Design, development and influence of super disintegrants on solid dispersion based taste masking orodispersible tablets of racecadotril

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Abstract:

Orodispersible tablets are a kind of solid dosage form that easily disintegrate or dissolve in water or a little amount of salivary fluid to generate a solution or suspension. Dispersible pills are a good option for patients of all ages who have trouble swallowing capsules and tablets, but notably young children and the elderly. Some drugs' bioavailability may be improved due to drug absorption in the oral cavity, as well as pregastric absorption of saliva-containing dispersed medicines that move down into the stomach. The current study used the direct compression method to manufacture orodispersible tablets (ODTs) of racecadotril employing sodium starch glycolate, crospovidone, and sodium croscarmellose as super disintegrants. The developed orodispersible tablets were assessed for several characteristics, including drug-polymer interaction, water absorption ratio, and *in-vitro* drug release studies. The tablets developed using the direct compression technique had a weight variation of less than 7.5%, a hardness of 3.07±0.35 to 3.94±0.33 kg/cm², a percentage friability of 0.41±0.78% to 0.95±0.33%, *in-vitro* dispersion times of 19±1.41 to 32±1.33 sec, drug content uniformity of 98.55±1.44 and 99.88±1.55%, wetting times of 32±1.28 to 49±1.55 sec, a water absorption ratio of 65.66±1.12% to 85.72±1.24% and disintegration times of 10±1.24 sec to 22±0.66 sec. Oro-dispersible tablets made with crospovidone (F6), which contain crospovidone at a concentration of 6%, were selected as the best batch due to rapid disintegration at 10 sec and relatively quick drug release of 99.82±1.55% at 8 minutes.

Key Words: Orodispersible tablets (ODT), Racecadotril, Antidiarrheal drug, Super disintegrants, Crospovidone.

Introduction:

Over the last three to four decades, orodispersible tablets (ODTs) have gained popularity as an alternative to traditional capsules and tablets because of their superior patient compliance, solubility, and stability characteristics[1, 2]. By creating a more user-friendly dosage form, recent innovations in novel drug delivery systems (NDDS) hope to improve patient compliance and, by extension, the safety and effectiveness of medicinal substances. Pharmaceutical advertising has contributed to the widespread availability of products that use fast-acting tablet technologies for dissolving or distributing substances[3]. As the patent life of a pharmacological entity nears its conclusion, it is common practice for pharmaceutical companies to develop a new and improved dosage form of that therapeutic entity. The introduction of a new, more effective dosage form may help a company gain more market exclusivity while simultaneously making the product more accessible to a wider range of patients[4]. Orodispersible tablets (ODT) are solid unit dosage forms that are similar to traditional tablets; however, they also comprise super disintegrants that cause them to dissolve in the mouth in the presence of saliva in under a minute[5].

Orodispersible tablets are defined by the European Pharmacopoeia as those that dissolve completely within three minutes in the mouth. Dispersible tablets, as defined by the Indian Pharmacopoeia, are uncoated tablets that dissolve evenly in water within a short amount of time at ambient temperature and may include permitted sweetening and flavoring components[6]. Orally disintegrating tablets (ODTs), mouth dissolving tablets (MDTs), quick-dissolving tablets (QDTs), and fast dissolving tablets (FDTs) all refer to the same kind of tablet used for instantaneous medication administration. Orodispersible tablets are excellent for patients who have difficulty in swallowing traditional tablets or hard capsules, such as pediatric and elderly patients, as well as individuals who do not have access to water when traveling or receiving chemotherapy[7].

The medication used to treat diarrhea is only available in adult strength, therefore it is important to give children the right dosage. The incorrect dose may come from cutting or breaking tablets, a frequent conversion technique for adult formulations to child dosage[8]. The taste of the medication is a critical component in determining therapy and medication compliance. In order to improve patient convenience, the current study set out to develop a dispersible tablet that included an antidiarrheal drug that swiftly dissolved and resulted in a

uniform dispersion in a matter of seconds[9]. The process for establishing solid dispersion depends on the rate of disintegration, which can be accelerated by increasing surface area to prevent precipitation inside the carrier, incorporating solids into the solution, and improving wetting properties as a result of direct interaction with the hydrophilic polymer carrier, which then takes the form of a meta-stable crystalline structure[10].

In order to change the kind of solid dispersion and drug release behavior, it is necessary to modify the drug/polymer ratio and choose the best approach. It is also regarded as a single-dose solid dispersion that is taken orally and administered inside the mouth cavity. This solid dispersion dissolves in saliva and begins its action rapidly[11]. The success or failure of an oral pharmaceutical formulation can be strongly connected with its flavour, making the taste of a pharmaceutical product a significant aspect[12].

Numerous pharmacological substances have an unpleasant aftertaste; thus, getting children and elderly patients to take their oral prescriptions regularly depends heavily on how well they taste[13]. Current treatment modalities concentrate on restoring fluid and electrolyte balance, eliminating infectious agents with antibiotics, and substantially reducing the duration of diarrhoea using antimotility medications. One of the most common health issues, diarrhoea affects people of all ages and costs countries a lot of money and human resources every year[14].

