculating the friability.

Potency and content uniformity test

Twenty tablets were crushed using a mortar and pestle and a powder equivalent to 5 mg of RDT was transferred into a 50 ml volumetric flask and the volume was made up with the mobile phase. The sample was sonicated for 10 min and suitably diluted to fit into the calibration curve range. The diluted samples were analysed using a UV-Visible Spectrophotometer at a wavelength (lambda max) of 232 nm. The experiment was performed in triplicate. For content uniformity, 10 tablets were individually weighed and transferred into a 50 ml volumetric flask and the same procedure was followed

as used for the potency test. Calculations were made as per the US Pharmacopeia test for dosage unit uniformity (USP, 2009a,b).

Disintegration test

In-vitro disintegration time of the rapid disintegrating tablets was determined following the procedure described by Gohel et al.[13] 10 mL of water at 25°C was placed in a petri dish of 10 cm diameter. The tablet was then carefully positioned in the center of the petri dish and the time required for the tablet to completely disintegrate into fine particles was noted. Measurements were carried out in replicates of six tablet (n=6) and mean SD values were recorded.

Dissolution test

The rapid disintegrating tablets were evaluated for their *in-vitro* release behavior in triplicate using a USP Type II dissolution apparatus (Electrolab Dissolution Tester TDT-6L) operated at 75 rpm and 37ºC with 400 ml of pH 4.5 acetate buffer as the dissolution medium. 2 mL samples were withdrawn at 5, 10, 15, 30, 45 and 60 mins, filtered through a 0.45 micron membrane filter, suitably diluted and analysed using an UV-VIS spectrophotometer at 232 nm.

RESULTS AND DISCUSSION

Solubility study

The solubility study was performed using shake flask method. The results (Fig. 2) obtained suggest pH dependent solubility of RDT. The drug solubility was found to be 326.47 µg/ml in pH 4.5 acetate buffer which was much greater than in pH 1.2 (0.1N HCl) buffer and pH 6.8 phosphate buffer.

Solid dispersion characterization

Phase solubility studies

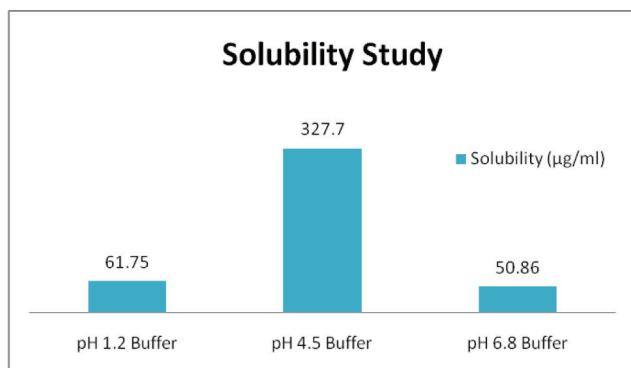There was an increase in the aqueous solubility of RDT solid dispersions prepared with poloxamer as indicated

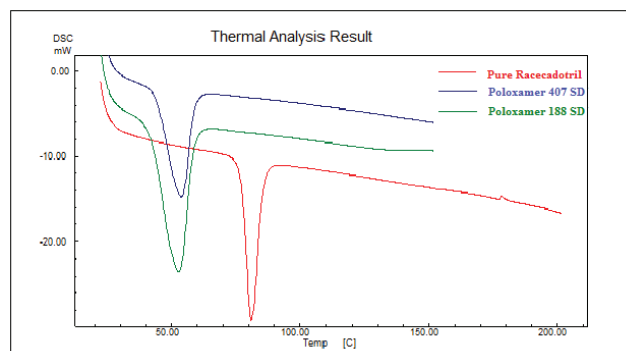**Figure 2:** Solubility of racecadotril.

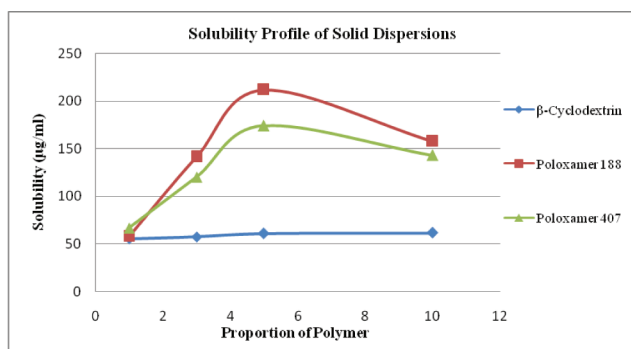**Figure 4:** DSC thermograms of pure drug and solid dispersions.

