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Investigation of Novel Multifunctional Co-Processed Excipient for Direct Compression

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Abstract: The main purpose of the present Study was to develop novel multifunctional pharmaceutical excipient for direct compression. In the present study, novel multifunctional excipient were developed by Co-precipitation method using Dicalcium phosphate and carboxymethylcellulose sodium in different ratios (9.9:0.1, 9.8:0.2, 9.7:0.3, 9.6:0.4, 9.5:0.5 and 9.4:0.6) The developed excipients were evaluated for the micromeritic studies and bulk powder properties in comparison with physical mixture. It was observed that multifunctional co-processed Excipient exhibited much better flow properties as compared to physical mixture. The effect of addition of co-processed excipient in a formulation containing poorly compressible and high dose drug (paracetamol and ibuprofen), medium dose drug (Aceclofenac) and low dose drug (simvastatin) was also studied. The results of dilution potential study reveal that up to 50% Paracetamol and Ibuprofen a poorly compressible drug, can be incorporated in the multifunctional directly compressible excipient. Conventional tablets of paracetamol, ibuprofen, Aceclofenac and Simvastatin were prepared using the multifunctional directly compressible excipient and evaluated for post-compression parameters. From the present study It can be concluded that prepared multifunctional directly compressible excipient serve as 'ready-to-compress' powder mixtures for any kind of drugs.

Key words: Co-processed excipient · Direct compression · Paracetamol · Ibufrofen · Acelofenac · Simvastatin · Co-precipitation method

INTRODUCTION

Tablets are most accepted dosage forms because of their low cost, ease of manufacturing, patient compliance, precise dosing and stability in comparison with liquid dosage forms. The art of tableting is performed by the three well-known methods i.e. wet granulation, dry granulation and direct compression [1, 2]. Recently most of the pharmaceutical manufacturer adapting direct compression technique because of several advantages like requirement of fewer unit operations which reduces overall product cost, increase stability of API's and simplicity of the direct compression method etc [3]. The direct compression process is highly influenced by powder characteristics such flow ability, compressibility and dilution potential. No Single-component excipient do not always provide the requisite performance to allow certain active pharmaceutical ingredients to be formulated or manufactured adequately [4] As a result, drug formulation scientists have dependent on combination of excipients. Such combinations fall into two broad categories: physical mixtures and co-processed excipients. Co-processed excipients are combinations of two or more excipients that possess performance advantages that cannot be achieved using a physical mixture of the same combination of excipients [5].

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 product with added value related to the ratio of its functionality/price another objective is to provide a synergy of functionality improvement as well as masking the undesirable properties [6]. Co-processing of excipient could lead to the formation of excipient with superior properties as compared to the simple physical mixture of their components. Development of co-processed directly

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compressible adjuvant start with selection of the excipients to be combined, their targeted proportion, selection of preparation method to get optimized product with desired Physico-chemical parameter and it ends with minimizing avoidance with batch-to-batch variation [1, 6].

Generally, a mixture of plastic and brittle material is used for co-processing. This mixture prevents storage of too much elastic recovery throughout compression, which results in a small amount of stress relaxation and a reduced propensity of capping and lamination in this manner resulting in optimum tableting performance [7]. The study described in this paper was undertaken to develop a novel co-processed, directly compressible multifunctional excipient that can serve as a base for any kind of active pharmaceutical ingredients. Carboxymethylcellulose sodium is familiar as a tablet binder and disintegrant. Carboxymethylcellulose sodium exhibits disintegration property due to capillary action; it has a self lubricating quality and thus, it requires less lubrication than other excipients. In addition, it exhibits inherent compatibility because of plastic deformation and limited elastic recovery. One of the few problems associated with Carboxymethylcellulose sodium is its very poor flowability and hygroscopicity which may lead to unsuitability for direction compression tableting. Dicalcium phosphate is mostly used as tablet diluents and having better flow as compared to Carboxymethylcellulose sodium. But major drawback associated with Dicalcium phosphate are extremely low compressibility making it difficult to form suitable tablet by direct compression and physically abrasive nature, leading an undesirable mouth feel as well as increase wear and tear tableting punches. In the present investigation combination of Carboxymethylcellulose sodium with Dicalcium phosphate and it is used in formulation of ibuprofen, paracetamol, aceclofenac and simvastatin conventional tablets.

MATERIALS AND METHODS

Materials: Ibuprofen, Paracetamol and simvastatin were received as gift sample from Mission Vivacare Limited, Pithampur, M. P., India. Aceclofenac was received as gift sample from Wockhard Research Centre D4 Chikalthana MIDC, Aurangabad. Dicalcium Phosphate was purchased from Burgoin. Sodium Hydroxide and Potassium Dihydrogen Phosphate was purchased from Ranbaxy Laboratories Limited. Ethanol was purchased from Changshu Yangyan Chemical, China. All others chemicals and reagents used were of Analytical Reagent Grade.

