ejpmr, 2023,10(4), 324-331

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

DEVELOPMENT OF CO-PROCESSED EXCIPIENTS TO IMPROVE GRANULAR CHARACTERISTICS AND DISSOLUTION OF TABLET CONTAINING AN INSOLUBLE DRUG

Dr. T. Mahesh Kumar*, G. Mathan Kumar and J. Manikandan

Department of Pharmaceutics, Sankaralingam Bhuvaneswari College of Pharmacy, Anaikuttam, Sivakasi - 626130, Tamil Nadu, India.

***Corresponding Author: Dr. T. Mahesh Kumar**

Department of Pharmaceutics, Sankaralingam Bhuvaneswari College of Pharmacy, Anaikuttam, Sivakasi - 626130, Tamil Nadu, India.

Article Received on 26/01/2023 **Article Revised on 16/02/2023** **Article Accepted on 09/03/2023**

ABSTRACT

The objective of this research was to develop co-processed excipients having improved granular properties and use it for enhancing the dissolution of BCS class II drug-piroxicam in tablet formulation. Excipients of different combinations were co-processed together by partial granulation method and the obtained granules were analysed for flow and compression properties. FT–IR spectroscopy employed to study the drug-excipients compatibility at 1:1 ratio. Tablets were prepared by directly compressing the blend of developed co-processed excipients with piroxicam drug and analyzed the quality parameters like weight variation, hardness, thickness, friability and disintegration. In vitro drug dissolution performed to study the drug release profile of the prepared formulations. One of the tablet formulation with co-processed excipient which contains combination of microcrystalline cellulose, sodium starch glycolate and surfactant exhibit synergistic effect on enhancement of drug dissolution and was comparable with market available reference product. Results of this study proved the suitability of the developed composition and process to use in formulation development of insoluble drug containing dosage forms.

KEYWORDS: Co-process, excipient, compatibility, synergistic effect, insoluble, dissolution.

INTRODUTION

Drug administration by oral route is considered to be more economical, convenient and any improvements in oral drug delivery technology can make significant differences in enhancing patient compliance and in-vivo drug bioavailability.[1] In oral route of drug delivery system, immediate release (IR) tablets are more popular and acceptable by pharmaceutical manufactures. Oral IR tablets are prepared using various techniques like wet granulation, dry granulation, direct compression, melt granulation, foam graluation, etc., Out of various techniques of tablet manufacturing, direct compression is more preferable method of tableting due to it require fewer processing steps, simplified validation, elimination of moisture, economical, high dilution potential, less chance of wear and tear of punches and improved drug stability compared with other techniques.[2-4] Although direct compression has several advantages, it also has some drawbacks which includes, segregation, poor reworkability, content uniformity problems, diluents interaction with drug to change the properties, poor compressibility of API in large dose drug, etc., Many of the currently available drugs and more than 80% of developing NCEs are difficult for adopting the direct compression method and more advanced diluents or excipients are required to facilitate the tabletting process.[5] Necessary modifications required to conquer the drawbacks related to excipients incorporating into direct compression process.

The International Pharmaceutical Excipient Council highlights excipients are included in pharmaceutical finished products to overcome some of the limitations of the active pharmaceutical ingredient(s) (APIs) concerning the manufacture and stability of those products, and to facilitate their use and release and/or delivery of the drug after its administration to the patient.[6] Excipients have substantial impact on the manufacturing process of different types of dosage forms, product quality and storage even though they are cosidered inactive.[7] Along with active pharmaceutical ingredients research, presently both academia and pharmaceutical excipient industry has been focusing on developing new type of excipients to support various formulation technology and dosage forms development. Pharmaceutical excipients contribute a major role in quality based design (QbD) of pharmaceutical development as per US FDA, which is vital component as 'critical material attributes'. In direct compression most formulations (70–80%) contains excipients at a higher concentration than the active drug. In pharmaceutical formulation, excipients have been

appropriately evaluated for safety and efficacy, and are intentionally included in a drug delivery system.[8] The major requirements for direct compressible excipients include compatibility, good flowability and high dilution potential.[9,10] Also, the excipient needs to meet improved functional properties to overcome the poor mechanical properties and low aqueous solubility of the emerging active ingredients, particularly BCS class II drugs.

A single excipient alone may not posesses all the necessary ideal characteristics and hence co-processed excipients are more important categories in the classification of pharmaceutical excipients.[11,12] To surmount various difficulties of using single excipients, co-processing is one of the best methods in which two or more excipients interacting at the sub-particle level to provide improved functionality.[13] Co processing lead to synthesis excipients with modified physical property without losing their chemical nature.[14,15] It could lead to the formation of excipients with superior properties compared to the simple physical mixtures of their components. In order to facilitate direct compression, specialized directly compressible excipients and grades of some high-dose drugs have been developed and marketed. These grades are prepared by various techniques to obtain particles with suitable micromeritic and physic-mechanical properties. Therefore a well-engineered co-processed excipient can play a vital role in fulfilling the basic requirements of direct compression.

