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Research Article

STATISTICAL SCREENING OF STARCH PASTE AND GUAR GUM ON HARDNESS AND DISINTEGRATION TIME OF FAST DISSOLVING TABLET

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ABSTRACT

The objective of this study was to find out the effect of starch paste and guar gum grade 4000 on hardness and disintegration of fast dissolving tablet by using one way ANOVA, polynomial equation and graphical presentation. As model formulations 9 formulations were prepared by using 3^2 factorial designs. The formulation variables, starch paste concentration and guar gum concentration were selected as the independent variables while hardness and disintegration time were selected as the dependent variables. A substantial better hardness (6.0±0.28) and low disintegration time of tablet (18±0.40) were at +1level of X1and X2.By one way ANOVA the F-value (11.98 and 3.88) and P- value (0.0438 and 0.0007) demonstrated that starch paste and guar gum were given significant effect on hardness and disintegration time of tablet. The polynomial equation was demonstrating the combined effect of both independent variables on dependent variable. The hardness was mainly effected by starch paste (b2=-0.78) but minutely effected by guar gum (b1=-0.58), that was also demonstrated by graphical presentation. The disintegration time was mainly affected by guar gum concentration (b1=-100) but minutely affected by starch paste (b2=-0.33), that was also demonstrated by graphical presentation.

Keyword: ANOVA, Polynomial equation, 3^2 factorial designs, F- Value, P- value

INTRODUCTION

Due to impaired swallowing ability, many elderly patients find it difficult to take some conventional dosage form such as tablet, capsule and powders. In order to solve this problem development of solid dosage that disintegrate rapidly or dissolve even when taken orally without water is being undertaken.[1, 2, 3, 4] These novel type of tablets that disintegrate/ dissolve/ disperse in saliva in less then a minute without the need of water.[5] Their characteristic advantage such as administration without water, any where, any time lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bed ridden, and patients who do not have easy access to water.[6,7] The bioavailability of some drugs, especially those suffering from a high first pass metabolism, can be improved due pregastric absorption and local gastro intestinal side effects are also expected to be reduced by formulating such dosage form.

Fast dissolving tablet is containing mostly synthetic or semi synthetic superdisintegrants in formulation like sodium starch glycol ate, ac-di –sol (sodium carboxy methyl cellulose) cross povidone. Guar gum is also a natural carbohydrate substance and is preferred over synthetic or semi synthetic substances because guar gum is relatively cheaper, abundantly available, nonirritating, nontoxic and completely inert. Still guar gum is used in sustained and delayed release tablet but could be a better option for fast disintegrating tablet because it has a better swelling capacity then other super disintegrating agent. [8, 9,10]

MATERIALS AND METHODS

Materials

Microcrystalline cellulose was purchased from Ases chemicals, Jodhpur. Mannitol, Talc, Mg-stearate and Camphor was purchased from Loba chemicals, Mumbai guar gum grade 4000 was purchased from guar gum factory Jodhpur. All other chemicals and reagents were of laboratory grade.

Identification: The identification of starch and guar gum was performed by FTIR spectra (Bruker)

