FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OFPIROXICAMBYSUPERDISINTEGRANTSCO-PROCESSING

Pushpendra Kumar Saini*and Namita Arora

Department of Pharmaceutical Sciences, Lords University, Alwar

Corresponding Author
Pushpendra Kumar Saini
Research Scholar
Department of Pharmaceutical Science, Lords University, Alwar, Rajasthan
Email: sainipushpendrakumar@gmail.com

Abstract:

The study evaluated two novel coprocessed excipients (with two methods) as disintegrants in a ODTspiroxicam tablet formulation. The tablets produced were assessed for mechanical properties with the use of friability and tensile strength while the release properties were assessed with wetting time, water absorption ratio, disintegration time and dissolution profile. The results obtained showed that the methods of coprocessing and disintegrant incorporation influenced the activities of the disintegrants. The novel disintegrantenhanced the mechanical properties of the tablets containing them as shown by lower friability and higher tensile strength of the tablets. The result further showed that the rate and amount of water absorbed, type of disintegrant and the method of disintegrant incorporation influenced the total amount of piroxicam released. The study concluded that the novel disintegrants will be effective in the formulation of Orodispersiblepiroxicam tablets.

Keywords: coprocessing, lyophilization, solvent evaporation, dissolution, friability, disintegration time, water absorption ratio, wetting time.

DOI Number: 10.48047/NQ.2022.20.12.NQ77716 **NeuroQuantology2022;20(12): 3922-3932**

INTRODUCTION

Tablets are the most preferred oral dosage forms due to their numerous advantages, which includes: ease of manufacture and administration, high physical and chemical stability, high patient compliance, convenient packaging/storage and the ability to provide accurately measured dose of thedrug[1-3]. However, its use in therapy is still associated with some challenges most especially among the geriatric and pediatric populations. Over the past two decades, Orodispersible tablet (ODTs),

apatient friendly dosage form, which disintegrates rapidly in the mouth upon contact with saliva, havegained increased importance, focus and patient acceptance because of their ability to addresses someof the challenges facing conventional tablets[4-6].

These ODTs obviate the need to swallow tablets thereby making drug usage more convenient for pediatric and geriatric patients who usually have compromised swallowing ability due to various physiological/psychological factors[7]. The convenienceof administration without water also enables dosing on the goî, which facilitates patient adherenceto the dosing regimen or administration[8].Various methods such as lyophilization, molding,cotton candy, direct compression or tabletingafter granulation have been used in the manufacture of ODTs[6]. Coprocessed multifunctional excipientsbased on polyols, disintegrants and binders with improved physico-mechanical properties (e.g.,pleasant mouth-feel, low hygroscopicity, better flowand compactability) have been used to conveniently manufacture ODTs with excellent disintegrationproperties without compromising the mechanical properties[8].

EXPERIMENTAL

Materials

The materials used were: Piroxicam, Cross carmellose sodium, Crospovidone, Micro crystalline cellulose,Aspartame, (Combitic Global Caplet, Sonipat), Lactose, Talc, Magnesium stearate (Lobachem, Mumbai)

Preparation of FDT

Orodispersible tablet (ODTs) were organized by direct compression method because of their several advantages[9-11].

- Easiest way to manufacture tablets.
- High doses can be accommodated.
- Use of conventional equipment.
- Limited number of processing steps.
- Less disintegration time.

The tablets were prepared by using single punch tablet machine (Cadmach, Ahmedabad) to produce flat faced tablets weighing 100 mg each with a diameter of 5 mm. A minimum of 50 tablets were ready for each batch.Before compression tablet blends were measured for mass-volume relationship (Bulk density, Tapped density, Hausner's ratio, Compressibility index) and flow properties (Angle of repose).

