Research Article

# Formulation and Optimization of Hydrochlorothiazide Mouth Dissolving Tablets by Using Co-Processed Superdisintegrants

**Jasmine Kaur Bhatia*, Rupinder Kaur, Sukhdev Singh, Rajwinder Kaur**
*Chandigarh College of Pharmacy, Landran, Mohali, Punjab, India.
***Corresponding author's E-mail:** Bhatiaccp@rediffmail.com

**Accepted on:** 01-05-2013; **Finalized on:** 31-07-2013.

**ABSTRACT**

The mouth dissolving tablets (MDTs) usually dissolve in the oral cavity within 15 seconds to 3 minutes. In another words a MDT is tablet that dissolves or disintegrate in the oral cavity without the need of water or chewing. Recently formulation scientist recognized that single component excipients do not always provide the required performance. Hence, there is a need to have excipients with multiple characteristics built into them such as better flow, low/no moisture sensitivity, superior compressibility and rapid disintegration ability. Co-processing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvement as well as masking the undesirable properties of individual. Co-processing excipients could lead to formation of excipients with superior properties compared with the simple physical mixture component. Co-processed particles of SSG and Crospovidone were prepared using a solvent i.e. Isopropyl Alcohol, which were used as a direct compressible excipients in mouth dissolving tablet formulation. The two super disintegrates were mixed in varied proportion (according to $3^2$ factorial design) by constant stirring until all the solvent was evaporated. The semi dried mixture of super disintegrates was passed through mesh screen size no. 60 and dried in tray dryer at 60°C. A two factor three level ($3^2$) factorial design is being used to optimize the formulation. Nine such different proportionate mixtures of super disintegrants were prepared accordingly. The concentration of processed Super disintegrants was then optimized for DT 35 secs. and friability 0.5% and used to formulate mouth dissolving tablet by direct compression method using other commonly used excipients and evaluated for disintegration time, wetting time, tablet hardness and percent friability. A decrease in disintegration time, % friability and wetting time was noted with tablet prepared by co-processed super disintegrants when compared with tablet formulated using SSG, Crospovidone alone or as compare to their physical mixtures.

**Keywords:** Co-processing, Factorial design, Hydrochlorothiazide, Mouth dissolving tablet.

## INTRODUCTION

Drug delivery systems are becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of physiochemical and biochemical parameters pertinent to their performance.[1] The oral route is very significant route of drug administration since this route is also a natural viaduct for transfer of materials to the system including food. The oral dosage forms are so prolific that their supremacy is not likely to face any serious challenge, at least, in the near future; the oral dosage forms may be intended either for local action on the oral mucosa or for systemic action.[2] Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because of low cost of therapy, ease of administration, accurate dosage, self-medication, pain avoidance. The most popular dosage forms being tablets and capsules, one important drawback of such dosage forms is 'Dysphagia' or difficulty in swallowing.[1] The difficulty is experienced in particular by paediatric and geriatric patients, but it also applies to people who are ill in bed and those active working patients who are busy or travelling, especially those who have no access to water and also in following conditions like: parkinsonism, motion sickness, unconsciousness and mentally disabled persons. To fulfil these medical needs, the pharmaceutical technologies have developed a novel type of dosage form for oral administration, the mouth dissolving tablets (MDTs), that disintegrate and dissolve rapidly in saliva without water.[3] The MDTs usually dissolve in the oral cavity within 15 seconds to 3 minutes. In another words a MDT is tablet that dissolves or disintegrate in the oral cavity without the need of water or chewing.[4] United States Pharmacopoeia (USP) approved these dosage forms as Orally Disintegrating Tablets. Recently European Pharmacopoeia adopted the term "Oro- dispersible tablet" for tablets that disperses readily and within 3 minutes in mouth before swallowing.[5] These tablets are also known as quick dissolves, orodispersible, fast melts, fast dissolving, fast disintegrating, rapid-dissolving, or orally dissolving tablets[6]. United States Food and Drug Administration (FDA) defined MDT as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue". The disintegration time for orally disintegrating tablets generally ranges from several seconds to about I minute.[7, 8] The basic approach used in development of MDT is the use of super disintegrants such as Crospovidone, croscarmellose, sodium starch glycolate etc. that provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. The bioavailability of some drugs may be increased due to absorption of drugs in oral cavity and due to pre-gastric absorption of saliva containing dispersed drugs that pass The basic approach

