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Formulation and Evaluation of Co-Processed Natural Super Disintegrants for Solid Oral Drug Delivery Systems.

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ABSTRACT

Fast dissolving tablets (FDTs) are those which dissolve quickly in presence of saliva or water. This study aimed to formulate and characterize Diclofenac Sodium FDTs using co-processed natural superdisintegrants of guar gum and banana starch. Equal amounts of guar gum and banana starch were blended by using solvent evaporation method. The obtained dried mass was then ground and passed through #60 mesh sieve and added to 9 different tablet formulations (F1-F9) by direct compression method. Initial formulation studies and compatibility studies were done by organoleptic test, solubility, melting point, UV, FTIR, DSC, XRD. The physical properties of the tablet formulations were studied by determining the flow properties, compression properties, hardness, friability, drug content, wetting time, disintegration time, in vitro dissolution and stability studies. This study shows that the powder blends showed good flow properties with the bulk density of 0.46-0.53 g/cm3, Carr's compressibility index less than 15%, Hausner ratio less than 1.25 and angle of repose less than 30o. Hardness of the tablets varied from 3.8-4.3 kg/cm2, friability less than 1% and drug content between 97.25%-99.96%. Formulation F9 with 20mg of co-processed material showed best results with wetting time of 21 seconds, disintegration time of 17 seconds and drug release of 96.4% after 15 minutes and 99.8% after 30 minutes. This indicates that guar gum and banana starch co-processed material should be explored further as natural superdisintegrant for Diclofenac Sodium FDTs. Further studies are needed to validate the results with detailed statistical analysis and comparison.

Keywords: Diclofenac Sodium; fast-disintegrating tablets; guar gum; banana starch; co-processed excipient; natural superdisintegrant; direct compression.

1. Introduction

Oral dosage forms are popular due to being easy to administer, convenient and economic. However, it can be hard to swallow conventional tablets in some patients, for example elderly people and those with disphagia. Fast disintegrating tablets can help overcome this problem by allowing the tablet to quickly disintegrate when exposed to saliva or aqueous liquid. This means the tablet needs to have an optimal balance between mechanical strength and fast wetting, disintegration and drug release.

Superdisintegrants can help cause disintegration within the tablet by swelling and capillary water absorption. Synthetic superdisintegrants are commonly used; however natural polymers have become an area of interest due to being available, renewable and potentially economic. However, they can have limitations due to variation in material properties, flowability and compressibility. Co-processing can be used to alter some of these physical properties of two excipients. This will help improve the handling of the powders and tablet properties without altering the chemical nature of the excipients.

Guar gum is a hydrophilic polysaccharide derived from plants. It has good water absorbing and swelling properties. Banana starch can also be used as it has good water absorbing properties and can aid tablet disintegration. Using both together can provide synergistic water absorbing and swelling properties. A co-processed guar gum and banana starch was produced and investigated for use in fast disintegrating tablets of Diclofenac Sodium using direct compression.

2. Materials and Methods

2.1 Materials

Diclofenac Sodium was taken as the model drug. Guar gum and banana starch were taken as the natural polymers to be co-processed. Other excipients such as microcrystalline cellulose PH102, lactose monohydrate, polyvinylpyrrolidone K30, talc and magnesium stearate were used as described in the

thesis formulation. Diclofenac Sodium was obtained from Yarrow Chem Products Pvt. Ltd., Mumbai, India while guar gum was procured from Loba Chemie Pvt. Ltd., Mumbai, India. Check lab documents for supplier and batch numbers of the rest of the materials.

2.2 Co-processed superdisintegrant preparation

Guar gum and banana starch were weighted and mixed well together to give a 1:1 ratio (50 g of each was used). Water (100-150 mL) was added gradually with stirring to produce a homogenous slurry. Continuous stirring for 30 mins. Drying in hot air oven (50 ± 2 oC) for 6-8 hours. Powdered and sieved through #60 mesh. Stored in an airtight container. Cream powder.

2.3 Fast disintegrating tablet formulation

Nine different formulations (F1-F9) were made using the direct compression method. Each tablet contained 50mg of Diclofenac Sodium with varying amounts of co-processed superdisintegrant (4mg for F1 up to 20mg for F9). Microcrystalline cellulose PH102, lactose monohydrate, PVP K30, talc and magnesium stearate were also used as described in the thesis formulation. Full amounts can be found below from the formulation table which were used in the formulation. Check lab documents for the final tablet weight.

