Design and Evaluation of a 3-Component Composite Excipient "Microcrystarcellac" as a Filler-Binder for Direct Compression Tabletting and it's Utilisation in the Formulation of Paracetamol and Ascorbic Acid Tablets

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Abstract

A research was conducted to design and evaluate a highly functional 3-component composite fillerbinder for direct compression. Tapioca starch (NTS) was modified physically at molecular level by annealing and enzyme hydrolyzed to obtain microcrystalline tapioca starch(MCTS) which was coprocessed with LMH and microcrystalline cellulose (MCC) to yield Microcrystarcellac (MSCL). NTS was extracted from cassava tuber (Mannihot esculenta crantz) using a standard method. The powder suspensions were prepared in concentration of 40

Index terms— Microcrystarcellac, Coprocessed Excipient, Directly compressible Excipient, Highly functional Filler-binder, Microcrystalline Tapioca Starch.

1 I. Introduction

he growing performance expectations of excipients to address issues such as flowability, compactibility, disintegration, dissolution and bioavailability also placed a demand for newer excipients with high functional property.

Co-processing excipients lead to the formation of excipient granulates with superior properties compared with physical mixtures of components or with individual components. They have been developed primarily to address the issues of flowability compressibility, and disintegration potential, with fillerbinder combinations being the most commonly tried. The combination of excipients chosen should complement each other to mask the undesirable properties of individual excipients and, at the same time, retain or improve the desired properties of excipient. For example, if a substance used as a filler-binder has a low disintegration property, it can be coprocessed with another excipient that has good wetting properties and high porosity because these attributes will increase the water intake, which will aid and increase the disintegration of the tablets.

Material science plays a significant role in altering the physicomechanical characteristics of a material, especially with regard to its compression and flow behaviour. Coprocessing excipient s offers an Design and Evaluation of a 3-Component Composite Excipient "Microcrystarcellac" as a Filler-Binder for Direct Compression Tabletting and it's Utilisation in the Formulation of Paracetamol and Ascorbic Acid Tablets properties. Materials, by virtue of their response to applied forces, can be classified as elastic, plastic, or brittle materials. Pharmaceutical materials exhibit all three types of behavior, with one type being the predominant response. Coprocessing is generally conducted with one excipient that is plastic and another that is brittle.. This particular combination prevents the storage of too much elastic energy during compression, which results in a small amount of stress relaxation and reduced tendency of capping and lamination 1 . A combination of plastic and brittle materials is necessary for optimum tabletting performance. Hence, coprocessing these two kinds of materials produces a synergistic effect, in terms of compressibility, by selectively overcoming, the disadvantages. Such combinations can help improve functionalities such as compaction performance, flow properties, strain-rate sensitivity, lubricant sensitivity or sensitivity to moisture or reduced hornification. Cassava tubers were washed and peeled to remove the outer skin and rind with the aid of a handy stainless knife. The peeled tubers were washed with freshly distilled water and rasped.

2 II. Materials and Methods

The rasp consists of a sheet of metal plate perforated with nails, clamped around a stainless bucket with the protrusions facing outwards. The tubers were then manually rasped to a pulp on the stationary grater (which is the metal plate perforated by nails). Water was applied in small quantities continuously to the rasper. The process was continued until the whole tubers were turned into a fine pulp in which most but not all of the starch granules were released.

After rasping, pulp from the sump was then pumped on to a nylon fastened /clamped around a stainless bucket. A small spray of water was applied to assist the separation of starch granules from their fibrous matrix and to keep the screen mesh clean while water was added, the mass were turned manually to aid the release of the granules. Starch granules carried with the water fall to the bottom of the bucket in which the sieve was placed. The starch milk was then allowed to sediment, by standing for a period of 8 h. The starch settled at the bottom of the bucket and the supernatant liquor decanted. The sediment / fine granules were centrifuged. After the removal of free water from the starch, cake was obtained. The starch cake was then crumbled into small lumps (1-3 cm) and spread out in thin layers on stainless trays and air dried for 120 h 2,3 .