Piroxicam is a potent non-steroidal anti-inflammatory drug used in first line drug therapy for the symptomatic relief of rheumatoid arthritis and osteoarthritis. Also it has Anti-pyritic and analgesic activity. The drug molucule comes under the BCS (Biopharmaceutical classification System) class II and possesses poor solubility and dissolution characteristics. Due to this it is low missible in biological fluid and establishing poor bioavailability.

The aim of the present study was to develop excipient of improved granular qualities by co-processing suitable excipient combinations at appropriate ratios. It was hypothesized to explore the developed co-processed excipient for formulating piroxicam, a class II insoluble drug into tablets by direct compression method to enhance its dissolution and physical characteristics. Additionally, both the co-processing and tablet preparation method would be simple, cost effective and easily scalable for commercial production. The current findings were also support the formulation development research of class II drug molecules of similar types.

MATERIALS AND METHODS

MATERIALS

Piroxicam was obtained as gift sample by Pharmafabrikon Ltd., (Madurai). Microcrystalline cellulose purchased from JRS Pharma, Mumbai. Sodium starch glycolate purchased from Vasa Pharma, Ahmedabad. Croscarmellose sodium purchased from Prachin chemical, Ahmedabad. Polyethylene glycol 400 purchased from Paxmy Speciality Chemicals, Chennai. Polyvinyl Pyrrolidone (PVP K30) purchased from Yarrow chemical products, Mumbai. Sodium lauryl sulphate (SLS) purchased from Reachem Laboratory Chem, Pvt. Ltd, Chennai. Magnesium stearate purchased from Vijlak Pharma Ltd., Hyderabad. Purified Talc purchased from Loba Chemie., Pvt. Ltd., Mumbai.

EXPERIMENTAL METHODS

Drug-excipient compatibility studies: The IR spectral studies of pure piroxicam, and the drug combined with equal proportion of proposed excipients were carried out to study the interaction of drug with excipients. The proposed excipient includes microcrystalline cellulose, sodium starch glycolate, croscarmellose sodium, polyethylene glycol 400, PVP K30, sodium lauryl sulphate, magnesium stearate and purified talc. Potassium bromide pellet was used to prepare the samples for IR spectroscopy study.

Preparation of Co-Processed Excipients and Piroxicam Formulations: Six formulations of directly compressed tablets of piroxicam using co-processed excipients were prepared. Preparation method includes two phases. The first phase was preparation of co-processed excipients by partial wet granulation technique and second phase was development of tablets by direct compression process.

Phase i. Method of preparation of co-processed excipients (CoEx.): Co-processed excipients are prepared by partial wet granulation method using a soluble binder. The excipients category selected for the preparation of different types of co-processed excipients includes diluent, binder, disintegrants and solubilizing agents. Microcrystalline cellulose was used as diluent due to its insoluble nature and having better compressibility. PVP K30 was used as binder as it is aqueous soluble and aid in drug dissolution. Sodium starch glycolate and croscarmellose sodium are super disintegrants widely used in many of pharmaceutical preparations and are used at 5% w/w concentration. The solubulizing agents PEG 400 (at 5% W/W concentration) and sodium lauryl sulphate (at 1% W/W concentration) were used to improve the solubility characteristics. The quantities of excipients used were at their optimum level of usage in tablet manufacturing. In Table 1, the composition of different co-processed granules (CoEx.1 to CoEx.6) prepared in this study was given. As per the Table 1 composition, the diluent microcrystalline cellulose and disintegrant sodium starch glycolate or croscarmellose sodium are mixed together to get a uniform dry mixture followed by partial wet granulation using aqueous PVP K30 binder solution. Wherever, sodium lauryl sulphate and PEG 400 in the formulation, were dissolved in the binder solution and incorporated into the dry mix for its uniform distribution while granulation. The wetted granules were dried at 55ºC to remove the excess moisture content. The dried granules

were sieved through 30#mesh sieve to get co-processed excipient granules. The granules were evaluated for various micromeritic behaviors before blending and its compression into tablets.

Table 1: Composition of Co-processed Excipient Granules.