used in development of MDT is the use of super disintegrants such as crospovidone, croscarmellose, sodium starch glycolate etc. that provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. The bioavailability of some drugs may be increased due to absorption of drugs in oral cavity and due to pre-gastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subject to first pass metabolism is reduced as compared to standard tablets.[9]

Recently formulation scientist recognized that single component excipients do not always provide the required performance. Hence, there is a need to have excipients with multiple characteristics built into them such as better flow, low/no moisture sensitivity, superior compressibility and rapid disintegration ability. Excipients with improved functionality can be obtained by developing new chemical excipients, new grade of existing materials and new combination of existing materials. New combinations of existing excipients are an interesting option for improving excipients functionality because all formulations contain multiple excipients. One such approach for improving the functionality of excipients is co processing of two or more excipients. Co-processing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvement as well as masking the undesirable properties of individual. Co processing of excipient could lead to formation of excipients with superior properties compared with the simple physical mixture of their components or with individual components.[10] In present study, formulation, evaluation & optimization of mouth dissolving tablet of Hydrochlorothiazide was done and studied the effect of co-processed super disintegrants (prepared according to ($3^2$) factorial design) on the tablet disintegration time and percent friability. Hydrochlorothiazide was selected for present study. It is diuretic of benzothiadiazine group and has proved very important and effective drug for management of edema and hypertension. It inhibits sodium reabsorption in the distal tubules causing increased excretion of sodium and water as well as potassium and hydrogen ions. Also it has less solubility in water so to increase its water solubility with the aim of reaching high serum concentration in short period of time is main reason for selection of this drug.[9, 11]

## MATERIALS AND METHODS

### Materials

Hydrochlorothiazide (HCTZ), crospovidone, microcrystalline cellulose (Avicel PH-102), mannitol (Pearlitol SD 200) were purchased from Allwell pharmaceutical company Chandigarh. Sodium starch glycolate and sodium stearyl fumarate were gift samples from Maruti Chemicals Pvt. ltd Ahmadabad. Sodium hydroxide, n-octanol, isopropyl alcohol, methanol and sodium saccharine were purchased from loba chemicals Mumbai, Potassium dihydrogen phosphate was purchased from Qualigens fine chemicals, ethanol was purchased from chamgshu yanguan chemical, China and Hydrochloric acid was purchased from Fisher scientific, Mumbai. All the other chemicals used were of analytical grade. Double distillation water (DDW) was prepared using in – house distillation unit (fabricated at Jencons).

### Methods

#### Preparation and evaluation of physical mixture and co-processed super disintegrants

The physical mixture of the SSG and Crospovidone was prepared by simple trituration technique of mixing using glass pestle and mortar. The co-processed super disintegrants were prepared as follows: blend of various concentrations of super disintegrants were prepared according to $3^2$ full Factorial design and were added to 65 ml of isopropyl alcohol in a beaker (250 ml capacity), stirred on a magnetic stirrer while maintaining the temperature between 50-60°C till most of the isopropyl alcohol has been evaporated. The wet coherent mass was sieved through 60 mesh screen size and obtained powder was dried in a tray dryer at a temperature 60°C for 20 minutes. The dried powder was again sifted through 60 mesh sieve, packed and stored in desiccator for further use. The prepared physical mixture and co-processed super disintegrants were evaluated for the mass-volume relationship, swelling properties and flow properties.[9] Results were shown in Table 1.