ii. Preparation of microcrystalline Tapioca Starch (MCTS) hundred gram (500 g) of tapioca starch granules were weighed into five places and each placed in a 1000 ml capacity conical flask. Six hundred millimeters (600 ml) of freshly distilled water was added to each content of the flask to make a suspension (= 40 %w/w). The pH of the medium was adjusted to between 6.5 and 7.0. All the flasks were placed on a digitalized water bath and the starches were annealed at 60 o C for 30 min. Each flask was dosed with 0.5 ml of ?-amylase (0.1 % v/w d.s) at 60oC on water bath and was allowed to stand for hydrolysis to take place at various length of specified time: 60, 120, 180, 240, and 300 min). At the end of the first 60 min., the enzyme reaction in one of the flasks was terminated by adjusting the pH to 2.0 with 0.4 N HCL after which the pH was raised to 6.5 with 0.4 N NaOH. The medium was filtered through a Buckner funnel; the residue was washed 3 times, with distilled water and finally dehydrated by adding enough isopropanol (99 %) (a water -miscible solvent) and the resulting dehydrated highly crystalline starches were air dried . These procedures were repeated for the remaining hydrolyzed starches at other times.

iii. Preparation of Three Component Composite Filler-Binder (Microcrystarcellac) by Codried method. The working formula for preparation of the novel three component composite excipient (microcrystarcellac).

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Material Batch % (w/w)

4 Five

The slurry form of annealed enzyme hydrolyzed tapioca starch (MCTS) (sieved fraction, <75 µ) was coprocessed with ?-lactose monohydrate (? -L-MH) (sieved fraction, <75 µ), and microcrystalline cellulose (MCC) (sieve fraction, <75 µ). The slurry was made by suspending the MCTS in a solution of Isopropranol and freshly distilled water in ratio 2:1 respectively. MCTS slurry was blended with ? -L-MH, and MCC at concentrations indicated in Table 1 as a dried mass relative to MCTS. The composite slurry was stirred vigorously with a stirrer until a semi-solid mass easily ball was formed. The composite mass was then granulated through a 1500 µ and codried at 60oC until a constant weight was reached. Codried granules were pulverized and sized by passing through mesh size 500 µm, and the fraction between >75 -250 µm was reserved. The powder and tabletting properties of the codried products were evaluated and compared to those of corresponding components and physical mixtures.

5 iv. Compactibility

The preliminary study was carried out to select few promising batches: (1) the best batch out of the five batches of hydrolyzed starch (MCTS) having the best tablet properties to be coprocessed with lactose and MCC, (2) the best two batches (out of five) of coprocessed filler-binder for microstructuring before compaction studies.

The native tapioca starch, and the microcrystalline tapioca starch at various time of hydrolysis were compressed on a single punch Erweka tabletting machine (Erweka, AR 400. Germany), fitted with 10.5 mm diameter flat faced punch and die. Tablet target was 500 mg, and pressure load used range from 4 to 7 KN.

The coprocessed filler-binder: MSCL (5 batches each) were subjected to the same procedure to streamline the batches to just two for effective research and particle restructuring. The batches chosen here were subjected to particle sieving and further employed for compaction studies.

6 v. Compaction Studies a. Preparation of Compacts

Compacts of weights, 500 mg, of each of the primary powders [tapioca starch, microcrystalline cellulose (MCC), lactose], annealed tapioca starch (ATS), annealed enzymatically hydrolyzed tapioca starch (MCTS), Microcrystarlac (B4 and B5), Microcrystarcellac (B2 and B3), physical mixture of MCTS and lactose; MCTS, lactose and MCC, were made using a single punch carver hydraulic hand press (model, C, Carver Inc. Menomonee Falls, Wisconsin, U.S.A) at machine compression force ranging from 2.5 KN to 12.5 KN. Fourty compacts were made at each compression level for individual material. Before compression, the die (10.5 mm diameter) and the flat faced punches were lubricated with a 1 % w/v dispersion of magnesium stearate in ethanol-ether (1:1). The compacts were stored over silica gel for 24 hours (to allow for elastic recovery and hardening and to prevent falsely low yield values) before evaluations. The dimensions (thickness and diameter) and weight uniformity of ten compacts were determined. The relative density, D, were calculated as the ratio of density of the compact, Dt to the particle density, Dp of individual powder or composite. The data obtained using 'ejected tablet method (out-of-die)' were used to obtain the Heckel plots. The weights, W, and dimensions were then determined respectively, and their relative densities, D, were calculated using the equation: **??**————————————-(1) Where V t is the volume of the tablet in cm 3 , and P s is the particle density of the solid material in gcm -3 .D = W/ [V t x P s] -

