World Journal of Pharmaceutical research

Volume 1, Issue 2,224-241. Research Article ISSN 2277 – 7105

DESIGN AND EVALUATION OF FAST DISSOLVING PROCHLORPERAZINE MALEATE TABLET

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Article Received on
14 March 2012,

Revised on 29 March 2012,

Accepted on 08 April 2012

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ABSTRACT

Fast dissolving tablet (FDT) has been growing interest during the last decade especially for elderly, children and patients who have swallowing difficulties. This dosage form is placed in the mouth, allowed to disperse or dissolve in the saliva, and then swallowed without the need of water. The problem of certain FDT is their low resistance and high friability. FDT having alone superdisintegrant have slow disintegration and high friability. The purpose of this study was to prepare and evaluate the superdisintegrant in promoting tablet disintegration and having low friability. Attempt was made to develop FDT of Prochlorperazine Maleate with the help of superdisintegrant. The tablets were evaluated for its percentage friability, disintegration time, wetting time, and hardness. In the investigation, a 32 full factorial design was used to investigate the combined influence of two formulation variables: amount of sodium starch glycolate and crospovidone. The results of multiple linear regression analysis revealed that for obtaining a hard and rapidly disintegrating dosage form. A checkpoint batch was also prepared to prove the validity of the evolved mathematical model. The concentration was optimized at which FDT disintegrate within 30 seconds and having friability 0.60%. A response surface plot is also presented to graphically represent the effect of the independent variables on the disintegration time and percentage friability. Optimized FDT should be prepared using an optimum concentration of sodium starch glycolate and crospovidone. Short-term stability studies indicated that there are no significant

changes in drug content and *in vitro* disintegration time. The optimized tablet was found to be stable and shelf life is predicted more than two years.

Keywords: Fast dissolving Tablet, Superdisintegrant, Prochlorprazine Maleate, Disintegration Time

INTRODUCTION

A fast dissolving system can be defined as a dosage form for oral administration, which when placed in mouth, rapidly dispersed or dissolved and can be swallowed in form of liquid. Recently fast dissolving formulation is popular as Novel Drug Delivery System because they are easy to administer and lead to better patient compliance. Pediatric and geriatric patient have difficulty (dysphasia) in swallowing the conventional dosage forms([1]). Fast dissolving drug delivery system may offer a solution to these problems. These dosage forms dissolve or disintegrate in the oral cavity within a minute without the need of water or chewing([2,3]). Tablet disintegration is a prerequisite to fast release of active ingredients from solid dosage form. The disintegrant is routinely integrated into a formulation to speed the process of disintegration. Despite all the theories proposed, however, there is still lack of a full understanding of the mechanism of disintegration. Proposed mechanism for the action of disintegrations include water uptake through wicking, swelling, deformation (shape) recovery, particle repulsion, and heat of wetting, through the latter 2 are not well supported by research([4]).

In recent years, scientist focused their attention on the formulation of quickly disintegrating tablets, the task of developing fast dissolving tablets is accomplished by using a suitable disintegrant. The widely used superdisintegrant are sodium starch glycolate (SSG), croscarmellose sodium (Ac-Di-Sol) and crospovidone. Each superdisintegrant has strength and weakness. In the present research, the preparation and evaluation of coprocessed disintegrant containing sodium starch glycolate and crospovidone was used. Coprocessing is defined as combining two or more established excipients by an appropriate process([5]). Coprocessing of excipients by could lead to formation of excipients with superior properties compared with simple physical mixture of their components or with individual components([6]). A large number of Coprocessed diluents are commercially available like Ludipress, Cellactose, and Starlac.

The use of coprocessing is a totally unexplored avenue in disintegrant. The SSG was chosen because of its high swelling capacity. Moreover, the disintegrant efficiency of SSG is

unimpaired by the presence of hydrophobic excipients. The crospovidone is selected due to the better compressibility compared with other superdisintegrant, high capillary activity, pronounced hydration capacity, and little tendency to form gel. SSG and crospovidone has fair to passable flow properties, and bulk density of SSG and crospovidone is 0.756 and 1.224 gm/cc respectively. Hence, if a physical mixture of superdisintegrant is used in high speed tabletting, the problem of segregation of the disintegrants may be encountered. One of the reasons for preparing the coprocessed superdisintegrant was to avoid the problem of segregation. A blend of swelling and wicking types of excipients may also prove to be efficient because the medium required for swelling will be brought into the tablet more easily if a wicking type of superdisintegrant is also present. Prochlorperazine maleate is a phenothiazine antipsychotic and widely used in prevention and treatment of nausea, vomiting including that associated with migraine or drug induced emesis([7,8])

The concept of formulating fast dissolving tablets containing prochlorperazine maleate offer a suitable and practical approach in serving desired objective of faster disintegration and dissolution characteristics with potential increased bioavailability.

The objective of the present research was to prepare and evaluate coprocessed superdisintegrant and to optimize their concentration for preparation of fast dissolving tablet of prochlorperazine maleate which disintegrates within 30 seconds and having friability 0.060%.