Method

Preparation of Physical Mixture: Weigh accurately the excipients according to their ratios and mixed together in a Polybag for 5 min using tumbling technique or in mortar pastel for few minutes. The ratio or proportion of excipients for preparation of physical mixture was selected according to their use in formulation. The DCP and NaCMC Ratio (9.9:0.1, 9.8:0.2, 9.7:0.3, 9.6:0.4, 9.5:0.5 and 9.4:0.6) were selected for the preparation of Physical Mixture.

Formulation of Co-Processed Excipient by Co-Precipitation Method: Carboxymethylcellulose sodium (0.1g) was dispersed in 50 ml of water and allows to swell it for few minute. DCP (9.9 g) was dispersed in 100 ml of water, Then DCP suspension was gradually added to the Carboxymethylcellulose sodium suspension under vigorous stirring until homogenization of the both excipient was accomplished, to which 20ml of ethanol was added under stirred mixing at room temperature for 10 min. The amounts of Carboxymethylcellulose sodium were 0.1, 0.2, 0.3, 0.4, 0.5, or 0.6 g, corresponding to the DCP: NaCMC ratios of 9.9:0.1, 9.8:0.2, 9.7:0.3, 9.6:0.4, 9.5:0.5 and 9.4:0.6, respectively. The co-precipitated product was collected by filtration through a Whatmann no.4 filter paper and then collected and tray-dried at 60°C for 2 hr in a hot air Oven. Then these mixtures of excipients were sifted through sieve no #44 to obtain the required particle size. This granule was dried at 60°C in tray dryer for overnight. After drying overnight the mixture was again sifted through sieve no #44 to Obtained required particle size of co-processed excipients. The pre-compression parameters like density's, Carr's index, Hausner's ratio,%porosity and angle of repose for co-processed excipients were measured. The optimum ratio was selected on the basis of compressibility index, angle of repose and their flow properties.

Evaluation of Pre-Compression Parameters

Angle of Repose: The angle of repose was determined by the fixed funnel method. The accurately weighed powder was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder. The powder was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured.

The angle of repose was calculated using the following equation [8].

$$\tan(\theta) = h/r \quad (1)$$

where 'h' and 'r' are the height and radius respectively of the powder cone.

Determination of Bulk Density (USP): It is the ratio of mass and bulk volume. It is required to decide the appropriate packing of dosage forms. 20 gm powder was allowed to flow in a fine stream into a graduated cylinder and final volume was noted [9]. It was determined by equation (2),

Bulk density = Wt. powder / Bulk volume (2)

Determination of Tapped Bulk Density (USP): The 20 gm powder was allowed to flow in a fine stream into a graduated cylinder of a mechanical tapping device. The measuring cylinder was tapped for 100 times and final tapped volume was noted [9]. It was calculated by using equation (3),

Tapped Density = Wt. powder/Tapped Volume (3)

Compressibility: It decides the flow properties of granules or powders. The percentage compressibility of a powder was a direct measure of the potential powder arch or bridge strength and stability [10]. Carr's index of each formulation was calculated according to equation (4),

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped Density}} \times 100 \quad (4)$$

Hausner's Ratio: It is essential to determine the compressibility strength of powders. It was determined by using equation (5),

Hausner's ratio = Tapped density/ Bulk density (5)

Lower Hausner's ratio (< 1.25) indicates better flow properties than higher ones (> 1.25) [11].

Characterization of Co-processed Excipients (Batch Cp5) by Analytical Technique

Fourier Transform Infrared (FTIR) Spectral Study: FTIR spectrum was recorded by using an FTIR-4100 spectrophotometer (Shimadzu Co. Japan). The wave number ranged from 400 to 4000 cm^{-1} with a resolution of 4 cm^{-1}. The FTIR spectra of DCP, carboxymethylcellulose sodium and co-processed excipient are shown in Figure No. 1, 2 and 3 respectively [12].

DSC Analysis: Thermo grams were obtained by using a differential scanning colorimeter at a heating rate 20° C/min over a temperature range of 100 to 300°C. The sample was hermetically sealed in an aluminium crucible. Nitrogen gas was purged at the rate of 40 ml/min, for maintaining inert atmospheres. The differential scanning calorimetry was performed on dicalcium phosphate, carboxymethylcellulose sodium, physical mixture of dicalcium phosphate and carboxymethylcellulose sodium and Co-processed excipients of dicalcium phosphate, carboxymethylcellulose sodium. The thermograms were shown in Figure No. 4 respectively [12, 13].