Heckle plots of ln (1/ 1 -D) versus applied pressure "P" 6 and Kawakita plots of P/C versus P, 7 were constructed for the composite excipients.

Linear regression analysis was carried out over a compression range 2.5, 5, 7.5, 10, and 12.5 KN. The parameters from Heckel plots were calculated. The Kawakita equation was employed to determine the extent of plastic deformation the material undergoes.

7 b. Moisture content

The moisture content (MC) of the powder was determined by weighing 100 g of the powder after which it was heated in an oven at a temperature of 105 °C until a constant weight was obtained.

The moisture content was then calculated with the following formula:MC = (1 -W t /W 0) X 100 ———— ——————**(2)**

vi. Determination of Flow Rate and Angle of Repose Angle of repose was determined using a standard method and equation 3 bellow. vii. Densities a. True (particle) densities

The true (particle) densities of the primary powders (tapioca starch and mcc-derived), annealed starch, annealed enzymatically hydrolyzed tapioca Where W t and W 0 represent weight of powder after time ' t' and the initial weight before heating respectively.

starch and the composite particles were determined by the liquid displacement method using a specific gravityD p =W/[(a + W) -b] x SG ——————(4)

Where, W, is the weight of powder, SG, is the specific gravity of the solvent, a, is the weight of bottle plus solvent, and, b, is the weight of bottle plus solvent plus powder. The measurement was performed in triplicate.

8 b. Bulk and Tap density

9 Bulk density

These parameters were determined by weighing 50 g quantity of each granule/powder and pouring into a 100 ml measuring cylinder. The volume (V o) was recorded as the bulk volume. The total weight of the granule/powder was noted. The bottom of the cylinder was raised 10 cm above the slab and made to fall on the platform continuously for 100 taps. The volume of (V t) of the granule was recorded, and this represents the volume of the granules minus the voids and is called the tapped volume. The final weight of the powder too was recorded as the tapped weight.

The bulk and tapped densities were calculated as:B d = W/V o ———————————————— ——————**(5)**B t = W/V t ————————————————**(6)**

Where, B d and B t , are bulk and tapped density respectively, and W, is the weight of the powder (50 g). The results presented are the mean of three determinations.

10 Carr's Index

Carr's Index (CI) = (? T? o)/? o x 100 % —————— (7) Where ? o is the poured or bulk density and ?k is the tapped density.

11 viii. Evaluation of Tablets

Weight variation Limit Test: The weights of 10 tablets were determined individually and collectively on a Metler balance (Denver, XP-300, U.S.A). The mean weight, percentage (%) deviation from the mean and standard deviation were calculated.

a. Thickness of Tablets The thickness of the tablets was measured with the aid of micrometer screw gauge. Five tablets were selected randomly and the thickness for each was measured and the mean value determined.

b. Hardness of tablets Crushing strength was determined using an electronic/digitalized tablet hardness tester (model EH O1, capcity 500 N,Indian).

12 c. Friability

The friability test was performed for the tablets formulated in a friabilator (Erweka, TA 3R). The weight of 10 tablets was determined on a Metler balance (Denver, XP -300, U.S. A). The tablets were placed in the friability and set to rotate at 25 r.p.m for 5 min after which the tablets were de-dusted gently and their weight determined. The difference was calculated and the percentage loss in weight and hence the value of the friability was calculated.