2.4 Pre-formulation studies and compatibility studies

Organoleptic properties, melting point, solubility and UV analysis were performed. Compatibility between drug and excipients and solid state properties were also studied using FTIR, DSC and XRD. Diclofenac Sodium had a λmax at 276nm. No major incompatibilities were found.

2.5 Evaluation of powder mixtures and tablets

Bulk density, tapped density, Carr's compressibility index, Hausner ratio and angle of repose were measured. Tablets were tested for hardness, friability, thickness/weight variation and drug content. Tablet disintegration was studied using wetting time, water absorption ratio and disintegration time. In-vitro dissolution was carried out on the different formulations (F1-F9). Optimised formulation was analysed for drug release kinetics and stability. Apparatus, dissolution media (volume), speed of rotation, sampling, assay method, number of replicates and duration/stability conditions were noted exactly as described in the lab methods section of the thesis.

3. Results and Discussion.

3.1 Pre-formulation and compatibility studies.

Pre-formulation studies indicated that Diclofenac Sodium and excipients chosen would be suitable for formulation. UV analysis showed λmax at 276nm. Analysis using FTIR, DSC and XRD indicated no major incompatibilities between drug and excipients and were in line with expected solid state properties. This was therefore suitable for direct compression formulation.

3.2 Properties of the co-processed excipient

The co-processed material was a free flowing, cream coloured powder. Guar gum was to provide swelling properties and banana starch to provide water absorption and wicking. The excipients had improved handling and hydration properties. If quantitative data is available, this should be included to show the extent of improvement between the separate polymers and co-processed excipient.

3.3 Powder flow and tablet properties.

All powders had similar properties with bulk densities between 0.46-0.53g/cm 3 with compressibility index <15, Hausner ratio <1.25 and angle of repose<30. This indicates suitable flow and compressibility for direct compression. Tablets had hardness within the range of 3.8-4.3kg/cm 2, friability <1% and drug content between 97.25-99.96%. Overall the formulations had suitable properties.

3.4 Wetting time, disintegration time and dissolution.

Amount of co-processed superdisintegrant was increased. As the amount of excipient increased so did the wetting and disintegration times decrease. This indicates improved water penetration and hydration. The optimised formulation was F9. It had a wetting time of 21 seconds and a disintegration time of 17 seconds. Diclofenac Sodium released from the formulation was 96.4% at 15mins and 99.8% at 30mins. This may be due to increased surface area for the drug to dissolve. However this is in-vitro data and does not indicate improved clinical efficacy or bioavailability.

3.5 Stability

The optimised formulation showed good stability over the course of the study. No major differences in appearance, drug content, disintegration time and dissolution were observed. A table can be seen below showing how long the formulation was stable for, what conditions it was stored under, when samples were taken and the results. Conclusions should only be made about stability under these conditions and for this duration.

4. Results.

Below are tables and figures showing the quantitative results from the experiments. All values have been taken directly from the thesis and any missing measurements or statistical data have not been guessed. The dissolution table shows the chosen formulations from the thesis (F1, F3, F5, F7 and F9).

Table 1. Pre-compression properties of powder blends

Formulation	Bulk density (g/cm³)	Tapped density (g/cm³)	Carr's index (%)	Hausner ratio	Angle of repose (°)
F1	0.46 ± 0.01	0.54 ± 0.01	14.81	1.17	30.25
F2	0.47 ± 0.01	0.55 ± 0.01	14.54	1.17	29.86
F3	0.48 ± 0.01	0.56 ± 0.01	14.29	1.16	29.42
F4	0.49 ± 0.01	0.57 ± 0.01	14.03	1.16	28.95
F5	0.49 ± 0.01	0.57 ± 0.01	14.03	1.16	28.61
F6	0.50 ± 0.01	0.58 ± 0.01	13.79	1.16	28.20
F7	0.51 ± 0.01	0.59 ± 0.01	13.56	1.15	27.84
F8	0.52 ± 0.01	0.60 ± 0.01	13.33	1.15	27.45
F9	0.53 ± 0.01	0.61 ± 0.01	13.11	1.15	26.92

Note: The thesis reports angle-of-repose values with standard deviations; the numeric mean values are shown here because the table layout is compact. Consult the source thesis table for the reported SD values.