Formulation of Conventional Tablets: The conventional tablets of different drugs like Ibuprofen, Paracetamol, Aceclofenac and Simvastatin were prepared by direct compression technique. The formulations were prepared

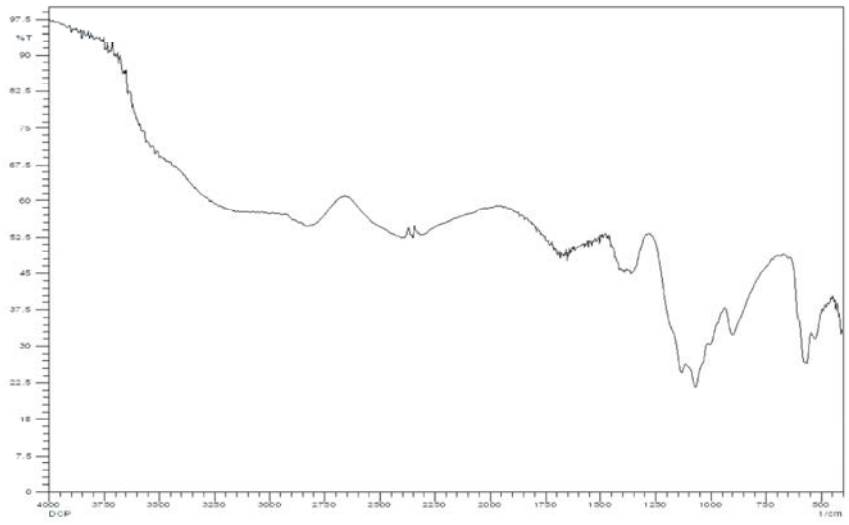

Fig. 1: FTIR spectrum of DCP

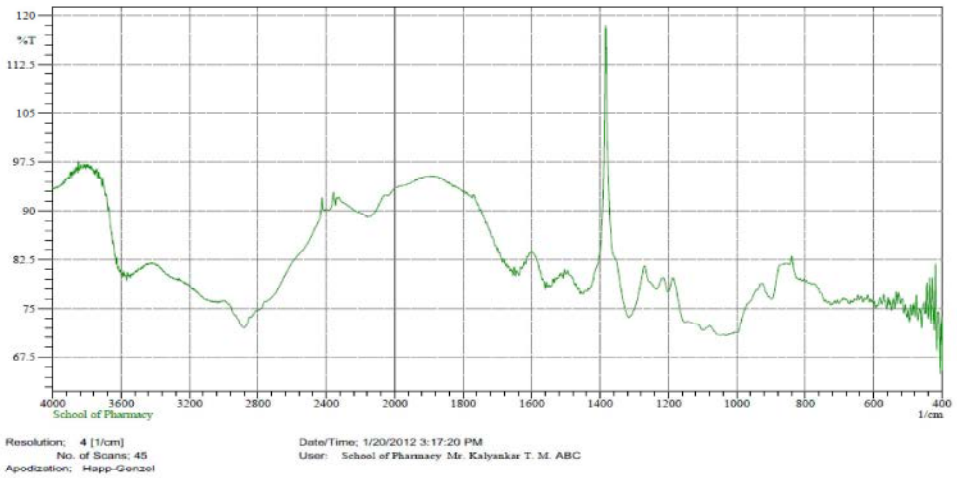

Fig. 2: FTIR spectrum of NaCMC

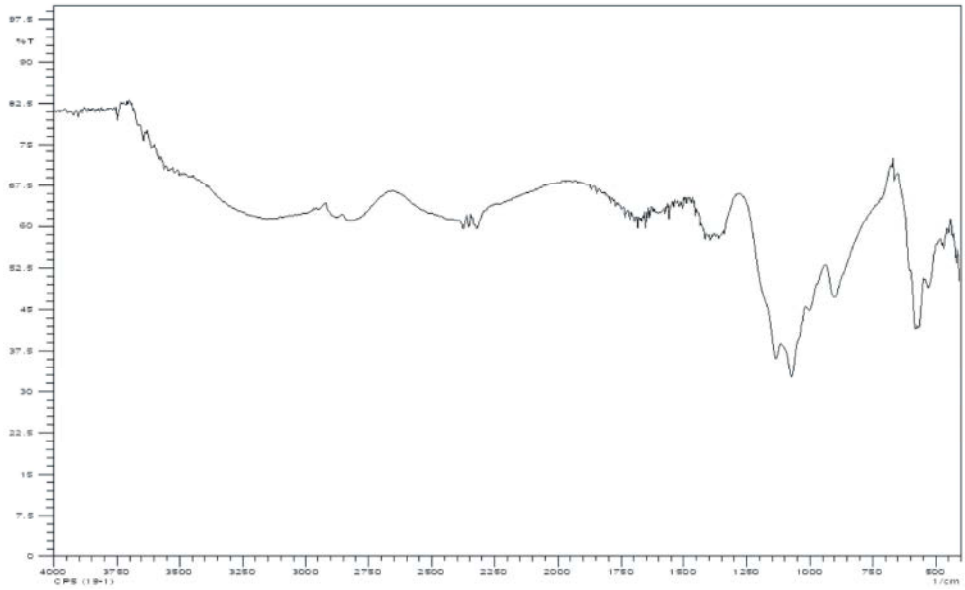

Fig. 3: FTIR spectrum of co-processed excipient

by using co-processed excipients (CP5). Accurately weighed quantities of drug and co-processed directly compressible excipient were blended homogeneously in a mortar and pestle and the resultant mixture was compressed into tablets using 12 station rotary tablet machine (Karnavati, Mumbai, India) using 10mm, 12mm, 9 mm respectively round concave punches at an optimum pressure.

Evaluation of Tablets (Post Compression Parameters)