Compact Volume: The volume of a cylindrical tablet having radius 'r' and height 'h' is given by the following equation. Compact density: The compact density of a tablet was calculated from the following equation. The tensile strength of the normal tablets (T) was determined at room temperature by diametral compression 9 using an hardness tester (model EH O1, capacity 500 N, Indian) and by applying the equation : **??**—————————————————————-(10) Where T is the tensile strength of the tablet (MNm-2), F is the load (MN) needed to cause fracture, d is the tablet diameter (m). Results were taken from tablets which split cleanly into two halves without any lamination. All measurements were made in triplicate, and the results given are the means of several determinations.T = 2 F / (?dt) -

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Compression pressure: This was derived from the relationship between the applied pressure and surface area.

15 C.P. =

Applied force e. Disintegration Time ??????..(11) Surface area of tablet Disntegration apparatus (Erweka, ZT 3, Germany) was employed. Three tablets were placed in each compartment of the disintegration basket which was lowered into a glass beaker (1 L capacity) filled with deionized water to 800 ml mark and in turn was placed i n a water bath maintained at 37 o C. The time taken for the disassociated tablet particles to pass through the mesh was recorded as the disintegration time. Average of three readings was taken as the disintegration time.

16 ix. Determination of dilution capacity

Ascorbic acid and paracetamol were used as model drugs representing both highly water soluble, Formulations were blended by method of dilution and lubricated with 1 % magnessium stearate. Each batch was compressed for 30 seconds on single moisture sensitive, and elastic/poorly water soluble active ingredient respectively.

Model drugs were blended in deferent ratios, ranging from 0 %, 5 %, 10 %, up to 50 % with MCTS, microcrystarlac and microcrystarcellac. 7.5 KN, target weight of 500 mg. Compacts were allowed to relax for 24 h post compression. Compact dimensions (diameter and thickness) were determined using a digitalized vernial caliper. Crushing strength was determined using an electronic/digitalized tablet hardness tester (model EH O1, capcity 500 N,Indian). A relationship between amount in percent (%) of model drug added to the formulation and the tensile strength will be generated.

In general, the capacity was expressed by the dilution potential as being an indication of the maximum amount of active pharmaceutical ingredient that can be compressed with the excipient, while still obtaining tablets of acceptable quality (that is, acceptable crushing strength average of 60 N, friability, < 1.0 %, good disintegration time < 15 min, and must meet the requirement of U.S.P weight variation limit test). Table 2 compares the granule properties of coprocessed MSCL (MCTS 40 %: LMH 40 %: MCC 40 %) with the direct physical mixtures of the same ratio, Starlac®, Cellactose® and MCC. The result illustrates an increase in flow properties of coprocessed MSCL over that of the direct physical mixture as reflected by flow rate 2.0 g/s, for the former and 0.45 g/s, for the later respectively. The corresponding angles of repose are 32 o and 47.8 o respectively. The compressibility indices as reflected in the table are: 13.4 % and 52 % respectively. All these results indicate improvement in both flow property and compressibility of MSCL after coprocessing over direct physical mixture of the same ratio. The coprocessed granules were restructured by sieving to remove the fine and granules greater than 250 µm. The MSCL granule distribution in percent cumulative retained oversize versus granule size in micrometer (Fig. **??**) shows that 100 % of the granules were within 90 -250 µm range. The free flowing characteristics of MSCL could be attributed to this structured granule size range.

17 III. Results and Discussion

were greater than 250 µm and all the granules (100 %) were greater than 90 µm, this range of granule size distribution was responsible for the improved flow property over individual and the direct physical mixture of the primary excipients. Fig. **??** was an illustration of the granule size compact density with pressure, and appears lower than the curves for the standard excipients this is due to low porosity of the former compare to the later. As the porosity approaches zero, plastic deformation may be predominant mechanism for all powder material (Heresy and Rees, 1971: York and Pilpel, 1972) Fig. 4.26 shows the result of the compactibility studies, it illustrates the relationship between compression pressure and radial tensile strength for MSCL. The curve is similar to Heckel plot, it has two portions, and the early part representing consolidation as a result fragmentation, and some degree of plastic deformation, followed by a linear portion illustrating the consolidation behavior as a result of plastic deformation.