**Table 1:** Evaluation of Super disintegrant

| Batch | Ratio | Bulk Density (g/cc) (Mean±SD)* | Tapped Density (g/cc) (Mean±SD)* | Hausner's Ratio (Mean±SD)* | Compressibility Index (%) (Mean ± SD)* | Angle of Repose (Θ) (Mean±SD)* |
|---|---|---|---|---|---|---|
| SSG | - - | 0.404±0.001 | 0.431 ± 0.001 | 1.04 ± 0.001 | 5.79 ± 0.003 | 23.60 ± 0.04 |
| Crospovidone | - - | 0.415±0.001 | 0.439 ± 0.001 | 1.08 ± 0.001 | 6.79 ± 0.001 | 27.62 ± 0.020 |
| Physical Mixture ($PM_o$) | 1:1 | 0.411 ±0.001 | 0.431 ± 0.002 | 1.06 ± 0.001 | 5.11 ± 0.008 | 35.43 ± 0.130 |
| Co-processed ($CP_o$) | 1:1 | 0.391 ±0.001 | 0.415 ± 0.001 | 1.05 ± 0.001 | 4.64 ± 0.002 | 22.37 ± 0.035 |

*Each value is average of six independent determinations

**Table 2:** Formulation and Evaluation of all trails

| Ingredients (mg) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | $PM_o$ | $CP_o$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SSG | 1.5 | 3 | 4.5 | 6 | 7.5 | - | - | - | - | - | 1.5 | 1.5 |
| CP | - | - | - | - | - | 1.5 | 3 | 4.5 | 6 | 7.5 | 1.5 | 1.5 |
| Mannitol (Pearlitol SD 200) | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 |
| Sodium Saccharine | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| MCC (Avicel PH 102) | 111 | 109.5 | 108 | 106.5 | 105 | 111 | 109.5 | 108 | 106.5 | 105 | 84.5 | 84.5 |
| Talc | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Sodium stearyl fumarate | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |
| Hydrochlorothiazide | - | - | - | - | - | - | - | - | - | - | 25 | 25 |
| **Evaluation of physico-chemical parameters of all trails** | | | | | | | | | | | | |
| Hardness* ($kg/cm^2$) | 2.6 ± 0.041 | 3.1 ± 0.102 | 3.7 ± 0.020 | 3.0 ± 0.026 | 3.2 ± 0.045 | 3.6 ± 0.044 | 3.4 ± 0.060 | 3.2 ± 0.026 | 3.6 ± 0.033 | 3.1 ± 0.039 | 3.100 ± 0.102 | 3.500 ± 0.102 |
| Friability** (%) | 0.45 ± 0.023 | 0.68 ± 0.023 | 0.74± 0.028 | 0.79 ± 0.038 | 0.93 ± 0.030 | 0.46± 0.046 | 0.51± 0.028 | 0.62± 0.028 | 0.73± 0.042 | 0.93± 0.037 | 0.587 ± 0.001 | 0.288 ± 0.001 |
| Wetting Time a (seconds) | 80.90 ± 0.223 | 69.85 ± 0.613 | 67.57± 0.401 | 40.13 ± 0.083 | 28.60 ± 0.069 | 31.8 ± 0.122 | 26.7± 0.081 | 20.6± 0.161 | 17.6± 0.039 | 14.02 ± 0.072 | 63.58 ± 0.917 | 42.00± 0.894 |
| Disintegration time*** (Seconds) | 89.33 ± 0.816 | 79.83 ± 0.753 | 71.66± 0.816 | 49.66 ± 0.816 | 37.66 ± 0.816 | 59.6± 0.816 | 51.8± 0.753 | 37.2± 0.983 | 32.0 ± 0.894 | 26.16 ± 0.753 | 75.41 ± 0.478 | 49.20 ± 0.436 |

SSG: Sodium starch glycolate; F1-F5= Formulation of Mouth Dissolving Tablet Using Sodium Starch Glycolate; F6-F10= Formulation of Mouth Dissolving Tablet Using crospovidone; $PM_o$= Physical mixture; $CP_o$= Co-processed mixture; *Each value is average of six independent determinations; a=20.

