Research Article

Formulation and Evaluation of Co-Processed MCC Core Pellets and Confirm Its Application in Layering of Drugs with Different Solubility

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ABSTRACT

Context: Microcrystalline cellulose (MCC) is an excellent excipient for production of core pellets by extrusion spheronization. Drug layering onto the MCC core pellets in a fluidized bed processor is an industrial applicable and scalable approach. However, it causes slow release rate of poorly water soluble drugs from the pellets. Objective: The aim of this work is to prepare and evaluate co-processed MCC core pellets using extrusion spheronization technique and to confirm utility of this core pellets into development of various drug layered pellets with acceptable mechanical properties and drug release profile. Materials and methods: Co-processed excipient pellets composed of MCC, crosscarmellose sodium and sodium bicarbonate were prepared by extrusion spheronization technique and evaluated for morphology, yield, bulk density, tapped density, Carr's index, Hausner's ratio, pellet size analysis, porosity, friability, and dispersion time. Ascorbic acid, atazanavir, isoniazid, efavirenz, eprosartan mesylate and nimesulide were used as model drugs with different solubility. Drugs were layered onto the core pellets into fluidized bed processor and drug layered pellets were evaluated for bulk density, tapped density, Carr's index, Hausner's ratio, pellet size analysis, porosity, friability, dispersion time, drug content and in vitro drug release. Results and discussion: Core as well as drug layered pellets exhibit adequate morphological, flow and mechanical properties. All drug layered pellets consisted of co-processed excipient core pellets showed significant increment in drug release rate compare to drug layered pellets consisted of MCC core pellets. Conclusion: Co-processed MCC core pellets can be used to coat variety of drugs with greater accuracy and consistency in drug layering.

Keywords: Microcrystalline cellulose, drug layering, fluidized bed processor, porosity, dissolution

1. INTRODCUTION

In recent years, drug formulation scientists have recognized that single-component excipient does not always provide the requisite performance to allow certain active pharmaceutical ingredients to be formulated or manufactured adequately. There is a strong need for new excipient in the market to modulate flow property, compressibility, solubility, disintegration, stability, dissolution and/or bioavailability of a drug molecule. Developing a new adjuvant is an uneconomical and laborious from the standpoint of safety and regulatory clearances. Hence, the formulation scientists are constantly

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working on modification of existing excipients to meet the ever-changing demands of industry. Co-processed excipients are combinations of two or more excipients that possess performance advantages that cannot be achieved using a physical admixture of the same combination of excipients. They offer substantial benefits of the incorporated excipients and minimize their drawbacks. They are produced using specialized manufacturing processes like granulation, agglomeration, co-crystallization, spray-drying, etc. [1].

"Pelletization" is an agglomeration process that converts fine powders or granules into small, free flowing, spherical or semi spherical units, referred as pellets. Pharmaceutical pellets are spherical beads with a mean size between 0.5 and 2 mm. Because of their narrow size distribution, regular shape and reproducible particle surface, they are ideal for coating and multiparticulate applications. They uniformly distribute throughout the gastrointestinal tract, invariably maximize drug absorption, reduce peak plasma fluctuations and minimize potential side effects without appreciably lowering bioavailability. Extrusion-spheronization is an established and widespread technique to produce pharmaceutical pellets [2,3].

Microcrystalline cellulose (MCC) this is the most widely used excipient for the production of pellets by extrusion-spheronization due to plasticity and cohesiveness of wet mass of MCC [4, 5]. The reluctance of MCC pellets to disintegrate in aqueous media results in slow drug release, especially in the case of poorly water- soluble drugs [6]. Goyanes A *et al*. developed a co-processed excipient composed of microcrystalline cellulose (MCC), sorbitol, chitosan and Eudragit E by wet massing technique and used this co-processed excipient to prepare pellets by extrusion–spheronization. They have used Indomethacin, nifedipine, furosemide, ibuprofen, prednisolone and hydrochlorothiazide as model drugs of different solubility [7]. Co-processing of MCC pellets with other suitable excipient by extrusion spheronization to improve dissolution rate of poorly water soluble drug has not been yet tried. The aim of this work is to prepare and evaluate co-processed MCC core pellets composed of MCC, crosscarmellose sodium (CCS) and sodium bicarbonate using extrusion spheronization technique and to confirm utility of this core pellets into development of various drug layered pellets with acceptable mechanical properties and drug release profile. Drug layering onto the co-processed excipient core pellets was performed in a fluidized bed processor. Ascorbic acid, atazanavir, isoniazid, efavirenz, eprosartan mesylate and nimesulide were used as model drugs with different solubility.