18 iii. Friability of MSCL (Placebo tablets) compression pressure on the friability of MSL compacts.

There is a direct relationship between tablet hardness and compression pressure. Friability declined with both increase in compression pressure and tablet hardness. It can be seen that as the compression pressure increases from 2.5 N to 12.5 N, friability also decreases from 1.25 % to 0.5 % for MSCL.

19 iv. Disintegration Time of MSCL (Placebo tablets)

The presence starch granules in MSCL are expected to impact disintegration property. The disintegration time is mostly influenced by tablet compression force on disintegration time for MSCL, Starlac, Cellactose and MCC. Disintegration time increases with increase in tablet hardness which is proportional to the applied pressure. The DT for all the compacts of MSCL formed between compression force 2.5 N and 12.5 N ranges from < 2min. to 3 min. The corresponding values for Starlac and Cellactose are: all < 1 min., and < 1 min to 17 mim., respectively. The B.P.C (1988) specified standard for conventional tablet to be 15 min. MSCL with disintegration time of 3 min. can be regarded as having a good inherent disintegrant property.ln 1/[1 -D] = kp + A

Where, D is the relative density of the compact, 1 -D is the pore fraction, and p is the pressure. 'A' and 'k' are constants of Heckel equation. The parameter A is said to relate to low pressure densification by interparticle motion, while the parameter k indicates the ability of the compact to densify by plastic deformation after interparticle bonding. Fig. ?? shows the plot of ln 1/[1 -D] vs p for MSCL, Starlac®, Cellactose® and MCC. The plot of MSCL can be divided into threephases, namely: 29 MNm -2 < p < 58 MNm-2, 58 MNm -2 < p < 116 MNm-2, and 116 MNm -2 < p < 144 MNm -2 , each of which basically obeys the Heckel equation. There is nonlinearity in the first phase (early stage) at low pressure which suggests that MSCL undergo fragmentation and rearrangement before plastic deformation ??Odeku and Itiola, 2007). Under low pressure (p < 58 MNm -2) the compaction would mainly result in the elimination of voids among the loose particles through rearrangement, fragmentation and some degree of plastic deformation, leading to rapid densification of MSCL. On the second phase from ~58 MNm -2 to ~116 MNm -2 , however, plastic deformation of MSCL particles would be responsible for the densification of MSCL compact. The third phase from ~116 MNm-2 to ~144 MNm-2, here, following decompression, an expansion in tablet height is represented by increased tablet porosity.

Table 3 show values of the mean yield pressure, P y ; the relative densities D o , D A , and D B for MSCL, Starlac®, Cellactose® and MCC. P y , is inversely related to the ability of the material to deform plastically under pressure. Low value of P y indicates a faster onset of plastic deformation (Odeku and Itiola, 1998). The P y obtained for MSCL, Starlac®, Cellactose® and MCC are: 22.3 MNm -2 , 143 MNm -2 , 24.2 MNm -2 and 25 MNm -2 respectively. From the values of P y stated above, MSCL shows faster onset of plastic deformation than Starlac®, Cellactose® and MCC. The yield value of MSCL reflects better densification at low pressure than Starlac®, Cellactose® and MCC. Shangraw et al.,(1981) explains that, a large value of slop (i.e., low P y value) is an indication that the onset of plastic deformation occurs at relatively low pressure and vise visa. This analysis has been extensively applied to pharmaceutical powders for both single and multi-component systems (Duberg and Nystrom, 1986;Itiola, 1991). D A , represents the total degree of densification at zero and low pressures

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ii. Tablet properties (Placebo tablets) free from chipping and lamination. This is an evidence of a good and acceptable tablet formulation.