### Preparation of mouth dissolving tablets (Trial batches)

Mouth dissolving tablets were prepared by direct compression technique. All the ingredients were passed through mesh screen no. 60 and weighed in geometrical order and the blend was then compressed into tablet. The tablets were prepared with super disintegrant alone, physical mixture (1:1), co-processed super disintegrants (1:1). The tablet formulation was shown in Table 2.

### Evaluation of mouth dissolving tablets

Six tablets were taken and their thickness was recorded using micrometer (Mitutoya, Japan). Tablet thickness is an important characteristic in reproducing appearance and also in counting by suing filling equipment.[12] For drug content uniformity as per USP, twenty tablets were taken and weighed individually, calculating the average weight, and comparing the individual weights to the average. The average weight of one tablet was calculated. The weight variation test would be satisfactory method of determining the drug content uniformity. [12] Hardness of the tablet of each formulation was determined using Monsanto hardness tester.[9] Friability of the tablets was determined using roche friabilator. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inch in each revolution. Preweighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were dedusted using a soft muslin cloth and reweighed. The friability (F %) is determined by the formula.[9]

$$F\% = (1- W_O / W)\times 100$$

Where, $W_0$ is initial weight of the tablets before the test and W is the weight of the tablets after test.

Disintegration of mouth dissolving tablets is achieved by saliva in the mouth, however amount of saliva in the mouth is limited and no tablet disintegration test was found in USP and IP to simulate *in vivo* conditions. 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 above the sieve. To determine disintegration time, 6 ml of phosphate buffer (pH 6.8), was placed inside the vessel in such way that 4 ml of the media was below the sieve and 2 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.[13] The method was followed to measure tablet wetting time. A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petri dish (ID = 6.5 cm) containing 6 ml of phosphate buffer (pH 6.8), A tablet was put on the paper and the time for the complete wetting was measured. Six trials for each batch were performed and the standard deviation was also determined.[14] *In vitro* dispersion time was measured by dropping a tablet in a glass cylinder containing 6 ml of Phosphate buffer (pH 6.8). Six tablets from each formulation were randomly selected and *in vitro* dispersion time was performed.[15] *In vitro* dissolution study of optimized formulation and marketed tablet were carried out using USP paddle method at 50 rpm in 900 ml

of Phosphate buffer (pH 6.8) as dissolution media, maintained at 37±0.5°C. 5 ml of aliquot was withdrawn at the specified time intervals (1 minute), filtered through whatmann filter paper and assayed spectrophotometrically at 271.8 nm. An equal volume of fresh medium, pre warmed at 37°C, was replaced into the dissolution media after each sampling to maintain the constant volume throughout the study.

### Factorial design

The experimental design was $3^2$ full-factorial design, and nine formulations (F11-F19) were prepared. The amount of super disintegrants $X_1$(SSG) and $X_2$(Crospovidone) were selected as independent variables. The amount of super disintegrants was optimized for dependent variables: disintegration time and percent friability. The low (-1), medium (0) and high (1) are the values of $X_1$(SSG) and $X_2$ (Crospovidone) respectively. All the possible nine batches were shown in Table 3.

## RESULTS AND DISCUSSION

In preliminary investigation, water dichloromethane, and isopropyl alcohol were used for co processing of the super disintegrant. Water was ruled out for further experiment because gel formation occurred due to the presence of starch. Dicloromethane was omitted because of floating of Crospovidone. Isopropyl alcohol was selected considering the absence of gel formation and phase separation.