2. MATERIAL AND METHODS

2.1. Materials

2.1.1. Excipients

Microcrystalline cellulose (MCC) pH 101 was received as a gift sample from RPG Life science, Ankleshwar, India. Crosscarmellose sodium (Yarrow Chem Products, Mumbai, India), sodium bicarbonate (S. D. Fine Chemicals Ltd. Mumbai, India), HPMC E5 LV (Yarrow Chem Products, Mumbai, India), talc (S. D. Fine Chemicals Ltd. Mumbai, India), hydrochloric acid (S. D. Fine chemicals Ltd., Mumbai, India), methanol and ethanol (S. D. Fine Chemicals Ltd., Mumbai, India) were purchased.

2.1.2. Active Ingredients

Ascorbic acid (Balaji Drugs, Surat, India), Atazanavir (Vapi Care Pvt. Ltd., Vapi, India), Isoniazid (S. D. Fine Chemicals Ltd., Mumbai, India), Efavirenz (Yarrow Chem Products, Mumbai, India), Eprosarten Mesylate (Vapi Care Pvt. Ltd., Vapi, India) and Nimesulide (S. D. Fine Chemicals Ltd., Mumbai, India) were used as model drugs.

2.2. Methods

2.2.1. Saturated solubility study of drugs in 0.1 N HCl

Saturated solubility study of all the selected drugs (Ascorbic acid, atazanavir, isoniazid, eprosartan mesylate, efavirenz and nimesulide) in 0.1 N HCl was performed using shake flask method. An excess amount of each drug was placed in a 25 ml glass flask containing 100 ml 0.1 N HCl. Flask

was covered with an aluminium foil and shaken (100 agitations/min) in orbital shaker for 24 hr at 37 ± 0.5^0C. After 24 hr, supernatant was withdrawn and filtered through 42 µm Whatman filter Paper. The filtrate was analyzed using a UV Visible spectrophotometer at specific wavelength after suitable dilution with 0.1 N HCl. Solubility measurements were performed in triplicate.

Table 1 Name of the drug and type of core pellets of batches F_1 to F_{12}

Sr. No.	Batch No.	Type of core pellets	Name of drug
1	F1	MCC core pellets	Ascorbic acid
2	F2	MCC core pellets	Atazanavir
3	F3	MCC core pellets	Isoniazid
4	F4	MCC core pellets	Efavirenz
5	F5	MCC core pellets	Eprosartan mesylate
6	F6	MCC core pellets	Nimesulide
7	F7	Co-processed excipient	Ascorbic acid
8	F8	Co-processed excipient	Atazanavir
9	F9	Co-processed excipient	Isoniazid
10	F10	Co-processed excipient	Efavirenz
11	F11	Co-processed excipient	Eprosartan mesylate
12	F12	Co-processed excipient	Nimesulide

2.2.2. Formulation and evaluation of MCC core pellets

The powder of MCC was weighed and granulating liquid composing of mixture of ethanol and water (40:60) was added until the wet mass was formed [8]. The wet mass was extruded through extruder having extruding screen with perforations 1 mm in diameter and 1.5 mm in thickness. The extrudates were spheronized in a spheronizer (Cronimach, India) at 1000 rpm. The resulting pellets were dried by hot-air oven at 50°C for 4 hr [9, 10]. MCC core pellets were evaluated for yield, flow property, compressibility, mean pellet size, porosity and friability.

Yield

The percentage yield of pellets were calculated by the following Equation 1.

$$\% \text{ yield of pellet} = \frac{\text{Practical yield of pellets}}{\text{Theoritical yield of pellets}} * 100 \quad \text{_____} Equation\ 1$$

Mean pellet size

Mean pellet size was estimated by the sieving method [11]. Sieves were arranged in a nest with the coarsest at the top. A sample of the dried pellets was placed on the top sieve and subjected to mechanical agitation. The sieve set was fixed and shaken for 10 minutes. The pellets retained on each sieve were weighed. The pellets were assigned the mesh number of the screen through which it passed or on which it was retained. It was expressed in terms of Arithmetic mean of the two sieves. Mean particle size was calculated using formula given in Equation 2.

$$Mean\ pellet\ size = \frac{\sum X_i F_i}{\sum F_i} \quad \text{_____} Equation\ 2$$

Where,
ΣXiFi = Weight size
ΣFi = Percentage weight retained

Flow property, compressibility and Porosity

Flow property and compressibility of MCC pellets were estimated by determining Hausner's ratio, Carr's index and angle of repose as per USP method. Porosity of pellets was determined by liquid displacement method [12, 13].