MSCL was subjected to compressibility and compactibility studies. The material was compacted using a single punch Carver hydraulic hand press (model, C, Carver Inc. Menomonee Falls, Wisconsin, U.S.A) over a pressure range of 2.5 to 12.5 KN. The MSCL tablets (Fig. 7) appeared smooth, Fig. 3 shows the effect of increasing hardness. Fig. 4 shows the effect of increasing and Chow, 1981). The relative density, D B , describes the phase of rearrangement of particles in the early stages ??Paronen and Juslin, 1983; ??itreveji et al., 1996), (Roberts and Rowe, 1985). Do, is used to describe the initial rearrangement phase of densification as a result of die filling. D o is equal to the ratio of bulk density at zero pressure to the true density of the powder (Chowhan of compression and tends to indicate the extent of particle or granule fragmentation. From Table 3 Where, a and b are constants ('a' gives the value of the minimum porosity of the bed prior to compression while 'b', which is termed the coefficient of compression, is related to the plasticity of the material) and C is the volume reduction, i.e., C = (V o -V)/ V o (here V o and V are initial volume and the volume after compression, respectively). The

Kawakita equation indicates that p/C is proportional to the applied pressure p. Fig. **??** shows the plot of p/C vs p for MSCL,"Starlac®, and Cellactose®. One can see that a linear relationship exists between p/C and p in the whole pressure range investigated at correlation coefficient (R 2 = 0.982), which indicates that the densification behavior of MCTS is consistent with prediction from the Kawakita equations. By best fitting of the experimental data to the equation above one obtains: p/C =1.64 p + 26.73 Hence, by relating the two formulae above, the value of "a" is obtained as 0.610 and "b as 0.0613 (1/b = 16.3).

The Di (=1 -a) indicates the packed initial relative density of tablets formed with little pressure or tapping **??**Lin and "Chain, 1995). Table 4 shows the Di values for MSCL, Starlac®, and Cellactose® as: 0.390, 0.474, and 0.286, respectively. It can be seen that at low pressure MSCL tablet is better packed than Cellactose tablets, but less in packing relative to Starlac tablet. This result is not far from the fact that packing of vi. Dilution capacity/potential Tablets formulated from MSCL (55 %) and PCM (45 %) as shown in Figure **??**1, were smooth, free from chipping and lamination. More so, tablets formulated from MSCL (50 %) and AA (50 %) were also characterized by the same good and acceptable tablet qualities.

a. Disintegration Time MSCL-Model drug Fig. 12 shows the declining disintegration time with increasing percentage of API. It can be seen that the DT of MSCL -PCM and MSCL -AA ranges between ~2.1min., down to ~0.42 min., for the former and ~3.8 min., down to 1.5 min., for the later respectively. One can see that the disintegrant properties of MSCL is more pronounced in the formulation containing poorly compressible and water insoluble API (PCM) than in formulation containing highly water soluble and moisture sensitive API (AA). compaction process. The lower the value of P k , the higher the degree of plastic deformation occurring during compression (Itiola, 1991). The pressure term P k has been shown to provide a measure of the total amount of plastic deformation occurring during compression (Odeku and Itiola, 1998). Hence, from the results of P k values, MSCL is more plastically deformed during compression than Starlac®, and Cellactose®. Fig. **??**0 and 11 Illustrates the relationship generated from the amount in percent (%) of API compressed with MSCL and the crushing strength. It can be seen that tablet strength declined with increasing amount of API until it reaches a point where the tablet strength, friability and the physical structure failed to meet the official standard. Table **??** showed the summary of the result of the dilution potential. MSCL was compacted with PCM and AA in predetermined percentages as model drug (API).One can see that MSCL was able to form acceptable compact with maximum of 45 % of the former (crushing strength is 70 N and friability, 0.6 %, disintegration time, 23 sec.), and with 50 % of the later (crushing strength is 68 N and friability, 0.4 %, disintegration time, 90 sec.). Hence, MSCL -PCM-45 % and MCTS -AA -50 % are both acceptable dilution capacity/potential. MSCL can therefore be used for formulating poorly compressible API, highly compressible, moisture sensitive API. a material with applied pressure is determined by deformation propensity.