Table 2. Post-compression evaluation of Diclofenac Sodium tablets

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Hardness (kg/cm²)	3.8	3.9	4.0	4.0	4.1	4.2	4.2	4.3	4.3
Thickness (mm)	3.21	3.24	3.26	3.28	3.29	3.30	3.31	3.33	3.35
Friability (%)	0.78	0.74	0.70	0.68	0.64	0.60	0.57	0.53	0.49
Drug content (%)	97.25	97.96	98.32	98.76	99.14	99.48	99.72	99.85	99.96
Wetting time (s)	62	57	52	46	41	36	31	26	21
Disintegration time (s)	58	52	46	40	34	29	25	21	17

Table 3. In-vitro cumulative drug release of selected formulations

Time (min)	F1 (%)	F3 (%)	F5 (%)	F7 (%)	F9 (%)
5	32.4	38.5	44.6	51.8	58.7
10	48.2	56.3	64.7	72.5	80.9
15	63.5	72.8	80.4	88.6	96.4
20	74.1	83.5	89.6	95.2	99.1
30	82.7	91.6	96.5	99.2	99.8

Table 4. Composition of Diclofenac Sodium fast-disintegrating tablets

Ingredient (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Diclofenac Sodium	50	50	50	50	50	50	50	50	50
Co-processed superdisintegrant	4	6	8	10	12	14	16	18	20
MCC PH102	110	108	106	104	102	100	98	96	94
Lactose monohydrate	30	30	30	30	30	30	30	30	30
PVP K30	5	5	5	5	5	5	5	5	5
Magnesium stearate	3	3	3	3	3	3	3	3	3
Talc	2	2	2	2	2	2	2	2	2
Total tablet weight	204	204	204	204	204	204	204	204	204

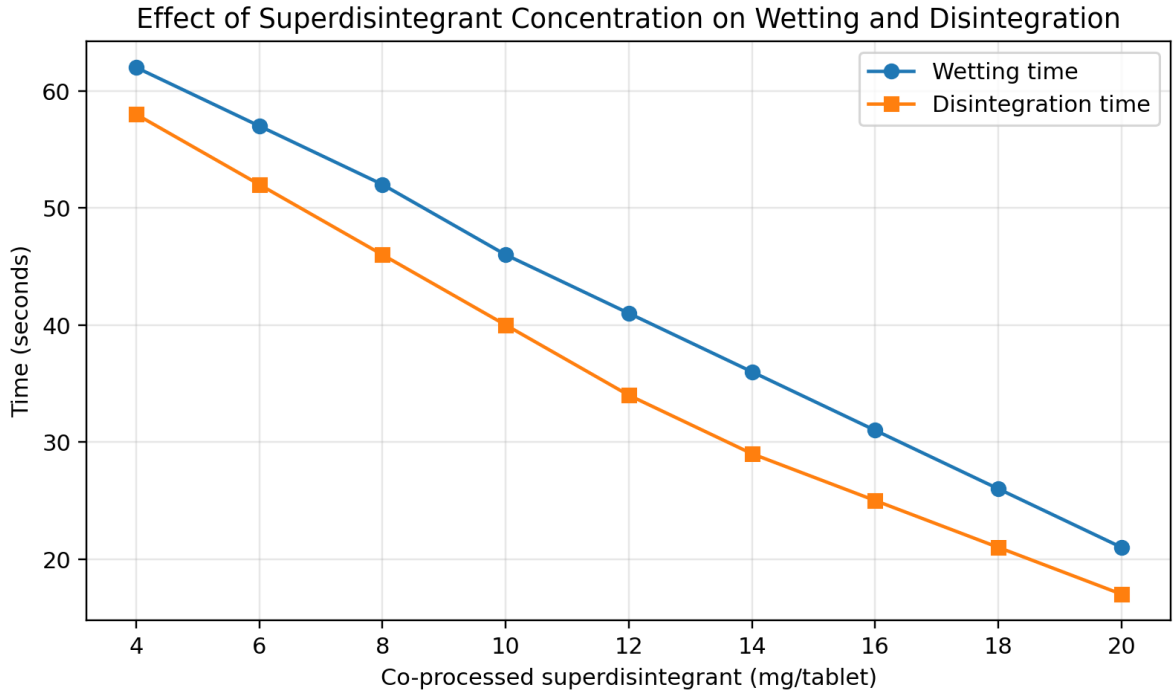


Figure 1. Relationship between co-processed superdisintegrant concentration, wetting time and disintegration time.

