Preparation and Assessment of Novel Coprocessed Superdisintegrant Consisting of Crospovidone and Sodium Starch Glycolate: A Technical Note

Submitted: March 24, 2006; Accepted: July 19, 2006; Published: February 2, 2007

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KEYWORDS: Crospovidone, sodium starch glycolate, coprocessing, disintegration, dissolution.

INTRODUCTION

Oral route of drug administration is perhaps the most appealing route for the delivery of drugs.[1] Of the various dosage forms administered orally, the tablet is one of the most preferred dosage forms because of its ease of manufacturing, convenience in administration, accurate dosing, stability compared with oral liquids, and because it is more tamperproof than capsules.[2,3] The bioavailability of drug is dependent on in vivo disintegration, dissolution, and various physiological factors. In recent years, scientists have focused their attention on the formulation of quickly disintegrating tablets. The task of developing rapidly disintegrating tablets is accomplished by using a suitable diluent and superdisintegrant.

Coprocessing is defined as combining 2 or more established excipients by an appropriate process.[3] Coprocessing of excipient could lead to formation of excipients with superior properties compared with the simple physical mixture of their components or with individual components.[3,4] A large number of coprocessed diluents are commercially available. The representative examples are Ludipress, Cellactose, and Starlac.

The use of coprocessing is a totally unexplored avenue in disintegrants. The widely used superdisintegrants are sodium starch glycolate, crospovidone, and croscarmellose sodium. Like diluents, each superdisintegrant has strengths and weaknesses. In the present investigation, the preparation and evaluation of coprocessed disintegrant containing crospovidone and sodium starch glycolate was explored. The reasons for the selection of crospovidone are as follows: better compressibility compared with other superdisintegrants,[5] high capillary activity, pronounced hydration capacity, and little tendency to form gels.[6] Moreover, the rate and extent of liquid uptake and swelling of crospovidone (Polyplasdone XL 10) are not reduced in 0.1 N hydrochloric acid when compared with aqueous medium.[7] The aqueous medium (water) represents disintegration medium and 0.1 N HCl represents gastric environment. Sodium starch glycolate was chosen because of its high swelling capacity.[8] Moreover, the disintegrant efficiency of sodium starch glycolate is unimpaired by the presence of hydrophobic excipients such as lubricants.[8] Sodium starch glycolate exhibits good flow (angle of repose <36º). The bulk density of crospovidone and sodium starch glycolate is 0.4 and 0.756 g/cm^3, respectively. Hence, if a physical mixture of superdisintegrants is used in high-speed tableting, 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 excipient may also prove to be efficient because the medium (usually water) required for swelling will be brought into the tablet more easily if a wicking (hydrophilic) type of superdisintegrant is also present.

The objective of the present investigation was to prepare and evaluate coprocessed superdisintegrant consisting of crospovidone and sodium starch glycolate. Lactose, microcrystalline cellulose, dibasic calcium phosphate dihydrate, cefixime trihydrate, and ibuprofen tablets were prepared to assess the efficacy of coprocessed superdisintegrant.

MATERIALS AND METHODS

Materials

Crospovidone, lactose Indian Pharmacopoeia (IP), microcrystalline cellulose (MCC), sodium starch glycolate (SSG), and hydroxypropyl methylcellulose (HPMC) 50 centipoise (cPs) were received as gift from Intas Pharma (Ahmedabad, India). Dibasic calcium phosphate dihydrate (DCPD) was received as a gift from Enar Chemie Pvt Ltd (Navsari, India). Cefixime trihydrate United States Pharmacopeia (USP) was received as a gift from Torrent Research Centre (Ahmedabad, India). Ibuprofen was received as gift from Zydus Cadila Health Care Ltd (Ahmedabad, India). Cab-O-Sil M5 was received as gift from Cabot Sanmar (Chennai, India). Magnesium stearate, starch, and talc were purchased from Apex Chemicals (Ahmedabad, India).