Table 1: Preparation of Tablets with Superdisintegrants

S.No	Ingredients (mg)	PC1	PC2	PC3	PC4	PC5	PC6*	PC7#	PC8$
1	**Piroxicam**	20	20	20	20	20	20	20	20
2	**Crospovidone**	1	0	2	0	2	1	1	1
3	**Croscaramellose sodium**	0	1	0	2	2	1	1	1
4	**Micro crystalline cellulose**	61	61	60	60	58	60	60	60
5	**Aspartame**	6	6	6	6	6	6	6	6
6	**Magnesium stearate**	5	5	5	5	5	5	5	5

7	**Talc**	5	5	5	5	5	5	5	5
8	**Aerosil**	1	1	1	1	1	1	1	1
9	**Pineapple flavour**	1	1	1	1	1	1	1	1
10	**Mannitol**	50	50	50	50	50	50	50	50
	Total	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

***: Physical Mixture #: Solvent Evaporation $: Lyophilize**

Pre compression Characterization

The quality of tablet, once formulated by rule, is generally expressed by the quality of physicochemical properties of blends. There are many formulations and process variables tangled in mixing steps and all these can affect the characteristics of blend produced. The description parameters for evaluating the flow property of mixed blends includes Bulk density, Tapped density, Hausner's ratio, Compressibility index and Angle of Repose.

Bulk density

Apparent bulk density (ρ_b)was determined by pouring the blend into a graduated cylinder.The bulk volume (V_b) and weight of powder (M) was determined[14-16].The bulk density was proposed using the formula: $\rho_b = \frac{M}{V_b}$

Tapped density

The measuring cylinder containing a recognized mass of blend was tapped 100 times using density apparatus. The constant minimum volume (V_t) involved in the cylinder after tappings and the weight (M) of the blend was measured[14-16].The tapped density (ρ_t) was designed using the formula: $\rho_t = \frac{M}{V_t}$

Compressibility index

The simplest way for measurement of flow of the powder is its compressibility, an indication of the luxury with which a material can be induced to flow[14-16].It is uttered as compressibility index (I) which can be calculated as follows: $I = \frac{\rho_t - \rho_b}{\rho_t} \times 100$

where, ρ_t = Tapped density; ρ_b = Bulk density

Hausner's Ratio

Hausner's ratio (HR) is an indirect index of affluence of powder flow. It is calculated by the following formula: $HR = \frac{\rho t}{\rho b}$ where, ρ_t is tapped density and ρ_b is bulk density.

Lower Hausner's ratio (<1.25) indicates improved flow properties than higher ones[17-19].

Angle of Repose

Angle of Repose was determined using funnel method. The blend was dispensed through a funnel that can be elevated vertically until a specified cone height (h) was achieved. Radius of the heap (r) was measured and angle of repose (θ) was calculated using the formula[17-19]

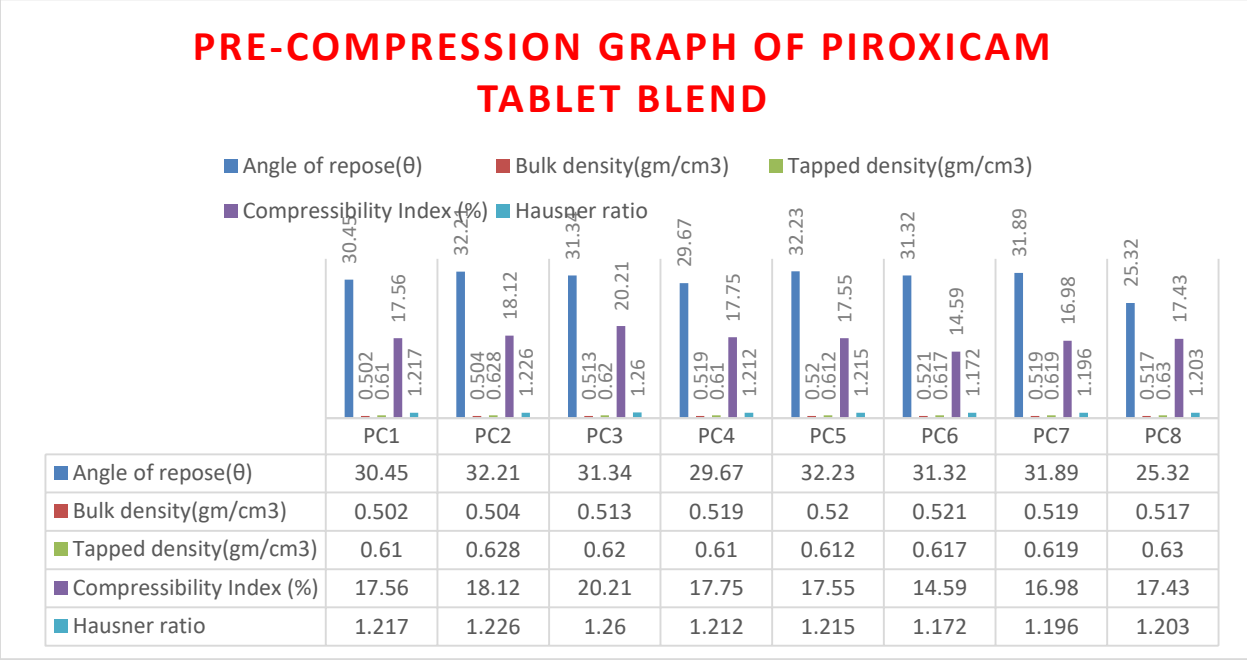
$$\tan\theta = \frac{h}{r}; \qquad \text{Therefore; } \theta = \tan^{-1}\left(\frac{h}{r}\right)$$