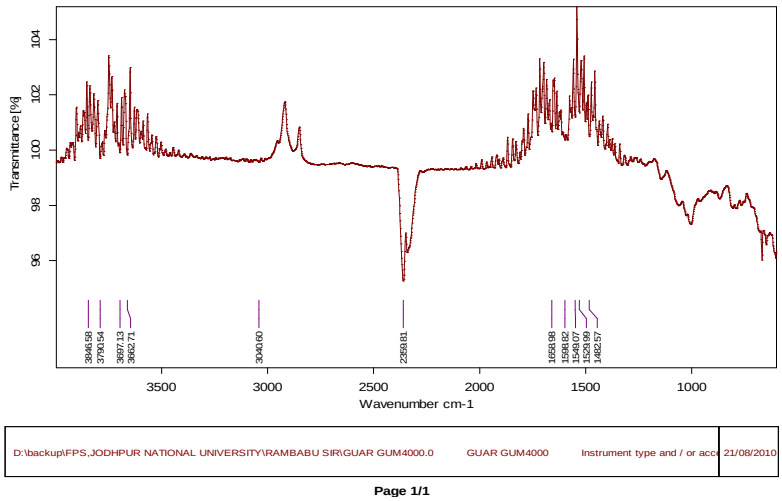

Fig. 1: FTIR graph of guar gum 4000

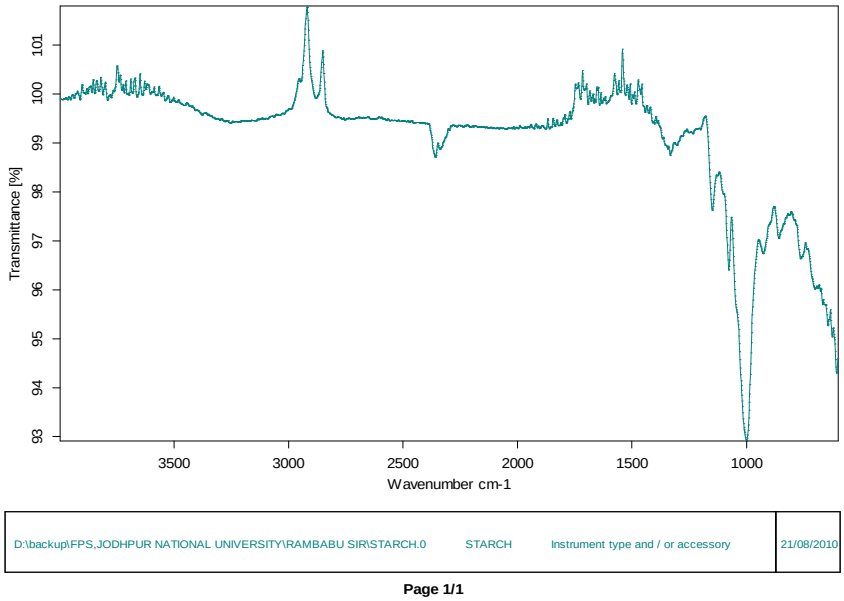

Fig. 2: FTIR graph of starch

Method

Preparation of fast dissolving tablets by wet granulation method

A full factorial design 3^2 was used for development of formulation the two variables, starch paste and guar gum were used for their lower to higher limit and found the influence of both ingredients on formulation. The starch paste concentration in formulation F1 5%, in F2 5%, in F3 5%, In F4 7.5%, In F5 7.5%, in F6 7.5%, in F7 10%, in F8 10% and in F9 10% were used.

The fast dissolving tablets were prepared by wet granulation method. Micro crystalline cellulose (MCC) and mannitol were used as diluents, Guar gum grade 4000 was used as a disintegrating agent, starch paste was used as a binder and magnesium stearate was used as a flow promoter. Micro crystalline cellulose (MCC) and mannitol were mixed together and a sufficient quantity of starch paste at different concentrations were added and mixed them to form a coherent mass. The wet mass was granulated using sieve no. 22 and regranulated after drying through sieve no. 44 and called as base granules. Guar gum, Mg- sterate, colloidal silica talc and aspartame were added as extra granularly. The all ingredients were mixed and compressed in to tablet using 6 mm punches on 8 station rotary tablet machine (Hardik engineers, Ahmedabad). Formulations of Zolmitriptan FDTs by direct compression method are shown in Table 1.[11]

Table 1: Formulation of Zolmitriptan FDTs by direct compression method

S. No.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Mannitol	65	62	59	65	62	59	65	62	59
2	Guar gum 4000	2	5	8	2	5	8	2	5	8
4	MCC	30	30	30	30	30	30	30	30	30
5	Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
6	Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
7	Starch Paste(%) q.s.	5	5	5	7.5	7.5	7.5	10	10	10
	Total weight (mg)	100	100	100	100	100	100	100	100	100

Formulation of fast dissolving tablet is affected by different concentration of binder and disintegration that's gives the affect on different evaluation parameters of tablet. Wet granules with various concentrations of guar gum and starch paste were made into 9 kinds of tablet to evaluate the effects of hardness and disintegration time of tablet. Therefore, starch paste and guar gum were selected as controlling factor, tablet hardness, and disintegration time were selected as response variables, and correlation regression was used to co- relate the controlling factors to the response variables.