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Table 1. Formulation of Lactose, DCPD, and MCC Tablets*

	Batch Code								
Materials	A1	A2	A3	B1	B2	B3	C1	C2	C3
Lactose granules	85	80	80	—	—	—	—	—	—
DCPD granules	—	—	—	85	80	80	—	—	—
MCC granules	—	—	—	—	—	—	85	80	80
Fines	10	10	10	10	10	10	10	10	10
Talc	5	5	5	5	5	5	5	5	5
Extragranular coprocessed superdisintegrant	—	5	2.5	—	5	2.5	—	5	2.5
Intragranular coprocessed superdisintegrant	—	—	2.5	—	—	2.5	—	—	2.5

*DCPD indicates dibasic calcium phosphate dihydrate; MCC, microcrystalline cellulose; and —, excipient not included in formulation. The amount is expressed in percentages. Coprocessed superdisintegrant contained 3 parts crospovidone and 1 part sodium starch glycolate.

Methods

Evaluation of Crospovidone, Sodium Starch Glycolate, and 3:1 Physical Blend of Crospovidone and Sodium Starch Glycolate

For the measurement of angle of repose, a glass funnel was secured with its tip at a given height (H) above a piece of graph paper placed on a horizontal surface. Powder was poured through the funnel until the apex of the conical pile touched the tip of the funnel. The angle of repose was calculated with the formula $\tan \alpha = H/R$, where α is the angle of repose and R is the radius of the conical pile.

The tablets were prepared by direct compression. Tablets of crospovidone and SSG were prepared by using flat-faced punches and die on a single-punch tablet machine (Cadmach Machinery Ltd, Ahmedabad, India). The tablets were evaluated for thickness using Dr Schleuniger Pharmatron Tablet tester 8M (Solothurn, Switzerland).

Preparation and Evaluation of Coprocessed Superdisintegrant

The coprocessed superdisintegrant was prepared as follows. A blend of crospovidone (7.5 g) and SSG (2.5 g) was added to 65 mL of isopropyl alcohol. The contents of the beaker (250 mL capacity) were stirred on a magnetic stirrer. The temperature was maintained between 65ºC and 70ºC, and stirring was continued till most of isopropyl alcohol evaporated. The wet coherent mass was granulated through 60-mesh sieve. The wet granules were dried in a tray dryer at 60ºC for 20 minutes. The dried granules were sifted on 60-mesh sieve and stored in airtight container till further use.

The angle of repose of the coprocessed superdisintegrant was measured as described above.

Preparation of Lactose, Dibasic Calcium Phosphate Dihydrate, and Microcrystalline Cellulose Tablets

Lactose was passed through a 60-mesh sieve, it was then granulated using 5% wt/vol solution of HPMC (50 cPs) as a binder. A 70:30 blend of water and isopropyl alcohol was used as a solvent for HPMC. The wet coherent mass was passed through a 20-mesh sieve. The wet granules were dried at 60ºC for 45 minutes in a tray dryer. The dried granules were passed through a 20-mesh sieve. Fines were removed by sifting the granules on a 40-mesh sieve. Granules of MCC and DCPD were similarly prepared. Lactose (10 g), DCPD (10 g), and MCC (10 g) required 5, 5, and 10 mL of the binder solution, respectively. Tablet formulations and mode of adding superdisintegrant are shown in Table 1. Tablets were prepared by using flat-faced punches and die on a single-punch tablet machine (Cadmach Machinery Ltd). The tablets were evaluated for crushing strength, friability, percentage reduction in friability, and disintegration time. Table 2 and Figure 1 display the results. MCC tablets were also prepared at low compaction pressure (batches D1-D3) to decrease the

Table 2. Results of Lactose, DCPD, and MCC Tablet Evaluation*

Batch Code	Crushing Strength (N)	Friability (%)	Disintegration Time (minutes.seconds)
A1	57	0.83	18.00
A2	74	0.57	3.30
A3	70	0.67	1.17
B1	108	0.83	>120.00
B2	84	0.64	38.00
B3	81	0.65	2.10
C1	161	0.13	29.30
C2	153	0.12	16.00
C3	140	0.13	14.00
D1†‡	52	0.60	1.10
D2†‡	62	0.23	1.00
D3†‡	56	0.49	0.30
E1†§	40	0.90	0.15
E2†§	50	0.56	0.05
E3†§	43	0.75	0.05

*DCPD indicates dibasic calcium phosphate dihydrate; MCC, microcrystalline cellulose; and HPMC, hydroxypropyl methylcellulose.
†Prepared at low compaction pressure.
‡HPMC 50 centipoise (cPs) 5% wt/vol solution was used as a binder.
§HPMC 50 centipoise (cPs) 2% wt/vol solution was used as a binder.