MATERIALS

Prochlorperazine Maleate, Sodium Starch Glycolate (SSG), Ac-Di-Sol, Lactopress, microcrystalline cellulose (PH102) and Crospovidone (CP) were a gift sample from Pharma Impex Lab (Kolkata, India). Talc and Magnesium stearate was purchased from Local Market. All other chemicals used were of analytical grade.

PREPARATION OF DISINTEGRANT BLEND (PHYSICAL MIXTURE AND COPROCESSED SUPERDISINTEGRANT)

The physical mixture of SSG and crospovidone was prepared by mixing them together in glass pestle motor. The coprocessed superdisintegrant was prepared as follows: blends of SSG and crospovidone in different ratio (1:1, 1:2, 1:3, 2:1, 2:3, 3:1, and 3:2) total weight of 10 g was added to 50 ml of isopropyl alcohol. The contents of beaker were stirred on a magnetic

stirrer. The temperature was maintained between 65-700C, and stirring was continued till most of isopropyl alcohol evaporated. The wet coherent mass was sieved through sieve no 100 the wet powder was dried in a tray drier at 600C for 20 minutes. The dried powder were sifted on 120-mesh sieve and stored in airtight container till further use. For the preliminary study and evaluation only physical mixture and coprocessed superdisintegrant was prepared in 1:1 ratio. Rest of ratio was prepared for the factorial design batch.

EVALUATION OF SSG, CROSPOVIDONE AND PHYSICAL BLEND OF SUPERDISINTEGRANT

Particle size analysis

The Malver Mastersizer, using a laser diffraction technique, was used to test the particle size distribution of superdisintegrants and their blends. The particle size of the dry powders was analyzed by feeding disintegrant powder directly into the system through a dry powder feeder. An external vacuum was connected to the other side to disperse and, at the same time, remove the particles from the system. To test the swelling of superdisintegrant in water and sorenson's buffer (pH 6.8, Saliva pH), disintegrant powder were first dispersed in a small volume of liquid and the ultrasonicated for 10 minutes. The suspension was transferred with a pipette to a small volume connected to a circulating cell, to achieve an optimal obscurity of 10% to 30%. The stirrer speed was set at 2500 rpm. The volume median diameter was recorded the average of 6 to 10 measurements. The ratio of particle diameter in the dispersing medium to the dry powders was used as an intrinsic swelling capacity of super disintegrant in the test medium.

Mass- volume relationship and flow properties([9])

For the mass-volume relationship bulk density (ρb), tapped density (ρt), hausner's ratio (RH = ρt / ρb) and compressibility index ($Ic = 100$(ρt – ρb) / ρb) was determined with the bulk/tapped densitometer9. The angle of repose was determined using funnel method. The blend was poured through a glass funnel that can be raised vertically until a specified cone height (h) was obtained. Radius of the conical pile (r) was measured and angle of repose (θ) was calculated using the formula tan θ = h/r.

Table 1: Evaluation of superdisintegrant

Code	Bulk Density (g/cc) ±SD	Tapped Density (g/cc) ±SD	Hausner's Ratio RH±SD	Compressibility Index *Ic±SD*	Angle of Repose (0) ±SD
SSG	0.759±0.005	0.945±0.004	1.250±0.004	20.029±0.234	36.18±0.174
CP	1.244±0.020	1.858±0.015	1.494±0.034	33.039±1.519	44.02±1.010
Physical Mixture (1:1)	0.892±0.008	1.158±0.040	1.299±0.039	22.946±2.268	37.83±1.714
Coprocessed (1:1)	0.624±0.002	0.701±0.004	1.122±0.004	10.855±0.332	24.42±0.627

Liquid uptake study

The liquid uptake characteristic of the loose disintegrant powder allows an evaluation of the both intrinsic swelling and the wettabilty of the studied superdisintegrant and their blends. A modified gravimetric liquid uptake apparatus([10,11]) was developed in our laboratory to facilitate the measuring of liquid uptake by the disintegrant was performed with both water and sorenson's buffer (pH 6.8) at room temperature. The apparatus consist of a Buchner funnel with a fritted disk to hold the sample and liquid holding vessel resting on an electronic digital balance (Shimadzu, Japan). The 2 parts were adjusted at the same horizontal level and connected by a plastic tube so that the liquid can flow freely from 1 side to the other. During the measurement, either 200 mg of disintegrant powder was placed on a piece of filter paper inside the sample holder. The liquid was then passively drawn into the sample from the feeder. The loss the loss of weight from the liquid holder was read from the electronic balance. Data were collected every two second until the saturation was reached.

Scanning electron micrographs

Finally to investigate the morphology of SSG, crospovidone and the formed coprocessed superdisintegrant in 1:1 ratio of SSG and crospovidone, scanning electron micrographs were taken using (JOEL, JSM-35, CF) scanning electron microscope; where the samples were previously sputter coated with gold.

Full factorial design

To know the actual amount of 2 superdisintegrant for the desirable property of fast dissolving tablets a 32 randomized full factorial design was used. In this design 2 factors are evaluated,

each at 3 levels, and experimental trials are performed at all 9 possible combinations([12]). The amount of SSG (X1), and the amount of crospovidone (X2), was selected as independent variables. The disintegration time and percentage friability were selected as dependent variables13.