**Table 3:** Factorial Design based hydrochlorothiazide mouth dissolving tablets formulation

| Batch code | $X_1$ (mg) | $X_2$ (mg) | DT (S) | Friability (%) |
|---|---|---|---|---|
| F11 | -1 | -1 | 54 | 0.32 |
| F12 | -1 | 0 | 42 | 0.39 |
| F13 | -1 | 1 | 34 | 0.47 |
| F14 | 0 | -1 | 45 | 0.49 |
| F15 | 0 | 0 | 38 | 0.57 |
| F16 | 0 | 1 | 26 | 0.64 |
| F17 | 1 | -1 | 30 | 0.68 |
| F18 | 1 | 0 | 22 | 0.74 |
| F19 | 1 | 1 | 17 | 0.79 |

| Coded values | Actual Values | |
|---|---|---|
| | $X_1$ | $X_2$ |
| -1 | 1.5 | 1.5 |
| 0 | 3 | 3 |
| 1 | 4.5 | 4.5 |

X1 indicates amount of SSG (mg); X2, amount of Crospovidone (mg); DT, disintegration time; F, friability.

**Table 4:** Fitted equation relating the responses disintegration time and percentage friability

| Coefficient | $b_0$ | $b_1$ | $b_2$ | $b_{12}$ | $b_1^2$ | $b_2^2$ |
|---|---|---|---|---|---|---|
| **DT** | 36.11 | -10.17 | -8.67 | 1.75 | -3.17 | 0.33 |
| **% friability** | 0.57 | 0.17 | 0.068 | -0.010 | -1.66 | -1.66 |

**Table 5:** Evaluation of optimized hydrochlorothiazide mouth dissolving tablets formulation ($F_{20}$)

| Ingredients | Amount (mg) |
|---|---|
| Hydrochlorothiazide | 25 |
| SSG | 1.31 |
| Crospovidone | 2.68 |
| MCC(Avicel PH-102) | 83.51 |
| Mannitol (Pearlitol SD 200) | 30 |
| Sodium saccharine | 3 |
| Talc | 3 |
| Sodium stearyl fumarate | 1.5 |
| **Parameters** | **Results** |
| Hardness (kg/cm$^2$) (Mean ± SD) * | 3.1± 0.141 |
| Friability (%) (Mean ± SD) * | 0.5 ± 0.006 |
| Disintegration time (sec) (Mean ± SD) * | 35 ± 0.087 |
| Wetting time (sec) (Mean ± SD) * | 26.60 ± 0.727 |
| Drug Content (%) (Mean ± SD) * | 96.4 ± 0.349 |
| Weight variation (mg) (Mean ± SD) [a] | 152.02 ± 1.36 |