Weight Variation: Twenty tablets were selected randomly and weighed individually. Calculated average weight and compared the individual tablet weight to the average [14].

Thickness and Diameter: Thickness and diameter of tablets was determined using Vernier Caliper. Three tablets from each batch were used and average values were calculated.

Hardness: Hardness is the force required breaking a tablet in a diametric compression test. For each formulation, the hardness of three tablets was determined using Pfizer Hardness tester.

Friability: Six tablets from each batch were selected randomly and weighed. These tablets were subjected to friability test using Roche Friabilator for 100 revolutions. Tablets dropping

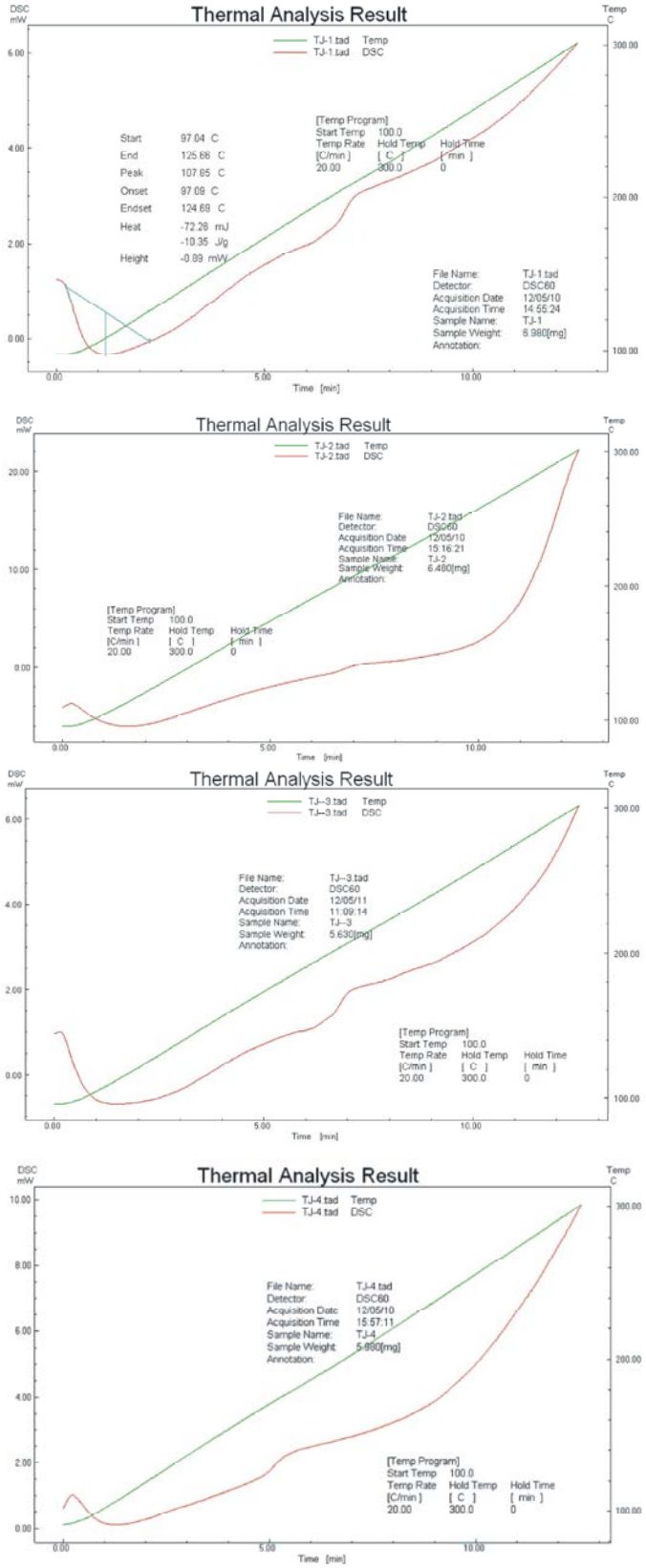

Fig. 4: DSC Thermogram of DCP, Na CMC and Co-processed excipient

Table 1: Specification for tablets as per Pharmacopoeia of India

Sr.No.	Average weight of Tablet	% Deviation
1	80 mg or less	10
2	More than 80 mg but less than 250 mg	7.5
3	250 mg or more	5