Preparation of fast dissolving tablets preliminary and factorial design batches

The raw materials were passed through a no. 100 screen prior to mixing. Prochlorperazine maleate, SSG, crospovidone, microcrystalline cellulose and lactose were mixed using a glass mortar and pestle. The blends were lubricated with 2% w/w talc and 2% w/w magnesium stearate. The blends ready for compression were converted into tablets using a single-punch tablet machine (Cadmach, Ahmedabad, India). The composition of the preliminary trial and factorial design batches is shown in Table 2 and Table 3 respectively.

EVALUATION OF TABLET PROPERTIES

The crushing strength of the tablets was measured using a Monsanto hardness tester. The friability of a sample of 20 tablets was measured using a Roche Friabilator. Twenty preweighed tablets were rotated at 25 rpm for 4 minutes([14]). The tablets were then reweighed after removal of fines (using no. 60 mesh screen), and the percentage of weight loss was calculated. The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers of 10 cm diameter were placed in a petridish with a 10 cm diameter. Ten milliliters of water containing amaranth, a water-soluble dye, was added to the petridish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time. A modified method was used to determine disintegration time of the tablets. A cylindrical vessel was used in which 10-mesh screen was placed in such way that only 2 ml of disintegrating or dissolution medium would be placed below the sieve. To determine disintegration time, 6 ml of Sorenson's buffer (pH 6.8), was placed inside the vessel in such way that 2 ml of the media was below the sieve and 4 ml above the sieve. Tablet was placed on the sieve and the whole assembly was then placed on a shaker. The time at which all the particles pass through the sieve was taken as a disintegration time of the tablet. Six tablets were chosen randomly from the composite samples and the average value was determined([15]). The dissolution of the tablet was performed in the same instrument used in disintegration time determination. The 6 ml Sorenson's buffer (pH 6.8) at 37±0.50C used as dissolution medium. Aliquots were

withdrawn at every minute and replaced by fresh media. The aliquots were filtered and diluted appropriately and analyzed by spectrophotometrically at 254 nm.

Optimization of the fast dissolving tablet

After application of full factorial design and with help of polynomial terms the optimized tablet was produced which have targeted to the DT 30 seconds and % Friability 0.6%. The optimization was done with the help of software Design Expert 7.1.6. The optimized concentration of the coprocessed SSG and crospovidone was incorporated in the tablet which was also used as the check point of the regression analysis model. The response surface prediction plots were formulated with the help of the software. The optimized fast dissolving tablet was prepared and evaluated for its physiochemical properties. The optimized tablet was subjected to short term stability studies at 40°C and 75% RH for 3 months.

Table 2: Preparation and evaluation of preliminary trial batches

Ingredients	T1	T2	T3	T4	T5	T6	T7	T8	T9*	T10#
SSG	1	2	3	4	-	-	-	-	2	2
Crospovidone	-	-	-	-	1	2	3	4	2	2
Avicel PH102	55	54	53	52	55	54	53	52	52	52
Lactopress	25	25	25	25	25	25	25	25	25	25
Mannitol	15	15	15	15	15	15	15	15	15	15
Talc	2	2	2	2	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2	2	2	2	2
Hardness (kg/cm2)	3.1 ±0.122	3.1 ±0.097	3.2 ±0.124	3.1 ±0.132	3.0 ±0.134	3.0 ±0.121	3.0 ±0.143	3.2 ±0.068	3.1 ±0.185	3.2 ±0.014
Friability (%)	0.413 ±0.025	0.465 ±0.023	0.526 ±0.054	0.565 ±0.013	0.311 ±0.032	0.339 ±0.053	0.456 ±0.014	0.585 ±0.017	0.885 ±0.029	0.574 ±0.011
Disintegration Time (seconds)	112 ±1.48	87 ±1.69	66 ±2.65	45 ±1.48	98 ±1.07	82 ±1.86	56 ±2.60	31 ±2.78	48 ±2.14	41 ±4.58
Wetting Time (seconds)	128 ±1.83	97 ±2.41	81 ±2.06	66 ±3.14	105 ±1.09	91 ±2.38	61 ±1.48	36 ±3.48	62 ±1.26	47 ±1.25

Table 3: 32 Full factorial design layout

Batch Codes	Variable Levels in Coded Form		Disintegration Time	% Friability
	X1 (mg)	X2 (mg)	DT (sec) ±SD	F (%) ±SD
FDT1	-1	-1	77±1.25	0..623±0.016
FDT2	-1	0	58±0.85	0.511±0.052
FDT3	-1	1	35±2.35	0.286±0.038
FDT4	0	-1	65±3.21	0.669±0.065
FDT5	0	0	41±4.58	0.574±0.011
FDT6	0	1	18±10.24	0.375±0.035
FDT7	1	-1	62±9.57	0.756±0.043
FDT8	1	0	42±1.98	0.651±0.018
FDT9	1	1	11±2.17	0.457±0.029
PCP	1	0.34	30.48	0.599

Coded values	Actual Values	
	X1	X2
-1	1	1
0	2	2
1	3	3

RESULT AND DISCUSSSION

In preliminary investigation, water, ethyl alcohol, dichloromethane, and isopropyl alcohol were used for coprocessing of the superdisintegrant. Water was ruled out for further experiment because gel formation occurs due to the presence of starch in SSG. Dichloromenthane was omitted because of floating of crospovidone and sedimentation of SSG. From ethyl alcohol and isopropyl alcohol, isopropyl alcohol was chosen because SSG is sparingly soluble in ethyl alcohol. Isopropyl alcohol was selected considering the absence of gel formation and phase separation.

