RESEARCH ARTICLE

Formulation, Optimization, and Comparative Evaluation of Rapidly Dissolving Tablets of Paracetamol using Natural and Synthetic Superdisintegrants

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ABSTRACT

Focusing on disintegration behaviour, dissolve performance, and tablet quality qualities, the present investigation attempted to develop, optimize, and compare Paracetamol rapidly dissolving tablets (RDTs) utilizing natural, synthetic, and combination superdisintegrants. A mixture of natural (banana starch and fenugreek seed mucilage) and synthetic (croscarmellose sodium and sodium starch glycolate) superdisintegrants were used in the direct compression approach to manufacture paracetamol RDTs. Angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio were among the pre-compression characteristics assessed for the manufactured powder mixes. Following the procedures suggested by the USP, the compressed tablets were tested for *in-vitro* dissolution profile, hardness, friability, drug content uniformity, wetting time, water absorption ratio, and disintegration time. Direct compression was a viable option for all formulations due to their satisfactory flow and compressibility. The product was found to meet the pharmacopeial criteria for hardness (ranging from 3.0-3.7 kg/cm²), friability (less than 1%), and drug content (97.9-99.8%) after compression. Results from an RDT-specific study showed that synthetic and hybrid superdisintegrants significantly improved wetting time, water absorption ratio, and disintegration time. Results for the most efficient hybrid formulation (F9) indicated the quickest disintegration time (13 s), greatest water absorption ratio (98%), and quickest wetting time (14 s). When compared to formulations based on synthetic (F6) and natural (F2) superdisintegrants, *in-vitro* dissolving experiments showed that F9 had better drug release, with 99.37% drug release within 30 minutes. Paracetamol RDTs disintegrate faster and dissolve better with the use of hybrid superdisintegrant systems, according to the study's findings. When mixed with synthetic agents, natural superdisintegrants have great promise as environmentally friendly excipients that can aid in the creation of sustainable, affordable, and patient-friendly oral dosage forms.

Keywords: Paracetamol, Rapidly dissolving tablets, Natural superdisintegrants, Synthetic superdisintegrants, Direct compression, *In-vitro* dissolution

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INTRODUCTION

Rapid-dissolving tablets enhance patient compliance by dissolving promptly in the mouth without the need for water[1]. The excellent solubility and permeability of paracetamol make it a prime option for RDT formulation. It is a BCS Class I medication[2]. Achieving fast tablet disintegration relies heavily on superdisintegrants. There has been a recent uptick in research towards biodegradable, natural alternatives to synthetic superdisintegrants[3]. This research looks at the effectiveness of Paracetamol RDTs with both natural and artificial superdisintegrants.

MATERIALS AND METHODS

Paracetamol procured from RS enterprises, Banana starch, Fenugreek mucilage isolated, Croscarmellose sodium, SSG, mannitol, Aspartame, Talc, Magnesium stearate procured from SD Fine Chemicals, Mumbai.

Isolation and Preparation of Natural Superdisintegrants

Banana Starch

To extract banana starch, the pulp of unripe bananas was wet milled, then washed and dried many times. After passing through a 60 mesh screen, the starch was gently acid treated to increase its swelling ability[4,5].

Fenugreek Seed Mucilage

Prior to boiling and filtering, the fenugreek seeds were immersed in distilled water. A 60-mesh sieve was employed to filter the powdered mucilage after it had been dried at 40 °C and precipitated with ethanol[6].

Direct Compression Technique

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Table 1: Composition of Paracetamol Rapidly-Dissolving Tablets

Ingredient (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9 (Hybrid)
Paracetamol	250	250	250	250	250	250	250	250	250
Banana starch	10	20	—	—	—	—	—	—	5
Fenugreek mucilage	—	—	10	20	—	—	—	—	5
Croscarmellose sodium	—	—	—	—	10	20	—	—	5
Sodium starch glycolate	—	—	—	—	—	—	10	20	5
Mannitol	75	65	75	65	75	65	75	65	65
Microcrystalline cellulose	50	50	50	50	50	50	50	50	50
Aspartame	5	5	5	5	5	5	5	5	5
Magnesium stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
Total weight (mg)	400	400	400	400	400	400	400	400	400

The Rapid-dissolving Paracetamol tablets were made using the direct compression method. Composition of RDT was given in Table 1. For consistent particle size and thorough mixing, measured out each ingredient and sieved them through a 60 screen. A homogenous combination of paracetamol and diluents (mannitol and microcrystalline cellulose, MCC) was initially prepared. The chosen superdisintegrants was thereafter included into the mixture and well blended to assurance uniform dispersion. To enhance the flow and compression properties, the glidant and lubricant were then gently mixed in. A tablet compression machine was used to compress the powder blend into tablets using 8 mm flat punches[7].