Co-processed excipient (CoEx.) No.	Composition			
			Disintegrant	**Solubilizer**
CoEx.1	Microcrystalline cellulose	PVP K30	Sodium starch glycolate	---
CoEx.2	Microcrystalline cellulose	PVP K30	Croscarmellose sodium	---
CoEx 3	Microcrystalline cellulose	PVP K30	---	Polyethylene glycol 400
CoEx.4	Microcrystalline cellulose	PVP K30	Sodium starch glycolate	Sodium lauryl sulphate
CoEx.5	Microcrystalline cellulose	PVP K30	Croscarmellose sodium	Sodium lauryl sulphate
CoEx.6	Microcrystalline cellulose	PVP K30	---	Polyethylene glycol 400 + Sodium lauryl sulphate

Phase ii. Preparation of directly compressed tablets of Piroxicam: The prepared co-processed granules were mixed geometrically with the pure piroxicam drug followed by addition of magnesium stearate and purified talc by blending. The blended granules with piroxicam drug was compressed using 12 mm shallow concave punch on 10-stations B-tooling single rotary tablet compression machine (Rimek mini press, India) to produce shallow convex-faced round tablet, weighing average weight of 150 mg. The thickness of the tablets kept about 3.5 mm to achieve hardness of more than 4.0 kg/cm^2. The same procedure was followed to compress all six formulations (F1 to F6) containing different co-processed excipients (CoEx.1 to CoEx.6). The unit composition of the tablet formulations was presented in Table 2.

Table 2: Composition of Piroxicam Tablet Formulations.

Composition (mg / tablet)	Tablet Formulation (F)					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
Microcrystalline cellulose	107	107	107	105.875	105.875	105.875
Sodium starch glycolate	7.5	0	0	7.5	0	0
Croscarmellose sodium	0	7.5	0	0	7.5	0
Polyethylene glycol 400	0	0	7.5	0	0	7.5
PVP K30	7.5	7.5	7.5	7.5	7.5	7.5
Sodium lauryl sulphate	0	0	0	1.125	1.125	1.125
Piroxicam	20	20	20	20	20	20
Magnesium stearate	5	5	5	5	5	5
Purified Talc	3	3	3	3	3	3
Average target weight of each tablet = 150 mg						

EVALUATION OF CO-PROCESSED EXCIPIENT GRANULES

Angle of Repose: The angle of repose of the powder or granules was determined by fixed funnel method to assess the flow property. Accurately weighed co-processed granules were taken in a beaker. The granules were allowed to flow through a funnel narrow opening freely onto the surface of the paper to form a cone shaped pile. The diameter and the height of the pile were noted. From, the diameter, radius was calculated. The angle of repose was calculated by using the following formula. The calculated value between 25–45 are considered satisfactory and >45 indicate poor in flow.

$$\text{Tan}\theta = h / r, \text{ and hence } \Theta = \text{Tan}^{-1} (h / r)$$

Where, h - Height of the pile, r - radius of the pile and θ - Angle of repose.

Bulk and Tapped Density: Bulk density is the ratio of mass of granules/powder to the bulk volume. It depends on the particle size distribution, shape and cohesiveness of the particle. Accurately weighted quantity of co-processed granules was carefully poured into graduated measuring cylinder through large funnel and volume was measured, which was called initial bulk volume. It is expressed in gm/ml and is given by the formula:

$$P_b = M \div Vo$$

Where, P_b = Bulk density, M = Mass of granules, Vo = Bulk volume of the granules

Tapped density is the ratio of mass of powder to the volume occupied by the powder after it has been tapped for a definite period of time. Weighed granules sample was transferred to a graduated cylinder and was placed on the tab density apparatus. The volume was measured by tapping for 500 times or more (upto getting constant volume). The tapped volume was noted. The tapped density was determined by the following formula:

$$P_t = M \div V_t$$

Where, P_t =Tapped density, M = Mass of granules and V_t =Tapped volume of the granules

Carr's Index: Based on the apparent bulk and tapped density, the Carr's Index or percentage compressibility was determined by the following formula. Carr's index value between 5 – 21 are considered satisfactory and >23 are poor in flow.

Carr's index (%) = [(Tapped density - Bulk density) ÷ Tapped density] × 100

Hausner's Ratio: Hausner's Ratio indicates the flow properties of granules/powders and is determined by the ratio of tapped density to bulk density. Hausner's ratio value of <1.25 indicates good flow, whereas >1.25 indicates poor flow.

Hausner's ratio = Tapped density ÷ Bulk density

EVALUATION OF COMPRESSED PIROXICAM TABLETS

Thickness and Hardness: Thickness of the individual tablet was measured using vernier caliper (Insize 150 mm Digital Basic – 1112-150). Six tablets were used for the test and average values with standard deviation (+/-) were calculated. The thickness was denoted in millimeter (mm). Tablet crushing strength or hardness is the force required to break the tablet in a diametric compression. The force is measured in kg÷cm^2. The hardness was tested using Monsanto hardness tester. When the thickness reduces the hardness of the tablet proportionally increases. Keeping of optimum thickness to obtain sufficient hardness was desired.