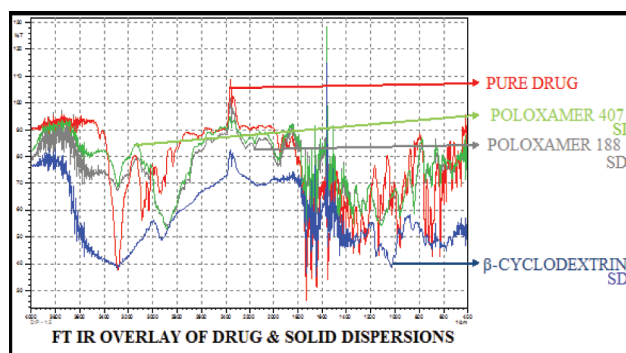**Figure 3:** Solubility profile of solid dispersions.

Figure 5: FT-IR spectra of pure drug and solid dispersions.

by the solubility profile (Fig. 3). The aqueous solubility increased as the drug to polymer ratio was increased from 1:1 to 1:5 and thereafter decreased as shown in Table 1. β-cyclodextrin was not beneficial in improving the drug solubility. The solubility of pure RDT in water was found to be 18.89 μg/ml. The aqueous solubility of solid dispersions with poloxamer 188 and 407 in the ratio 1:5 (drug:polymer) was found to be 70.75 and 58.07 μg/ml respectively, which corresponded to a 3-fold increase in solubility.

Physicochemical characteristics of solid dispersion formulations

Differential scanning calorimetry

The crystallinity and amorphicity of individual components and solid dispersion formulations were tested by DSC studies. Figure 4 shows the DSC thermogram of pure RDT showed a sharp endothermic peak at 83ºC corresponding to its melting point, that confirmed its crystallinity. In the thermograms of solid dispersions (Fig. 4), no drug melting endotherms were observed which suggests a complete conversion of crystalline drug into its amorphous form or the crystalline portion of the drug was too low in comparison to its amorphous content.

Fourier transform infrared spectroscopy

The FTIR spectrum of pure drug and the solid dispersion prepared using different polymers by solvent

evaporation method were taken and are as shown in the Figure 5. The FTIR spectrum of RDT showed absorption bands of C-H stretching in aromatic ring at 3050 cm^{-1}, N-H stretching in amide at about 3300 cm^{-1} and C-O stretching present in carbonyl group, ester and amide in the range of 1650–1770 cm^{-1}. The peaks showed no significant changes in the material characteristics when the solid dispersions of the drug prepared with poloxamer 188 and poloxamer 407 were assessed, indicating the absence of interaction between the components.

XRD analysis

The X-ray diffraction patterns for the RDT and the solid dispersion are depicted in Figure 6 and 7. The XRD pattern of RDT showed numerous sharp, narrow and intense peaks, claiming its high crystallinity. The patterns of the poloxamers also showed few peaks indicating its crystallinity nature. It was observed that, the number and intensity of the peaks were found to more in the SD samples. The bases of the peaks in the SD samples were also found to be sharper in nature confirming the crystallinity. These conclusions from XRD analysis can be taken as confirmation for crystallinity in the samples.

Rapid disintegrating tablet characterization

Weight variation, hardness and friability

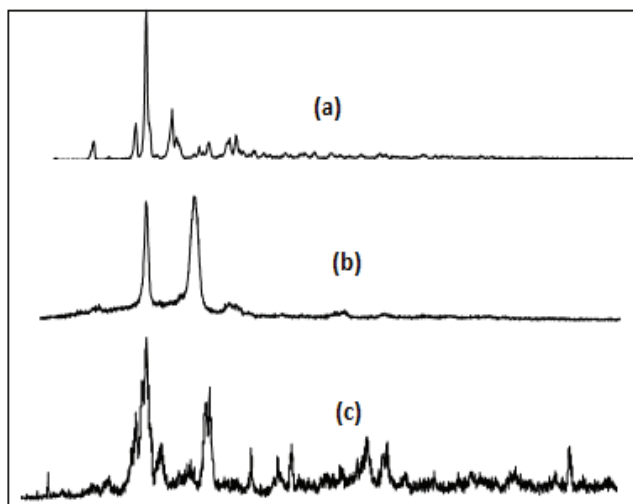The deviation from the average weight was found to be less than 3% for all the formulation batches as seen

Figure 6: XRD pattern of (a) Pure drug, (b) Poloxamer 188, (c) Solid dispersion.
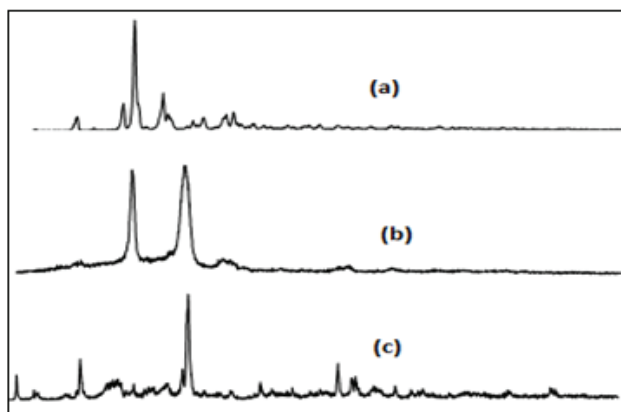

