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FORMULATION DEVELOPMENT, EVALUATION AND COMPARATIVE STUDY OF EFFECTS OF SUPERDISINTEGRANTS IN FAST DISINTEGRATING TABLETS OF *RUBIA CARDIFOLIA*

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ABSTRACT

In current study, fast disintegrating tablet of *Rubia cardifolia* has been prepared by using super-disintegrants. *Rubia cardifolia* is an anti-emetic drug that is also used for treatment of skin diseases, spleen disorders, anti tumor effects in different doses. The purpose is to get the quicker onset of action and better patient compliance. Super-disintegrants are major participants in fast disintegrating tablets. Cross Povidone, Sodium starch glycollate and Crosscarmellose sodium are used in this study and their comparative disintegrating efficacy is studied. Pre-compression and post-compression characteristics are evaluated. It has been concluded that cross povidone gives the best results as super-disintegrant while preparing fast disintegrating tablets of *Rubia cardifolia.*

KEYWORDS: Fast Disintegrating Tablets, superdisintegrants, *Rubia cardifolia.*

INTRODUCTION

Oral route is considered to be most acceptable route of drug administration owing to better patient compliance and ease of self administration. Amongst different solid and liquid dosage forms for oral administration, tablets are most preferred as they are easy to manufacture and accurate dose is administrated.[1-3]

Most of herbal formulations are administered in form of powders, which tends to stick to buccal mucosa leading to difficulty in swallowing and bad after effects. Here, in this study, an attempt has been made to formulate and evaluate fast disintegrating tablets (FDTs) of and herbal drug. *Rubia cardifolia* has been chosen as model drug in this study. *R. cardifolia,* common name Manjishtha, belongs to rubiaceae family. It is used in treatment of ulcers and known for its anti-emetic effect. It is also used in treatment of skin diseases, spleen disorders, anti tumor effects in different doses.

To formulate FDTs, the key ingredient is superdisintegrant. These agents have capability of disintegrating the tablets into particulate fragments in very less time, as soon as they come in contact with body fluids. These may act by different mechanisms, swelling, wicking, repulsive forces and deformation. Desirable features of superdisintegrants include good compressibility, flow properties, poor solubility, poor gel formation capacity, good hydration capacity and complexation. Taking these into consideration, three superdisintegrants were chosen and formulation was optimized.[4-7]

MATERIALS AND METHODS

Materials
Roots of *R. cardifolia* were procured from Total Herbs Solution, Mumbai, microcrystalline sodium, cross povidone, sodium starch glycollate, talc, magnesium stearate were procured from Loba Chemie Pvt. Ltd., Mumbai.

METHODOLOGY

a. Pre-formulation Studies
Pre-formulation studies involve test to understand different physical and chemical properties of drug substance alone and when it is combined with excipients. It involves.

1. Angle of Repose
Angle of repose was determined by passing the powder through funnel till the resulting heap formed on surface reaches to tip of funnel. Circumference of the heap was drawn on surface paper, without disturbing heap. The height and diameter of heap was determined and values for put in expression to find out angle of repose.

$$\text{Tan } \emptyset = h/r$$

Where, h = height of cone, r = radius of cone

2. Bulk Density

Passed the powder through sieve no #18, to break up lumps. Pour the powder in 250 ml cylinder, leveled it without compacting it. Read the unsettled apparent volume (V_0).

$$Bulk\ Density = M/V_0$$

Where, M = Mass of powder taken

3. Tapped Density

The powdered sample was loaded in cylinder of tapped density tester and was tapped at rate of 300 drops/ min. Tap the cylinder 500 times and measured tapped volume (V_a). Repeat the procedure at 750 tappings and measured the tapped volume (V_b). As the difference between V_a and V_b was less than 2%, V_b was considered at final tapped volume(V_f).

$$Tapped\ Density = M/V_f$$

Where, M = Mass of powder taken

4. Carr's Index

It is indicator of compressibility of powders/granules.

$$Carr's\ Index\ (\%) = \frac{(Tapped\ density - Pour\ Density)}{Tapped\ Density} \times 100$$

5. Hausner Ratio

$$Hausner\ Ratio\ (\%) = \frac{Tapped\ density}{Pour\ Density} \times 100$$

b. Formulation Development

The tablets were formulated using direct compression method and optimized at two levels:

I- Effect of diluents: The tablets were formulated using lactose (Formulation A), avicel (Formulation B) and dicalcium phosphate (Formulation C) as diluents (Table I).