Evaluation of SSG, crospovidone and physical blend of superdisintegrant Particle size analysis and swelling

The volume median diameters of superdisintegrants in different media was determined are given in Fig. 1. According to the volume median diameters, SSG swells 120% in sorenson's

buffer pH 6.8, and 260% in water. A significant reduction in swelling capacity is also observed in physical mixture as well as coprocessed superdisintegrants. The strong decrease in swelling capacity of chemically modified starch may attribute to the converting of the carboxymethyl sodium moieties to its free acid form in acidic medium. Since the acid medium form has less hydration capacity than its salt form, the liquid holding capacity of the disintegrant particle reduces after deionization in the slightly acidic medium. Therefore, the total degree of substitution and the ratio of basic to acidic substituent's are potential factors determining the extent of influence of medium pH on the water uptake and swelling properties of disintegrants and blends particles. Unlike the other superdisintegrant and their blends, there is no apparent change in the swelling capability of the nonionic polymer crospovidone in both media. The percentage of increase in diameter for SSG, crospovidone, physical mixture and coprocessed superdisintegrant is 260%, 23%, 398%, and 657% in water and 120%, 38%, 205%, and 460% in sorenson's buffer pH 6.8 respectively. Therefore, the large difference in swelling capacity between superdisintegrants in water is less significant in slightly acidic medium. The results clears that the physical mixing and coprocessing gives better swelling than used alone due to its combined effect.

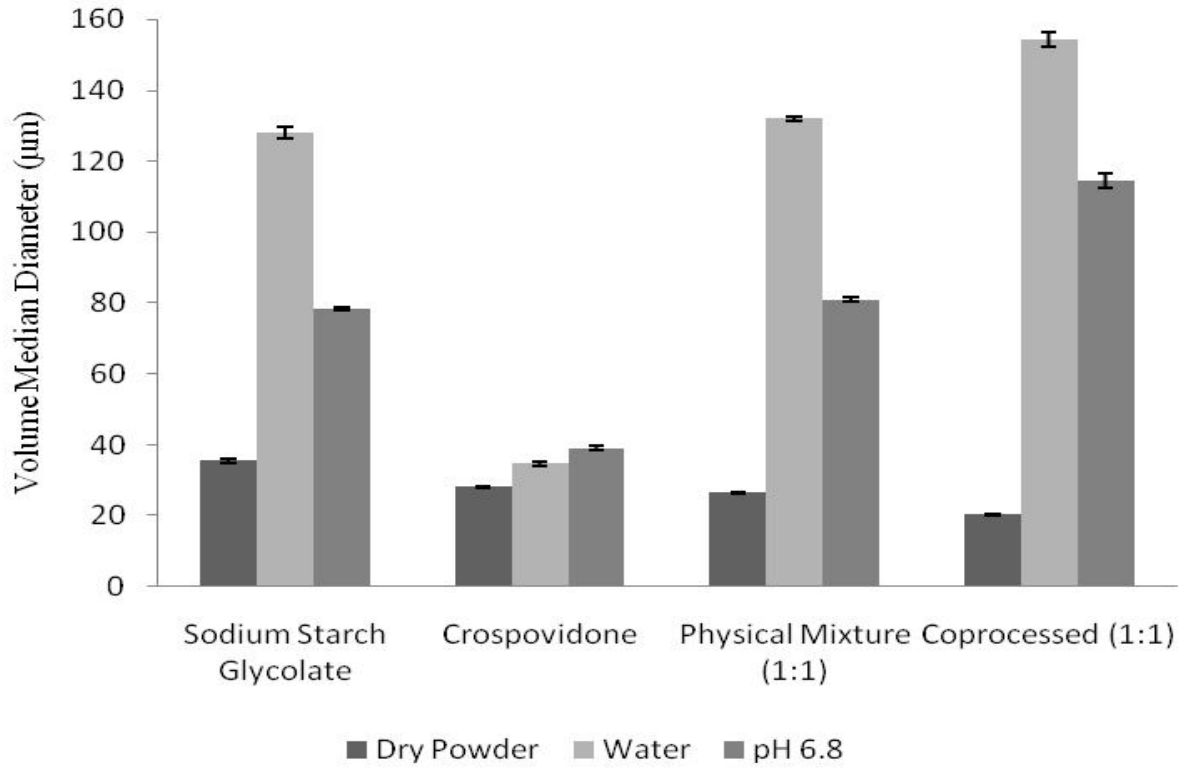

Figure 1: Volume median diameter of superdisintegrant and their blends in different media (n=6).

Mass- volume relationship and flow properties

Table 1 reports the bulk density, tapped density, Compressibility Index (*Ic*) and Hausner's Ratio for all studied batches. According to literature data powder with a *Ic* between 5 to 18% are suitable for producing tablets, and those with a Hausner's Ratio below 1.25 are exhibited good flowability. Only coprocessed superdisintegrant batch is fallen in the limit/range. On the evaluation of superdisintegrant angle of repose of the physical mixture and coprocessed SSG: Crospovidone (1:1) was found to be 380 and 240 respectively. According to USP, good flow (angle of repose between 200 and 300) was shown by coprocessed superdisintegrant. Therefore, it was concluded that particle size distribution of the excipients would be kept the same to avoid the tabletting problem that is dependent on the flow of powder from hopper to die cavity. The results were shown in Table 1 for angle of repose.