Racecadotril acts as a peripherally acting enkephalinase inhibitor and is a safe and effective antisecretory antidiarrheal drug. The patient's perception of the efficacy of medical treatment rises when the frequency and volume of bowel movements decrease. Studies have shown that racecadotril may reduce the severity and duration of both infectious and noninfectious cases of acute diarrhoea[15, 16]. Due to its high therapeutic index, lack of CNS effects, and pure antisecretory action, racecadotril is an ideal anti-diarrhea medication for orodispersible dosage forms. Patients would benefit from orodispersible rehydration because they would have a large reduction in stools and a quicker recovery[17, 18].

The size and hardness of the tablet affect how rapidly the dosage form dissolves. Preparing orodispersible tablets requires mixing many super disintegrants of varying strengths. The current research using dispersible tablets might compromise the efficacy and safety of the therapy for young children and elderly patients by hiding the unpleasant taste of the drugs and producing its dispersible tablet.

Materials and Methods:

Racecadotril was received as a gift samples from Swapnroop Drugs and Pharmaceuticals Aurangabad. Eudragit EPO was purchased from Dow chemical Inc, Mumbai. Sodium starch glycolate, Crospovidone, and Croscarmellose sodium were purchased from BASF Company, Mumbai. Avicell PH 102 was purchased from FMC Biopolymer, Mumbai. Sucralose was purchased from J.K. Sucralose INC, Ghaziabad. All other materials used were of analytical grade and procured from commercial sources.

Pre-compression evaluation of powder blends:

Physical properties:

Angle of repose (θ):

It is described as the greatest angle that can be made between the horizontal plane and the surface of the powder pile. It was done with a fixed funnel. A flat, horizontal surface was fastened with a funnel that had its tip raised to a specific height (h), above which graph paper was laid out. Powder was poured slowly and carefully via a funnel until its peak reached the end of the device[19]. These investigations were conducted both before and after lubricant/glidant incorporation. Next, the angle of repose (θ) was determined.

$\theta = \tan^{-1}(h/r)$

Where, θ - Angle of repose,

h - Height of pile,

r - Radius of the base of the pile.

Bulk density (D_b):

A bulk density apparatus was used to measure the density of the dried granules by measuring accurately weighted samples in a cylinder to measure and recording the sample's volume and total weight[20].

Bulk density is determined using the below formula and its units are gm/ml.

$D_b = M / Vo$

Where, Db - Bulk density (gm/ml)

M - Weight of granules (gm)

Tapped density (D_t):

In order to calculate the tap density, an accurately weighted quantity of the dried granules was placed in a measuring cylinder, and the volume of the granules after 100 taps, as well as the total granule weight were recorded.

$D_t = M / V$

Where, D_t- Tapped density (gm/ml),

M - Weight of granules (gm)

V - Tapped volume of granules (ml)

Compressibility index:

It is easy to compress a powder. The compressibility index was calculated by inserting the dry granules in a measuring cylinder, noting the initial volume (V0), and then remeasuring the volume after 100 taps (V). Table 1 lists the different characteristics of the flow[21].

Compressibility index = $(1- V/ V_0) X 100$

Where, V_0-Volume of powder/granules before tapping.

V-Volume of powder/granules after 100 tappings.

Hausner's ratio:

The Hausner's ratio is a number that is correlated to the flow ability of a powder or granular blend.

Hausner's Ratio = TD / BD

Where, TD -Tapped density, BD -Bulk density

Table 1: Flow properties of powders

S. No	Flow Properties	Angle of Repose (θ)	Flow Properties	Hausner's Ratio	Compressibility Index (%)
1	Excellent	25-30	Excellent	1.0-1.11	<10
2	Good	31-35	Good	1.12-1.18	11-15
3	Fair	36-40	Fair	1.19-1.25	16-20
4	Passable	41-45	Passable	1.26-1.34	21-25
5	Poor	45-46	Poor	1.35-1.45	26-31
6	Very poor	55-56	Very poor	1.46-1.59	32-37

7	Very very poor	>66	Very very poor	>1.60	>38

Drug-Excipient compatibility studies:

The FTIR method may be used to identify the role of different functional groups of drugs and excipients by analyzing substantial changes in the shape and location of absorbance bands. Individual samples, with the addition of the drug and excipient blend, were pulverized in a mortar and carefully mixed with potassium bromide (1:100) for 3-5 minutes before being compacted into a disc by applying pressure of 5 tonnes for 5 minutes in a hydraulic press. The pellet was placed in a sample container and scanned in an FTIR spectrophotometer from 4000 to 400 cm^{-1}. The distinctive peaks of all samples and mixes were then collected[22].

Formulation development & procedure for preparation of taste masked dispersible tablets:

Development of formulation in the present study was mainly based on the type of carriers, for solid dispersion preparation, and polymers for coating of the formed solid dispersion granules. Formulation of Racecadotril (10mg) orally dispersible tablets by direct compression of the coated solid dispersion involves use of polyethylene glycol-6000 as a carrier.

- Initially formulations were prepared using the carrier namely PEG 6000 of which gave better taste masking & disintegration of the solid dispersion granules.
- Weighed quantities of drug (Racecadotril), orange flavor and sweetener (Sucralose) were taken in a poly bag and mixed for 30 minutes and mixed uniformly.
- 2% PEG 6000 was weighed and was melted in a clean petridish, until a clear solution was formed.
- The above prepared drug mixture was added slowly to the polymer melt.
- This mixture formed was rapidly cooled which resulted in a hard mass, which was then sieved through #20.
- These formed granules were coated with 1% solution of HPMC and Eudragit EPO, where Eudragit EPO favoured better taste masking.
- In another beaker 1% solution of Eudragit EPO was prepared with water.
- This solution was poured over drop by drop wise to the above prepared drug granules, where a soft mass was formed and which on sieving through #30 mesh gave polymer coated granules.