Table I: Formula For Tablet By Varying Diluents.

Ingredient	A	B	C
Powdered roots of *Rubia cardifolia*	1000 mg	1000 mg	1000 mg
Avicel	370 mg	-	-
Lactose	-	370 mg	-
Dicalcium phosphate	-	-	370 mg
PVP	50 mg	50 mg	50 mg
Talc	50 mg	50 mg	50 mg
Magnesium stearate	30 mg	30 mg	30 mg

II- Effect of superdisintegrants: The tablets were formulated using crosspovidone (Formulation A11 – A13), sodium starch glycollate (Formulation A21 – A23) and croscarmellose sodium as superdisintegrants (Formulation A31 – A33). (Table II)

Table Ii: Formula For Tablet By Varying Superdisintegrant.

Ingredient	A11	A12	A13	A21	A22	A23	A31	A32	A33
Powdered roots of *Rubia cardifolia*	1000mg	1000 mg	1000 mg	1000 mg	1000 mg	1000 mg	1000 mg	1000 mg	1000 mg
Avicel	310 mg	290 mg	270 mg	330 mg	320 mg	310 mg	360 mg	350 mg	340 mg
PVP	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
Cross Povidone	60 mg	80 mg	100 mg	-	-	-	-	-	-
Sodium starch glycollate	-	-	-	40 mg	50 mg	60 mg	-	-	-
Crosscarmellose sodium	-	-	-	-	-	-	10 mg	20 mg	30 mg
Talc	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
Magnesium stearate	30 mg	30 mg	30 mg	30 mg	30 mg	30 mg	30 mg	30 mg	30 mg

c. Evaluation of formulation

1. Weight Variation

Twenty tablets were selected at random, weighed and average weight was calculated.

2. Friability

Pre-weighed tablets were placed in friabilator, which was then operated at 100 revolutions. The tablets were de-dusted and reweighed.

3. Hardness

Tablet hardness was determined using Monsanto Hardness Tester.

4. Wetting Time

Tissue papers were cut and placed on petri dish. Tablets were placed on surface of tissue paper. Water was poured through graduated pipette. Time required to just wet the tablet, till it wets the tissue surface wet is the wetting time.

5. Wetting Volume

The volume required to wet the tablets in above procedure (for determination of wetting volume) was determined.

6. Disintegration Test

Six tablets were introduced in the disintegration test apparatus assembly, using disc. Water at $37\ ^oC \pm 2^oC$ was used as disintegration medium and time taken for disintegration of tablets with no residue remaining in apparatus was noted.

RESULT AND DISCUSSION

The pre-compression characteristics of formulations A, B, C and A11-A33 were evaluated and results are indicated in Table III, V. All the values are indicating good flow characteristics of powders.

The post-compression parameters are listed in Table IV, VI. The weight variation test has proved that there was least batch to batch variation, result of all formulation comply with IP limits. Mechanical strength data also complied with IP limits and further supported by results of friability test. All the formulations showed friability less than 0.9%, with no sign of breakdown on tablets. Formulation-to-formulation variations were observed but all were within limits. This indicates that these formulations can easily be handled and transported. The disintegration time wa less than 1 minute in all cases except formulation A31. Rapid disintegration is attributed to rapid uptake of fluid, swelling and bursting effect. Amongst all, A12 was found to show least disintegration time and considered to be optimized formulation. Amongst different diluents, avicel showed the best results for robustness. So, it was selected for further evaluation. Amongst different super-disintegrants, cross povidone is the choice of excipients, as the disintegration time is observed to be least with cross povidone.

TABLE III: Pre-Compression Characteristics Of Powders For Study Of Effect Of Diluents (N=3).