Liquid uptake study

The liquid uptake study of superdisintegrant powders and blends describes the dynamic process of particle swelling upon wetting. The liquid uptake of the 2 superdisintegrants and their blends in both media is given in Fig. 2. Similar to the particle size analysis, major difference in liquid uptake between two pH media is observed for SSG. The dramatic decrease in both the rate and extent of liquid uptake of SSG demonstrates its reduced hydration capacity and wettabilty in slightly acidic medium. The crospovidone behaves the same in the both media during liquid uptake, which is consistent with the particle size distribution analysis. On the other hand physical mixture and coprocessed superdisintegrant shows the good uptake of liquids, rather than alone 2 superdisintegrants. This is due to the spherical shape of SSG. Generally spherical shaped SSG particles more likely absorb water and retain it rather than transfer it to the next particle. In other words, the water transferring rate between particles is slower than the swelling rate of individual particle. Here the crospovidone plays an important role to uptake a liquid and transfer it to next particle. So the combination of these two superdisintegrant is much more useful to prepare fast dissolving tablets.

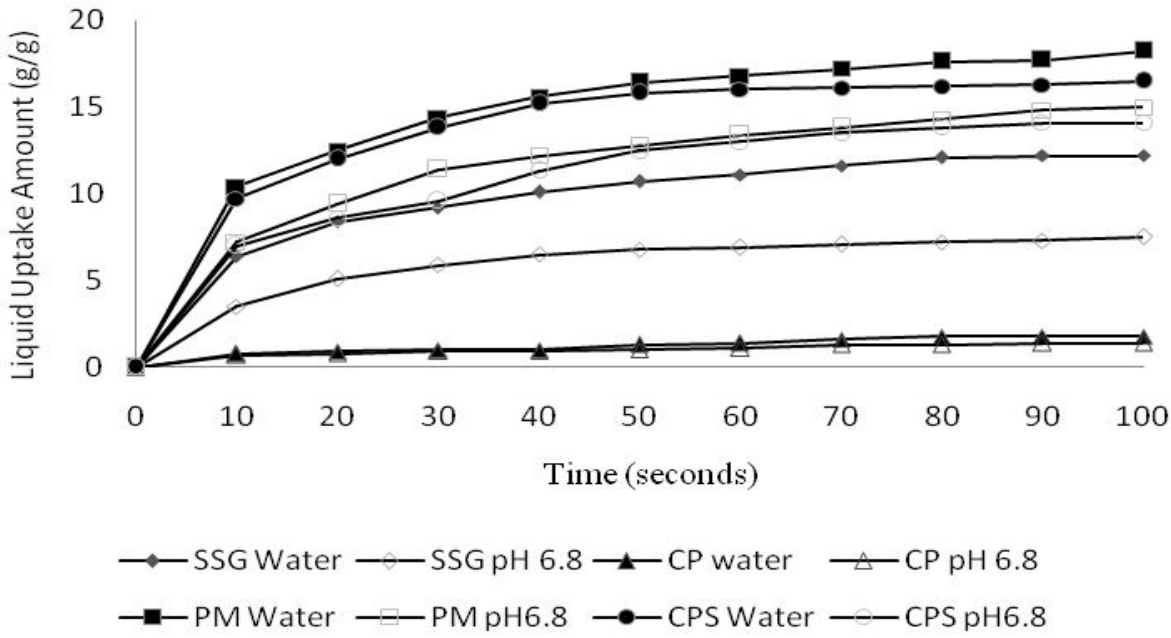

Figure 2: Liquid uptake by superdisintegrants and their blends from water (solid symbol) and sorenson's buffer (pH 6.8) with respect to time SSG indicates, Sodium Starch Glycolate; CP, Crospovidone; PM, Physical Mixture; CPS, coprocessed superdisintegrant (n=6).

Scanning electron microscopy

The morphology and surface properties of SSG, crospovidone and coprocessed superdisintegrant were visualized using scanning electron microscopy shown in Fig. 3. All powder batches are presentenced in magnificence of X150. From these micrographs we observe clear difference between the structure and size of superdisintegrants. The all above results was proved by these micrographs.