*Each value is average of six independent determinations; a=20

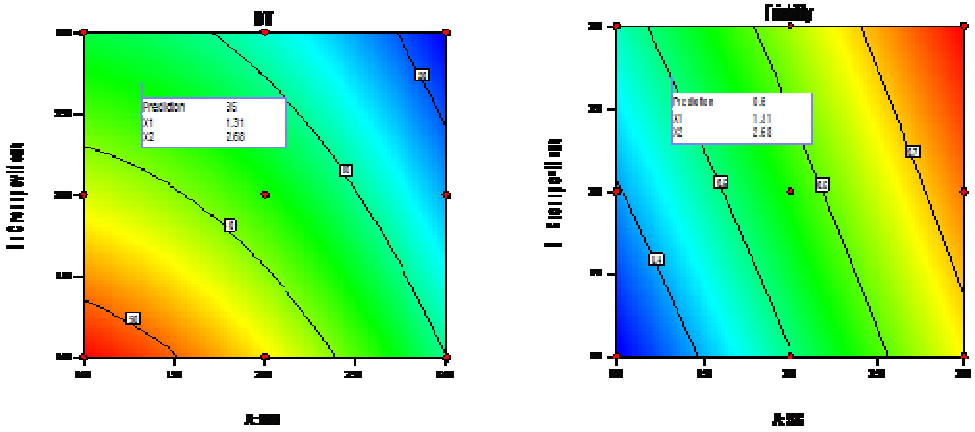

**Figure 1:** Contour plot for disintegration time and percent of friability

**Evaluation of super disintegrants alone, their physical mixture and co-processed mixture**

Table 1 reports the bulk density, tapped density, compressibility index, Hausner's ratio and angle of repose for all studied batches. According to literature data, powder having a compressibility index having between 5 to 16% is suitable for producing tablets, and those with a Hausner's ratio below 1.25 are exhibited good flow ability. Co processed super disintegrant batch falls in the prescribed limit/range. The angle of repose of co-processed super disintegrants was found to be < 25° which indicate excellent flow in comparison to physical mixture of super disintegrants > 30° due to granule formation.

**Evaluation of mouth dissolving tablets with super disintegrant alone, physical mixture and co-processed mixture**

The preliminary trials were conducted by using 1 to 5% w/w super disintegrants SSG and Crospovidone. The tablets with Crospovidone showed more profound results for all the characterization parameters as compared to SSG but not to be 30 seconds and friability is also increased consequently as shown in table 2. The results in Table 2 clears that the disintegration time and percent friability have a great difference in physical mixture and co-processed super disintegrants (Batch $PM_o$ and $CP_o$). The use of a physical mixture of super disintegrants resulted in increased friability probably due to low compressibility of excipients. So by co-processing 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 co-processed super disintegrants so we selected co-processed mixtures for further studies.

**Evaluation of factorial batch**

The results shown in Table 3 indicated concentration dependent disintegration in batches prepared using co-processed Sodium starch glycolate and Crospovidone. The absorption and swelling is responsible for faster water uptake; hence it facilitates wicking action of Crospovidone in bringing about faster disintegration. Tablets with lower friability (≤ 0.5%) may not break during handling on machines and or shipping. One of the primary requirements of MDTs is faster disintegration. Considering these results, it may be concluded that co-processed super disintegrant is superior to physical mixture for formulating the MDTs. In order to investigate the factors systematically and optimize the tablet for DT 35 seconds and % F less than 0.5%, a factorial design is applied in the present investigation.

**Optimization of the mouth dissolving tablet**

The optimization of the mouth dissolving tablet was decided to target disintegration time 35 second and percent friability is 0.5%. The optimized concentration was obtained by software as clears in the surface response prediction curves shown in figure 1. Optimization results or coefficient values for disintegration and friability were shown in Table 4. A checkpoint batch HMD was prepared at $X_1$= 1.31 and $X_2$ = 2.68 as actual values. From the full model, it is expected that the friability value of the checkpoint batch should be 0.5, and the value of disintegration time should be 35 seconds table 5 indicates that the results are as expected. Thus we can conclude that statistical model is mathematically valid.

***In vitro* drug release studies**

*In vitro* drug release experiments were performed at 37±0.5°C in dissolution apparatus for the optimized formulation and conventional marketed tablets- Aquazide 25 (150 mg).The drug release was at the end of 5 minutes was more than 90% from optimized tablet whereas only 25.52% was released from marketed conventional tablet after 5 minutes.

**Effect of independent variables (concentration of SSG and Crospovidone) on dependent variables (DT and % friability)**

The results of multiple linear regression analysis reveal that, on increasing the concentration of either sodium starch glycolate or crospovidone, a decrease in disintegration time is observed; both the coefficients $b_1$

and $b_2$ bear a negative sign. When higher percentage of sodium starch glycolate is used, the water uptake and subsequent disintegration are thus facilitated. It is obvious that in the presence of higher percentage of disintegrant Crospovidone, wicking is facilitated. An increase in the concentration of sodium starch glycolate and Crospovidone leads to an increase in friability because the coefficient $b_1$ and $b_2$ bears a positive sign. When a higher percentage of sodium starch glycolate and Crospovidone was used, low compressible tablets were produced, which were mechanically weak. Results are shown in Table 4.