- Hence, PEG 6000 was selected as the solid dispersion carrier and Eudragit EPO was chosen as the taste masking coating polymer.
- All of the excipients, including the diluent, disintegrants, and lubricant, were precisely measured and sieved through mesh sizes of 40 and 60, respectively, for the experimental formulation.
- Using a double cone blender set at 100 rpm for 10 minutes, we successfully combined the drug polymer complex with the other excipients.
- Stearic acid and aerosil were added to the well-blended mixture after being passed through #32 and well mixed.
- Finally, orally dispersible tablets were prepared by direct compression using different concentrations of super disintegrants like crospovidone (polyplasdone), croscarmellose sodium (Ac-Di-Sol), and sodium starch glycolate (explotab) of the prepared granules with 8 mm punch and 8 stations rotary tablet compression machine of Shakti Pharmatech Pvt Ltd. The formulation was tabulated in table.2.

Table 2: Formulations of racecadotril oro-dispersible tablets prepared by using different super disintegrants

Ingredient (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Racecadotril- DPC	30	30	30	30	30	30	30	30	30
Sodium starch glycolate (Explotab)	3.5 (2%)	7 (4%)	10.5 (6%)	-	-	-	-	-	-
Crospovidone (Polyplasdone),	-	-	-	3.5 (2%)	7 (4%)	10.5 (6%)	-	-	-
Croscarmellose sodium (Ac-Di-Sol),	-	-	-	-	-	-	3.5 (2%)	7 (4%)	10.5 (6%)
Mannitol	86.5	83	79.5	86.5	83	79.5	86.5	83	79.5
Avicell PH 102	50	50	50	50	50	50	50	50	50
Orange flavour	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Sucralose	1	1	1	1	1	1	1	1	1

Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Aerosil	1	1	1	1	1	1	1	1	1
Total (mg)	175	175	175	175	175	175	175	175	175

Note: DPC – Drug polymer complex,

Evaluation of oro-dispersible tablets:

Hardness:

Mansanto's hardness tablet tester apparatus was used to measure the hardness of tablets that were randomly picked from various formulations. After setting the scale to zero, the load was steadily raised until the tablet broke. A measurement of the tablet's hardness may be found in the load at the exact point where it broke. Kg/cm^2 was used to measure hardness. Three measurements were taken, and the average was computed[23].

Thickness:

The tablet's thickness must be the same for all tablets of the same overall dimensions. The thickness was measured using Vernier Callipers. By utilizing a digital vernier scale, investigators averaged the thickness of three tablets from each batch that had been individually preweighed. Three separate measurements were averaged to obtain the final tally[24].

Weight variation:

From each batch, twenty tablets were handpicked at random, and the mean mass of these tablets was calculated using the total mass of all tablets. Individual measurements were compared to the mean mass. In terms of percentage difference, the weight fluctuation should be within acceptable ranges[25, 26]. The IP or BP weight variation limitations for tablets are shown below (table 3).

The below formula has calculated the % deviation:

$$\% \text{ Maximum deviation} = (W_3\text{-}W_2/ W_3) \times 100$$

$$\% \text{ Minimum deviation} = (W_3\text{-}W_1/ W_3) \times 100$$

Where, W_1 = Minimum weight of tablet in mg.

W_2 = Maximum weight of tablet in mg.

W_3 = Average weight of tablet in mg.

Table 3: Maximum allowed deviation in tablet weight variation in percent.

The highest weight differences permitted	Tablets average weight milligrams
	IP or BP
± 10	< 80
± 7.5	80 - 250
± 5	> 250

Friability:

Friability is a measure of how well a tablet holds up under stress and damage caused while it is manufactured, packaged, shipped, and handled by the end user. Friability may be evaluated using a Roche friability testing device. Tablets that lose less than 1.0% of their weight during compression are often accepted. The friability was determined using the following formula[27, 28].

$$\% \text{ Friability} = 1 - (\text{loss in weight} / \text{initial weight}) \times 100$$

Disintegration time:

How quickly a tablet breaks down into smaller pieces is defined by a metric called disintegration time. The disintegration testing apparatus uses a basket rack configuration of six glass tubes, each of which has a 10-mesh screen. Six pills were placed in tubes, and the whole basket was placed in 900 ml of water maintained at 37 degrees Celsius. Using a standard motor-driven device, the tablet is pushed up and down a distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minute, maintaining a height of 2.5 cm above the water's surface throughout. The time it took for each pill to completely disintegrate was recorded[29, 30].

Wetting time:

A piece of tissue paper that had been folded in half and placed inside a petri dish that had a diameter of 10 centimetres and contained 10 millilitres of water. A tablet was put on the tissue paper, and it was allowed to take up all of the moisture that was there. After that, the amount of time required to completely rehydrate the pill was tallied[31, 32].

Water absorption ratio:

A square of tissue paper that had been folded in half twice was placed inside of a petri dish that had a diameter of 10 centimetres and an interior capacity of 5 millilitres. A tablet was positioned on the tissue paper, and time was allowed for it to completely absorb the liquid[33, 34].

After being dampened, the pill was given a second weighing. The water absorption ratio, denoted by R, was calculated by using the following equation.