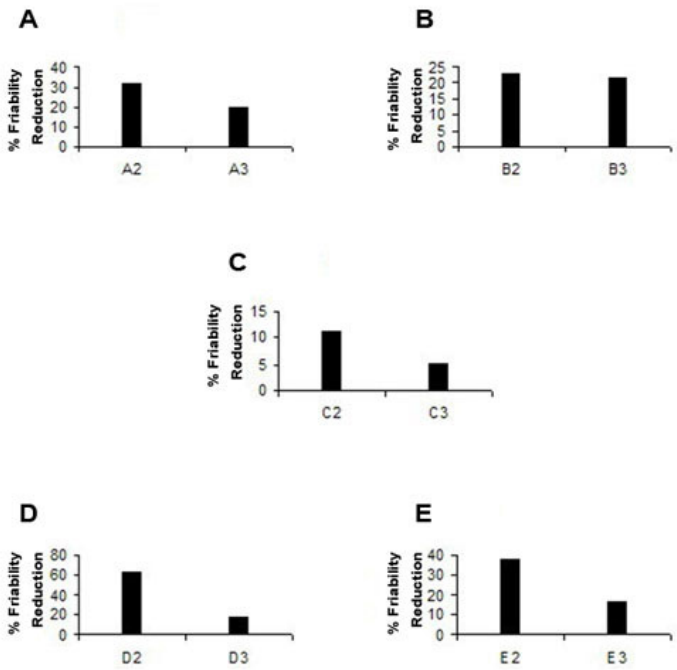

Figure 1. Percentage friability reduction (A) lactose tablets, (B) DCPD tablets, (C) MCC tablets (high compression pressure, 5% wt/vol binder solution, (D) MCC tablets (low compression pressure, 5% wt/vol binder solution), and (E) MCC tablets (low compression pressure; weak binder solution, 2% wt/vol). DCPD indicates dibasic calcium phosphate dihydrate; and MCC, microcrystalline cellulose.

crushing strength. Batches E1 to E3 were prepared using weak binder solution (2% wt/vol HPMC).

Crushing strength of the tablets was measured using Dr Schleuniger Pharmatron Tablet tester 8M.

Friability was evaluated from percentage weight loss of 20 tablets tumbled in a friabilator (USP XXIII, model EF2, Electrolab, Mumbai, India) at 25 rpm for 4 minutes. The tablets then were dedusted, and the loss in weight caused by fracture or abrasion was recorded as percentage weight loss. Percentage friability reduction was calculated by considering the friability of batch containing no disintegrant as 100% (Figure 1).[9]

The time required for disintegration of 6 tablets placed in the tubes of a USP disintegration test apparatus (model ED2L, Electrolab) was measured at 37ºC ± 2ºC using 900 mL distilled water.[9]

Effect of Magnesium Stearate and Cab-O-Sil

Two additional batches of granules of DCPD were prepared as described earlier. In one batch, physical mixture of superdisintegrant was used and in the other, coprocessed superdisintegrant. In both batches, intragranular and extragranular disintegrant was 2.5% each. The mixing time with 1% magnesium stearate (lubricant) was either 2 or 5 minutes. In selected batches, Cab-O-Sil was used at 0.25% in addition to magnesium stearate. In all the batches, 10% fines and 5% talc were also added. The composition and results are shown in Table 3.