Table 2: Factorial design for formulation batches

Batch No.	X1	X2	$X1^2$	$X2^2$	X1X2	Disintegration Time(sec.)	Hardness (Kg/cm^2)
1	-1	-1	1	1	+1	80±0.577	3±0.28
2	0	-1	0	1	0	62+±0.457	3.2±0.17
3	+1	-1	1	1	-1	49±0.192	3.4±0.19
4	-1	0	1	0	0	70±0.5	4±0.23
5	0	0	0	0	0	54±0.15	4.2±0.34
6	+1	0	1	0	0	38±0.65	4.5±0.2
7	-1	+1	1	1	-1	48±0.34	5±0.21
8	0	+1	0	1	0	28±0.28	5.5±0.23
9	+1	+1	1	1	+1	18±0.40	6.0±0.28

Table 3: Independent variables with their actual values

Coded Values	Actual Values of guar gum(mg)	Actual Values of starch paste (%)
-1	2	5
0	5	7.5
+1	8	10

Evaluation Parameter

Weight variation (I.P monograph 1996) Friability (Roche fribilator), Hardness (Monsanto hardness tester) and thickness (vernier calipers) were determined. Wetting and swelling time were determined for tablet because wetting time is required for complete wetting of tablet in buccal cavity and swelling time is required for destruction of tablet in buccal cavity. Wetting time is determined by covered the tablet in tissue paper and applied the eosin dye on surface of tablet and placed it in Petri dish which containing 10 ml phosphate (6.8 pH) buffer. Swelling time was determined by placed the tablet in 10 ml phosphate buffer and noted the time when the tablet was swelled.

RESULT AND DISCUSSION

By using 3^2 factorial designs 9 batches of fast dissolving tablet were prepared by wet granulation method varying 2 independent variables: concentration of guar gum and concentration of starch paste. The disintegration time and hardness, which were taken as a dependent variables, were determined and result were recorded (Table 2).A substantial better hardness (6.0±0.28) and low disintegration time of tablet (18±0.40) were at +1level of X1and X2.The reason of better hardness and low disintegration time of tablet may be because the higher concentration of starch paste and guar gum. The starch paste concentration is mainly affecting the hardness of tablet that is proved by one way ANOVA test. According the table no.4 the F value was found to be 11.98 that is greater than tabulated value (3.63) at 2 degree of freedom and 16 degree of freedom at 95% confidence interval. The P- value was found to be 0.0007 at 95% confidence interval that is less than 0.05. The F- value and P-value indicate that the Starch paste concentration is giving a highly significant effect on hardness of tablet. (Software used prism version 3.0)

Table 4: ANOVA –Influence of formulation variables on the response factors

Source of variance	D.F.	Sum of square	Mean square	F value
Tablet hardness	2	0.6156	0.3078	11.98
Starch paste concentration	8	26.30	3.288	127.9
Residual	16	0.4111	0.0256	

On other hand the concentration of guar gum is mainly affecting the disintegration of tablet that is proved by one way ANOVA test. According the table no. 5 the F value was found to be 3.86 that is greater than tabulated value (3.63) at 2 degree of freedom and 16 degree of freedom at 95% confidence interval. The P- value was found to be 0.0438 at 95% confidence interval that is less than 0.05. The F- value and P-value indicate that the guar gum concentration is giving a significant effect on disintegration time of tablet.

Table 5: ANOVA –Influence of formulation variables on the response factors

Source of variance	D.F.	Sum of square	Mean square	F value
DT time	2	2.036	1.18	3.86
Guar gum	8	9400	1175	4465
Residual	16	4.210	0.2631	

The reason for better hardness and low disintegration time of tablet may be because the starch paste concentration increases the binding capacity of tablet and higher guar gum concentration increases the swelling capacity of tablet that is why tablet is required less time for disintegration.

But it was seen that, further increases the concentration of guar gum, the tablet is required more time to disintegrate because on higher concentration of guar gum is swell up and form a gel like structure which create a problem for disintegration of tablet.[12]

The polynomial terms was also used to evaluate the response. A statistical model, $Y = b_0 + b_1 X_1 + b_2 X_2 + b_{12} X_1 X_2 + b_{11} X_1 X_1 + b_{22} X_2 X_2$, incorporating interactive and polynomial terms was used to evaluate the responses; where Y is the dependent variable, b_0 is the arithmetic mean response of the nine runs and b_i is the estimated coefficient for the factor X_i. The main effects (X_1 and X_2) represent the average result of changing one factor at a time from its low to high value.

The interaction terms ($X_1 X_2$) show how the response changes when two factors are simultaneously changed. The polynomial terms ($X_1 X_1$ and $X_2 X_2$) are included to investigate nonlinearity. The DT and hardness for the nine batches (F1 to F9) showed a variation (i.e., 18 to 80 s and 3.0 to 6.0, respectively given in table no 2).