$R\ (\%) = 100\times(W_2 - W_1) / W_1$

Where W_1 is the weight before water absorption and W_2 is the weight after water absorption, respectively.

***In-vitro* dispersion time:**

To determine the *in-vitro* dispersion time, one tablet was placed in a beaker that had 10 millilitres of pH 6.8 phosphate buffer at a temperature of 37 ± 0.5°C. The time required for complete dispersion was then determined[35, 36].

Drug content:

The purpose of the content homogeneity test is to ensure that there is little variation in the amount of active ingredient contained in each tablet across a batch. After picking five pills at random, we were able to calculate their mean weight. After being carefully weighed and crushed in a mortar, the tablets were averaged out to get the amount of an average tablet. The samples were then diluted with 6.8 phosphate buffer solution to the required concentration before being split between three 100 ml volumetric flasks. The drug was stored for 24 hours and shook repeatedly to ensure complete dissolution. The combinations were filtered, and then diluted as needed[37]. Maximum 231 nm absorbance was used to compare each tablet to a blank standard and report the medication content.

Dissolution studies:

The in-vitro dissolution examination was performed at 37 ± 0.5 degrees Celsius with 50 revolutions per minute using 900 millilitres of phosphate buffer solution with a pH of 6.8 as the dissolving medium. The USP dissolution apparatus Type II (Paddle type) was employed for the experiment. Following the removal of aliquots of the dissolving liquid, the absorbances of the filtered solutions were evaluated using an ultraviolet spectrophotometer set at 231 nanometers. Six separate trials were carried out for each individual batch. It was determined how to calculate and publish the average percentage of medication release together with the standard deviation[38].

Assessment of Taste Masking:

Since taste perception differs from person to person, evaluating taste masking requires establishing the rate at which drugs are released from taste-masked complexes in addition to other time-consuming in-vivo assessments of drug release and efficiency.

***In-vivo* taste evaluation:**

Before conducting the research task, detailed permission from each participant was sought after receiving approval from the institution's human experimentation committee. Under the direction of a licensed medical practitioner, this study was carried out in accordance with the recommendations made by the committee[39, 40].

A taste evaluation was performed on six healthy male human volunteers (aged 18-55 years) who provided informed permission. The drug-polymer combination was placed on the tongue for 30 seconds before being spat out. The optimized orodispersible tablet formulation was applied to the tongue and allowed to dissolve completely. Taste was assessed and given using a scale of bitterness, with 0 being bitterless, 1 being barely bitter, 2 being moderately bitter, and 3 being strongly bitter[41].

Stability study of oro-dispersible tablets:

A formulation's stability may be described as the period of time from the date of manufacturing until its chemical activity is at least at the labeled level and its physical features have not altered noticeably or negatively. The stability of the active ingredient must be a primary factor in deciding whether to approve or decline the use of dosage forms for medications in any reasonable dosage form design and review process.

According to the ICH Guidelines, stability assessments should be carried out at 40°C/75%RH for 6 months whereas long-term stability tests should be conducted at 25°C/60% RH. If there is a noticeable shift in these stability conditions, the formulation should be evaluated in an intermediate temperature and humidity level, such as 30°C and 65%RH. Drug product stability testing starts with formulation development and lasts until the compound or commercial product expires[42]. The stability testing time and various temperatures are shown in the table 4. The current study entails placing the optimised batch in HDPE bottles and exposing them to stable conditions of 40°C ±2°C/75% RH ±5% RH.

Table 4: ICH-recommended storage conditions for stability studies

Study Conditions	Storage conditions	Minimum time period
Accelerated	40°C ± 2°C/75% RH ± 5% RH	6 months
Intermediate	30°C ± 2°C/65% RH ± 5% RH	6 months
Long-term	25°C ± 2°C/60% RH ± 5% RH	12 months

Results and Discussion

Racecadotril dispersing tablets were made using a technique that included super-disintegrants sodium starch glycolate, crospovidone and croscarmellose sodium in varying ratios. Nine formulations in all were developed.

Pre-compression physical characteristics of powder blends:

Physical properties of racecadotril:

Interparticulate interactions influence the bulking properties of powder. A comparison of the bulk density and tapped density can give a measure of the relative importance of this interaction in a given powder; such a comparison is often used as an index of the ability of the powder to flow. The bulk density and tapped density were found to be 0.74g/cm^3 and 0.82g/cm^3 respectively. A simple indication of ease with which a material can be induced to flow is given by application of a compressibility index. The value for the % compressibility index of racecadotril was found to be 12.63 % and Hauser's ratio of 1.32. The precompression properties of racecadotril active pharmaceutical ingredient were tabulated in table.5.

Table 5: Evaluation of precompresion properties of racecadotril

Parameters	Values
Angle of Repose (θ)	29
Bulk Density (g/cc)	0.74
Tapped Density (g/cc)	0.82
% Compressibility index	12.63
Hausner's ratio	1.32

Angle of repose:

The findings that were identified for an angle of repose for each of the formulations are shown in Table 6. The numbers were found to fall anywhere between 25.97±0.06 to 29.85±0.07 degrees, give or take a few degrees. All of the formulations had angles of repose that were less than 30 degrees, which is an indication of excellent flow.

Bulk density:

For all of the formulas, the bulk density and tapping density ranged from 0.54gm/cm^3 to 0.63gm/cm^3 and from 0.67 gm/cm^3 to 0.71 gm/cm^3. The numbers found were within a good

range, and there were no big differences between the bulk density and the tapped density. These answers help us figure out how much the powder can be compacted (Table 6).