Friability: Friction and shock are the force that most often causes tablets to chip, cap or break. The friability test is closely related to tablet hardness and designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling, and shipping. It is usually measured by the Roche friabilator. Twenty tablets were weighted and placed in the apparatus where they are exposed to rolling and repeated as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100–500 revolutions, the tablets were weighted and the weight was compared with the initial weight. The loss due to abrasion is measure of the tablet friability. The value was expressed as % and maximum weight loss should not be more than 1% of the weight of the tablet being tested during the friability test is considered generally acceptable. The percent friability was determined by using following formula:

Percentage Friability = (Initial weight - Final weight x 100) ÷ (Initial weight)

Weight Variation Test: This is an in process quality control test. These tests are primarily based on the comparison of the weight of the individual tablet of a sample of tablets with an upper and lower percentage limit of the observed sample average. As per the USP the % difference allowed for the uncoated compressed tablets weighing between 80 mg to 250 mg is 7.5%. Ten tablets were selected randomly and average weight was determined. Subsequently, individual tablets were weighed and compared with average weight. Not more than two tablets should differ in their average weight by more than percentage allowed limit of 7.5%.

Disintegration Time: The in-vitro disintegration test was carried out at 37 ± 2^{0}c in 900 ml distilled water using disintegration test apparatus. One tablet was placed in each of the six tubes of the apparatus containing distilled water. One disk was added to each tube. The time taken for the complete disintegration of the tablets with no mass remaining in the mesh was noted. Less disintegration is desired to achieve better dissolution for immediate release tablets.

INVITRO DRUG RELEASE STUDY

Preparation of Standard Curve of Piroxicam: 8.2 ml of 0.1N hydrochloric acid (HCL) was mixed in distilled water and made up to 1000 ml with distilled water. Accurately weighed 20 mg of piroxicam drug was dissolved in 0.1N HCL buffer solution and the volume was made up to 100 ml using 0.1N HCL buffer pH 1.2 in a volumetric flask. From this above solution 25 ml was pipetted out and made up to 50 ml using 0.1N HCL buffer solution. From this 50 ml of stock solution 1 ml, 2 ml, 3 ml, 4 ml, 5 ml were pipetted out into a series of 10 ml volumetric flask and made up to the mark with 0.1N HCL buffer solution to get drug concentration in the range of 10 to 50 µg/ml. The absorbance of the resulting solution was then measured at 354 nm using UV spectrometer against 0.1N HCL buffer pH 1.2 as blank, as shown in Table 3. The standard curve was obtained by plotting concentration (µg/ml) values in X- axis and absorbance values in Y-axis, as given in Figure 1.

Table 3: Absorbance of Piroxicam in pH 1.2 Buffer.

S.No.	Concentration	Absorbance at 354 nm
1.	10 µg/ml	0.328
2.	20 µg/ml	0.652
3.	30 µg/ml	0.997
4.	40 µg/ml	1.345
5.	50 µg/ml	1.716

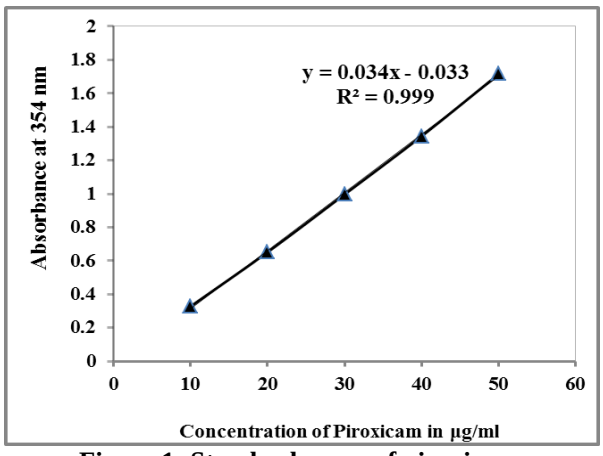

Figure 1: Standard curve of piroxicam.

Dissolution Method: *In vitro* release of piroxicam tablets was studied using USP Type II dissolution

apparatus (Paddle), with 900 ml of dissolution medium maintained at 37 ± 2^0C at 50 rpm. 0.1 N HCL buffer pH 1.2 was used as a dissolution medium. 5 ml of the sample were withdrawn at suitable time intervals of 10, 20, 30, 45 and 60 minutes and are replaced by fresh quantity of dissolution medium. The collected samples after filtration were analyzed spectrophotometrically at 354 nm against 0.1 HCL buffer pH 1.2 as blank and percentage of drug release was determined.

RESULTS AND DISCUSSION

Drug excipients compatibility study: IR spectral analysis of pure piroxicam drug compared with IR spectra of drug-excipients mixture. The spectra were recorded over the wave number in between 4000 - 500 cm^{-1} in a shimadzu FT-IR (model – 8400S) spectrophotometer. It was observed that there was no change in peaks in the drug mixture when compared to pure drug; it indicates absence of drug - excipient interaction, as shown in Figure 2(a) and 2(b).