where, θ is angle of repose; h is height of cone; r is radius of cone.

Table 2: Characterization of Tablets Blends

Batch Code	Angle of repose(θ)	Bulk density(gm/cm^3)	Tapped density(gm/cm^3)	Compressibility Index (%)	Hausner ratio
PC1	30.45	0.502	0.610	17.56	1.217
PC2	32.21	0.504	0.628	18.12	1.226
PC3	31.34	0.513	0.620	20.21	1.26
PC4	29.67	0.519	0.610	17.75	1.212
PC5	32.23	0.520	0.612	17.55	1.215
PC6	31.32	0.521	0.617	14.59	1.172
PC7	31.89	0.519	0.619	16.98	1.196
PC8	25.32	0.517	0.630	17.43	1.203

n=6, ±S.D



	PC1	PC2	PC3	PC4	PC5	PC6	PC7	PC8
Angle of repose(θ)	30.45	32.21	31.34	29.67	32.23	31.32	31.89	25.32
Bulk density(gm/cm3)	0.502	0.504	0.513	0.519	0.52	0.521	0.519	0.517
Tapped density(gm/cm3)	0.61	0.628	0.62	0.61	0.612	0.617	0.619	0.63
Compressibility Index (%)	17.56	18.12	20.21	17.75	17.55	14.59	16.98	17.43
Hausner ratio	1.217	1.226	1.26	1.212	1.215	1.172	1.196	1.203

Figure. 1 Response Pre-compression data of meloxicam tablet blend

Preparation of physical mixture and co-processed superdisintegrants

Mixture of numerous concentrations of superdisintegrants were prepared bestowing to factorial design batches. The physical mixture of CCS and crospovidone was organized by mixing them together in glass pestle motor. The co-processed superdisintegrant was prepared as follows:

1) **Solvent Evaporation Technology**:
   Blends of croscarmellose sodiumand crospovidone in diverse proportion, total weight of 10 g were added to 50 ml of isopropyl alcohol. The contents of beaker were stirred on a
   Magnetic stirrer. The temperature was kept between 65-70^0 and stirring was continual till
   utmost of ethyl alcohol evaporated. The wet coherent mass was sieved through sieve no.100the wet powder was dried in a tray drier at 60^0 for 20 minutes. The dried powder was siftedon 120 mesh sieve and stored in airtight container.

2) **Lyophilized Technology**:
   The Blends of CCS and CP in diverse ratio, total weight of 10 g was added to 50 ml of water. Resulting solution was taken into round bottom flask and frozen for 2 hours followed with condenser temperature of -77. 50C.When complete freezing was achieved RBFs were removed from freezing chamber, vaccum was Pragmatic and sample were bare to lyophilization for 4 hours with vaccum of 0.02 mbar. Complete sublimation of water transpired and dried mass remained in RBF. Dried powder was detached from freeze dryer and placed in desiccator. Wet coherent mass was sieved through sieve no.100 the wet powder was dried in a tray drier at 60^0 for 20 minutes. The dried powder was sifted on 120 mesh sieve and stored in airtight container till additional use.

Development of Orodispersible tablet (ODTs)with physical mixture and coprocessed superdisintegrants

The superdisintegrants (croscarmellose sodiumand Crospovidone) coprocessed by solvent evaporationand lyophilization techniques were used to develop the tablets. All the ingredients were passed through sieve no. 60 and were co-grounded in a glass pestle motor. The tablets were prepared by using single punch tablet machine (Cadmach, Ahmedabad) to produce flat faced tablets weighing 100 mg each with a diameter of 5 mm. A minimum of 50 tablets were ready for each batch.Before compression tablet blends were measured for mass-volume relationship (Bulk density, Tapped density, Hausner's ratio, Compressibility index) and flow properties (Angle of repose).