Table 2: Dilution Potential study of various batches of optimized formulation

		Formulations				
Model Drug	Ingredients	FD1	FD2	FD3	FD4	FD5
Ibuprofen	Agglomerates of formulation CP5 (%)	90	80	70	60	50
	Ibuprofen (%)	10	20	30	40	50
Paracetamol	Agglomerates of formulation CP5 (%)	90	80	70	60	50
	Paracetamol (%)	10	20	30	40	50

from a distance of six inches with each revolution. Tablets were removed dedusted and reweighed [15, 16].

Following formula was used to calculate the friability

$$F(\%) = \frac{\text{Initial wt.} - \text{Final wt.}}{\text{Initial wt.}} \times 100 \quad (6)$$

Disintegration Test: Disintegration time of the tablets was determined using USP tablet disintegration tester. To test disintegration time, one tablet was placed in each tube of the apparatus and basket rack was positioned in a 1L beaker of distilled water, at 37°C. The apparatus was operated till complete disintegration of all the tablets and the disintegration time for each tablet noted. The mean disintegration time was calculated [17].

Dilution Potential: Dilution Potential is the amount of poorly compressible drug that can be satisfactorily compressed into tablet with a directly compressible adjuvant. Dilution potential of agglomerates of formulation CP5 was evaluated by using Ibuprofen and Paracetamol as a model drugs [18, 19] (Table 2).

Water Absorption Ratio% (Wetting Study): Twice folded tissue paper was placed in a Petri dish having an internal diameter of 5 cm containing 6 ml of distilled water. A tablet was carefully placed on the surface of the tissue paper in the Petri dish. The time required for water to reach the upper surface of the tablet and to completely wet it was noted as the wetting time. The Water Absorption Ratio (R) was determined using the following equation (7),

$$\text{Water absorption ration (R)} = \frac{W_a - W_b}{W_b} \times 100 \quad (7)$$

Where, W_b is the weight of the tablet before water absorption and Wa is the weight of the tablet after water absorption [20].

***In vitro* dissolution Study:** *In vitro* dissolution studies for ibuprofen, paracetamol, aceclofenac and simvastatin conventional tablet were carried out by using USP Dissolution Apparatus II paddle type at 50 rpm in 900 ml of dissolution media, maintained at 37±0.5°C. The study was carried for 2 h and at predetermined time intervals (0, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120 minutes) 2 ml aliquots were withdrawn, filtered and assayed spectrophotometrically at λmax 221nm, 243nm, 275nm and 238nm using double beam UV Visible Spectrophotometer (Shimadzu, Model 1700, Japan). An equal volume of fresh medium, which was pre-warmed at 37°C, was replaced into the dissolution medium after each sampling to maintain the sink condition throughout the study. Dissolution study was performed in triplicate for each formulation.

RESULTS AND DISCUSSION

Evaluation of Pre-Compression Parameters: Co-processed directly compressible excipient were prepared by co-precipitation method by using dicalcium phosphate and carboxymethylcellulose sodium in different ratios (9.9:0.1, 9.8:0.2, 9.7:0.3, 9.6:0.4, 9.5:0.5, & 9.4:0.6). The co-processed excipient was evaluated for their pre-compression parameters in comparison with physical mixture of dicalcium phosphate and carboxymethylcellulose sodium. The angle of repose of co-processed excipients was found to be < 27.18 which indicates excellent flow in comparison to physical mixture of same component >36.66 due to the less percentage of fines. As the concentration of carboxymethylcellulose sodium increases the physical mixture shows poor flow properties may be due to hygroscopic nature of carboxymethylcellulose sodium.

The value of Carr's index between 5–15 and 12–16 indicates excellent and good flow ability, respectively while values greater than 21 indicate poor flow ability [19]. All the batches of physical mixture (PM1, PM2, PM3, PM4, PM5 and PM6) failed to meet the selection criteria. Co-processed excipient exhibit Carr's index in range of 13.97- 23.30% and the hausners ratio in the range of 1.17-1.28. The batch CP5 exhibits excellent flow properties and compressibility hence it was selected as optimized batch. (Table 3, 4)

Characterization of Co-Processed Excipients (batch CP5) by Analytical Technique

Fourier Transform Infrared (FTIR) Spectral Study: FTIR absorption spectrum of DCP, NaCMC and Co-processed excipients was taken and the spectral assignments for major bands were in consistent with the structure of DCP and NaCMC. The FTIR Spectra of DCP, NaCMC and Co-processed excipient are shown Figure No. 01, 02 & 03 respectively. The prominent peak of DCP at 2825.72, 1132.21, 898.83, 578.64 and 466 cm^{-1} are present in co-processed excipients indicating that there was no interaction between the excipients.