Figure 2(a)

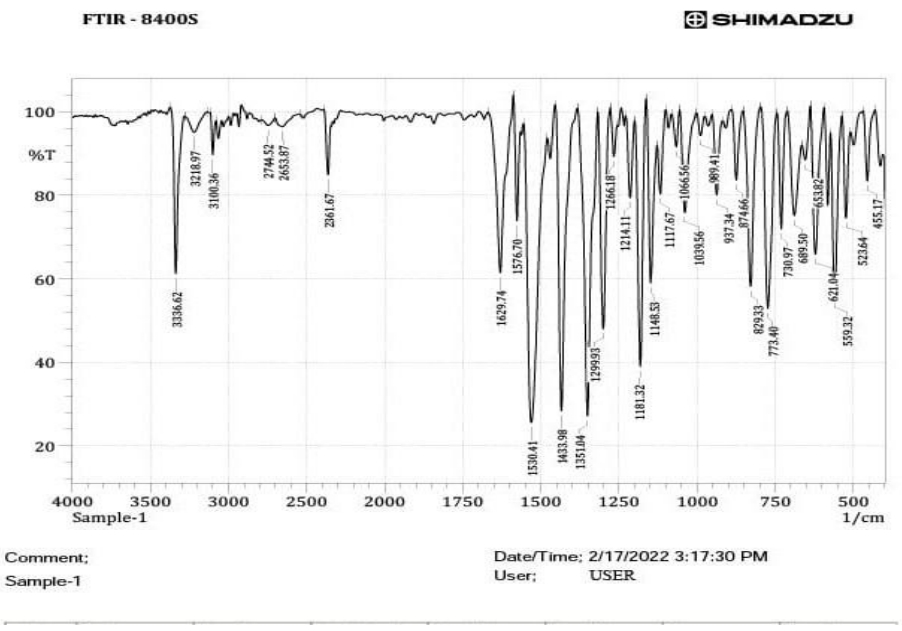

Figure 2(b)

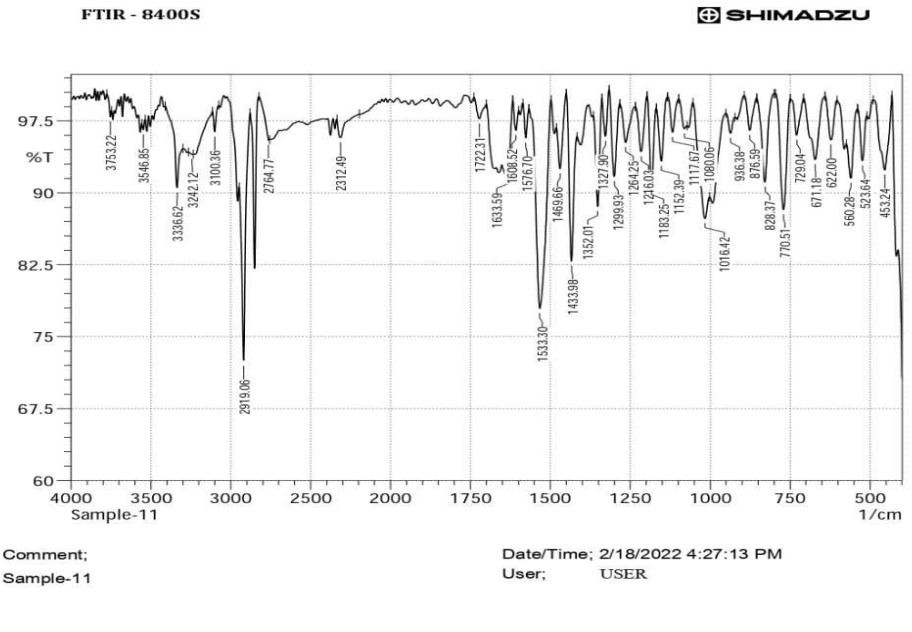

Figure 2: FT-IR Spectrum of: (a) Pure drug Piroxicam and (b) Mixture of Piroxicam drug and Excipients.