Preparation and Evaluation of Cefixime Tablets

Cefixime tablets were prepared. The mixture of cefixime trihydrate (224 mg per tablet), intragranular superdisintegrant (Table 4), and DCPD (53 mg per tablet) was granulated with 2.5% wt/vol solution of HPMC (0.14 mL per tablet). A 70:30 blend of water and isopropyl alcohol was used as a solvent for HPMC. The wet coherent mass was passed through a 20-mesh sieve. The granules were dried at 60ºC for 60 minutes in a tray dryer. The dried granules were passed through 20-mesh sieve. Magnesium stearate (3 mg per tablet) and Cab-O-Sil (1.5 mg per tablet) were dry blended. In each tablet, 15 mg of superdisintegrant was added as per the scheme shown in Table 4. The experimental design was 3^2 full-factorial design, and 9 formulations were prepared. The 2 independent variables were the mode of addition of superdisintegrant (X_1) and the type of superdisintegrant (X_2). The low (−1), medium (0), and high (+1) values of X_1 were intragranular, intragranular plus extragranular, and extragranular; the low (−1), medium (0), and high (+1) values of X_2 were crospovidone, coprocessed superdisintegrant, and SSG, respectively. Tablets were prepared using a single-punch tablet machine (Cadmach Machinery Ltd). The average weight of each tablet was 300 mg.

Cefixime tablets were evaluated for crushing strength, friability, and disintegration time as described earlier. An in vitro drug dissolution study of cefixime tablets was performed by using USP apparatus (basket operated at 100 rpm) in 0.05 M potassium phosphate buffer (900 mL, pH 7.2, 37ºC). Samples (5 mL) were withdrawn at a predetermined

Table 3. Results of Lubricant and Glidant Sensitivity Test for DCPD Tablets*

Batch Code	Lubricant Mixing Time (minutes)	Cab-O-Sil (%)	Crushing Strength (N)	Disintegration Time (minutes.seconds)
PM1	2	—	40	3.00
PM2	5	—	39	3.00
PM3	2	0.25	49	3.43
PM4	5	0.25	49	3.14
CP1	2	—	38	2.30
CP2	5	—	36	2.38
CP3	2	0.25	40	2.45
CP4	5	0.25	40	2.19

*DCPD indicates dibasic calcium phosphate dihydrate; PM, physical mixture; CP, coprocessed; and —, excipient not included in formulation.

Table 4. Results of 3^2 Full-factorial Design (Batches CF1-CF9)

Batch Code	X_1	X_2	Crushing Strength* (N)	Friability* (%)	Disintegration Time* (seconds)	Drug Dissolved in* 2 minutes (%)	Drug Dissolved in* 5 minutes (%)
CF1	Intragranular	Crospovidone	73	0.67	200	32	78
CF2	Intragranular	Coprocessed super disintegrant	74	0.56	180	38	78
CF3	Intragranular	Sodium starch glycolate	73	0.51	330	17	39
CF4	Intra+Extragranular†	Crospovidone	77	0.68	260	30	70
CF5	Intra+Extragranular†	Coprocessed super disintegrant	78	0.59	170	32	72
CF6	Intra+Extragranular†	Sodium starch glycolate	75	0.61	360	16	43
CF7	Extragranular	Crospovidone	69	0.67	960	24	42
CF8	Extragranular	Coprocessed super disintegrant	71	0.60	840	30	47
CF9	Extragranular	Sodium starch glycolate	61	0.62	1020	12	22

*Dependent variables.

†Intra+Extragranular indicates that the ratio of intragranular to extragranular superdisintegrants is 1:1.

time interval. The samples were filtered through a 0.45-μm membrane filter, diluted, and assayed at 288 nm using a UV-visible spectrophotometer (1700, Shimadzu, Kyoto, Japan).[9]

Preparation and Evaluation of Ibuprofen Tablets

Ibuprofen tablets were prepared by direct compression. Ibuprofen (400 mg per tablet, 60-mesh sieve), coprocessed superdisintegrant (Batch IB1), or physical mixture of superdisintegrant (Batch IB2) containing 3 parts of crospovidone and 1 part of sodium starch glycolate (192 mg), magnesium stearate (6 mg), and Cab-O-Sil (3 mg) were blended. Angle of repose of both the batches was measured using the method described earlier. Ibuprofen tablets containing coprocessed superdisintegrant were prepared with the single-punch tablet machine. The average weight of each tablet was 601 mg.