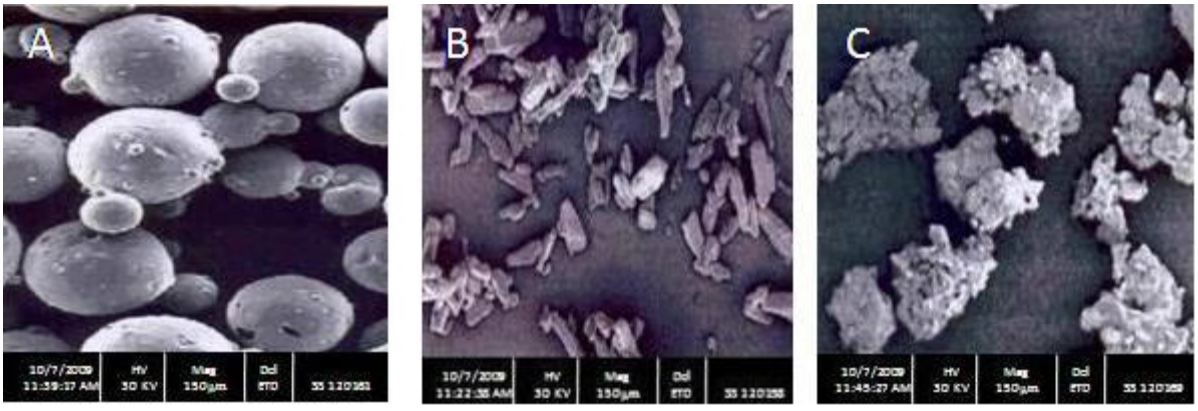

Figure 3: Scanning electron micrographs at same magnificence A. sodium starch glycolate; B. crospovidone; C. coprocessed superdisintegrant.

Evaluation of preliminary trial and factorial design batch

The preliminary trials were conducted by using 1 to 4% w/w superdisintegrants sodium starch glycolate and crospovidone. On the basis of the results obtained in the preliminary screening studies, the batch containing SSG and crospovidone showed the fastest disintegration in very high concentration but not to be 30 seconds and friability is also increased consequently. The results in Table 2 clears that the disintegration time and percent friability have a great difference in physical mixture and coprocessed superdisintegrants. The use of a physical mixture superdisintegrant agent resulted in increased friability probably due to low compressibility of excipients. So by coprocessing of SSG and crospovidone may decrease the percent friability of the tablets. The result of preliminary examination revealed that tablets containing 1:1 physical mixture of SSG and crospovidone showed a higher friability than that of tablet of coprocessed superdisintegrant.

The results shown in Table 3 indicate that concentration-dependent disintegration was observed in batches prepared using coprocessed SSG and crospovidone. The absorption and swelling is responsible for faster water uptake; hence it facilitates wicking action of crospovidone in bringing about faster disintegration. It is worthwhile to note that as the concentration of SSG is increased, the wetting decreased. Tablets with lower friability (≤ 0.6%) may not break during handling on machines and/or shipping. The response surface plots are shown in Fig. 4. One of the primary requirements of immediate release preparation is faster disintegration. Considering these results, it may be concluded that coprocessed superdisintegrant is superior to physical mixture for formulating the fast dissolving tablets. In order to investigate the factors systematically and optimize the tablet for DT 30 seconds and % F less than 0.6%, a factorial design was employed in the present investigation.

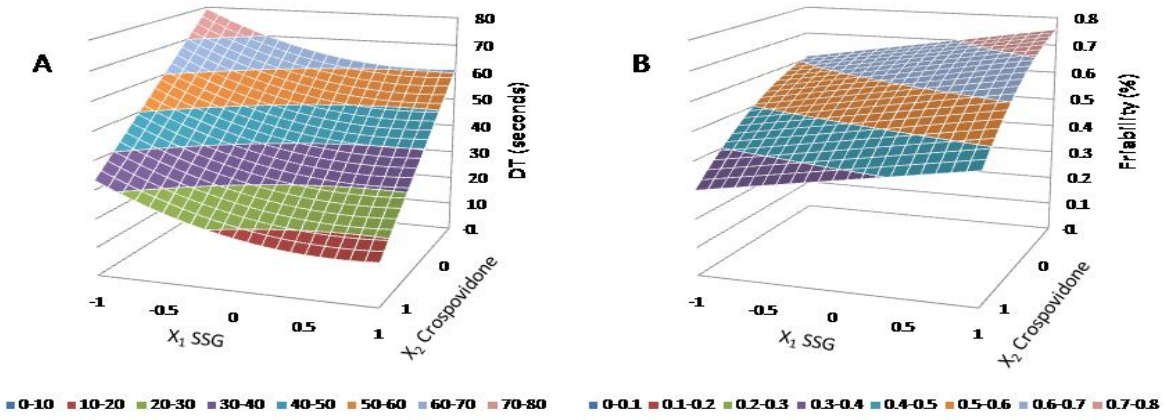

Figure 4: Response surface plot A. disintegration time B. percent friability.

Factorial Design

The amount of SSG (X1) and the crospovidone (X2) were chosen as independent variables in a 32 full factorial design. A statistical model incorporating interactive and polynomial terms was used to evaluate the responses

$$Y = b0 + b1X1 + b2X2 + b11X1X1 + b22X2X2 + b12X1X2 \quad (1)$$

Where, Y is the dependent variable, b0 is the arithmetic mean response of the 9 runs, and b1 is the estimated coefficient for the factor X1. The main effects (X1and X2) represent the average result of changing 1 factor at a time from its low to high value. The interaction terms (X1X2) show how the response changes when 2 factors are simultaneously changed. The polynomial terms (X1X1 and X2X2) are included to investigate nonlinearity. The disintegration time and percentage friability for the 9 batches (FDT1 to FDT9) showed a wide variation (ie, 11 - 76 seconds and 0.286% - 0.756%, respectively).