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Table 4 shows the values of 1/b (P k) obtained for MSCL, Starlac®, and Cellactose® as: 16.3, 19.1, and 17.0 respectively. The reciprocal of b yields a pressure term, P k , which is the compression pressure, required to reduce the powder bed by 50 % (Shivanand and Sprockel, 1992). The value of P k gives an inverse measurement of plastic deformation during vii. Brittle Fracture Index (BFI) Both MSL and MSCL possessed BFI values as 0.1 and 0.08 respectively (Theoretical value range is 0 -1). BFI has been used as a measure of plastoelasticity of pharmaceutical powders. A low BFI value indicates the ability of the material to relieve localized stresses while a value approaching unit indicates a tendency of the material to laminate or cap.

The P values obtained at 95 % confidence interval for MSL and MSCL sampled at 6 months interval were >0.05, hence, the mean of differences does not differ significantly.

The P value obtained for MSL-PCM paired with Cellactose-PCM was >0.05, the result was considered not significant.

The P value for MSCL-AA paired with Cellactose-AA was >0.05, the result was also considered not significant.

23 IV. Conclusion

The crushing strength for NTS, ATS and MCTS are: 30 N, 90 N and 100 N after 3 h of annealing and hydrolysis respectively, compressed at 6 metric units.

MSCL have improved functionality over direct physical mixture of the primary excipients. The compression pressure, required to reduce the powder bed by 50 % (onset of plastic deformation) P y (yield value) are: MSCL (22.3 MNm -2)>Cellactose (24.2 MNm -2)>MCC (25 MNm -2)> Starlac (143 MNm -2). The degree of plastic deformation occurring during compression (P k) is in the following order: MSCL (16.3 MNm -2)> Starlac®(17 MNm -2)>MCC (18.6 MNm -2)>Cellactose® (19.1 MNm -2). From these two parameters (Py and Pk), MSCL has been established to be more superior to the three standard excipients namely: Starlac, Cellactose, and MCC.

The dilution potential obtained for MSCL compacted with paracetamol (PCM) and ascorbic acid (AA) as active drug (API) are: 50 % AA with MSCL, 45 % PCM with MSCL. MSCL is superior in functionality than Starlac, Cellactose and MCC. The hardness of MSCL active ingredient in 15min, and it can be seen from the table that the T90% ranges from 12-14min for the formulations, and they compared favourably with Cellactose® and much better than Starlac ®.

From the table 4.18, the rate constants obtained from dissolution data presents the following sequence of dissolution order: KD at t = 10min. MSCL -AA (11.0 x 10 -3 mg min -1) > Cellactose -AA (10.3 X 10-3) Cellactose -PCM (9.3 x 10 -3 mg min -1) > MSCL -PCM (7.5 x 10 -3 mg min -1).

MSCL performed better than MSL, Starlac ®, and rated equal with Cellactose® in PCM and AA tablet formulations in terms of functionality. It can be used to formulate low dose up to 225 mg poorly soluble and poorly compressible API (i.e., 45 % of tablet weight) in which PCM represents the class of drug. Moreover, it formed better tablet with low dose up to 250 mg poorly compressible, highly soluble and moisture sensitive API (i.e., 50 % of tablet weight) this class of drug is represented by AA.

The combination of plastic and brittle materials in both MSL and MSCL helped to reduce storage of elastic property. Lamination or capping is s normally a result of high storage of elasticity. viii. In-vitro Drug ig.13 also illustrate the graphs of percentage (%) drug release versus time (min) for MSCL -PCM and MSCL-AA. The table 4.19 shows T90% to be 13min and 12min respectively, and 100% of the drugs were released from both formulations in 15 min. The dissolution rate constant (KD) for both formulations at 10min were calculated to be 7.5 x 10-3 mg min-1 and 11.0 x 10-3 mg min-1 respectively.