Percentage compressibility or Carr's consolidation index:

Powder mixture compressibility was calculated using the Carr's consolidation index formula. Table 6 shows that the tablet combination of the different formulations flows very well, with % compressibilities ranging from 10.01 to 12.12.

Hausner's ratio:

Based on the information provided by bulk density and tapped density, Hausner's ratio of powder mix was established. All the formulas have a Hausner's ratio between 1.10 and 1.13, which means the powder flows very well (Table 6).

Table 6: Pre-compression parameters of oro-dispersible tablets

Formulation Code	Angle of Repose* (ɵ)	Bulk Density* (g/cc)	Tapped Density* (g/cc)	Compressibilty Index (%)	Hausner's Ratio
F1	26.82±0.04	0.56±0.067	0.67±0.075	11.94	1.10
F2	28.42±0.04	0.58±0.034	0.69±0.084	10.01	1.12
F3	29.21±0.05	0.60±0.057	0.66±0.046	10.09	1.10
F4	25.97±0.06	0.54±0.056	0.64±0.076	10.93	1.12
F5	28.43±0.04	0.58±0.067	0.66±0.057	12.12	1.10
F6	29.85±0.07	0.57±0.087	0.64±0.035	10.93	1.12
F7	27.14±0.07	0.62±0.046	0.68±0.057	10.09	1.11
F8	28.68±0.05	0.57±0.048	0.67±0.068	10.82	1.10
F9	26.23±0.06	0.63±0.047	0.71±0.047	10.14	1.11

*: Mean ± S.D (n = 3),

Drug-Excipient compatibility studies:

Formulation F6 oro-dispersible tablet FTIR spectra were compared to those of the standard drug. Racecadotril's FTIR spectra are characterized by N-H amide stretching (3383.19 cm^{-1}), C=O ester group stretching (1752.92 cm^{-1}), C=C aromatic stretching (1588.35 cm^{-1}) and C-S stretching (1270.56 cm^{-1}); the physical mixture of directly compressible tablets similarly displays peaks of a similar kind. The lack of any new peaks and the existence of all drug peaks in

F6 indicate that there is no interaction between the medications and the carrier or coating material.

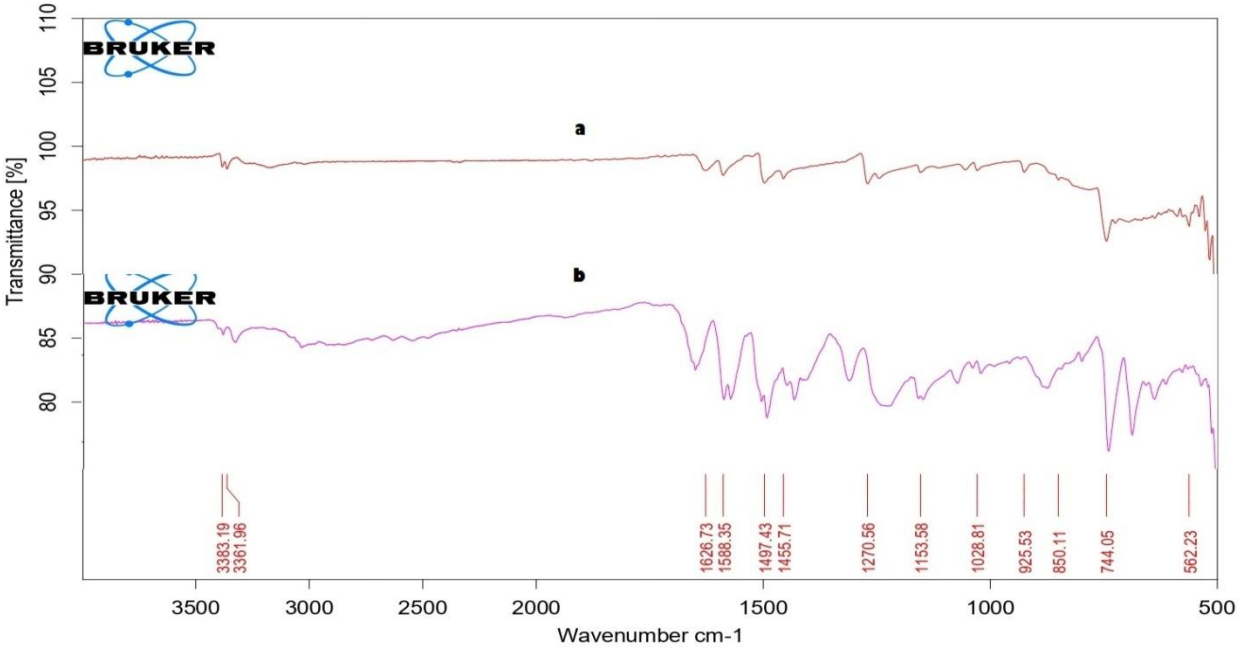

Figure 1: FT-IR spectra of a) pure drug and b) optimized formulation

Hardness:

During formulation development and manufacture, the hardness of the tablets were monitored at regular intervals. The hardness was 3.07±0.35 to 3.94±0.33 kg/cm^2, allowing for the needed integrity during handling and transit. The hardness of all formulations was determined to be within an acceptable range because they are designed to be disseminated on the tongue for between 15 sec and 3 minutes, therefore excessive hardening is not recommended. The findings are shown in Table 7.