The data clearly indicate that the disintegration time and percentage friability values are strongly dependent on the selected independent variables. The fitted equation relating the responses disintegration time and percentage friability to the transformed factor are shown in Table 4. The polynomial equations can be used to draw conclusions after considering the magnitude of coefficient and the mathematical sign it carries (ie, positive or negative). Table 4 shows the results of the analysis of variance (ANOVA), which was performed to identify insignificant factors. The high values of correlation coefficient for disintegration time and percentage friability (Table 5) indicate a good fit.

Table 4: Summary of results of regression analysis

Response (Full Model)	b0	b1	b2	b11	b22	b12
Disintegration Time	42.55	-9.16	-23	6.16	-2.33	-2.5
Percentage Friability	0.573	0.074	-0.155	0.008	-0.051	0.009

Table 5: Calculations for testing the model in portions

For Disintegration Time

	df	*SS*	*MS*	*F*	*Sign. F*	R^2
Regression	5	3790.111	758.022	335.518	0.000256	0.9982
Residual	3	6.777	2.259			
Total	8	3796.889				

For % Friability

	df	*SS*	*MS*	*F*	*Sign. F*	R^2
Regression	5	0.182	0.0365	454.847	0.000162	0.9986
Residual	3	0.000241	8.03E-05			
Total	8	0.182938				

Effect of independent variables on dependent variables

The results of multiple linear regression analysis reveal that, on increasing the concentration of either SSG or crospovidone, a decrease in disintegration time is observed; both the coefficients b1 and b2 bear a negative sign. When higher percentage of SSG is used, higher water uptake swelling and deformation of the SSG take place, which gives internal pressure to tablet to disintegrate due the swelling of the disintegrant. The water uptake and subsequent disintegration are thus facilitated. It is obvious that in the presence of higher percentage of superdisintegrant crospovidone, wicking is facilitated.

An increase in the concentration of SSG leads to an increase in friability because the coefficient b1 bears a positive sign. When a higher percentage of SSG is used, low compressible tablets are produced, which are mechanically weak. The increase in the concentration of crospovidone results in decreased friability values because b2 bears a positive sign. Crospovidone is known to produce mechanically strong tablets. Results were shown in response surface plot for disintegration time and percent friability (Fig. 4.).

Optimization of the fast dissolving tablet

The optimization of the fast dissolving tablet was decided to target disintegration time 30 second and percent friability is 0.6%. The optimized concentration was obtained by software as clears in the surface response prediction curves. Optimization results were shown in Table

6 (Fig. 5.). A checkpoint batch PCP was prepared at X1 = 1 level and X2 = 0.34 level. From the full model, it is expected that the friability value of the checkpoint batch should be 0.599, and the value of disintegration time should be 30.48 seconds. Table 7 indicates that the results are as expected. Thus, we can conclude that the statistical model is mathematically valid. The optimized formula was characterized for its blend properties and tablet characterization. The drug release was at the end of 5 minutes was more than 90%. The drug release was followed first order kinetics. The optimized tablet was subjected to short term stability studies at 40°C and 75% RH for 3 months. Studies indicated that no significant change in appearance of the tablets, disintegration time, and percentage friability were observed. The drug release after the period of stability studies was found to be similar.

The similarity factor “f2 value” was observed 92.84. The shelf life of the optimized tablet was predicted more than two years (821 days).

Table 6: Optimization of fast dissolving tablet

Constraints			
Name	Goal	Lower Limit	Upper Limit
SSG	is in range	-1	1
Crospovidone	is in range	-1	1
DT (sec)	is target = 30	11	76
Friability (%)	is target = 0.6	0.286	0.756

Solution				
SSG (X1)	Crospovidone(X2)	DT (sec)	Friability (%)	Desirability
1.00	0.34	30.48	0.599	0.993

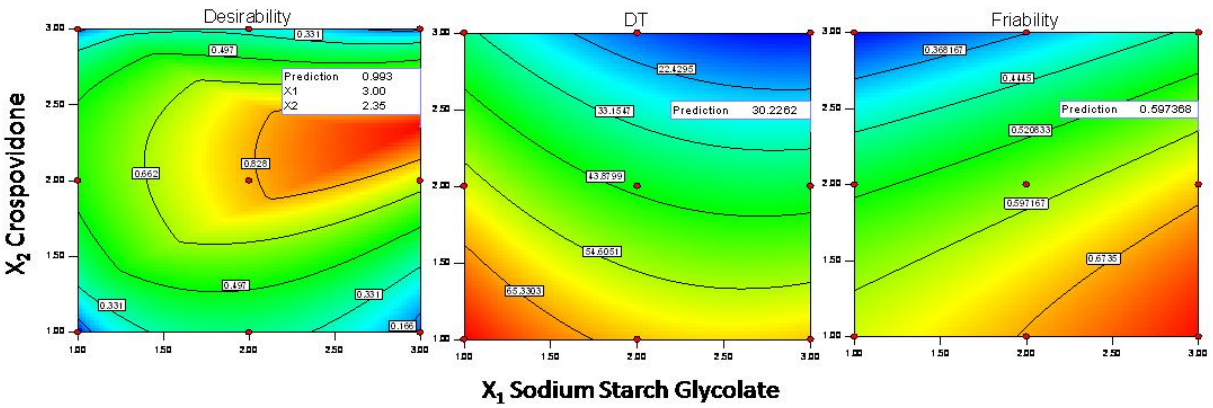

Figure 5: Response surface prediction plot

Table 7: Preparation and characterization of optimized formulation (n=6)