## CONCLUSION

Co-processing of excipients could lead to formulation of excipients with superior properties compared with the simple physical mixture of their components or individual components. It was cleared that the disintegration time and percent friability have a great difference in physical mixture and co processed super disintegrants. By the co processing technology the friability of tablets was also decreased. So it may be concluded that co-processed super disintegrant is superior to physical mixture for formulating the MDTs. Full factorial design ($3^2$) was used for the optimization of formulation to get DT equals to 35 seconds and friability 0.5%. The data clearly indicate that the disintegration time and percentage friability values are strongly dependent on the selected independent variables. On increasing the concentration of either Crospovidone or sodium starch glycolate disintegration time was decreased and friability increased.

## REFERENCES


1. Kaur T, Gill B, Kumar S, Gupta GD, Review article mouth dissolving tablets: a novel approach to drug delivery, Int J Curr PharmaResearch, 3(1), 2011, 1-7.
2. Mithal BM, editor, A textbook of pharmaceutical formulation, 6th edn. Vallabh publication, 2010, 11.
3. Chang R, Guo X, Burnside BA, Couch RA, Fast dissolving tablets, Pharm Technonogy, 24(6), 2000, 52-58.
4. Kuchekar BS, Atul, Badhan C, Mahajan HS, Mouth dissolving tablets: A novel drug delivery system, Pharma Times, 35, 2003, 7-9.
5. Fu Y, Yang S, Jeong SH, Kimura S, Park K, Orally Fast Disintegrating Tablets: Developments, Technologies, Taste-Masking and Clinical Studies, Crit Rev Ther Drug Carrier Sys, 2l, 2004, 433-76.
6. Wayne C, Dipan R, Ann D, Selecting Super disingrants for Orally Disintegrating Tablet Formulations, Pharmaceutical Technology, 8, 2006, 226-229.
7. Seong Hoon Jeong, Yuuki Takaishi,Yourong Fuc, Kinam Park, Material properties for making fast dissolving tablets by a compression method, J Mat Chem, 18, 2008, 3527-3535.
8. Deshmukh KR, Patel V, Verma S, Pandey A, Dewangan P, A review on mouth dissolving tablet techniques, Int J Research Ayu & Pharm, 2(11), 2011, 66-74.
9. Shailesh Sharma S, Bhardwaj P, Gupta GD, Formulation, Evaluation & Optimization of Mouth Dissolving Tablets of Losartan Potassium: Effect of Co-processed Super disintegrants, International Journal Pharma & Bio Archives, 1(1), 2010, 76-83.
10. Gohel MC, Parikh RK, Brahmbhatt BK, Shah AR, Preparation and Assessment of Novel Co-processed Super disintegrant Consisting of Crospovidone and Sodium Starch Glycolate: A Technical Note, AAPS PharmSciTech, 8(1), 2007, 1-7.
11. Jha SK, Vijayalakshmi P, Karki R, Goli D, Formulation and evaluation of melt-in-mouth tablets of haloperidol, Asian J Pharmaceutics, 2(4), 2008, 255-260.
12. United States Pharmacopoeia, Rockville.MD: USP Convention, Inc 32 revision, NF 27; 2009.
13. Late SG, Yi-Ying Y, Banga AK, Effect of Disintegration Promoting Agent, Lubricants and Moisture Treatment on Optimized Fast Disintegrating Tablets, Int J Pharm, 365, 2009, 4-11.
14. Bi Y, Sunada H, Yonezawa Y, Danjo K, Otsuka A, Lida K, Preparation and Evaluation of a Compressed Tablet Rapidly Disintegrating in Oral Cavity, Chem Pharm Bull, 44, 1996, 2121-2127.
15. Gohel MC, Bansal G, Bhatt N, Formulation and Evaluation of Orodispersible Taste Masked Tablets of Famotidine, Pharma Bio World, 3, 2005, 75-80.


**Source of Support:** Nil, **Conflict of Interest:** None.