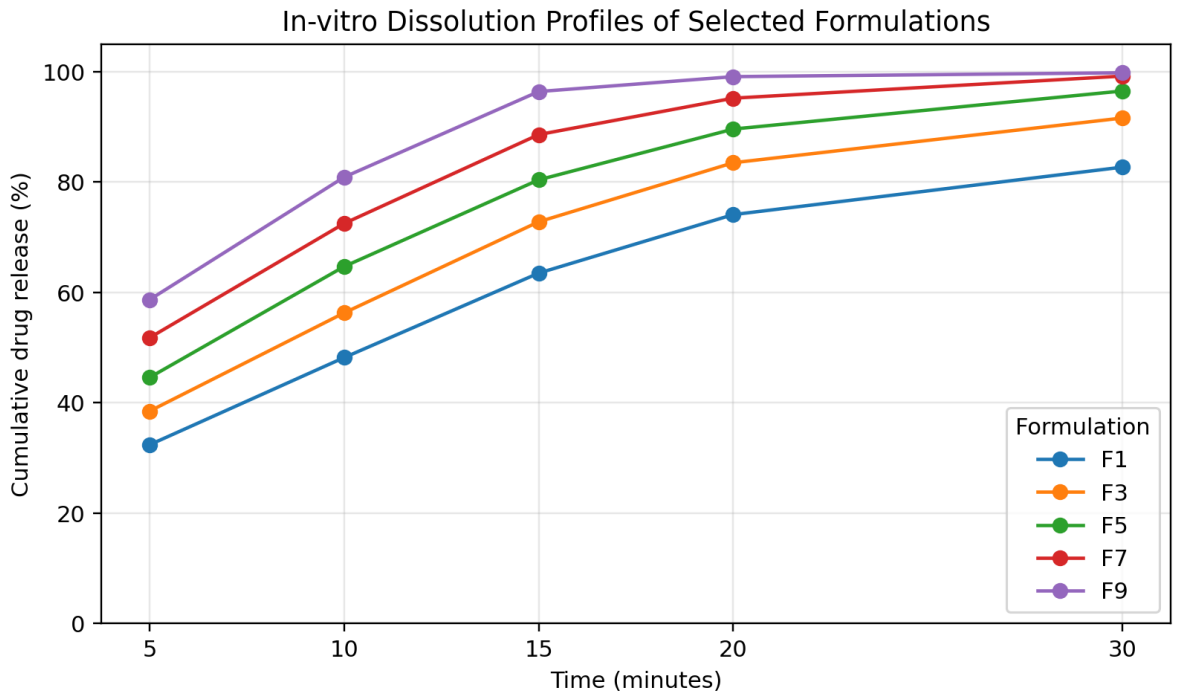


Figure 2. In-vitro dissolution profiles of selected formulations (F1, F3, F5, F7 and F9).

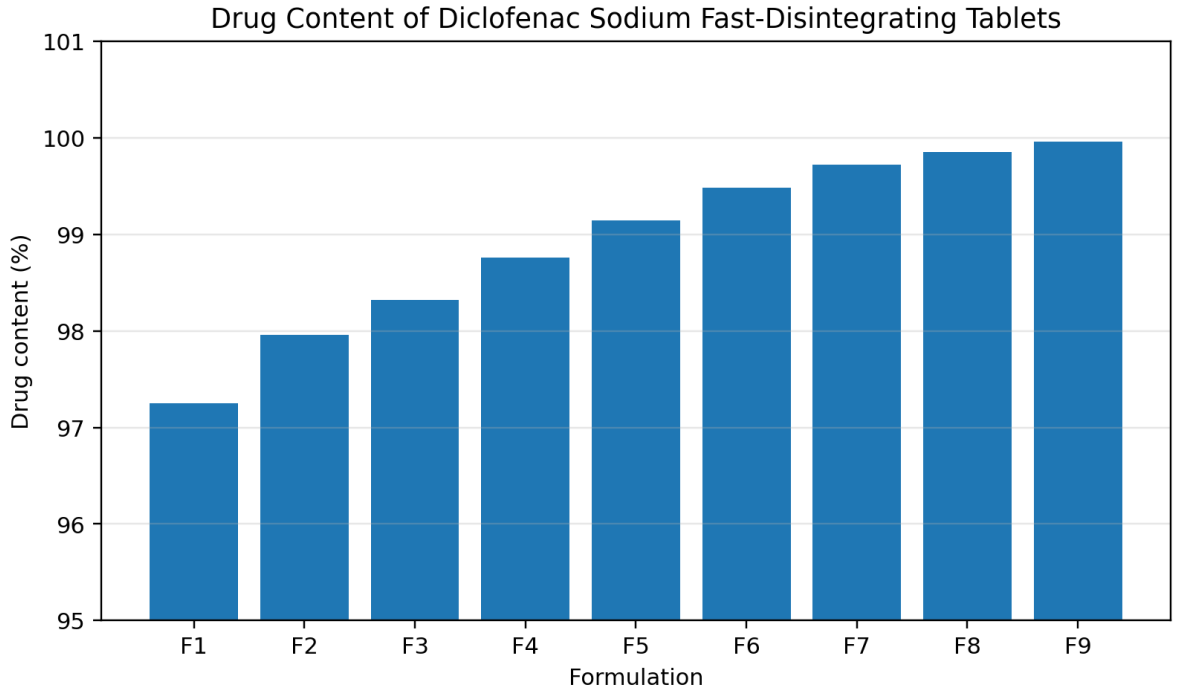


Figure 3. Drug content (%) across formulations F1–F9.