Table 6: Regression analysis data

Response	bo	b1	b2	b12	b11	b22
DT	49.67	-100	-0.33	20.00	-10.33	-14.67
Hardness	4.31	0.022	-0.78	-0.56	0.24	0.58

*b1= affect of guar gum; *b2= affect of starch paste

The Design expert design version 8.0.6 soft ware was used to calculate the polynomial equation and data are given in table no: 3. When placed all values of data in polynomial equation and the equation is Y=49.67-100X1-0.33X2+20.00X1X2-10.33b11-14.67X2X2.

The data clearly indicate that the DT and hardness values are strongly dependent on the selected independent variables. In table the negative sign indicate that the independent variable give the more effect on dependent variable i.e. the guar gum concentration is

giving main effect on disintegration time and starch paste is giving main effect on hardness of tablet.[13,14, 15]

Interaction Study between Guar gum and Starch Paste for Hardness

The effect of starch paste and guar gum on hardness and disintegration can be explained by graphical presentation. A study of guar gum and starch paste on hardness is showing in following graph. By this graph at 5% starch paste concentration (B1 level 1of B), guar gum concentration is increased, the hardness is linearly increased. At 7.5 starch paste concentration(B2 level of B), the hardness of tablet is increased from 2mg to 5mg of guar gum(level 1 of A to level 2 of A) but again guar gum concentration is increased the hardness of tablet is decreased. At 10% concentration of starch paste(B3 level of B) The hardness of tablet shown dramatically variation, at 2mg of guar gum the hardness of tablet is maximum but increase the concentration of guar gum the hardness is decreased, but again guar gum concentration is increased, the tablet hardness is also increased.