Precompression micromeritic properties of co-processed granules: Angle of repose of co-processed excipients granules of six combinations prepared (CoEx.1 to CoEx.6), were measured by funnel method and the result showed that the values were in between 32.3° to 34.4°. The angle of repose within 35° indicates good flow property for granules of all the formulations. The bulk and tapped density of the granules of all the formulation was measured by using bulk density apparatus. The bulk density was found in the range of 0.325 to 0.363 g/cm^3 and the tapped density in the range of 0.379 to 0.442 g/cm^3. These observed values to be substituted in the formula for calculating compressibility index and Hausner's Ratio to analyze the flow properties. The compressibility index and Hausner's ratio were calculated using bulk density and tapped density data. The co-processed excipient granules containing microcrystalline cellulose with sodium starch glycolate (CoEx.1, CoEx.4); and microcrystalline cellulose with croscarmellose sodium (CoEx.2, CoEx.5) showing compressibility index in between 12 – 16%, which falls in the category of "Good". The granules having microcrystalline cellulose with PEG 400 (CoEx.3, CoEx.6.) possess compressibility index of about 18 – 21%, which falls in the category of "Fair". Overall, the compressibility index of the granules was found to be within acceptable range, which indicates that all the granules prepared were having satisfactory flow properties. The hausner's ratio was found to be less than 1.25 for all the prepared granules of co-processed excipients (CoEx.1 to CoEx.6), hence having good flow behavior for its compression into tablets. In Table 4 micromeritic properties of the prepared granules of six different co-processed excipients were mentioned.

Table 4: Precompression Micromeritic Properties of Co-processed Excipients Granules.

Co-processed excipient (CoEx.) granules	Angle of repose (θ)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Compressibility index (%)	Hausner's ratio
CoEx.1	33.1±1.89	0.363±0.005	0.432±0.010	15.0	1.19
CoEx.2	33.1±1.89	0.359±0.007	0.442±0.030	14.7	1.23
CoEx.3	34.4±0.50	0.353±0.005	0.437±0.020	19.2	1.24
CoEx.4	32.3±1.50	0.325±0.001	0.379±0.040	14.2	1.17
CoEx.5	33.7±1.24	0.338±0.002	0.396±0.030	14.6	1.17
CoEx.6	32.4±2.40	0.326±0.003	0.403±0.012	19.1	1.24

The differences between the granules were due to their density differences because of the granulation parameters used; hence this needs to be further optimized by scale up batches. Good flow of granules and its compressibility index of lower value will make this process commercially viable and ease the compression process, increase the production output and avoid compression related problems.

Post Compression Parameters of Piroxicam Directly Compressed Tablets: The average thickness of all the formulation was found to be within the range of 3.40 mm to 3.52 mm. The hardness of the tablets was found within the range of 4.5 to 5.8 kg/cm^2. The results showed that tablets of all the formulation possess uniform thickness and hardness, and there was no significant difference between all the formulations manufactured using different co-processed excipients. The friability of the formulated tablets containing sodium starch glycolate, croscarmellose sodium and polyethylene glycol 400 (F1, F2, and F3) and its combination with sodium lauryl sulphate (F4, F5, and F6) was within the limit of 1%. It revealed that good adhesion of tablet ingredient after compression and granules having adequate strength. For weight variation analysis, ten tablets from each formulation were selected randomly and weighed individually. Not more than two tablets should go more than the limit of variation. The weight variation of piroxicam tablets was found within the range of 144 to 156 mg (Target: 150 mg) and all the formulated tablet batches complies weight variation test. The disintegration time for the formulations manufactured was found to be between 4.0 mins to 18.1 mins. Tablets containing sodium starch glycolate, croscarmellose sodium (F1 and F2) and it's combination with sodium lauryl sulphate (F4 and F5) showed less disintegration time of about 4 – 5.6 minutes, whereas formulation with PEG 400 (F3) and its combination with sodium lauryl sulphate (F6) showed more disintegration time of about 16 – 18.1 minutes. The difference was due to wicking and swelling effect of the super disintegrant added. Sodium starch glycolate swells up to 300 times to its volume and croscarmellose sodium rapidly swells up to 4–8 times its original volume. PEG 400 can improve the solubility of the drug in the medium but playing least role in tablet disintegration. Based on this result the important role of super disintegrants incorporated was well understood. In Table 5 the results of physical parameters for all the 6 batches of tablets compressed were presented.

Table 5: Physical parameters of compressed piroxicam tablet formulations.

Formulation No.	Average Thickness (mm)	Average Hardness (Kg/cm^2)	Friability (%)	Weight Variation (mg)	Disintegration time (Maximum value in Minutes)
F1	3.40±0.15	5.8±0.6	0.5	150±1.7	5.4
F2	3.42±0.10	5.7±0.5	0.5	150±2.9	5.6
F3	3.50± 0.16	4.8±1.0	0.7	150±1.4	18.1
F4	3.44± 0.06	5.3±0.8	0.6	150±1.0	4.0
F5	3.52± 0.12	5.0±1.0	0.7	150±1.1	4.5
F6	3.46± 0.08	4.5±1.0	0.9	150±3.8	16.0