Thickness:

Vernier calipers were used to gauge the thickness of three tablets that were chosen at random. The values for tablet thickness ranged from 2.31±0.01 to 2.37±0.03 mm. The findings are shown in Table 7.

Weight variation:

The weight variation was strictly watched since any deviation to either the lower or upper limit would result in issues with decreased medication content or toxicity. As a result, the percentage of weight variation was 1.18 - 1.92%, the weight variation test was passed for all formulations. None of the formulas were going over the 7.5% IP limit. As the outcome, it was

determined that all of the formulations met the Indian Pharmacopoeia criteria. The findings are shown in Table 7.

Friability:

Due to their dispersible composition, orodispersible tablets have slightly higher Friability test results. Therefore, it is essential to maintain a balance between the developed formulations' disintegration and friability qualities. Finally, the friability values of the obtained formulations were optimized within the permitted ranges, and the tablets were extremely stable. The range of all formulations' percentage friability, which was determined to be within the limit (i.e., 1%) is between 0.41±0.78% and 0.95±0.33%. The findings are shown in Table 7.

Disintegration time:

Tablet disintegration time is the most critical factor to consider when designing orodispersible tablets. Table 7 displays the findings, which show that the disintegration durations for all tablet formulations varied from 10±1.24 seconds to 22±0.66 seconds. Disintegration rates of tablets with crospovidone as the superdisintegrant were quicker than those with croscarmellose sodium, and slower than those with sodium starch glycolate. Because crospovidone readily absorbs water by wicking from the medium, swelling, and burst action, formulations containing it dissolve more rapidly. Tablets made with croscarmellose sodium and sodium starch glycolate are slow to dissolve because of their tendency to become gel-like. Some of the rapid swelling of these pills after being wet may be attributable to the process of deformation. All formulations completed disintegration in under the maximum allowed duration of 3 minutes at a simulated salivary pH of 6.8. These results suggest that the wicking type disintegrant crospovidone may be used to reduce the disintegration time. According to the USP, this is the best time for an ODT to disintegrate. The findings are shown in Table 7.

Table 7: Evaluation of post compression parameters of formulations

Formulation Code	Hardness[a] (kg/cm^2)	Thickness[a] (mm)	Weight Variation[b] (mg)	Friability[a] (%)	Disintegration time[a] (sec)
F_1	3.15±0.19	2.33±0.04	175±1.37	0.64±0.33	22±0.66
F_2	3.83±0.23	2.33± 0.06	176±1.92	0.51±0.41	18±0.56
F_3	3.07±0.35	2.31±0.05	175±1.24	0.95±0.33	16±0.63

F_4	3.44±0.46	2.36±0.07	175±1.18	0.73±0.66	18±0.48
F_5	3.94±0.33	2.31±0.01	169±1.35	0.67±0.22	15±0.25
F_6	3.52±0.63	2.32±0.03	175±1.56	0.53±0.43	10±1.24
F_7	3.72±0.33	2.37±0.03	176±1.19	0.63±0.66	21±0.61
F_8	3.47±0.89	2.32±0.02	169±1.33	0.41±0.78	19±0.85
F_9	3.33±0.15	2.36±0.05	176±1.84	0.43±0.15	15±0.19

a: Mean ± S.D (n = 3), b: 20

Wetting time:

The internal makeup of tablets has a direct bearing on how easily they wet. The swelling capacity of super disintegrants and the water absorption capacity of varied formulations determine the wetting time. Wetting periods of crospovidone-containing tablets were found to be shorter than those of tablets containing sodium croscarmellose or else sodium starch glycolate superior disintegrants. These results agreed with those of the disintegration test. The formulas' wetting times ranged between 32±1.28 and 49±1.55 seconds. The findings are shown in Table 8.

Water absorption ratio:

It was investigated how well the different disintegrants wicked water into the small tablets. As the concentration of super disintegrants raised from 2 to 6 percent, the water absorption ratio, or "R," increased. The rise in "R" may be caused by crospovidone absorbing more water than sodium starch glycolate and croscarmellose sodium at greater concentrations. Tablets containing crospovidone rapidly wick water to maintain body hydrated. The water absorption ratio ranged between 65.66±1.12 % and 85.72±1.24%. The findings are shown in Table 8.

***In-vitro* dispersion time:**

All of the formulations' in-vitro dispersion times fell between 19±1.41 and 32±1.33 seconds. All of the formulations in the current investigation dispersed in less than 56 seconds, meeting the statutory standard (<3 min) for dispersible tablets. The findings are shown in Table 8.

Drug Content:

All of the pills' percent drug content was identified to be between 98.55±1.44 and 99.88±1.55%, which was within permissible limitations. The findings are shown in Table 8.