DSC Analysis: The DSC analysis indicated that exothermic peak of DCP and endothermic peak of NaCMC are intact in co-processed excipients and physical mixture indicating that both amorphization and crystallization has occurred in co-processed excipients, it may be due to absorption of moisture, therefore on inspecting DSC spectra it can be concluded that changes are physical. In DSC analysis of co-processed excipients neither sharp endothermic nor exothermic peak was observed, suggesting that the complex of co-processed excipient is amorphous in nature. DSC Thermograms of DCP, NaCMC, Physical mixture and Co-processed excipient are shown in Figure no. 04, 05, 06 and 07 respectively.

Table 3: Powder characterization of various physical mixtures

	Formulations					
Micrometric properties	PM1	PM2	PM3	PM4	PM5	PM6
Bulk Density (±SD)	0.425	0.4285	0.5	0.5263	0.4761	0.4545
	(±0.048)	(±0.042)	(±0.05)	(±0.043)	(±0.023)	(±0.027)
Tapped Density (±SD)	0.6296	0.6428	0.7692	0.8333	0.7692	0.7407
	(±0.079)	(±0.032)	(±0.014)	(±0.31)	(±0.017)	(±0.027)
Carr's Index (±SD)	32.49	33	34.99	36.84	38.10	38.63
	(±2.00)	(±3.61)	(±5.15)	(±2.71)	(±1.81)	(±1.33)
Hausners Ratio (±SD)	1.48	1.50	1.538	1.58	1.61	1.62
	(±0.044)	(±0.076)	(±0.10)	(±0.060)	(±0.041)	(±0.029)
% Porosity (±SD)	32.5	33	35	36.8	38.09	38.63
	(±0.7)	(±0.52)	(±0.76)	(±0.38)	(±1.01)	(±0.677)
Angle Of Repose (±SD)	30.76	32	33.68	34.55	36.05	36.66
	(±0.34)	(±0.28)	(±1.55)	(±0.25)	(±0.404)	(±0.165)

Table 4: Powder characterization of various co-processed excipients

	Formulations					
Micrometric properties	CP1	CP2	CP3	CP4	CP5	CP6
Bulk Density (±SD)	0.555	0.555	0.625	0.583	0.588	0.5714
	(±0.027)	(±0.071)	(±0.071)	(±0.061)	(±0.048)	(±0.065)
Tapped Density (±SD)	0.7142	0.666	0.7692	0.70	0.6896	0.7142
	(±0.026)	(±0.067)	(±0.065)	(±0.099)	(±0.05)	(±0.044)
Carr's Index (±SD)	23.30	16.76	18.75	16.71	13.97	20.0
	(±1.37)	(±2.17)	(±2.86)	(±3.79)	(±1.09)	(±1.27)
Hausners Ratio(±SD)	1.28	1.2	1.23	1.20	1.17	1.24
	(±0.015)	(±0.032)	(±0.0435)	(±0.060)	(±0.02)	(±0.01)
%Porosity (±SD)	22.22	16.66	18.75	16.66	13.88	20.0
	(±0.80)	(±0.659)	(±0.629)	(±0.671)	(±0.506)	(±0.73)
Angle Of Repose (±SD)	27.18	24.57	25.02	24.37	23.04	25.73
	(±0.626)	(±0.623)	(±0.731)	(±0.815)	(±0.989)	(±0.789)

Table 5: Physico-Chemical Characterization of different drug Tablets

	Formulations			
Evaluation tests	IF1	PF1	AF1	SF1
Weight variation	404.3 ±4.73	653.6 ±8.40	198.95±5.41	104.6±6.95
Hardness (kg/cm2)	5±0.5	3.5±0.40	4.5±0.65	5.3±0.7
Diameter (mm)	10±0.25	12±0.40	3±0.025	0.52±0.035
Thickness (mm)	2±0.05	9±0.30	2±0.03	0.57±0.03
Friability (%)	0.80±0.055	9±0.5	1±0.049	O.57±0.06
Disintegration time(min)	8±0.76	15±0.96	1±0.5	5±0.49
Water absorption ratio	15.23±0.24	29.62±0.56	37.68±0.86	43.84±0.85