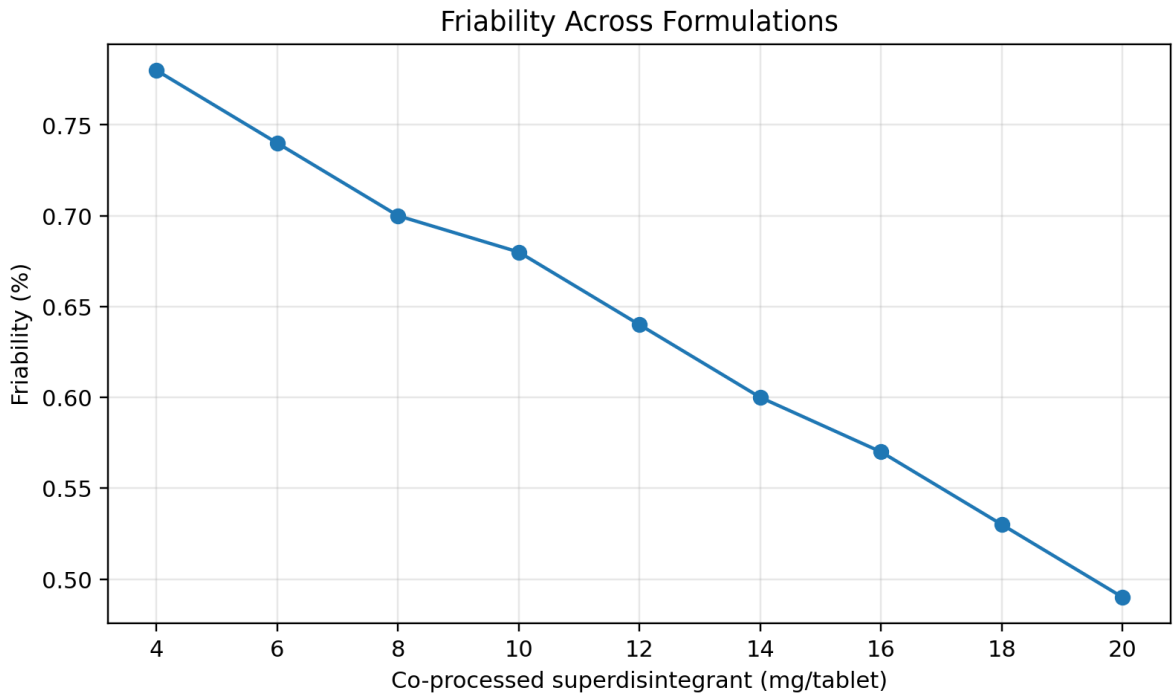


Figure 4. Friability (%) across formulations F1–F9.

5. Interpretation

Results from increasing the amount of co-processed superdisintegrant used from 4mg/tablet to 20mg/tablet showed a reduction in both wetting time (62s to 21s) and disintegration time (58s to 17s). The highest drug release was seen for formulation F9 within the chosen dissolution set. Drug release was 96.4% at 15mins and 99.8% at 30mins. The drug content was also increased from 97.25% (F1) to 99.96% (F9). Friability results reduced from 0.78% to 0.49%. These can be considered as trends but cannot be claimed as significant without replicate data and proper statistical analysis.

6. Conclusion

A co-processed natural superdisintegrant was successfully made using a 1:1 ratio of guar gum and banana starch. This was added to Diclofenac Sodium fast disintegrating tablets using direct compression. All the powder flow properties and tablet quality properties were found to be acceptable. Formulation F9, with 20mg of the co-processed excipient, had the fastest wetting time (21s) and disintegration time (17s). It also released the drug fastest with 96.4% drug release at 15mins and 99.8% drug release at 30mins. The guar gum and banana starch combination appear to have potential to be developed further within the limitations of the in-vitro data presented. Further comparison experiments, full statistical analysis, validation of the method and stability testing would be required before claiming that this is superior, scalable and will have any clinical benefits.

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