Table 8: Evaluation of racecadotril oro-dispersible tablets by using superdisintegrants

Formulation code	Wetting Time[a] (sec)	Water absorption ratio[a] (%)	*In-vitro* dispersion time[a] (sec)	Drug content[a] (%)
F_1	49±1.55	65.66±1.12	32±1.33	99.87±1.84
F_2	41±1.16	75.39±1.81	28±1.25	99.63±1.32
F_3	36±1.25	82.18±1.58	23±1.66	98.55±1.44
F_4	43±1.09	69.25±1.32	26±1.72	99.33±1.62
F_5	37±1.14	77.77±1.19	22±1.75	99.21±1.43
F_6	32±1.28	85.72±1.24	19±1.41	99.88±1.55
F_7	46±1.36	68.13±1.73	31±1.56	98.65±1.13
F_8	39±1.66	76.89±1.46	26±1.33	99.19±1.16
F_9	35±1.33	83.63±1.97	22±1.49	99.07±1.27

a: Mean ± S.D (n = 3),

Dissolution studies:

In-vitro dissolving studies showed that the formulations which comprise sodium starch glycolate (F1-2%, F2-4%, and F3-6%) showed 99.97±1.93%, 99.01±1.26, and 99.22±2.48% drug release, respectively. This points out that as the quantity of sodium starch glycolate grew, the time it took for it to dissolve reduced as it quickly absorbs water, generating swelling that causes tablets and granules to dissolve quickly, as shown in Fig 2.

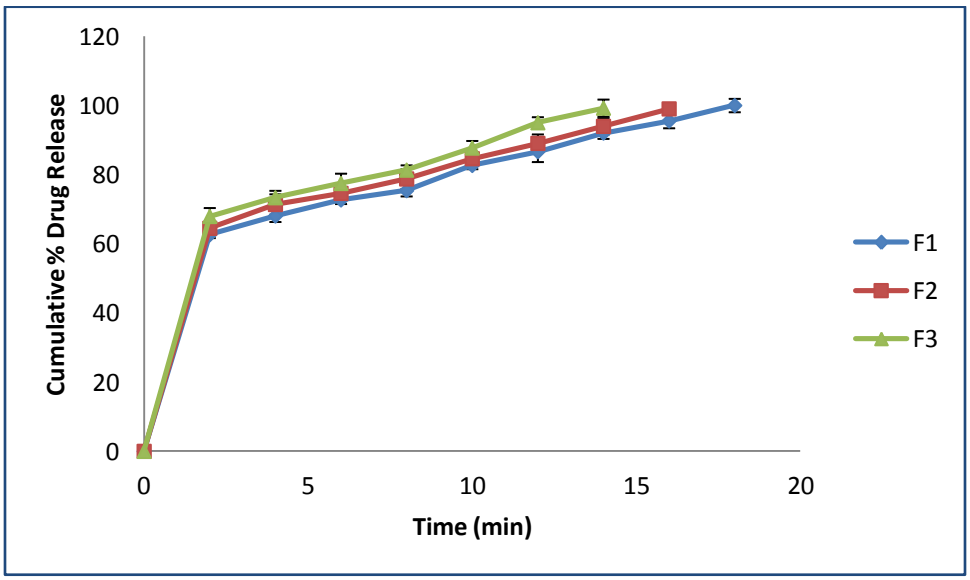

Figure 2: Dissolution graph for F1, F2 and F3

In-vitro dissolving experiments revealed that the release rates of the drug from the crospovidone formulations (F4-2%, F5-4%, and F6-6%) were 99.72±1.96%, 100.72±1.41, and 99.82±1.55%, respectively. This indicates how, as the amount of crospovidone increased, the time it took for it to dissolve reduced because it has great swelling qualities and hygroscopic, or water-attracting, capabilities, as shown in Fig 2.

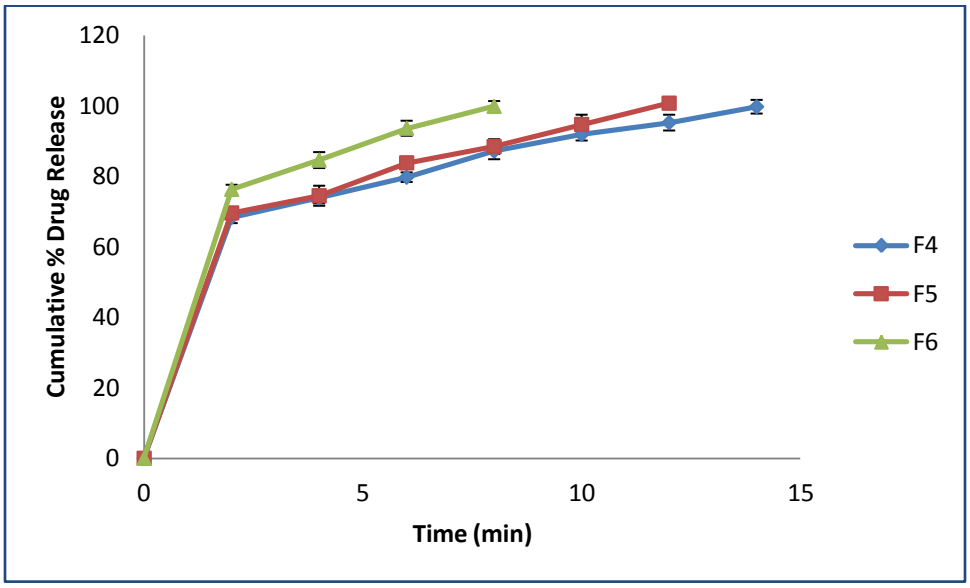

Figure 3: Dissolution graph for F4, F5 and F6

Croscarmellose sodium formulations (F7-2%, F8-4%, and F9-6%) released the medication at rates of 99.47±2.71%, 99.44±2.75, and 99.63±1.19%, respectively, according to in-vitro dissolving tests. This demonstrates how, as the amount of croscarmellose sodium increased, the time it took for it to dissolve decreased as a way to speed up the breaking up of a tablet, shown in Fig 3.