After compression of powder blends, the prepared tablets were evaluated for organoleptic features like color, odor, taste, diameter, thickness and physical characteristics like hardness, friability, disintegration time, wetting time, % drug release.

Post Compresion characterization

After compression of powder blends, the prepared tablets were evaluated for organoleptic features like color, odor, taste, diameter, thickness and physical characteristics like hardness, friability, disintegration time, wetting time, % drug release. The results are shown in Table 5.

General appearance

The general appearance of a tablet, its visual identification and over all 'elegance' is essential for consumer acceptance. This includes tablet's size, shape, color, presence or absence of an odor, taste, surface texture, physical flaws etc[20].

Tablet thickness

Ten tablets were taken and their thickness was evaluated using micrometer (Mityato, Japan).

Weight variation

The weight variation test would be acceptable method of determining the drug content uniformity. As per USP[21], twenty tablets were

taken and weighted individually, calculating the average weight, and comparing the distinct tablet weights to the average. The average weight of one tablet was calculated.

Hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet in direction to break the tablet. The confrontation of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation was determined using Pfizer Hardness Tester[20].

Friability

Friability of the tablets was determined using Roche friabilator. This device subjects the tablets to the collective 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. Pre weighed sample of tablets was located in the friabilator and were subjected to 100 revolutions. Tablets were dedusted by means of a soft muslin cloth and reweighed. The friability (F %) is determined by the formula

$$F\% = \left(1 - \frac{Wo}{W}\right) X 100$$

Where, W_0 is initial weight of the tablets before the test and W is the weight of the tablets after test[13-16].

Wetting time

Wetting time of the tablets was measured by means of a piece of tissue paper (12 cm X 10.75 cm) folded twice, placed in a small petridish (ID = 6.5 cm) comprising of 6 ml of Sorenson's buffer (pH 6.8). A tablet was put on the paper, and the time for the whole wetting was measured[22-23].

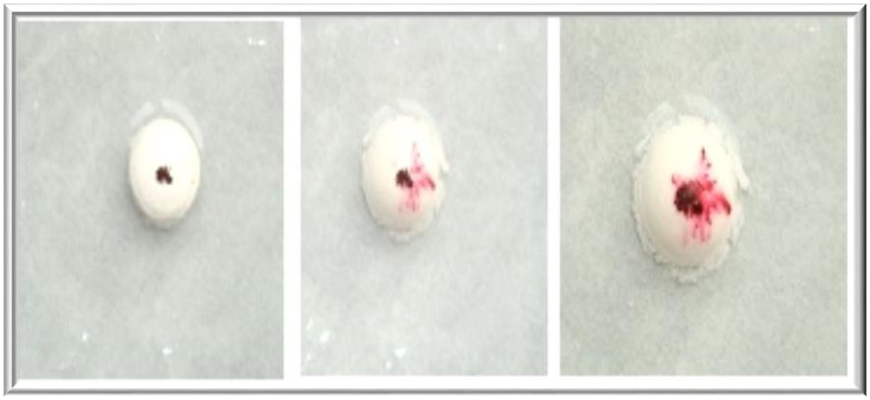


Figure2: *In vitro* Wetting Property

Disintegration test

Disintegration of Orodispersible tablet (ODTs) is attained in the mouth due to the action of saliva, however amount of saliva inthe mouth is restricted and no tablet disintegration test was found inUSP and IP to simulate *in vivo* conditions[24]. A alteredmethod was used to determine disintegration time of the tablets.A cylindrical vessel was used in which 10 meshscreen was placed in such way that only 2 ml of disintegrating ordissolution medium would be located under the sieve (Figure 4.2). Todetermine disintegration time, 6 ml of water was placed inside the container in such way that 4 ml of the mediawas underneath the sieve and 2 ml above the sieve. Tablet was placed onthe sieve and the entire assembly was then placed on a shaker.The time at which all the particles pass through the sieve wastaken as a disintegration time of the tablet. Six tablets were chosenrandomly from the complex samples and the average value wasdetermined[25].