Figure 7: XRD of (a) Pure drug, (b) Poloxamer 407, (c) Solid dispersion.

from the results of the weight variation test. As the average weight of the tablet is 300 mg, the permissible limit for weight variation is 5% as per the Indian Pharmacopeia 2007. The average hardness for all the batches was found to be between 4.5–5.5 kg/cm². The friability for all the batches was found to be less than 0.9%. The tablets comply with the standards for weight variation, hardness and friability as shown in Table 3.

Potency and content uniformity test

The prepared formulations comply with the standard specifications for potency and content uniformity. Table 3 shows that all the tablets were found to be in the range of $100 \pm 5\%$.

Disintegration time

The FDA recommends a disintegration time of 30 sec or less for rapid disintegrating tablets based on the USP disintegration test (FDA guidance, 2008). Superdisintegrants are commonly used to reduce the disintegration time and to speed the drug release and potentially increase the absorption process of a drug. They are used in low concentrations, usually 1–10% of tablet weight. The mechanism by which they reduce the disintegration time is swelling, wicking and volume expansion (Quadir and Kolter, 2006).

Disintegration time of rapid disintegrating formulations varied from 19.83 ± 1.66 sec for formulation-F3 to 41.81 ± 2.49 sec for formulation-F4 as shown in Table 3. As seen from the results of disintegration test, the disintegration time was much lesser for formulations with Kollidon® CL-SF than for the formulations with sodium starch glycolate when used in same proportions. These observations could be explained by the fact that Kollidon has the ability to reach 90% maximum swelling pressure in a short period (32.9 sec) compared to sodium starch glycolate (Quadir and Kolter, 2006).

Dissolution testing

The *in-vitro* dissolution behavior of RDT from various solid dispersion formulation and marketed product (MP) was examined in Acetate buffer (pH 4.5) as shown in Figure 8. The data obtained from the dissolution study shows the complete drug release within 60 mins for all the six formulations. Model independent approaches like mean dissolution time (MDT), T_{50}, and T_{90} were calculated for all the batches and compared with the marketed product using One Way ANOVA. The best batch among the six (batch F-3) was further compared with the marketed product using difference (f1) and similarity (f2) factors (Fig. 9).

Table 3: Evaluation of Rapid Disintegrating Tablets					
Formulation	Hardness (kg/cm²)	Friability (%)	Potency (%)*	Content Uniformity (range, %)	Disintegration Time (secs)*
F1	5.0	0.81	98.59 ± 1.94	97.57–101.56	29.59 ± 2.94
F2	4.5	0.67	96.78 ± 2.14	98.48–100.76	23.83 ± 2.01
F3	5.0	0.73	97.95 ± 1.99	99.34–101.17	19.83 ± 1.41
F4	5.5	0.49	98.77 ± 0.88	96.48–99.91	41.81 ± 2.49
F5	5.0	0.84	95.96 ± 1.37	98.79–102.34	34.83 ± 1.66
F6	5.0	0.68	99.21 ± 2.05	99.75–101.31	28.30 ± 1.29

*Values indicated as mean ± SD
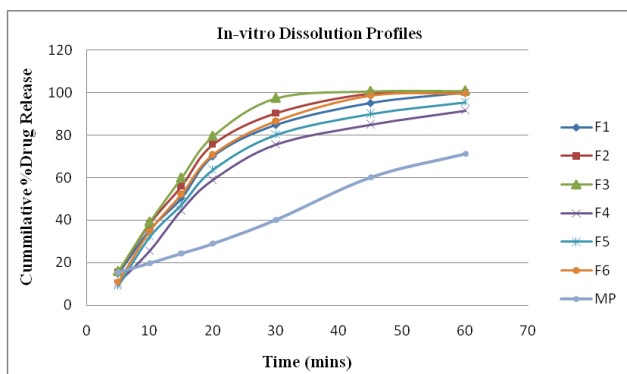
Figure 8: *In-vitro* dissolution profiles of the prepared formulations & marketed product.
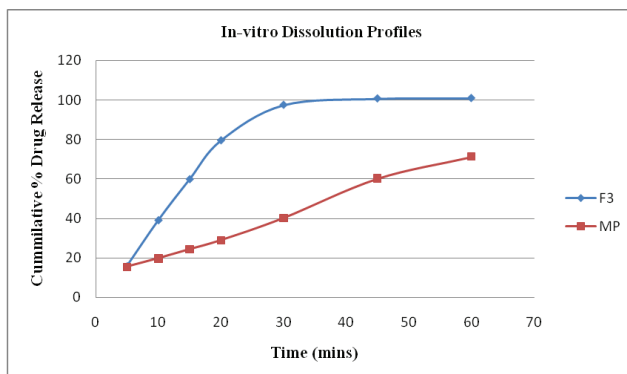
Table 4: Results of Dissolution Studies