Friability

Ten g pellets (Fs) and 200 glass beads having 4 mm diameter were placed in a friabilator (Hardik Machinery, India). The sample was subjected to falling shocks for 10 min at a rotational speed of 25 rpm followed by removal of fines through a 250 µm mesh. The fraction above 250 µm (Fa) was used to calculate the friability of pellets according to Equation 3 [14].

$$\% \text{ Friability} = \frac{Fs - Fa}{Fs} \text{ X } 100 \quad \text{_____} Equation\ 3$$

2.2.3. Formulation and evaluation of co-processed excipient core pellets

The required quantities of MCC (82.56%), Sodium Bicarbonate (10.00%) and CCS (7.44%) were weighed and mixed for 10 min [15]. Granulating liquid composing of mixture of ethanol and water (40:60) was added to the mixture until the wet mass was formed. The wet mass was extruded

through extruder having extruding screen with perforations 1 mm in diameter and 1.0 mm in thickness. The extrudates were spheronized in a Spheronizer (Cronimach, India) at 700 rpm until spherical pellets were obtained. The resulting pellets were dried by hot-air at 50°C for 4 hr. Co-processed excipient core pellets were evaluated in the same manner as of MCC core pellets.

Scanning Electron Microscopy (SEM) study

Surface morphology of co-processed excipient core pellet was observed using scanning electron microscopy. Aspect ratio was calculated using image analysis software (Image J).

Fourier Transform InfraRed (FTIR) study

To confirm absence of chemical change in co-processed excipients, FITR spectrum of optimized co-processed excipients was compared with FTIR spectrum of MCC and physical mixture consisted of MCC, CCS and sodium bicarbonate. FTIR spectra were recorded in Shimadzu FTIR spectrometer within range was 400 to 4000 cm^{-1}. Optimized co-processed excipient was in pellet form hence it was crushed into powder for FTIR study.

Stability studies

Samples of co-processed excipient core pellets were kept at 40°C/75% RH and at room temperature for six months in high-density polyethylene (HDPE) bottle. Core pellets were analyzed at 0, 3 and 6 month to check the stability of co-processed excipient pellets.

2.2.4. Formulation of drug layered pellets of batches F_1 to F_{12}

Preparation of coating dispersion

Coating dispersion was composed of drug, binder (HPMC E-5), anti-adherent (talc), dye and solvents (water and alcohol). Hydroxypropyl methylcellulose (HPMC) E-5 LV (5%) was added to 70 ml water-alcohol mixture (50:50) under continuous stirring for 30 min. Four percentage drug was slowly added to the solution with continuous stirring. Finally Talc (1%) and dye were added to the above dispersion and volume as made up with alcohol: water (50:50) up to 100 ml. The dispersion was passed through 100 # sieve.

Drug layering of pellets in fluidized bed processor

Coating dispersion was layered on to the core pellets in a fluidized bed processor (Cronimach, India) by the suspension layering technique. 400g of core pellets were loaded into fluidized bed and warmed before treatment with 400 ml of drug dispersion [11]. Name of drug and type of core pellets in batches F_1 to F_{12} are mentioned in table 1.

For the drug layering, the inlet air temperature was 54°C, the outlet air temperature was 46°C, the nozzle outlet was 0.5 mm in diameter, the atomizing air pressure was ranged between 0.8 and 0.9 bar, blower rate was maintained in the range of 3 to 6 and the solution was sprayed at an initial pumping rate of 3.5 rpm gradually increasing upto 6 rpm as the coating process proceeded. The coating process was continued till 400 ml dispersion was coated onto it.

2.2.5. Evaluation of drug layered pellets

Drug layered pellets were evaluated for yield, flow property, compressibility, mean pellet size, porosity and friability in the same manner as of MCC core pellets.

Dispersion study

Pellet dispersion study was performed in water using a modified tablet disintegration tester (Figure 4.1). Sieve no. 30 having 500 µm aperture size was kept at the top and the bottom of the tube of disintegration apparatus. After filling 500 mg pellets in each tube, they were inserted in the standard tablet disintegration tester. Dispersion time of drug layered pellets consisted of MCC core and co-processed excipient core pellets were compared. Absence of pellets between sieves was considered as complete dispersion.