Ibuprofen tablets were evaluated for crushing strength, friability, and disintegration time as described earlier. An in vitro drug dissolution study of ibuprofen tablets was performed using USP apparatus (paddle operated at 50 rpm) in phosphate buffer (900 mL, pH 7.2, 37ºC). Samples (5 mL) were withdrawn at a predetermined time interval. The samples were filtered through a 0.45-μm membrane filter, diluted, and assayed at 221 nm using a UV-visible spectrophotometer.[9]

Preparation and Evaluation of Ibuprofen Capsule

Ibuprofen capsules were prepared. A blend of ibuprofen (400 mg), magnesium stearate (4 mg), and Cab-O-Sil (2 mg) was filled in hard gelatin capsules.

Ibuprofen capsules were evaluated. An in vitro drug dissolution study of ibuprofen capsules was performed similar to that described for ibuprofen tablets except that a basket was used in place of the paddle to prevent floating of capsules.

Results and Discussion

Flow properties of the powder can be judged from the angle of repose. The powder flow depends on 3 general areas: (1) the physical properties of the particle (eg, shape, size, compressibility): (2) the bulk powder properties (eg, size distribution, compaction); and (3) the processing environment (eg, storage, humidity).[10] A chapter on powder flow has been recently introduced in *USP 29–NF 24*.[9] Angle of repose, Hausner ratio, flow rate through an orifice, and shear cell methods are included in the chapter. The angle of repose of crospovidone and SSG was 43º and 33º, respectively. The results reveal that crospovidone and SSG exhibited passable and good flow, respectively, from the view point of USP. The angle of repose of 3:1 physical blend of crospovidone and SSG was 42º. Therefore, granulation is recommended to improve flow.

Formulation scientists generally use superdisintegrants for developing rapidly disintegrating tablets or for improving dissolution of active pharmaceutical ingredients from solid dosage forms. The superdisintegrants are used from as low as 4% to as high as 66% in fast dissolving formulations or for improving dissolution of active pharmaceutical ingredients.[11] Therefore compressibility of the superdisintegrant is an important attribute. To assess compressibility, both the superdisintegrants were compressed on a single-punch tablet machine using the same die volume and compaction pressure. Crospovidone formed thinner tablets (2.69 mm), while SSG formed relatively thicker tablets (4.47 mm). The diameter of the tablets was 8.8 mm. The results of thickness measurement reveal that crospovidone exhibits better compressibility.[12]

Wet granulation was employed to prepare the coprocessed superdisintegrant. In the preliminary investigation, water, ethyl alcohol, isopropyl alcohol, and dichloromethane were used for preparation of granules. Water was ruled out for further experimentation because of gel formation of SSG. Dichloromethane was omitted because of floating of crospovidone

and sedimentation of SSG. From ethyl alcohol and isopropyl alcohol, isopropyl alcohol was chosen for further processing because SSG is sparingly soluble in ethanol. Isopropyl alcohol was selected considering the absence of gel formation and phase separation.

In the preliminary trials, 2 batches of coprocessed superdisintegrant were prepared using crospovidone and SSG at ratios of 3:1 (Batch I) and 1:1 (Batch II). Lactose tablets containing 5% extragranular disintegrant of either batch were prepared. The crushing strength and friability of the lactose tablets were not distinguishable. The tablets prepared using coprocessed superdisintegrant of Batch I showed a relatively faster disintegration time. Therefore, it was chosen for further studies.

The angle of repose of the physical mixture of crospovidone and SSG (3:1), coprocessed superdisintegrant (60-mesh sieve), and coprocessed superdisintegrant (sieve fraction 60/85 mesh) was found to be 42º, 41º, and 38º, respectively. According to USP, fair flow (angle of repose between 36º and 40º) was shown by coprocessed superdisintegrant (sieve fraction 60/85 mesh). Therefore, it was concluded that particle size distribution of the extragranular fraction of excipients would be kept the same to avoid any tableting problem that is dependent on the flow of granules from hopper to die cavity.