Table 6: Results for dilution potential study

		Formulations				
Model Drug	Parameters	FD1	FD2	FD3	FD4	FD5
Ibuprofen	Hardness (kg)	5±0.25	4.80±0.1	4.50±0.12	3.60±0.2	3.50±0.21
	Friability (%)	0.33±0.11	0.49±0.075	0.62±0.08	0.75±0.04	0.87±0.02
	Disintegration time (min)	13±0.52	11.5±0.62	9±0.50	8.56±0.25	8±0.5
Paracetamol	Hardness (kg)	4.5±0.18	4±0.10	3.80±0.104	3.30±0.15	3.00±0.26
	Friability (%)	0.38±0.035	0.45 ±0.065	0.53±0.076	0.77±0.036	0.84±0.025
	Disintegration time (min)	15±0.59	12±0.73	8±0.75	6±0.43	5±0.55

Table 7: Dissolution data of different formulations containing Co-processed excipient

		%CDR			
Sr. No.	Time(min)	IF1	PF1	AF1	SF1
1	5	9.8677±0.090	4.0584±0.93	21.1250±0.089	6.6592±0.051
2	10	12.4121±0.068	7.4913±0.087	28.9219±0.052	11.7188±0.078
3	20	17.1313±0.075	12.9443±0.74	41.2361±0.068	22.8435±0.032
4	30	22.4159±0.069	17.1935±0.19	47.8275±0.026	35.0018±0.073
5	40	27.2077±0.12	21.2285±1.33	50.4333±0.59	41.1332±0.086
6	50	32.9180±0.27	24.3919±0.62	59.7947±0.62	46.2691±0.12
7	60	38.4392±0.22	31.2936±0.81	63.6767±0.87	55.4520±0.37
8	70	42.9130±0.32	41.6484±2.06	65.3169±1.04	60.6193±0.69
9	80	54.0054±0.35	56.4842±1.32	71.4606±1.47	72.8605±0.61
10	90	65.6771±2.94	69.0887±0.048	83.8675±1.09	80.0839±0.50
11	100	77.9798±1.11	78.1574±0.85	92.8017±1.98	85.3049±0.12
12	110	91.3690±2.13	85.3172±3.29	95.2553±2.12	88.5193±0.88
13	120	95.4546±1.51	97.1044±0.39	98.7139±2.31	92.7493±1.50