Drug content of drug layered pellets

Five hundred mg of pellets were crushed and transferred to 100 ml volumetric flask. 50 ml of methanol was added and sonicated for 20 min. The volume was adjusted up to mark with metha-

nol. The solution was filtered through Whatmann filter paper and diluted with methanol. The absorbance of the diluted solution was recorded using UV Visible spectrophotometer (UV-3092, Lab India, India) at 296 nm to calculate drug content per 500 mg of pellets.

In vitro drug release of drug layered pellets

Pellets equivalent to 20 mg of telmisartan were used for the dissolution studies. The dissolution was performed in 900-mL 0.1 N HCl using USP dissolution apparatus I (TDT 06T, Electrolab, India) equipped with a basket which was operated at the speed of 100 rpm and temperature of 37±0.5 °C. The amount of drug released was measured at suitable time interval using UV Visible spectrophotometer (UV-3092, Lab India, India) at 292 nm. Each dissolution study was performed in triplicate. One way ANOVA was used to check whether differences in % drug release at 30 min (% Q_{30}) between drug layered pellets consisted of co-processed excipient core pellets and that of MCC core pellets were statistically significant or not. The software package SPSS was used for statistical analysis.

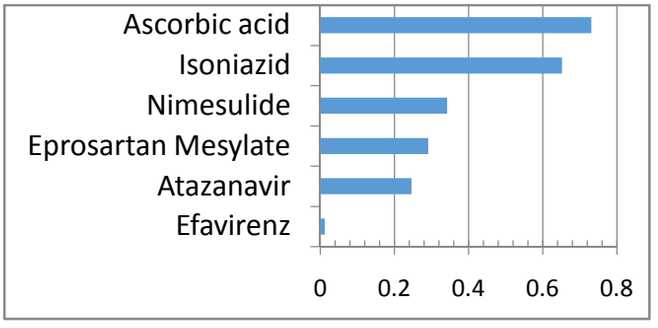

Figure 1: Saturated solubility of drug in 0.1 N HCl (mg/ml)

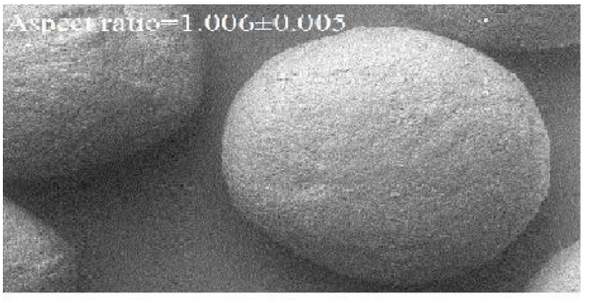

Figure 2: SEM image of optimized co-processed excipient pellets

3. RESULTS AND DISCUSSION

3.1. Saturated solubility study of drugs in 0.1 N HCl

Saturated solubility of different drugs is reported in figure 1. Solubility of drugs follow following order: Ascorbic acid> Isoniazid >Nimesulide >Eprosartan mesylate> Atazanavir> Efavirenz which is in accordance with BCS classification. Ascorbic acid is BCS class 1 drug (High solubility and high permeability) and Isoniazid is BCS class 3 (High solubility, low permeability) drug. Nimesulide, Eprosartan mesylate and Atazanavir are BCS class 2 drugs (Low solubility, high permeability) and Efavirenz is BCS class 4 drug (Low solubility, low permeability). Reason for selection of drugs with different solubility was to confirm utility of the developed co-processed excipient to all BCS class of drugs and thereby to prove versatility of the developed co-processed excipient.

3.2. Evaluation of MCC and co-processed excipient core pellets

The results of evaluation of MCC core pellets and co-processed excipient core pellets are reported in table 2 and 3, respectively. Both pellets exhibited excellent flowability and compressibility of the core pellets. There was not much difference in yield and mean pellet size of MCC and co-processed excipient core pellets. Porosity of co-processed excipient was more compare to MCC pellets due to presence of crosscarmellose sodium and sodium bicarbonate in the formulation. Friability of MCC pellets was less than co-processed excipient pellets indicated better mechanical strength of MCC pellets. However, both (MCC and co-processed excipient) core pellets exhibited acceptable friability (less than 1%w/w). Porosity was found to be directly proportional to the friability. Both (MCC and co-processed excipient) core pellets showed acceptable flow and mechanical properties and hence could be used further for drug layering process in fluidized bed processor.