Pre-Compression Evaluation

The powder mixes designated for compression underwent pre-compression assessment to evaluate their flow and compressibility properties. The angle of repose was assessed to analyse the flow characteristics of the powder mixtures. The bulk density and tapped density were assessed to evaluate the packing capacity of the powders in both loose and tapped states. Carr's compressibility index and Hausner's ratio were derived using these numbers to evaluate the compressibility and flow characteristics of the blends. These parameters are essential for achieving consistent die filling and effective tablet production during the direct compression process[8,9].

Post-Compression Evaluation

Hardness

The hardness of the compressed tablets was assessed with a Monsanto hardness tester or a Pfizer hardness tester. For each formulation, five tablets were randomly chosen, and the force necessary to fracture each tablet was documented in kg/cm². The mean hardness value was computed and presented alongside the standard deviation. Hardness guarantees adequate mechanical strength to endure handling and packing[10].

Friability (%)

Utilizing a Roche Friabilator, the percentage of friability was determined. The Friabilator was set to run at 25 rpm for 4 minutes (100 revolutions), and a sample of 10 tablets was carefully weighed and placed in it. The tablets were subsequently reweighed after dedusting. The formula was used to calculate the friability (%):

$$\%\ Friability\ =\ ((Initial\ Weight\ (W1) - End\ Weight\ (W2))/(Initial\ Weight\ (W1))\ \ x\ 100$$

Table 2: Pre-Compression Parameters results

Formu-lation	Angle of Repose (°)	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner's Ratio
F1	28.4	0.54	0.63	14.29	1.17
F2	27.9	0.55	0.64	14.06	1.16
F3	29.1	0.53	0.62	14.52	1.17
F4	28.6	0.54	0.63	14.29	1.17
F5	26.8	0.56	0.64	12.50	1.14
F6	26.1	0.57	0.64	10.94	1.12
F7	28.4	0.54	0.63	14.29	1.17
F8	27.9	0.55	0.64	14.06	1.16
F9	24.9	0.59	0.65	9.23	1.10

A friability of less than 1% indicates acceptable mechanical resistance[11].

Drug Content

Five tablets were crushed from each batch for the purpose of drug content analysis. After dissolving 250 mg of Paracetamol in 100 mL of phosphate buffer pH 6.8, sonicating, filtering, and diluting it accordingly, the final solution was prepared. A UV-visible spectrophotometer was used to detect the absorbance at 243 nm. For the purpose of achieving a consistent distribution of the active ingredient, the drug content (%) was determined[12].

Wetting Time

In order to find the wetting time, the Petri dish method was employed. 10 ml of distilled water was added to a Petri dish along with a circular piece of tissue paper. The time it took for a tablet to become fully moistened after being put on the tissue was recorded in seconds. Rapid disintegration can be achieved with a shorter soaking time.

Water Absorption Ratio

The water absorption ratio is a measure of a material's capacity to absorb water in relation to its weight or volume. This ratio is influenced by the material's structure, porosity, and water retention capabilities. Water absorption ratio (R) was determined using the formula:

$$Water\ Absorption\ Ratio\ =\ 100\ (Wa\ -\ Wb)\ /\ Wb$$

In this context, Wa is the tablet's original weight and Wb is its weight after being fully wetted. Before and after being immersed in distilled water to ensure full wetting, the tablets were weighed. A faster disintegration rate is associated with a higher water absorption ratio.