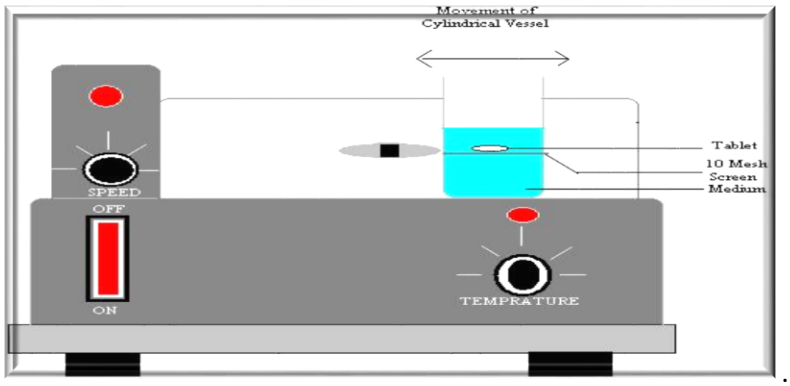


Figure3: Disintegration Test Apparatus

***In-vitro* Release Study**

The dissolution studies of new as well as conditioned ODT's were carried out using BP type II dissolution test apparatus[16]. The tablets were positioned in dissolution vessel containing 900 ml of 0.1 N HCl maintained at 37ºC ± 0.5 and stirred at 50 rpm. Samples (5 ml) were collected periodically at different time intervals (1, 2, 3, 4, 5 min) and substituted with fresh dissolution medium. The absorbance was determined spectrophotometrically at 284 nm. Dissolution contours were constructed as shown in Fig.4.8. Concentrations were calculated using calibration curves established in respective media. Taking into account, the loss of drug in aliquot replaced, the correction factor was used as shown in eq[25].

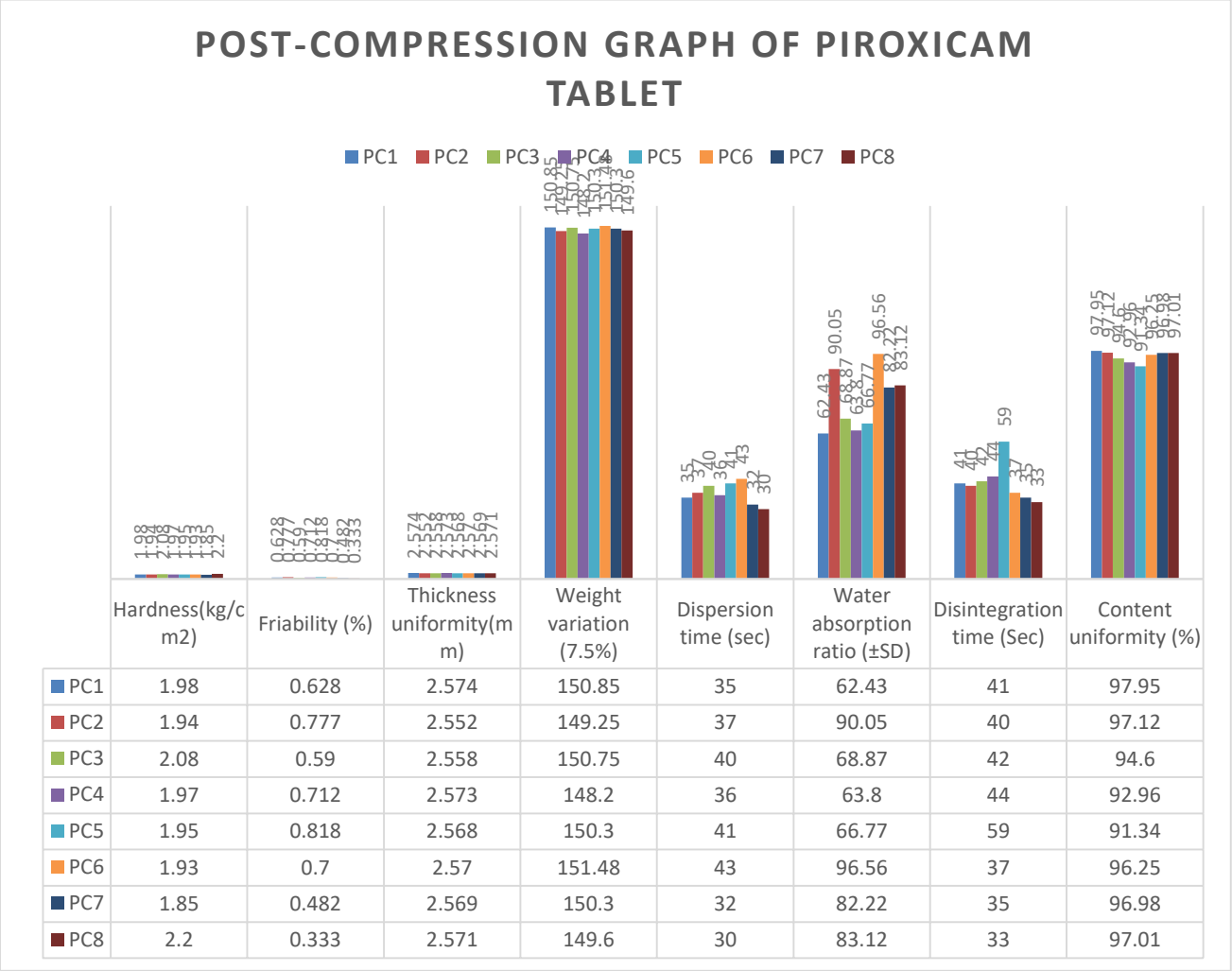
$$C_i = Ai + \frac{Vs}{Vt}\sum_{i=1}^{n-1} Ai\left(\frac{Vt}{Vt - Vs}\right)$$