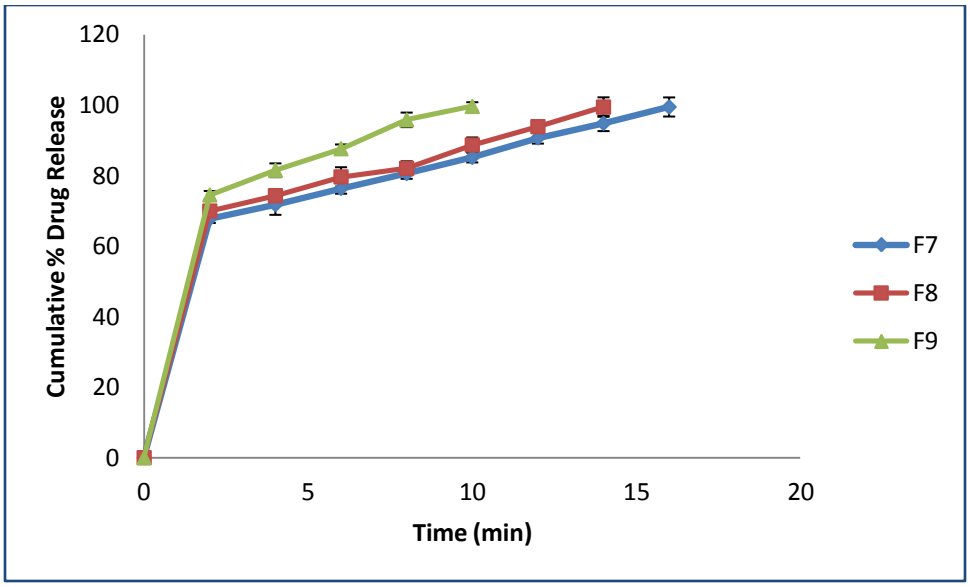

Figure 4: Dissolution graph for F7, F8 and F9

Oro-dispersible tablets produced with crospovidone (F6) outperformed the other nine formulations in terms of dissolution and disintegration time. It disintegrates in 10 seconds and dissolves to 99.82±1.55% in 8 minutes. Additionally, formulation F6, which contains crospovidone at a concentration of 6%, was chosen as the optimal batch due to its rapid drug release (99.82±1.55% at 8 minutes) and rapid disintegration (10 sec). As a result of the porous particle shape of crospovidone super disintegrants in the formulation F6, saliva is drawn into the oro-dispersible tablet by capillary action, causing secondary swelling, the breaking of inter particulate bonds, and rapid tablet disintegration.

***In-vivo* Taste evaluation:**

The taste test was carried out with the assistance of six human volunteers in good health, and the results are shown in Table 9. After being complexed with Eudragit EPO and racecadotril, the bitter taste of the medicine was either significantly reduced or completely masked. As a result, throughout this inquiry, attempts were made to increase flavor masking and give excellent qualities in the tablet's delivery characteristics.

Table 9: Comparative taste evaluation

Degree of Bitterness*				
Time	**30 seconds**	**1 minute**	**2.5 minutes**	**5 minutes**
Pure drug	3	2	2	1
Drug- polymer mixture (PEG)	1	0	0	0
Optimized formulation (F6)	0	0	0	0

*Results are the mean of 3 observations

i.e. 0=tasteless, 1=slight bitter, 2=moderate bitter, 3=strong bitter.

Stability study of oro-dispersible tablets:

The stability of the optimized formulation F6 was investigated for 3 and 6 months, and the tablets' drug content, dissolution, and disintegration were evaluated. Studies on the accelerated short-term stability of the above-mentioned promising formulation (at 40°C/75°F for 3 months) have revealed no appreciable changes in the formulation's physical characteristics, drug content, or *in-vitro* dispersion time. The outcomes were as shown in Table 10 below.

Table 10: Tests for stability studies of the optimized formulation

S No.	**Test**	**3rd Month**	**6th Month**
		40°C ± 2°C/75% RH ± 5% RH	40°C ± 2°C/75% RH ± 5% RH
1	Drug Content	99.78 ± 2.36 %	99.13 ± 1.59 %
2	Disintegration time (sec)	10 ± 0.53	10 ± 1.15
3	Dissolution at 10 min	99.14 ± 1.33 %	98.66 ± 2.29 %

Mean ± S.D (n = 3),

Conclusion:

For the purpose of hiding the drug's bitter flavour, Eudragit EPO was used to coat the racecadotril solid dispersion with PEG 6000 as a carrier. In this research, a handful of super disintegrants were used to explore how they would affect the disintegration and dissolution of tablets. Increasing the drug-to-super disintegrant ratio from 2 to 6% improved dissolving properties and shortened the disintegration time. The FTIR analysis showed that the formulations were safe to use since the medication and excipients did not react negatively with one another. In

vitro disintegration time, dispersion time, and drug release were all greatly speeds up in formulations made using a wide range of super disintegrants, and the resulting pills tasted great and felt great in the mouth. With respect to in-vitro release, the optimum formulation was F6, which included 4% crospovidone. Based on the dissolving profiles, it was determined that the F6 formulation had the best drug release (99.82±1.55%) after 8 minutes. As a result, it became clear that racecadotril oral dispersible tablets are feasible to develop and will be employed as a new medicine dosage form for both young and old patients due to their high compliance rates.

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Conflict of interest:

There are no conflicts of interest declared by the authors.

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