To investigate the versatility of the coprocessed superdisintegrant of Batch I; lactose, DCPD, and MCC tablets were prepared and evaluated for crushing strength, percentage friability, and percentage friability reduction due to incorporation of disintegrant. The results shown in Table 2 and Figure 1 demonstrate that the crushing strength and the percentage friability reduction of the lactose tablets were higher when the disintegrant was added in extragranular form. The probable reasons could be facilitated flow and densification of the granule in die. Furthermore, it is interesting to note that lactose tablets containing coprocessed superdisintegrant showed relatively faster disintegration despite increase in crushing strength and decrease in friability. The possible reason for faster disintegration may be attributed to increased water uptake by lactose tablets. The tablets containing DCPD and MCC were prepared to investigate the effect of coprocessed superdisintegrant (Batch I) on the functionalities of tablets.

The results shown in Table 2 reveal that tablets (Batches B2, B3, and C2, C3) containing insoluble excipients and coprocessed superdisintegrant showed substantial decrease in disintegration time as compared with the respective batches B1 and C1 containing no disintegrant. The disintegration time for DCPD tablets without and with disintegrant was more than 2 hours and less than 3 minutes, respectively. DCPD shows higher fragmentation propensity as compared with lactose. This could be one of the reasons for higher crushing strength of DCPD tablets compared with lactose tablets. The slightly higher disintegration time of DCPD tablets compared with lactose tablets may be attributed to higher crushing strength (greater than 80 N) and poor aqueous solubility. With DCPD, friability of tablets also decreased upon addition of coprocessed superdisintegrant. Friability of DCPD tablets without coprocessed superdisintegrant was 0.83%, which was reduced to 0.65% on addition of coprocessed superdisintegrant.

The disintegration time of MCC tablets decreased from 30 minutes (without any disintegrant) to 14 minutes on addition of coprocessed superdisintegrant (Batches C1 and C3). The high disintegration time of MCC tablets may be attributed to high crushing strength (more than 140 N of Batches C1, C2, and C3). The probable reason for higher crushing strength may be superior intrinsic compressibility of MCC or presence of higher amount of binder. The extremely strong binding property of MCC is mainly caused by hydrogen bonds between the plastically deformable, adjacent cellulose particles.[13] It is worthwhile to note that MCC required 10 mL binder, whereas lactose and DCPD each required 5 mL of binder. The crushing strength of MCC tablets was highest amongst the 3 diluents. Three batches of MCC tablets (Table 2, Batches D1-D3) were prepared at lower compaction pressure, so that tablets with crushing strength between 40 and 70 N were obtained. Also, 3 additional batches of MCC tablets (Table 2, Batches E1-E3) were prepared using HPMC 50 cPs (2% wt/vol) as a binder at lower compaction pressure. The results shown in Table 2 reveal that the MCC tablets of Batch D3 showed quick disintegration (30 seconds) as compared with that of tablets of Batch C3 (14 minutes). It is concluded that disintegration time of MCC tablets is strongly influenced by crushing strength. The MCC tablets prepared using HPMC 50 cPs (2% wt/vol) as binder and coprocessed superdisintegrant exhibited satisfactory friability 0.75% (Batch E3) and acceptable crushing strength 43 N (Batch E3).[2,14] The disintegration time of Batch E3 was only 5 seconds. The results reveal that besides the type of diluents, binder concentration and crushing strength also play a major role in controlling disintegration of tablets.

Lactose is a water-soluble excipient, and hence it works as an auxiliary disintegrant. Microcrystalline cellulose works as an auxiliary disintegrant because of its higher water-absorbing capacity. The purpose of the present study was to evaluate superdisintegrant. Hence, DCPD was selected for further studies to evaluate the coprocessed superdisintegrant.