Table 2: Evaluation of flow properties and average particle size of MCC core pellets

%yield	Carr's index (%)	Hausner's ratio	Angle of repose* (^{0})	Mean Pellet Size* (µm)	Porosity*(%)	Friability* (%)
95.5±4.4	7.77	1.084	26±0.95	719.10±14.23	30.6±6.65	0.21±0.02

***mean (n=3) ± SD**

Table 3: Evaluation of flow properties and average particle size of co-processed excipient core pellets

%yield	Carr's index (%)	Hausner's ratio	Angle of repose* (^{0})	Mean Pellet Size* (µm)	Porosity* (%)	Friability* (%)
84.39±4.62	7.32	1.079	27±0.12	719.9±13.9	47.2±4.67	0.39±0.04

***mean (n=3) ± SD**

Table 4: Results of stability study of optimized co-processed excipient (core) pellets

Time	Carr's index (%)	Hausner's ratio	Mean pellet size*(µm)	Friability* (%)	Porosity* (%)	Dispersion time* (min)
0	3.01	1.031	770.76± 9.72	0.17±0.02	56.27±2.06	22.09 ± 1.14
Product stored at accelerated condition of 40°C/75% RH						
3 month	3.01	1.031	765.34± 11.72	0.16±0.02	57.59±3.07	21.67 ± 2.01
6 months	3.02	1.030	771.34± 9.04	0.16±0.03	57.19±4.02	21.58 ± 2.01
Product stored at room temperature						
3 month	3.01	1.031	770.16± 11.90	0.16±0.02	58.62±2.97	22.18 ± 1.86
6 months	3.01	1.030	765.16± 10.22	0.16±0.02	57.54±3.13	22.27 ± 3.47

***mean (n=3) ± SD**

Table 5: Results of yield, bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose of drug layered pellets of batches F_1 to F_{12}

Batch	Type of core pellet	Drug	%yield*	Bulk density* (g/cm^3)	Tapped density* (g/ cm^3)	Carr's index(%)	Hausner's ratio	Angle of repose* (^{0})
F_1	MCC	Ascorbic acid	75.12±4.23	0.50±0.02	0.51±0.01	1.96	1.02	22.42±0.16
F_7	CP**		76.94±3.19	0.76±0.020	0.80±0.02	5.0	1.04	23.14±0.12
F_2	MCC	Atazanavir	84.22± 5.12	0.83±0.01	0.86±0.02	3.48	1.04	22.56±0.15
F_8	CP**		82.86± 4.25	0.74±0.01	0.76±0.02	2.6	1.03	22.96±0.5
F_3	MCC	Isoniazid	76.02± 4.34	0.50±0.01	0.52±0.02	3.84	1.05	23.50±0.55
F_9	CP**		78.74± 3.92	0.64±0.02	0.68±0.02	5.88	1.06	23.43±0.85
F_4	MCC	Efavirenz	74.92± 5.11	0.57±0.02	0.59±0.01	3.38	1.07	23.96±0.12
F_{10}	CP**		66.58±3.28	0.61±0.02	0.64±0.02	4.68	1.08	22.44±0.41
F_5	MCC	Eprosartan	84.75±3.07	0.71±0.02	0.73±0.02	2.73	1.04	22.50±0.15
F_{11}	CP**	Mesylate	80.29±4.82	0.52±0.03	0.53±0.02	1.88	1.05	22.40±1.9
F_6	MCC	Nimesulide	86.22±4.33	0.62±0.02	0.65±0.01	4.61	1.05	23.41±0.34
F_{12}	CP**		84.13±5.10	0.73±0.02	0.76±0.02	3.94	1.10	23.51±0.77

***mean (n=3) ± SD; **CP: Co-processed excipient**

Scanning Electron Microscopy (SEM) study

SEM photomicrograph of co-processed excipient pellets (Figure 2) showed that the pellets were spherical in nature and had a smooth surface. Aspect Ratio (AR) was found to be 1.006 which assured sphericity of the pellets.

Fourier Transform InfraRed (FTIR) study

The FTIR spectrum of MCC powder, co-processed excipient and physical mixture is displayed in figure 3. The peaks of MCC pellets were preserved in physical mixture as well as co-processed excipient which confirmed absence of any chemical reaction while co-processing. Co-processed excipient doesn't involve any chemical reactions in existing approved excipients.

Stability study

There was no significant difference ($p < 0.05$) was observed among results of Hausner's ratio, Carr's

index, mean pellets size, porosity, friability and dispersion time of the developed co-processed excipient core pellets at 0, 3 and 6 months which proved stability of the developed co-processed excipient upto 6 months at accelerated conditions (Table 4).