Table 3: Post-Compression Characterization

Batch Code	Hardness(kg/cm2)	Friability (%)	Thickness uniformity(mm)	Weight variation (7.5%)	Dispersion time (sec)	Water absorption ratio (±SD)	Disintegration time (Sec)	Content uniformity (%)
PC1	1.98	0.628	2.574	150.85 ±0.6	35	62.43±6.74	41	97.95
PC2	1.94	0.777	2.552	149.25± 0.4	37	90.05±3.82	40	97.12
PC3	2.08	0.590	2.558	150.75± 0.2	40	68.87±5.44	42	94.6
PC4	1.97	0.712	2.573	148.20± 0.3	36	63.80±2.51	44	92.96
PC5	1.95	0.818	2.568	150.30 ±0.8	41	66.77±4.90	59	91.34
PC6	1.93	0.700	2.570	151.48 ±0.4	43	96.56±2.34	37	96.25
PC7	1.85	0.482	2.569	150.30 ±0.4	32	82.22±4.56	35	96.98
PC8	2.20	0.333	2.571	149.60	30	83.12±3.	33	97.01

				±0.2		25		

n=6, ±SD



	Hardness(kg/cm2)	Friability (%)	Thickness uniformity(mm)	Weight variation (7.5%)	Dispersion time (sec)	Water absorption ratio (±SD)	Disintegration time (Sec)	Content uniformity (%)
PC1	1.98	0.628	2.574	150.85	35	62.43	41	97.95
PC2	1.94	0.777	2.552	149.25	37	90.05	40	97.12
PC3	2.08	0.59	2.558	150.75	40	68.87	42	94.6
PC4	1.97	0.712	2.573	148.2	36	63.8	44	92.96
PC5	1.95	0.818	2.568	150.3	41	66.77	59	91.34
PC6	1.93	0.7	2.57	151.48	43	96.56	37	96.25
PC7	1.85	0.482	2.569	150.3	32	82.22	35	96.98
PC8	2.2	0.333	2.571	149.6	30	83.12	33	97.01

Figure. 4 Response of Post-compression data of piroxicam tablet

Table 4: Percentage drug release profile

S.No	Time (min)	% drug Release							
		PC1	PC2	**PC3**	**PC4**	**PC5**	**PC6**	**PC7**	**PC8**
1	0	0	0	0	0	0	0	0	0
2	1	15.4	13.37	12.37	18.92	10.98	12.53	11.48	12.33
3	2	21.6	29.67	29.6	29.13	22.19	26.6	22.69	52.55
4	3	35.4	40.38	38.37	41.08	31.06	38.37	32.31	35.82
5	4	49.66	59.59	42.51	51.57	38.54	47.26	47.12	58.76