Superdisintegrants are generally used for developing mouth-dissolve tablets or for improvement of solubility for active pharmaceutical ingredients. The primary requirement of both dosage forms is quicker disintegration. The results of preliminary examination revealed that tablets containing 3:1 physical mixture of crospovidone and SSG showed higher

Table 5. Regression Output for Dependent Variables (Batches CF1-CF9)

Dependent Variables	b_0*	b_1*	b_2*	b_{12}*	b_{11}*	b_{22}*	R^2†
Crushing strength	(78.66)‡	(–3.16)‡	(–1.66)‡	(–2.00)‡§	(–6.50)‡	(–3.00)‡§	(0.94)‡
	76.66	–3.16	–1.66		–6.50		0.78
Friability	(0.60)‡	(0.03)‡	(–0.05)‡	(0.03)‡	(–0.02)‡§	(0.04)‡	(0.97)‡
	0.58	0.03	–0.05	0.03		0.04	0.93
Disintegration time	(180.00)‡	(351.66)‡	(48.33)‡	(–17.50)‡§	(325.00)‡	(125.00)‡	(0.99)‡
	180.00	351.66	48.33		325.00	125.00	0.99
Drug dissolved	(33.66)‡	(–3.50)‡	(–6.80)‡	(0.75)‡§	(–0.50)‡§	(–11.50)‡	(0.98)‡
(%) in 2 minutes	33.66	–3.50	–6.80			–11.50	0.98
Drug dissolved (%)	(72.77)‡	(–14.00)‡	(–14.33)‡	(4.75)‡	(–10.66)‡	(–16.66)‡	(0.99)‡
in 5 minutes	72.77	–14.00	–14.33	4.75	–10.66	–16.66	0.99

*b_i represents coefficient.

†R^2 is the square of the multiple regression coefficient.

‡The parenthesis represent the values of the coefficient for full model ($Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}X_1^2 + b_{22}X_2^2$).

§Insignificant interaction terms at $\alpha = 0.05$.

crushing strength than that of tablets of coprocessed superdisintegrant. One of the primary requirements of immediate release preparation is faster disintegration. It is well known to formulation scientists that the tablets with higher crushing strength show longer disintegration time. Considering these results, it may be concluded that coprocessed superdisintegrant is superior to powder blend for formulating quick-disintegrating tablets. The only precaution that should be taken is proper handling of softer tablets (less hard tablets) during manufacturing. It is worthwhile to note that when superdisintegrants are used for solubility enhancement, a high percentage of superdisintegrant is present in drug-superdisintegrant ensembles. The active pharmaceutical ingredient may be loaded in the ensembles during preparation of coprocessed superdisintegrant. The work on drug-disintegrant ensemble is under way, and the results will be published later.

The results shown in Table 3 reveal that all the tablets disintegrated in less than 4 minutes, indicating the efficacy of both the physical mixture of superdisintegrants as well as coprocessed superdisintegrant. The crushing strength of DCPD tablets prepared using physical mixture plus Cab-O-Sil (Batches PM3 and PM4) was higher than that of tablets prepared using physical mixture of superdisintegrants. It is well known that tensile strength of the tablets depends on the particle size.[13] The crushing strength of tablets prepared using coprocessed superdisintegrant remained almost unaltered on addition of Cab-O-Sil (Batches CP3 and CP4). The results reveal that coprocessed superdisintegrant is not sensitive to the addition of Cab-O-Sil. It is worthwhile to note that formulation chemists generally use glidant such as Cab-O-Sil in all the tablet formulations. The advantages of less hard tablets have been mentioned earlier.

The design layout, results, and regression output for cefixime trihydrate tablets are shown in Tables 4 and 5, respectively. The results reveal that the disintegration time and percentage drug dissolved in 2 and 5 minutes were strongly influenced by the mode of addition of superdisintegrant (X_1) and type of superdisintegrant (X_2). The order of efficacy of tablet disintegration, in each group (same level of X_1), was coprocessed superdisintegrant > crospovidone> SSG. The amount of drug dissolved at 2 minutes and the disintegration time showed inverse relationship in each group. The tablets of Batches CF7 to CF9 showed higher disintegration time probably because the disintegrant was not included in the granules.