3.3. Evaluation of drug layered pellets of batches F_1 to F_{12}

The results of evaluation of drug layered pellets of batches F_1 to F_{12} are pellets are shown in table 5 and 6. Hausner's ratio, Carr's index and angle of repose indicated excellent flowability and compressibility of pellets of all the batches. Size of pellets of all batches was in acceptable range (0.5 to 1.5 mm). Friability of drug layered pellets consisted of MCC core pellets were less than the co-processed excipient core pellets but it was within acceptable limit (less than 1%w/w). Drug layered pellets prepared using MCC core pellets did not disperse even up to 90 min. All drug layered pellets prepared using optimized co-processed excipient core pellets completely dispersed within 26.17 ± 2.14 min due to presence of superdisintegrant and pore former in the formulation. High porosity and faster dispersion favoured faster drug release from drug layered pellets having co-processed excipient core pellets compare to MCC pellets. Cumulative % drug release at 30 min (% Q_{30}) was kept as one of the most critical quality attributes for drug product development as it is immediate release product. Percentage Q_{30} for all the drugs in pellets with MCC core pellets was in the range of 47.92 to 60.32%, hence there was a need for co-processing of MCC with other excipient to improve drug dissolution rate. Solubility of drugs showed definite impact on % Q_{30}. As solubility of drug increased, % Q_{30} from pellets also increased. Percentage porosity of drug layered pellets with co-processed excipient core pellets was higher than the MCC core pellets. Comparative *in vitro* drug release profile of drug layered pellets consisted of MCC pellets and co-processed excipient core pellets are displayed in figure 4.

In co-processed excipient, sodium bicarbonate was added as a pore former and crosscarmellose sodium was added as a superdisintegrant with MCC which enhanced the porosity of the formulation, reduced friability and increased % $Q_{30.}$ As per one way ANOVA, statistically significant differences (sig. value < 0.05) were found between percent Q_{30} of drug layered pellets consisted of co-processed excipient core pellet and those of MCC core pellets. Kallai N *et al.* prepared Isomalt, Sugar, and Microcrystalline Cellulose Inert cores and drug was layered onto it. He noticed significant difference in drug release in all three pellets. Starter cores potential influences on drug release but there is still only limited data available about the effect of the starter core on layered drug. In present study, co-processed excipient core pellets favors solvent entry into the pellets due to high porosity compares to MCC pellets. Pellets filled with medium could be beneficial to the dissolution of drugs with poor solubilities [16].

4. CONCLUSION

Co-processed MCC core pellets consisted of co-processing of MCC with sodium bicarbonate and crosscarmellose sodium by extrusion spheronization technique was successfully formulated and evaluated. Flowability, compressibility and mean pellet size of developed co-processed excipient core pellets were similar with MCC core pellets but porosity and friability of co-processed excipient core pellets were higher than the MCC core pellets. Drugs with different solubility were successfully layered onto the developed core pellets in fluidized bed processor. Drug layered pellets consisted of co-processed excipient core pellets exhibited acceptable pellet size, flow property, compressibility, friability and porosity. Porosity, friability, drug content and %Q_{30} of drug layered pellets consisted of co-processed excipient core pellets were higher than the MCC core pellets. There was a significant improvement in dispersion time and drug release rate from drug layered pellets consisted of co-processed excipient core pellets compare to MCC core pellets due to presence of pore former and superdisintegrant in the formulation. Developed co-processed MCC core pellets can be used to coat drugs with different solubility. Hence, its commercial viability needs to be exploited in all cases.

Table 6: Results mean pellet size, porosity, friability, drug content/500 mg of pellets and % drug release at 30 min (%Q_{30}) of drug layered pellets of batches F_1 to F_{12}

Batch	Type of core pellet	Drug	Mean pellet size* (µm)	Porosity* (%)	Friability* (%)	Drug content (mg) */500 mg of pellets	%Q_{30}
F_1	MCC	Ascorbic acid	745.53±12.38	30.67±1.80	0.38±0.03	21.48 ±2.12	60.32± 0.47
F_7	CP**		656.68±14.91	48.40±2.86	0.42±0.01	20.82 ±3.86	77.41± 3.20
F_2	MCC	Atazanavir	695.35±11.54	31.46±1.63	0.28±0.02	22.64 ±4.12	52.75± 1.66
F_8	CP**		698.68±14.26	54.98±1.76	0.56±0.01	25.75 ±3.28	73.85± 5.43
F_3	MCC	Isoniazid	726.76±13.37	31.80±1.80	0.32±0.01	38.21 ±1.16	53.21± 1.02
F_9	CP**		745.33±9.17	44.66±0.77	0.39±0.03	39.25 ±1.92	72.30± 1.15
F_4	MCC	Efavirenz	688.29±10.28	39.34±2.03	0.32±0.02	37.65 ±1.67	47.92± 0.40
F_{10}	CP**		675.37±14.22	43.91±0.26	0.46±0.03	38.91 ±3.02	57.19± 1.87
F_5	MCC	Eprosartan	745.36±5.69	31.01±0.99	0.38±0.04	25.71 ±2.16	53.31±2.32
F_{11}	CP**	Mesylate	733.65±10.15	45.24±1.01	0.5±0.06	22.93 ±3.19	70.11±1.41
F_6	MCC	Nimesulide	698.47±13.35	35.57±1.93	0.33±0.01	30.64 ±4.01	53.50±1.87
F_{12}	CP**		685.36±10.86	42.62±1.77	0.56±0.02	27.45 ±3.68	70.61±2.09