In-vitro drug release study: Piroxicam tablet formulations prepared using various co-processed excipients were subjected to *in vitro* drug release studies. The percentage drug release from the formulation F1, F2, F3, F4, F5, and F6 at the end of 60 mins were found to be 70±1.6%, 40±1.9%, 24±1.3%, 100±2.6%, 59±3.3%, and 35±3.1% respectively. Formulation F4 prepared by using combination of microcrystalline cellulose with sodium starch glycolate and 1% sodium lauryl sulphate showed better drug release when compared to other formulation prepared using croscarmellose sodium and polyethylene glycol. The difference was due to easy swelling ability and wicking capacity of sodium starch glycolate when compared with other excipients. The percentage of drug release from the formulation F3 and F6 was found to be less due to longer tablet disintegration time and lesser solubility of piroxicam in the dissolution medium. When comparing the formulation F1, F2 and F3 (without surfactant) with F4, F5, and F6 (similar composition but additionally having surfactant sodium lauryl sulphate) showed increased percentage of drug release. Surfactant used in these formulations playing a vital role in piroxicam drug dissolution. In presence of surfactant, the water uptake was good, and hence water absorption ratio was high, thereby about 10 - 30% increase of the drug release from the granules. By comparing all, the formulation F4 prepared by using co-processed excipient having combination of microcrystalline cellulose with sodium starch glycolate and sodium lauryl sulphate exhibit better drug release of 100%. Also, formulation F4 was in-vitro equivalent with market available piroxicam tablets in compare to other formulations which were showing lesser drug release. The drug release data and dissolution release profile comparison were presented in Table 6 and Figure 3, respectively.

Table 6: Comparative drug dissolution of prepared formulations and market product.

S. No.	Time Interval (Minutes)	Drug Release (%) of Formulations with Co-processed excipients.						Drug Release (%) of Marketed Formulation
		F1	F2	F3	F4	F5	F6	
1	10	33 ± 2.3	15 ± 1.3	12 ± 1.7	82 ± 2.2	19 ± 1.3	20±1.2	98 ± 2.3
2	20	49 ± 3.4	22 ± 0.8	15 ± 2.5	96 ± 3.2	31 ± 2.4	23±2.2	97 ± 3.4
3	30	56 ± 1.3	33 ± 1.3	18 ± 3.6	98 ± 2.5	41 ± 1.6	27±3.2	100 ± 2.1
4	45	62 ± 1.5	38 ± 1.2	20 ± 2.2	99 ± 2.4	52 ± 2.7	32±1.4	101 ± 1.8
5	60	70 ± 1.6	40 ± 1.9	24 ± 1.3	100 ± 2.6	59 ± 3.3	35±3.1	99 ± 2.4
Statistical evaluation for significance between Test Formulations (F1 to F6) and Market product (M) – Two tailed pair t test (α = 0.05), degree of freedom = 4								
	T Value	F1 Vs M*	F2 Vs M*	F3 Vs M*	F4 Vs M*	F5 Vs M*	F6 Vs M*	
		7.5955	16.1091	45.8238	1.3117	8.6913	30.0957	
	Difference considered to be	Statistically significant	Statistically significant	Statistically significant	Not Statistically significant	Statistically significant	Statistically significant	
*M – Market Product. Not Statistically significant difference: Obtained T value < T critical value of 2.776. Statistically significant difference: Obtained T value > T critical value of 2.776.								

Statistical Analysis: Each of dissolution experiments conducted for six tablets from all the formulations F1 – F6 and for market product. Six time points (10 min – 60 min) of dissolution along with its standard deviation (±) for each tablet were recorded. Individually, statistical significant test performed for each point of dissolution between the developed test formulations and the market product. Results were represented in Table 6. Statistical analysis proves that formulation F4 was comparable with market product without any statistical difference and hence it was well predicted to meet the bioequivalence criteria to provide better systemic bioavailability.