Disintegration Time

Table 3: Post-Compression Parameters

Formulation	Hardness (kg/cm²)	Friability (%)	Drug Content (%)
F1	3.1	0.68	98.2
F2	3.0	0.72	97.9
F3	3.2	0.65	98.6
F4	3.1	0.70	98.0
F5	3.4	0.55	99.1
F6	3.5	0.52	99.4
F7	3.5	0.50	99.2
F8	3.6	0.51	99.3
F9	3.7	0.45	99.8

Table 4: RDT-Specific Evaluation

Formu-lation	Wetting Time (s)	Water Absorption Ratio (%)	Disintegration Time (s)
F1	42	62	58
F2	38	68	52
F3	40	65	55
F4	36	70	48
F5	28	85	32
F6	25	88	28
F7	27	84	33
F8	24	87	27
F9	14	98	13

A disintegration test instrument approved by the USP was used to determine the disintegration time of the tablets. Each of the six tubes of the apparatus was filled with one tablet, and the equipment was run in 900 mL of distilled water maintained at 37 ± 0.5°C. The number of seconds it took for the pill to dissolve entirely, leaving no trace, was recorded. The predicted disintegration time for rapidly dissolving tablets is less than 60 seconds[13].

***In-Vitro* Dissolution Profile**

A USP Type II (paddle) dissolving equipment was used to assess the oral bioavailability of the medication *in vitro*. The tablets were placed into 900 mL of phosphate buffer (pH 6.8) that was kept at 37 ± 0.5°C and rotated at 50 rpm using a paddle. At 5, 10, 15, and 30-minute intervals, 5 mL of sample buffer was removed and replaced with 5 mL of fresh buffer to keep the sink conditions constant. After filtering and diluting the samples as needed, a UV-visible spectrophotometer was used to detect absorbance at 243 nm. In order to assess the dissolution profile, the percentage of medication released was computed and plotted against time[14,15].

RESULTS

Pre-Compression Evaluation

In Table 2 represent the pre-compression parameters of all the formulations (F1-F9). Before compressing the powder mixes into tablets, it is important to measure their flow and compressibility using characteristics such as bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio.

The values of the angle of repose varied between 24.9° and 29.1°. The best flow qualities were shown by Formulation F9, with an angle of repose of 24.9°, while Formulation F3 had the highest, at 29.1°, indicating somewhat worse flow than the other formulations. All values were below 30°, which is indicative of passable to medium flow characteristics and is appropriate for direct compression.

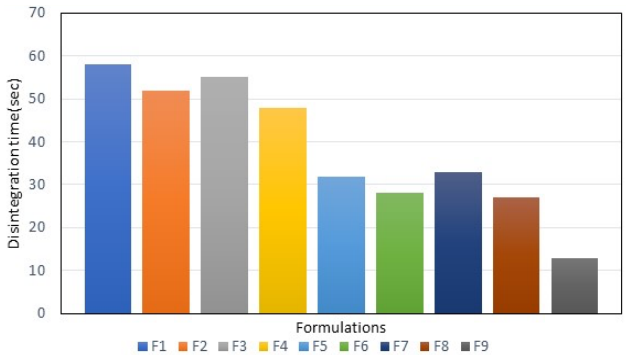

Figure 1: Effect of superdisintegrants on disintegration time

There was a wide range of bulk density values (0.53-0.59 g/mL) and tapped density (0.62-0.65 g/mL). The somewhat greater bulk density (0.57-0.59 g/mL) and tapped density (0.64-0.65 g/mL) of Formulation F6 and Formulation F9, respectively, indicate that these blends have improved packing ability. Consistent powder compaction was shown by the fact that the bulk-to-tapped density ratio stayed within a reasonable range.

The values of the Carr's index varied between 9.23% and 14.52%, whereas the range of Hausner's ratio was 1.10 to 1.17. While F3 exhibited the greatest values (Carr's index 14.52%, Hausner's ratio 1.17), which is still within the permitted range for direct compression, Formulation F9 had the lowest values (9.23%) and showed outstanding flowability and compressibility (1.10).

The results showed that all of the formulations were good candidates for direct compression tablet compression based on their flow and compressibility characteristics measured before compression. It is worth mentioning that formulations with hybrid superdisintegrants systems (F9) demonstrated better packing and flow characteristics when contrasted with formulations with solely native (F1-F4) or synthetic (F5-F8) agents.