Tablet Preparation by using Coprocessed	
Ingredients (mg)	PCP
Prochlorperazine Maleate	15.00
SSG	03.00
Crospovidone	02.35
Avicel PH102	53.65
Lactopress	15.00
Mannitol	10.00
Talc	02.00
Magnesium stearate	02.00
Blend Characterization±SD	
Bulk Density (gm/cc)	0.356±0.013
Tapped Density (gm/cc)	0.392±0.001
Hausner's Ratio	1.103±0.041
Compressibility Index (%)	9.277±3.382
Angle of Repose (o)	22.637±0.222
Tablet Characterization±SD	
Weight (mg)	99.178±0.238
Thickness (mm)	2.358±0.239
Hardness (kg/cm2)	3.7±0.2.31
Friability (%)	0.598±0.003
Disintegration Time (seconds)	30±3.60
Wetting Time (seconds)	39±2.08
Drug Content (mg/Tab.)	14.859±0.022
% Drug Release (5 min.)	90.701±0.415

CONCLUSION

A laser diffraction particle size analyzer proved to be an effective tool for determining the intrinsic swelling of disintegrant particles in different media. The results correlated with liquid uptake and swelling measurements made on neat disintegrant powder, physical mixture and coprocessed superdisintegrant. Coprocessed superdisintegrant consisting sodium starch

glycolate and crospovidone exhibited good flow and compression properties. The results of a 32 full factorial design revealed that the amount of sodium starch glycolate and crospovidone significantly affect the dependent variables, disintegration time, and percentage friability. It is thus concluded that by adopting a systematic formulation approach, an optimum point can be reached in the shortest time with minimum efforts.

The area where further work can be done include using a lyophilization, spray dryer or microwave for preparation of coprocessed superdisintegrant.

REFERENCES

1. Seager H, Drug delivery products and the zydis fast dissolving dosage forms, J. Pharm. Pharmacol., 1998, 50, 375-382.

2. Habib W,Khankari R, Hontz J, Fast-dissolving drug delivery systems: critical review in therapeutics, Drug Carrier Systems., 2000, 17, 61-72.

3. Bi Y, Sunada H, Yonezawa Y, X Dayo K, Otsuka A, Iida K, Preparation and evaluation of a compressed tablet rapidly disintegrating in oral cavity, Chem. Pharm. Bull., 1996, 44, 2121-2127.

4. Augsburger LL, Brzecko AW, Hahm HA, Characterization and functionality of superdisintegrants, in: J. Swarbik, J.C. Boylan (Eds.), Encyclopedia of Pharmaceutical Technology, Marcel Dekker Inc., New York, 2000, pp. 269-291.

5. Michoel, Rombaut P, Verhoye A, Comparative evaluation of co-processed lactose and microcrystalline cellulose with their physical mixtures in the formulation of folic acid tablets, Pharm. Dev. Technol., 2002, 7, 79-87.

6. Gohel MC, Jogani PD, A review of co-processed directly compressible excipients, J. Pharm. Pharm. Sci., 2005, 8, 76-93.

7. Casey JF, Lasky JJ, Klett C, Hollister LE, Treatment of schizophrenic reactions with phenothiazine derivatives. a comparative study of chlorpromazine, triflupromazine, mepazine, prochlorperazine, perphenazine, and Phenobarbital, The Am. J. Psychiatry., 1960, 117, 97-105.

8. Gralla RJ, Osoba D, Kris MG, Recommendations for the use of antiemetics: evidence-based, clinical practice guidelines, J. of Clinical Oncology., 1997, 17**,** 2971-2994.

9. Aulton ME, The Science of Dosage form Design, first ed., Churchill Livingstone, New York, 1996.

10. Shah U, Augsburger L, Evaluation of the functional equivalence of crospovidone NF from different sources. part 2. standard performance test, Pharm. Dev. Technol., 2001, 6, 419-430.

11. Kamp HVV, Bolhuis GK, De Boer AH, Lerk CF, Lie-A-Huen L, The role of water uptake on tablet disintegration. Design of an improved method for penetration measurements, Pharm. Acta. Helv., 1986, 61, 22-29.

12. S. Bolton, Pharmaceutical Statistics, first ed., Marcel Decker Inc., New York, 1990.

13. Franz RM, Browne JE, Lewis AR, Experiment design, modeling and optimization strategies for product and process development, in: H.A. Liberman, M.M. Reiger, G.S. Banker (Eds.), Pharmaceutical Dosage Forms: Disperse Systems, Marcel Dekker Inc., New York, 1988, pp. 427-519.

14. Schiermeier S, Schmidt PC, Fast dispersible ibuprofen tablets, Eur. J. Pharm. Sci., 2002, 15, 295-305.

15. Late SG, Yi-Ying Y, Banga AK, Effect of disintegration promoting agent, lubricants and moisture treatment on optimized fast disintegrating tablets, Int. J. Pharm.,2009, 365, 4-11.