For selection of the best batch among all batches (CF1-CF9), the results were compared (Table 4). Batches CF2 and CF5 appear to be equally good. To select the best batch among these batches, the particles formed on disintegration of tablet were observed. One tablet of Batch CF2 and CF5 was placed into Petri dishes containing 25-mL distilled water. The Petri dishes were kept undisturbed for 10 minutes. Microscopy was used to measure the size of the disintegrated particles. The average particle size of batch CF2 and CF5 was 39 μm and 75 μm, respectively. Hence, Batch CF2 was ranked as the best batch.

A batch similar to CF2 was prepared (Batch CF2 PM), wherein coprocessed superdisintegrant was replaced with physical mixture of superdisintegrant containing 3 parts of crospovidone and 1 part of SSG. The results for Batch CF2 PM were crushing strength, 71 N; friability, 0.65%; disintegration time, 230 seconds; and percentage drug dissolved at 2 and 5 minutes, 21% and 49%, respectively. When the results of both the batches (CF2 and CF2 PM) were compared, it was found that Batch CF2 was superior to Batch CF2 PM in all respects (ie, crushing strength, friability, disintegration time, percentage drug dissolved at 2 and 5 minutes). Complete drug release was observed at 25 and 40 minutes from Batch CF2 and CF2 PM, respectively. It is therefore concluded that coprocessed superdisintegrant is far superior to

the physical mixture of superdisintegrant in case of dissolution enhancement of drug.

The superdisintegrants are normally used at low concentration (<10%). However, they have been explored by researchers across the world as solubility modifiers at much higher concentrations.[11,15] In the present study, coprocessed superdisintegrant/physical mixture of superdisintegrant was used at a higher concentration (>10%) for dissolution enhancement, while the maximum permissible limits for crospovidone and SSG mentioned in the Inactive Ingredient Guide were kept in mind while designing the experiment.[16] The potency range for crospovidone in oral tablet is 1.3 to 180.0 mg, while for SSG the potency range for oral tablets is 0.031 to 738.0 mg.[16] The formulated coprocessed superdisintegrant contained 3 parts crospovidone and 1 part SSG. The coprocessed superdisintegrant containing 144 mg of crospovidone and 48 mg of SSG was used for fabricating ibuprofen tablets containing 400 mg of the drug (Batch IB1). Similarly, the physical mixture of superdisintegrant containing 3 parts of crospovidone and 1 part of SSG was incorporated in Batch IB2. According to USP, passable flow (angle of repose = 43º) was shown by Batch IB1 and poor flow (angle of repose = 47º) was shown by Batch IB2.[9] Batch IB2 was ruled out for further studies as it exhibited poor flow. The superiority of coprocessed superdisintegrant is proved over physical mixture. The tablets of Batch IB1 exhibited acceptable crushing strength (50 N),[14] satisfactory friability (0.70%),[2] and fast disintegration (12 seconds). The in vitro dissolution study of tablets of Batch IB1 revealed that complete drug release was obtained in 5 minutes. The in vitro dissolution study of ibuprofen capsules revealed that complete drug release was noticed in 60 minutes. From the results of in vitro dissolution study of batch IB1 and ibuprofen capsule, it is evident that there is a noticeable improvement in dissolution rate of ibuprofen by using coprocessed superdisintegrant. The dissolution enhancement may be attributed to increased hydrophilicity.

The areas where further work can be done include using a fluid bed dryer or microwave dryer for drying granules and a spray dryer for preparation of coprocessed excipient, trying different ratios of crospovidone and SSG, and using other combinations of superdisintegrants.

Summary and Conclusion

Coprocessed superdisintegrant consisting of crospovidone and SSG exhibited good flow and compression characteristics. Cefixime trihydrate and ibuprofen tablets containing coprocessed superdisintegrant exhibited quick disintegration and improved drug dissolution.

Acknowledgments

Generous support from Intas Pharma (Ahmedabad, India), Enar Chemie Pvt. Ltd. (Navsari, India), Torrent Research Centre (Ahmedabad, India), Zydus Cadila Health Care Ltd. (Ahmedabad, India), and Cabot Sanmar (Chennai, India) is gratefully acknowledged.

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