***mean (n=3) ± SD; **CP: Co-processed excipient**

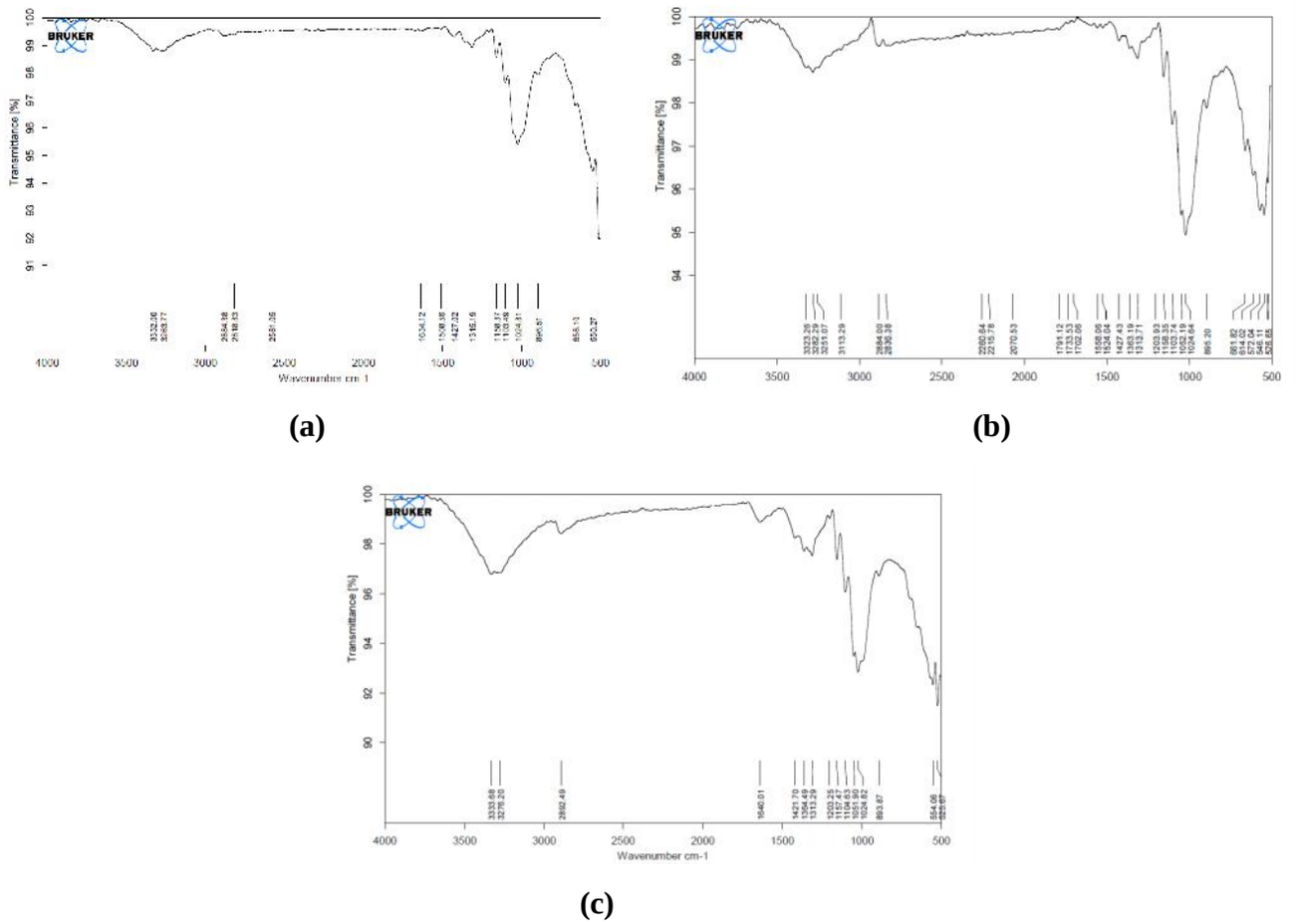

Figure 3: FTIR study of (a) MCC (b) Physical mixture of MCC with CCS and sodium bicarbonate (c) Optimized co-processed excipient pellets