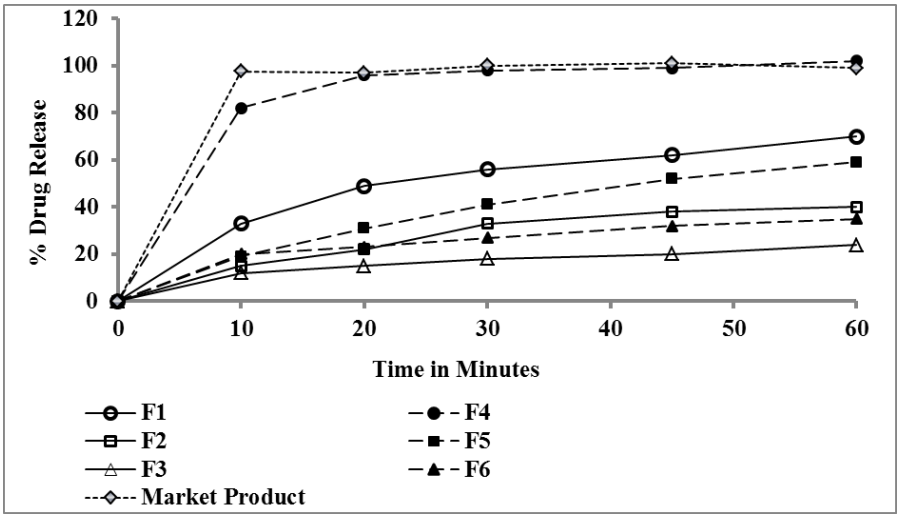

Figure 3: Dissolution Profile comparison of Piroxicam Tablet Formulations prepared using Co-processed Excipient contains: MCC* + Sodium starch glycolate (F1) Vs. MCC* + Croscarmellose sodium (F2) Vs. MCC* + PEG400 (F3) Vs. MCC* + Sodium starch glycolate + Sodium lauryl sulphate (F4) Vs. MCC* + Croscarmellose sodium + Sodium lauryl sulphate (F5) Vs. MCC* + PEG400 + Sodium lauryl sulphate (F6) Vs. Market Product. *MCC – Microcrystalline cellulose.

CONCLUSION

It was concluded that formulation developed with the co-processed excipient containing combination of microcrystalline cellulose, sodium starch glycolate and sodium lauryl sulphate (F4) was observed to have rapid disintegration and maximum percentage of drug release in compared to other formulations. Also it was comparable with marketed product with respect to drug release and other quality requirements of immediate release oral tablets. The synergistic effect by the combination of super disintegrant and surfactants along with microcrystalline cellulose leads to enhanced dissolution rate of insoluble class II category drug. The excipients used in this study improve the granular properties for its flow and compression into tablets. Additional advantages over marketed product include reduction in average tablet weight, cost effective and orally consumable. The technique of co-processing the excipients and tablets preparation by direct compression method in this present work can be industry adaptable, cost effective and overcome issues of conventional manufacturing process. Further necessary scale up and in-vivo bioavailability / bioequivalence studies can be performed to establish its commercial manufacturability and in-vitro in-vivo correlation.

ACKNOWLEDGEMENTS

The authors are grateful to Pharmafabrikon Ltd., Madurai, Tamil Nadu, India for providing the drug sample and Ayya Nadar Janaki Ammal College, Sivakasi, Tamil Nadu, India for facilitating the FT–IR spectroscopy analysis for this research work.

REFERENCES

1. Hetal Patel, Mukesh Gohel. J Crit Rev., 2016; 3(2): 48-56.
2. Sanjay S Patel, Natvarlal M Patel. Int J Pharm Pharm Sci., 2009; 1(1): 125-148.
3. Mohammad Kashif Iqubal, Pranjal Kumar Singh, Dr. Mohd. Shuaib, A Iqubal, Monika Singh. Int J of pharm research and development, 2014; 6(1): 49-57.
4. Michael E Aulton, Kevin M G Taylor. Aulton's Pharmaceutics. The Design and Manufacture of Medicines. 5th ed, Elsevier, 2017.
5. John Rojas, Ira Buckner, Vijay Kumar. Drug Dev and Ind Pharmacy, 2012; 38(10): 1159-1170.
6. Guideline for Excipients Industry; The International Pharmaceutical Excipient Council, 2017; Ver(1): 1-17.
7. Ashok Katdare, Mahesh V. Chaubal. Excipient Development for Pharmaceutical, Biotechnology and Drug Delivery Systems. 1st ed. New York; Informa Healthcare USA Inc, CRC Press., 2006.
8. Liew Kai Bin, Anand Gaurav, Uttam Kumar Mandal. Int J Pharm Pharm Sci., 2019; 11(1): 1-9.
9. Gohel MC, Pranav D Jogani. J Pharm Pharmceut Sci., 2005; 8(1): 76-93.
10. Sharma SK, Alam MN, Jaimini M, et al. *International Journal of Current Trends in Pharmaceutical Research*, 2013; 1(3): 205-214.
11. Abhay Kumar Mourya, Sunil K Prajapati, Jain SK, Ajay Kumar, Atul Kumar Thakran, Shashi Alok. Int J of Pharm Sci and Research, 2012; 3(2): 610–614.
12. Mukesh Mohite, Sayli Sarnaik, Akshay Lingayat. Journal of Science and Technology, 2020; 5(5): 85-89.
13. Chowdary KPR, Ramya K. Int. Journal of Comprehensive Pharmacy. Pharmacie Globale, 2013; 4(2): 1-5.
14. Mamatha B, Srilatha D, Sivanarayani CH, Kumar Desu P, Venkateswara Rao P. World journal of pharmaceutical Research, 2017; 6(15): 224-237.
15. Patel L, Jitendra P, Umesh U. Int J Pharm Res and Applications, 2020; 5(2): 270-283.