6	5	58.77	69.98	56.77	61.33	42.6	56.33	53.12	75.54
7	6	63.89	79.04	67.65	69.32	53.92	66.33	58.12	92.8

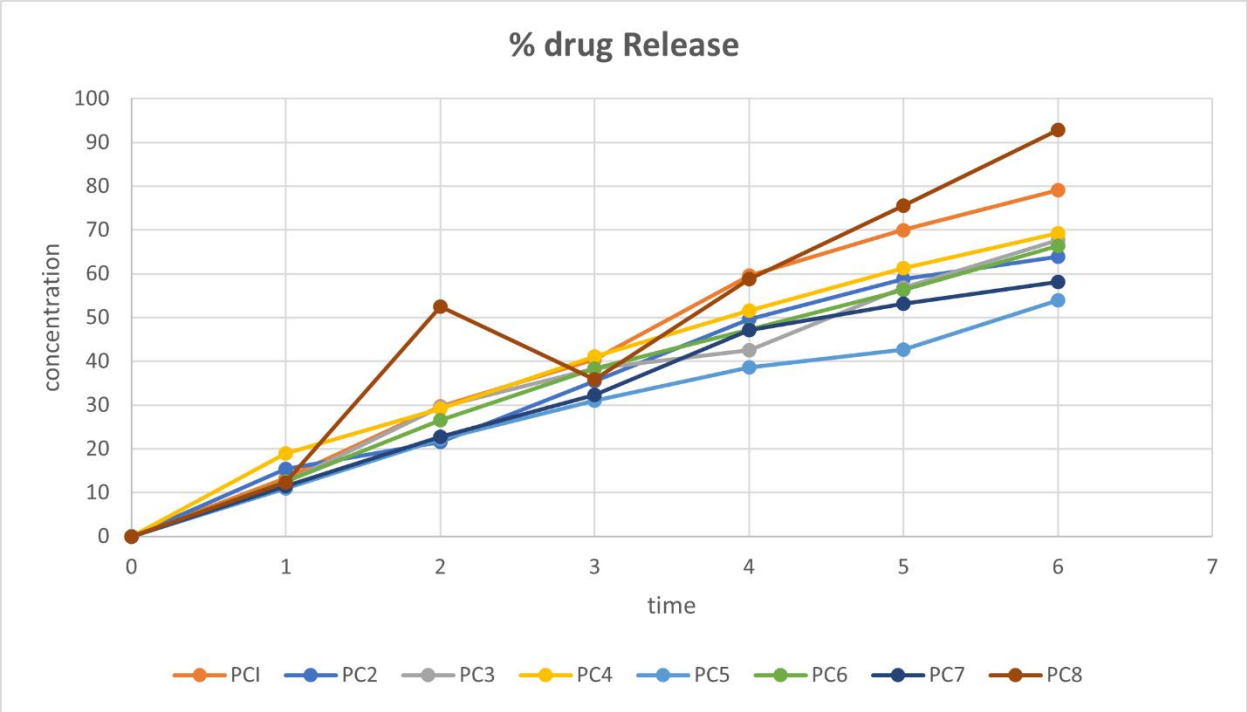


Figure 5 percentage drug release

CONCLUSION

From the results obtained from the study, it can be concluded that:

The method employed (solvent evaporation and lyophilization) in coprocessing excipients would affect the properties of the excipients and the effect they have on the formulations in which they are used.

The coprocessed disintegrants consisting of croscarmellose sdoium and crospovidone, when used in the formulation tablets would enhance the mechanical properties of the resulting tablets.

The rate/amount of water intake into the tablets and wetting time and disintegration time would be limiting factors in early onset of drug dissolution and bioavailability.

Disintegrants coprocessed by lyophilization techniques would be effective disintegrants in the formulation of ODT of piroxicamwith disintegration times of less than 1 min without compromising the mechanical properties of the tablets.

Thus piroxicam ODT produced from the disintegrants coprocessed by lyophilization technique provides better drug dissolution and bioavailability in cost effective manner.

REFRENCES

1. Rubinstein M.H.: in Pharmaceutics: the science of dosage form design. Aulton, M.E. Ed.
ELBS 21st edn., p. 304, Longman group Ltd., UK 1988.
2. Patel S., Kaushal A.M., Bansal AK.: AAPS PharmSciTech. 8 (4), E110 (2007).