Powder blend qualities, including tablet uniformity, hardness, and disintegration behaviours, may be improved by combining native and synthetic superdisintegrants, according to this.

Post-Compression Evaluation

Paracetamol rapidly dissolving tablet (RDT) post-compression quality features, including percentage drug content, friability, and hardness, are listed in Table 3. Mechanical strength, dose consistency, and patient satisfaction are all critically dependent on these characteristics.

All of the tablet formulations had hardness values between 3.0 and 3.7 kg/cm². The natural superdisintegrant-containing formulations F1–F4 had considerably lower hardness values (ranging from 3.0 to 3.2 kg/cm²), in contrast to the synthetic superdisintegrant–containing formulations F5–F8 and the hybrid system–containing formulations F9.

Improved particle packing and inter-particulate bonding may explain the progressive rise in hardness (F7-F9) seen in formulations, which do not negatively impact fast disintegration. For quickly dissolving tablets, all hardness

values were within the permitted range, guaranteeing enough mechanical strength for transit and handling.

All of the formulations had friability values < 1%, which means they had great mechanical strength. The friability values for formulations F1–F4 were between 0.65 and 0.72%, but formulations F5–F9, which contained synthetic and hybrid superdisintegrants, had lower values, ranging from 0.45 to 0.55%. Formulation F9 had the least amount of friability (0.45%), which means it has stronger tablets. This is probably because the combination of natural and synthetic superdisintegrants improves binding and compaction.

All formulations met the pharmacopeial criteria (95-105%), with drug content ranging from 97.9% to 99.8%. While F1–F4 were native superdisintegrant formulations with somewhat lower drug content values, F5–F9 were hybrid and synthetic formulations with greater drug content values and more consistent drug distribution. Formulation F9 had the greatest drug concentration at 99.8%, which is a sign of great blending efficiency and even distribution of Paracetamol in the tablet matrix.

All formulations were found to meet the pharmacopeial quality criteria in the post-compression examination. In contrast to formulations that just used native or synthetic superdisintegrants, those that included F7-F9 showed better mechanical strength, reduced friability, and increased drug content uniformity. This exemplifies the benefit of developing strong, high-quality fast-solving tablets by mixing natural and synthetic superdisintegrants.

Rapid dissolving tablets' (RDTs') capacity to soak up saliva, turn moist, and dissolve quickly determines how well they work. Table 4 displays the data for each formulation (F1-F9), including their wetting time, water absorption ratio, and *in-vitro* disintegration time.

A wetting time of 14–42 seconds was recorded. The wetting periods of formulations F1–F4, which include native superdisintegrants, were somewhat longer (36-42 s), suggesting that water penetrated the tablet matrix at a slower rate. Due to their increased swelling and wicking capacity, formulations F5-F6, which were made using synthetic superdisintegrants, exhibited much shorter wetting periods (25-28 s). Formulations F7–F9, which showed much more improvement; formulation F9 hybrid had the fastest wetting time, at 14 seconds. The quick wetting is caused by the combination of natural and artificial superdisintegrants, which work together to improve capillary action and speed up water absorption.

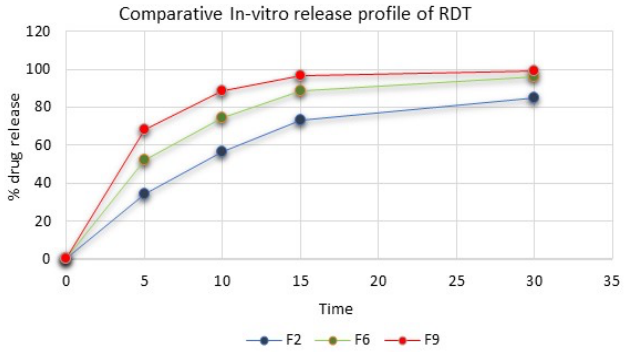

Figure 2: Comparative *in-vitro* release profile of RDT

Table 5: *In-Vitro* Dissolution Profile (% Drug Released)

Time (min)	F2	F6	F9
0	0	0	0
5	34.22	52.13	68.42
10	56.73	74.42	88.79
15	72.87	88.56	96.72
30	85.14	96.12	99.37

Formulations ranged in water absorption ratio from 62% to 98%. F1–F4 tablets containing native superdisintegrants absorbed less water (62%–70%) than F5–F6 tablets containing synthetic superdisintegrants (85-88%).The best hydration capacity was demonstrated by Formulation F9, which had the highest water absorption ratio at 98%. Superdisintegrants swell more quickly in water, which speeds up pill breakdown and increases patient compliance.