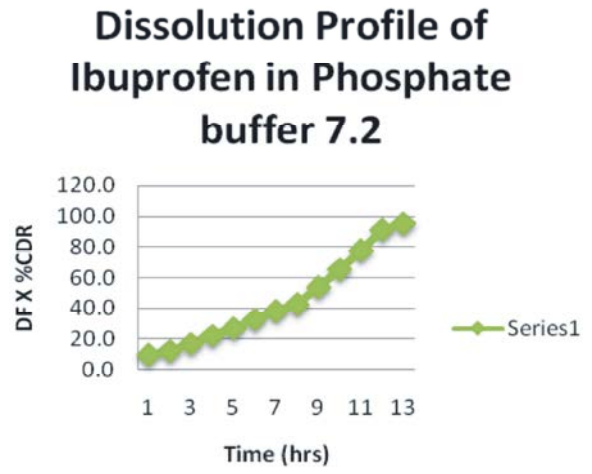

Fig. 5: Dissolution Profile of IF1

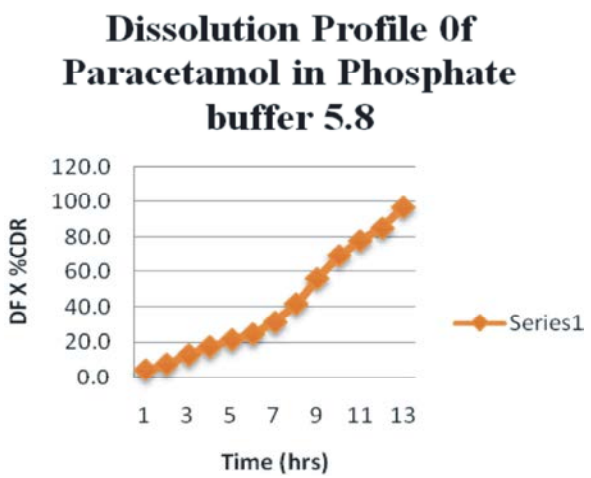

Fig. 6: Dissolution Profile of PF1

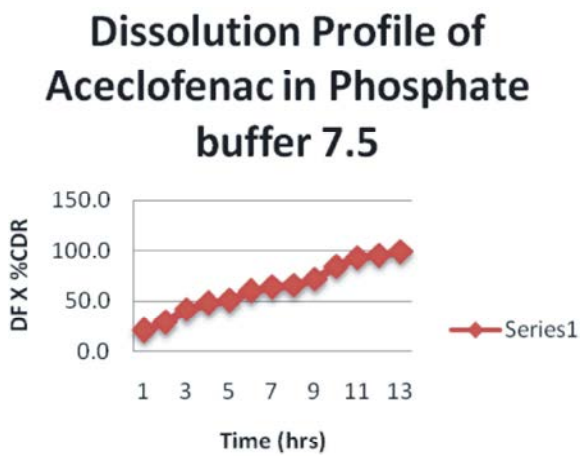

Fig. 7: Dissolution Profile of AF1

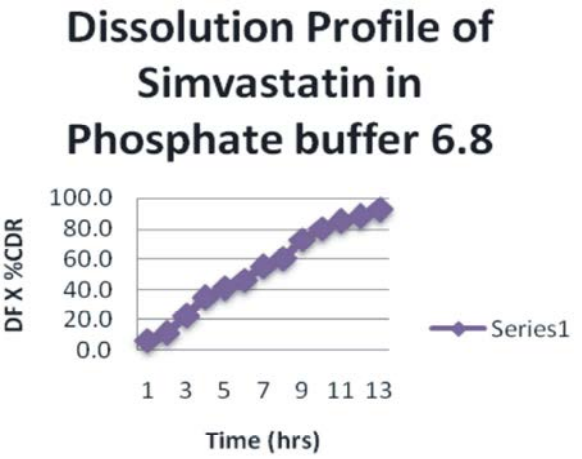

Fig. 8: Dissolution Profile of SF1

Drug Excipient Interaction Study: Physical mixture of drug and excipient was characterized by FTIR spectral analysis for any physical as well as chemical alteration of the drug characteristics. From the Fig. 3. It can be concluded that there was no interference in the functional group as the principle peaks of the Ibuprofen, Paracetamol, Aceclofenac and Simvastatin was found to be unaltered in the drug-excipient physical mixtures, indicating they were not any interaction of excipient with drug.

Evaluation of tablet

Physical Evaluation of Tablet: Conventional tablets of ibuprofen, pracetamol, aceclofenac and simvastatin were prepared by using directly compressible co-processed excipient (CP5). The tablets obtained were of uniform weight due to the uniform die fill, with acceptable variations as per IP specifications i.e 5% for ibuprofen and paracetamol, 7.5% for aceclofenac and simvastatin.

Hardness of all different drugs formulation was in the range of 3.5±0.40 to 5.3±0.7 KP which is acceptable. All the different drug formulations show friability within the acceptable range i.e <1% hence passes friability test. The results of friability indicate that the tablets were mechanically stable and could handle the rigors of transportation and handling. Thickness of all different drug formulation was between 1±0.049 to 3±0.025 mm indicating fairly acceptable tabletting. The disintegration time of all formulation were found to be good because none of the tablet disintegrate greater than 15 minute which is IP limit for uncoated tablet, within all formulation The AF1 gives best disintegrating time i.e. 1 minute. Wetting time and water absorption ratio, are important criteria for understanding the capacity of disintegrant to swell in the presence of little amount of water were found to be in the range of 15.23-43.84%43.84. From above observations, it can be concluded that the concentration of binder and ratio of diluents are important criteria for the preparation of directly compressible excipients. (Table)

Dilution Potential Study: Tablets were prepared by using 10-50% paracetamol and Ibuprofen. It was arbitrarily decided to select a batch, which shows friability < 1%. It was quite evident from the result shows that 50% paracetamol and ibuprofen Gave acceptable results (Table)

The In-vitro Dissolution Study: The in-vitro rug release profiles of ibuprofen, paracetamol, aceclofenac and simvastatin are shown in fig. An in-vitro dissolution study showed that more than 90% ibuprofen, paracetamol, aceclofenac and simvastatin was released at the end of 2 hr from tablets prepared using co-processedexcipient of batch CP5. (Table)

CONCLUSION

Multifunctional excipient was prepared by incorporating one excipient into the particle structure of other excipient by using co-precipitation method. The co-precipitation method has been found to be potential alternative method for the production of directly compressible excipient. From this study it was concluded that the multifunctional excipient shows better properties than the physical mixture of their component.

In the present study co-processing of DCP & NaCMC exhibited improved flowability as measured by angle of repose, compressibility index & hausner's ratio, the lower% of fines could be the reason for improved flow.

Combination of DCP & NaCMC was successful in improving the compatibility of drug substances such as ibuprofen, paracetamol (poorly compressible, high dose), Aceclofenac (medium dose) and Simvastatin (low dose). Tablets prepared from multifunctional excipient exhibit acceptable crushing strength and disintegration into primary particle. From the results of this study it can be concluded that co-processed excipient containing DCP and NaCMC can be used as potential multifunctional directly compressible excipient. The proposed co-precipitation technique requires only short processing time which is an advantage over spray drying technique. From the present study it can be concluded that prepared multifunctional directly compressible excipient may be serve as 'ready-to-compress' powder mixtures for any kind of drugs.

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