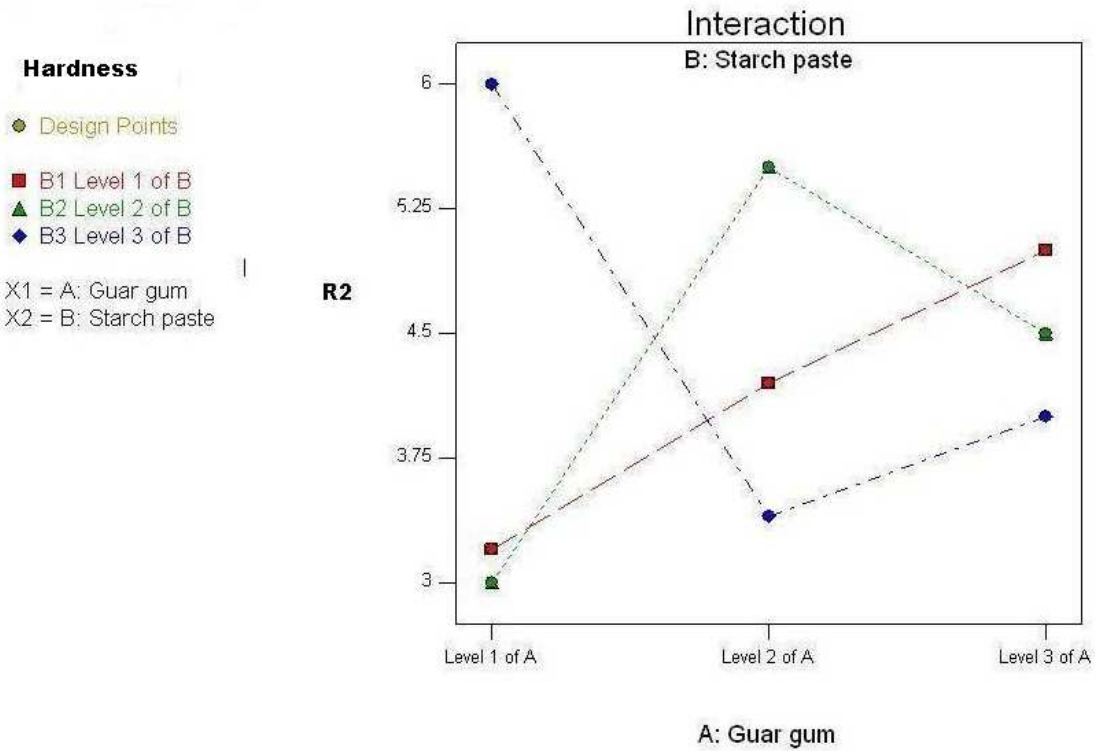

Fig. 3: Interaction Study between Guar gum and Starch Paste for Hardness

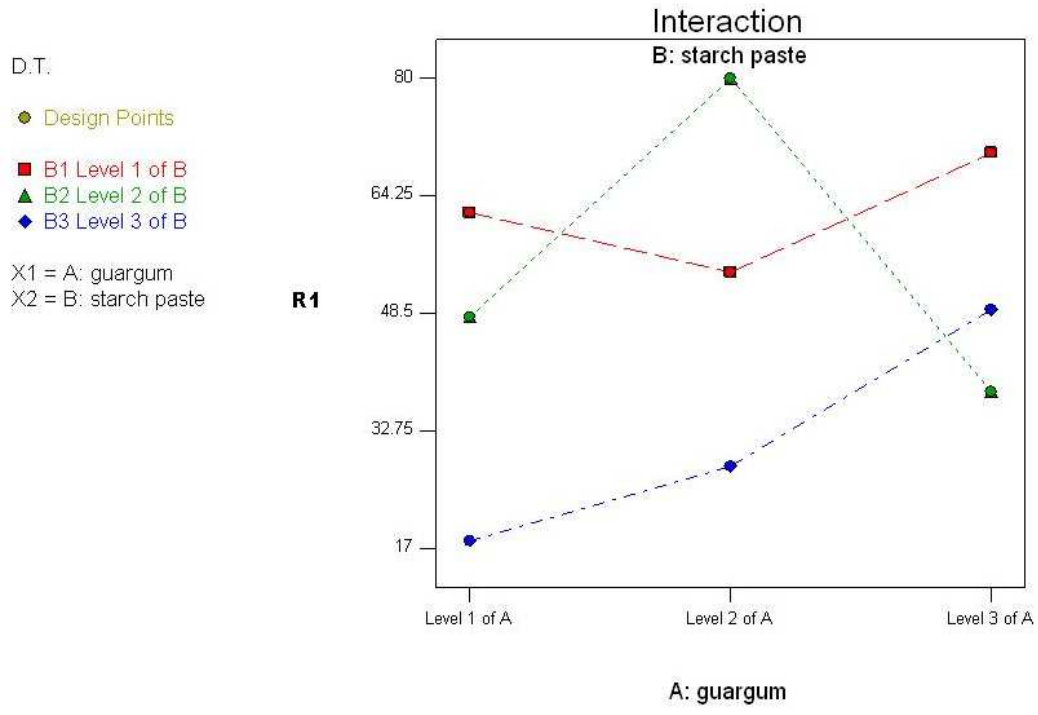

Fig. 4: Interaction Study between Guar gum and Starch Paste for Disintegration Time

Interaction Study between Guar gum and Starch Paste for Disintegration Time

A study of guar gum and starch paste on Disintegration time is showing in following graph. By this graph at 5% starch paste conc. (B1 level 1of B), guar gum concentration is increased, and the disintegration time is decreased on 5 mg concentration of guar gum(level 2 of A),and it again increase on 10mg of guar gum concentration (level 3 of A). At 7.5 starch paste concentration(B2 level of B), the disintegration time of tablet is increased from 2mg to 5mg of guar gum(level 1 of A to level 2 of A) but again guar gum concentration is increased the disintegration time of tablet is decreased. At 10% concentration of starch paste (B3 level of B) the disintegration time of tablet is linearly increased when guar gum concentration is increased from 2mg to 8mg (level 1 of A to 3 level of A).

By graphical presentation and polynomial equation, a combined affect of starch paste and guar gum was seen that, the hardness was mainly affected by starch paste concentration but it minute affected by guar gum concentration, which was indicated by negative sign of b2(-0.78) that was less than b1 value(-0.58). Since the guar gum concentration was mainly affecting the disintegration time of tablet (b1=-100) but it also minutely affected by starch paste concentration (b2=-0.33).

CONCLUSION

The study demonstrated that 3^2 factorial designs is useful tool to understand the effects the various formulation parameters in the preparation of fast dissolving tablet and to predict the best composition for a particular response. The one way ANOVA study demonstrated only one independent variable response on one dependent response like, effect of starch paste on hardness and guar gum on disintegration. But polynomial equation and graphical presentation demonstrated the combined effect of starch paste and guar gum on hardness and disintegration time. It is also conclude that guar gum 4000 grade could be an option of disintegrating agent in development of fast dissolving tablet.

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