The disintegration time of RDTs is an important metric since it influences the ease of administration and the time it takes for the drug to start working. Figure 1 showing the effect of superdisintegrants on disintegration time. The disintegration periods of the Formulations F1–F4, which contained just native superdisintegrants, were somewhat longer (48–58 s), although they were still within the permitted range for RDTs. The disintegration time of the synthetic superdisintegrant formulations (F5-F6) was found to be 28-32 seconds shorter. Hybrid formulation F9 disintegrated in 13 seconds, which is much less time than the pharmacopeial restrictions for orally disintegrating tablets.

Wetting time and disintegration time showed a significant inverse association, whereas water absorption ratio and disintegration efficiency showed a positive link. Fastest disintegration was seen in Formulation F9, which had the shortest wetting time and the greatest water absorption, proving that the hybrid superdisintegrant system was successful.

Table 5 shows the *in-vitro* dissolution characteristics of 9 different formulations of rapidly dissolving paracetamol tablets. The selected formulas stand in for three different types of superdisintegrant: native (F2), synthetic (F6), and hybrid (F9). As part of our dissolving investigations, we used a USP Type II dissolution equipment and a phosphate buffer with a pH of 6.8.

Formulation F2 exhibited 34% medication release at 5 minutes, suggesting a slower dissolving rate linked to the native superdisintegrants' restricted swelling and wetness. Formulation F6, on the other hand, showed a 52.13% drug release, which is indicative of the much better efficacy of synthetic superdisintegrants in facilitating quick tablet disintegration and drug diffusion. The fast wetting, high water absorption ratio, and quickest disintegration time of formulation F9 were responsible for its much greater initial drug release of 68% within 5 minutes, as noted in earlier studies.

Subsequently, at 10, 74.42% (F6), 88.79% (F9), and 56.73% (F2) of the drug was released. The addition of synthetic and hybrid superdisintegrants clearly shows improved release kinetics in the dissolution trend. In comparison to F6's 88.56% release and F2's 72.87% release,

F9 reached 96.37% drug release by 15 minutes. After 30 minutes, the medication was nearly completely released by formulation F9 (99.37%), formulation F6 (96.12%) and F2 (85.14%). These results reveal that the hybrid superdisintegrants system greatly enhances the efficiency of dissolving.

Figure 2 show the comparative *in-vitro* release profile of paracetamol RDT. F9 has the quickest disintegration time (13 s), greatest water absorption ratio (98%), and shortest wetting time (14 s), all of which are highly correlated with its better dissolving profile. A greater surface area of Paracetamol is available for dissolution, and the tablet matrix is quickly disintegrated as a result of the dissolving medium's fast penetration. While F6's dissolution was better than F2's, it was still worse than F9's. This suggests that synthetic superdisintegrants alone do not improve dissolution as much as when combined with natural superdisintegrants.

CONCLUSIONS

The study conclusively demonstrates that rapidly dissolving tablets of Paracetamol can be successfully developed using both natural and synthetic superdisintegrants. While natural superdisintegrants alone provided acceptable performance, synthetic superdisintegrants offered faster disintegration and dissolution. However, the combination of natural and synthetic superdisintegrants (hybrid system) resulted in synergistic enhancement of tablet performance. Among all formulations, Formulation F9 emerged as the optimized formulation, exhibiting Excellent pre-compression flow properties, Superior mechanical strength with minimal friability, Rapid wetting and disintegration, nearly complete drug release within 30 minutes. The findings highlight the potential of natural superdisintegrants as eco-friendly and biodegradable alternatives, especially when used in combination with synthetic agents. This hybrid approach not only improves tablet performance but also supports the development of cost-effective, patient-friendly, and sustainable oral dosage forms.

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