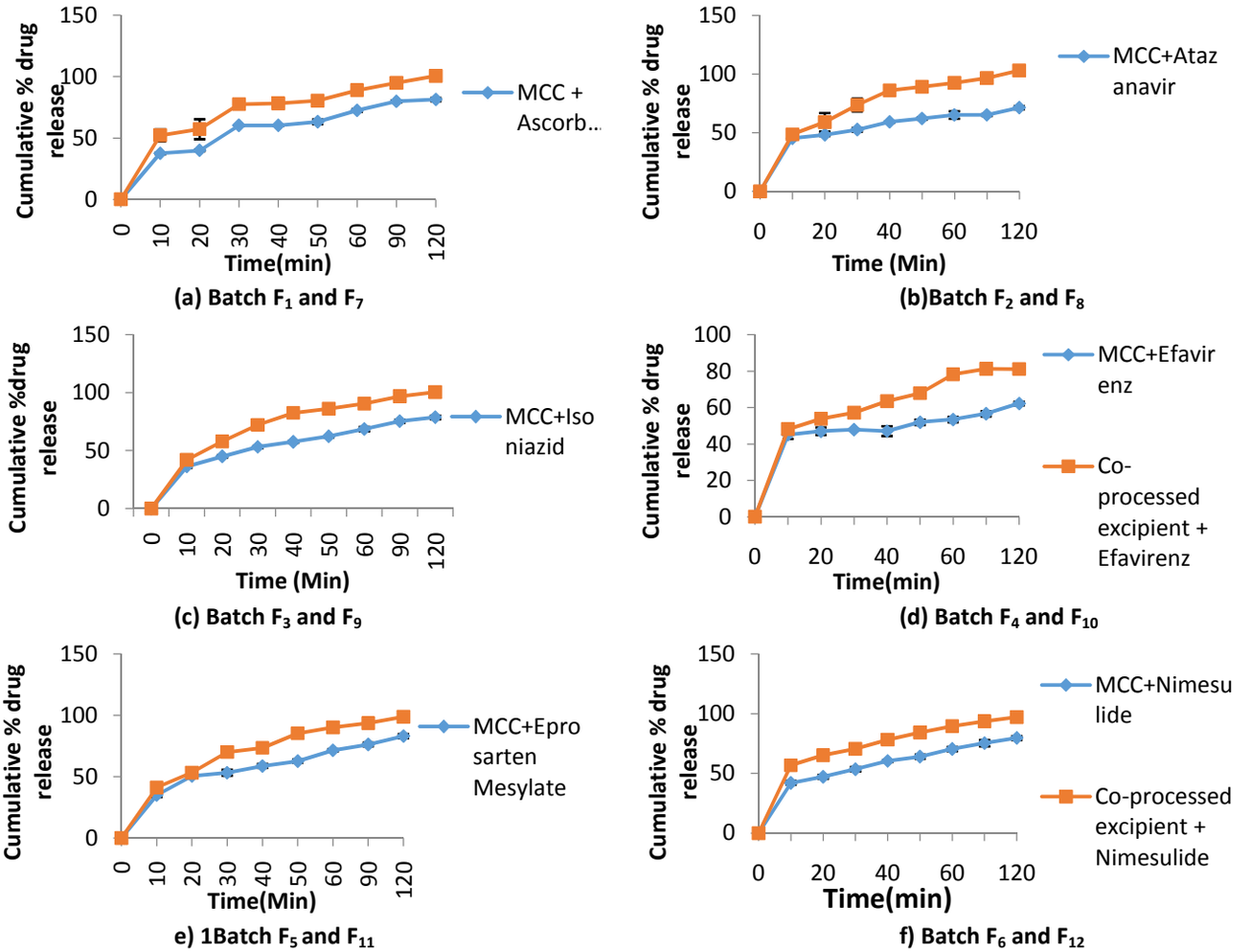

Figure 4: Comparative dissolution of drug layered pellets consisted of MCC core pellets with co-processed excipient core pellets

5. ACKNOWLEDGEMENT

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