Formulation	MDT (mins)	T_{50} (mins)	T_{90} (mins)
F1	17.34 ± 0.44	13.15 ± 0.21	43.67 ± 0.68
F2	15.08 ± 0.82	11.6 ± 0.09	38.53 ± 0.30
F3	13.85 ± 0.27	10.63 ± 0.17	35.31 ± 0.57
F4	19.00 ± 0.18	17.14 ± 0.34	56.94 ± 1.13
F5	18.18 ± 0.23	15.06 ± 0.39	50.03 ± 1.31
F6	16.53 ± 0.03	12.87 ± 0.24	42.74 ± 0.80
MP	40.53 ± 0.65	34.33 ± 0.15	114.05 ± 0.50

Values indicated as mean±SD
MDT = Mean Dissolution Time
MP = Marketed Product

Figure 9: *In-vitro* dissolution profiles of formulation F3 & marketed product (MP).

MDT, T_{50} and T_{90}

The MDT is the arithmetic mean of *in-vitro* dissolution profiles. T_{50} and T_{90} are the time required to release 50% and 90% of the drug from the formulations, respectively. The values of MDT, T_{50} and T_{90} varied from 13.85 ± 0.27 (F3) to 19.00 ± 0.18 mins (F4), 10.63 ± 0.17 (F3) to 17.14 ± 0.34 mins (F4) and 35.31 ± 0.57 (F3) to 56.94 ± 1.13 mins (F4) respectively (Table 4). The MDT, T_{50} and T_{90} of the marketed formulation were found to be 40.53 ± 0.65, 34.33 ± 0.15 and 114.05 ± 0.50 mins respectively. From the results of One Way ANOVA MDT, T_{50} and T_{90} of all the six formulations were statistically significant ($p < 0.01$) when compared with the marketed product. Both Kollidon® CLSF and SSG decreased the T_{50} and T_{90} values but Kollidon® CLSF at a concentration of 4% (F3) was found to show the best results.

Difference and similarity factors

The formulation F3 (the best formulation among the six as seen from MDT, T_{50} and T_{90} values) was further compared with the marketed product using difference (f1) and similarity (f2) factors. The difference factor was found to be 89.91 while the similarity factor was 21.11. The results suggest that the two formulations are different and confirm the inference obtained from MDT, T_{50} and T_{90} data.

Thus there is significant increase in solubility and dissolution rate of the solid dispersion of poorly soluble Racecadotril. Enhancement in the solubility and dissolution of Racecadotril could be correlated to the chemical structure of highly water soluble Poloxamer. Arrangement of hydrophilic portion; ethylene oxide (EO) and hydrophobic core; propylene oxide (PO) blocks in poloxamer results in an amphiphilic nature, which has the properties to self assemble into micelles in aqueous solution; the hydrophobic core can act as reservoir for the drug, while the hydrophilic portion acts as interface between the aqueous medium and the drug. At higher concentration, these monomolecular micelles associate to form aggregates of varying size, which have the ability to solubilize the drugs. In the dry state, the particles are in close contact or adhered to the polymer particles as a result of mixing. When the mixture comes in contact with water, the polymer particles might have hydrated rapidly into polymer solution and solubilizing the adjacent drug particles.[14–16] Hydrogen bonding may be possible when the drug is molecularly dispersed in the carrier (solid solution). Along with this, improvement in the wettability may be the possible reason for solubility as well as the dissolution enhancement. Wettability and the solubilization of the drug are improved due to presence of diffusion layer of high carrier concentration around the drug particles which may be formed during solvent evaporation. The solubilized drug diffuses to and gets diluted in the bulk of dissolution medium.[16–17]

CONCLUSION

The solid dispersion of RDT with poloxamer 188 and 407 greatly enhanced its aqueous solubility. The solubility increased as the drug to polymer ratio was increased from 1:1 to 1:5 and thereafter decreased. Thus the optimum drug to polymer ratio was found to be 1:5.

The solid dispersion prepared using Poloxamer 188, when formulated into rapid disintegrating tablets using Kollidon® CL-SF and sodium starch glycolate as disintegrants, showed decreased disintegration time and enhanced dissolution characteristics. From the dissolution profiles, MDT, T_{50} and T_{90} it was seen that the prepared formulations were better than the marketed formulations. The formulation (F3) with Kollidon® CL-SF in a concentration of 4% gave the best *in-vitro* release profile. The superiority of the formulation (F3) over the marketed formulation was proved using One Way ANOVA and confirmed using difference (f1) and similarity (f2) factors.

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