Formulation Code	Bulk Density g/ml	Tapped Density g/ml	Angle of Repose	Hausner's Ratio	Carr's Index
A	0.617 ± 0.07	0.733 ± 0.12	22.4 ± 0.31	1.20 ± 0.15	16.99 ± 0.24
B	0.625 ± 0.33	0.755 ± 0.22	20.8 ± 0.44	1.11 ± 0.22	16.32 ± 0.63
C	0.643 ± 0.29	0.778 ± 0.62	20.1 ± 0.21	1.06 ± 0.34	15.19 ± 0.81

Tablet Iv: Post-Compression Characteristics Of Tablets For Study Of Effect Of Diluents (N=3).

Formulation Code	Weight Variation (mg)	Hardness (kg/cm$^{2)}$)	Friability (mm)
A	Complies	4.0 ± 0.11	0.382 ± 0.19
B	Complies	3.8 ± 0.24	0.492 ± 0.43
C	Complies	3.8 ± 0.33	0.419 ± 0.51

Table V: Pre-Compression Characteristics Of Powders By Varying Superdisintegrants (N=3).

Formulation Code	Bulk Density g/ml	Tapped Density g/ml	Angle of Repose	Hausner's Ratio	Carr's Index
A11	0.609 ± 0.16	0.747 ± 0.44	23.6 ± 1.2	1.23 ± 0.19	17.12 ± 0.57
A12	0.633 ± 0.23	0.767 ± 0.17	22.8 ± 0.56	1.19 ± 0.72	15.99 ± 0.07
A13	0.610 ± 0.32	0.788 ± 0.67	21.6 ± 0.99	1.16 ± 0.66	15.82 ± 0.13
A21	0.598 ± 0.34	0.713 ± 0.23	27.2 ± 0.45	1.27 ± 0.59	17.56 ± 0.07
A22	0.603 ± 0.66	0.727 ± 0.34	26.4 ± 0.32	1.24 ± 0.71	16.89 ± 0.08
A23	0.608 ± 0.11	0.736 ± 0.59	25.7 ± 0.67	1.19 ± 0.51	16.11 ± 0.22
A31	0.617 ± 0.23	0.729 ± 0.29	26.1 ± 0.99	1.21 ± 0.88	15.88 ± 0.78
A32	0.622 ± 0.31	0.742 ± 0.81	24.3 ± 0.81	1.18 ± 0.22	15.35 ± 0.91
A33	0.637 ± 0.55	0.611 ± 0.22	29.9 ± 0.45	1.27 ± 0.89	16.66 ± 0.86

Tablet Vi: Post-Compression Characteristics Of Tablets By Varying Superdisintegrants (N=3).

Formulation Code	Weight Variation (mg)	Hardness (kg/cm^2)	Friability (mm)	Wetting Time (s)	Wetting Volume (ml)	Disintegration Time (s)
A11	Complies	3.9 ± 0.17	0.411 ± 0.22	52 ± 0.32	11.6 ± 0.91	43 ± 0.99
A12	Complies	4.2 ± 0.98	0.492 ± 0.32	59 ± 0.12	12 ± 0.76	36 ± 0.36
A13	Complies	5.0 ± 0.71	0.501 ± 0.71	59 ± 0.53	13.3 ± 1.21	48 ± 0.78
A21	Complies	4.9 ± 0.45	0.538 ± 0.33	72 ± 0.66	19 ± 1.23	59 ± 1.02
A22	Complies	5.1 ± 0.41	0.542 ± 0.61	76 ± 0.74	20.2 ± 0.89	58 ± 0.88
A23	Complies	5.1 ± 0.75	0.566 ± 0.89	81 ± 0.47	21 ± 0.66	55 ± 1.56
A31	Complies	5.2 ± 0.66	0.576 ± 0.63	78 ± 0.44	23 ± 1.11	70 ± 1.01
A32	Complies	5.7 ± 0.59	0.577 ± 0.53	88 ± 0.34	23.7 ± 0.67	56 ± 2.02
A33	Complies	5.8 ± 0.81	0.581 ± 0.81	82 ± 0.51	29.2 ± 0.88	51 ± 1.89

CONCLUSION

The formulation A12 prepared by direct compression method, having cross povidone as superdisintegrant and avicel as diuent was proved to be best amongst all formulations. The order in which drug disintegration was observed was Cross Povidone > Sodium starch glycollate > Crosscarmellose sodium.

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