3. Saha S., Shahiwala A.F.: Expert Opin. Drug Deliv. 6, 197 (2009).
4. Pfister W., Gosh T.: Pharm. Technol. 29, 138 (2005).
5. Al-khattawi A., Mohammed A.R.: Expert Opin. Drug Deliv. 10, 651(2013).
6. Brniak W, Jachowicz R, Krupa A, Skorka T, Niwinski K.: Pharm. Dev. Technol. 18, 467(2013).
7. Varia I., Venkataraman S., Hellegers C.: Psychopharmacol. Bull. 40, 47 (2007).
8. Soh J.L.P., Grachet M., Whitlock M., Lukas T.:Pharm. Dev. Technol.., 18, 172 (2013)
9. Mishra DN, Vijaya KSG. Rapidly disintegrating oral tablets of meloxicam. Indian Drugs 2006, 43(2); 117-121.
10. Bi YX, Sunda Y, Yonezawa Y, Danjo K. Evaluation of rapidly disintegrating tablets prepared by a direct compression method. Drug Dev Ind Pharm 1999; 25 (5): 571-581.
11. Sreenivas SA, Gadad AP, Dandagi PM, Mastiholimath VS, Patil MB. Formulation and evaluation of ondeanesetron hydrochloride directly compressed mouth disintegrating tablets. Indian Drugs 2006; 43(1): 35-38.
12. Zhao N, Augsburger LL. Functionally compression of 3 classes of superdisintegrants in promoting aspirin tablet disintegration and dissolution. AAPS Pharm Sci Tech 2005; 6(4): 634-640.
13. Kuchekar BS, Mahajan HS, Bandhan AC. Mouth dissolve tablets of salbutamol sulphate: a novel drug delivery system. Indian Drugs 2004; 41(10): 592-598.
14. Khan S, Kataria P, Nakhat P, Yeole P. Taste masking of ondansetron hydrochloride by polymer carrier system and formulation of rapid-disintegrating tablets. AAPS Pharm Sci Tech 2007; 8(2): E1-E7.
15. Sunada H, Bi Y. Preparation, evaluation and optimization of rapidly disintegrating tablets. Powder Technology 2002; 122: 188-198.
16. Marshall K, Compression and consolidation of powdered solid. In: Lachman L, Liberman HA and Kaning JL, Eds., The Theory and Practice of Industrial Pharmacy, 3rd Edn., Varghese publishing house, Mumbai, 1987; 66-99.
17. Gorman EA, Rhodes CT, Rudnic EM. An evaluation of croscarmellose as a tablet disintegrant in direct compression systems. *Drug Dev Ind Pharm* 1982; 8(4): 397–410.
18. Chaudhari PD, Chaudhari SP, Kolhe SR, Dave KV, More DM. Formulation and evaluation of Orodispersible tablet (ODTs) of famotidine. Indian Drugs 2005; 42(10): 641-649.
19. Lindberg N, Palsoson M, Pihl A, Freeman R, Zetzener H, Enstad G. Flowability measurements of pharmaceutical powder mixtures with poor flow using five different techniques. Drug Dev Ind Pharm 2004; 30(7): 785-791.
20. Cooper J, Gunn C. Powder flow and compaction. In: Carter SJ, Eds., Tutorial Pharmacy, 3rd Edn., CBS publishers and distributors, New Delhi, 1986; 211-233.
21. Banker SB, Anderson NR, Tablets. In: Lachman L, Liberman HA and Kaning JL, Eds., The Theory and Practice of Industrial Pharmacy, 3rd Edn., Varghese publishing house, Mumbai, 1987; 293-345.
22. United States Pharmacopoeia 30/ NF25. The Official Compendia of Standards. Electronic edition. Rockville, MD: United States Pharmacopoeial Convention Inc. 2007.
23. Late SG, Yi-Ying Y, Banga AK. Effect of disintegration promoting agent, lubricants and moisture treatment on

optimized Orodispersible tablet (ODTs). Int. J Pharm 2009; 365: 4-11.

24. Dissolution. The British Pharmacopoeia, Vol. 4, London: Her Majesty's Stationary Office 2009: A296, Appendix XII B.
25. Singh B, Kaur T, Singh S. Correction of Raw Dissolution Data for Loss of Drug and Volume during Sampling. *Indian J Pharm Sci*1997; 59(4): 196-199.