24 ix. Statistics

Figure 1:

[1] [2] [3] [4] [5]

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[1] © 2012 Global Journals Inc. (US) © 2012 Global Journals Inc. (US) 2

[2] © 2012 Global Journals Inc. (US) bottle with Xylene as displacement fluids, and the particle density, D p , computed according to the following equation: Design & Evaluation of A 3-Component Composite Excipient "Microcrystarcellac" As A Filler-Binder for Direct Compression Tabletting & it's Utilisation in The Formulation of Paracetamol & Ascorbic Acid Tablets

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[5] Design & Evaluation of A 3-Component Composite Excipient "Microcrystarcellac" As A Filler-Binder for Direct Compression Tabletting & it's Utilisation in The Formulation of Paracetamol & Ascorbic Acid Tablets

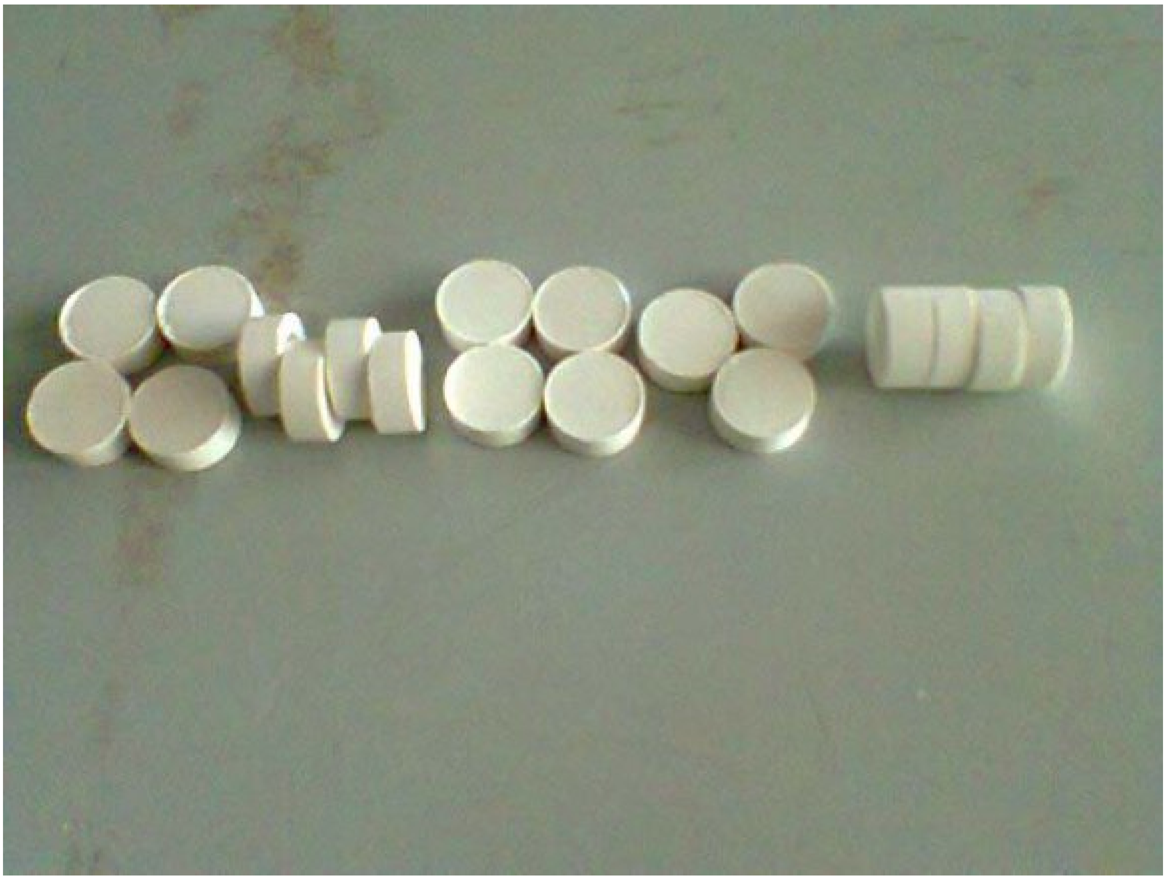
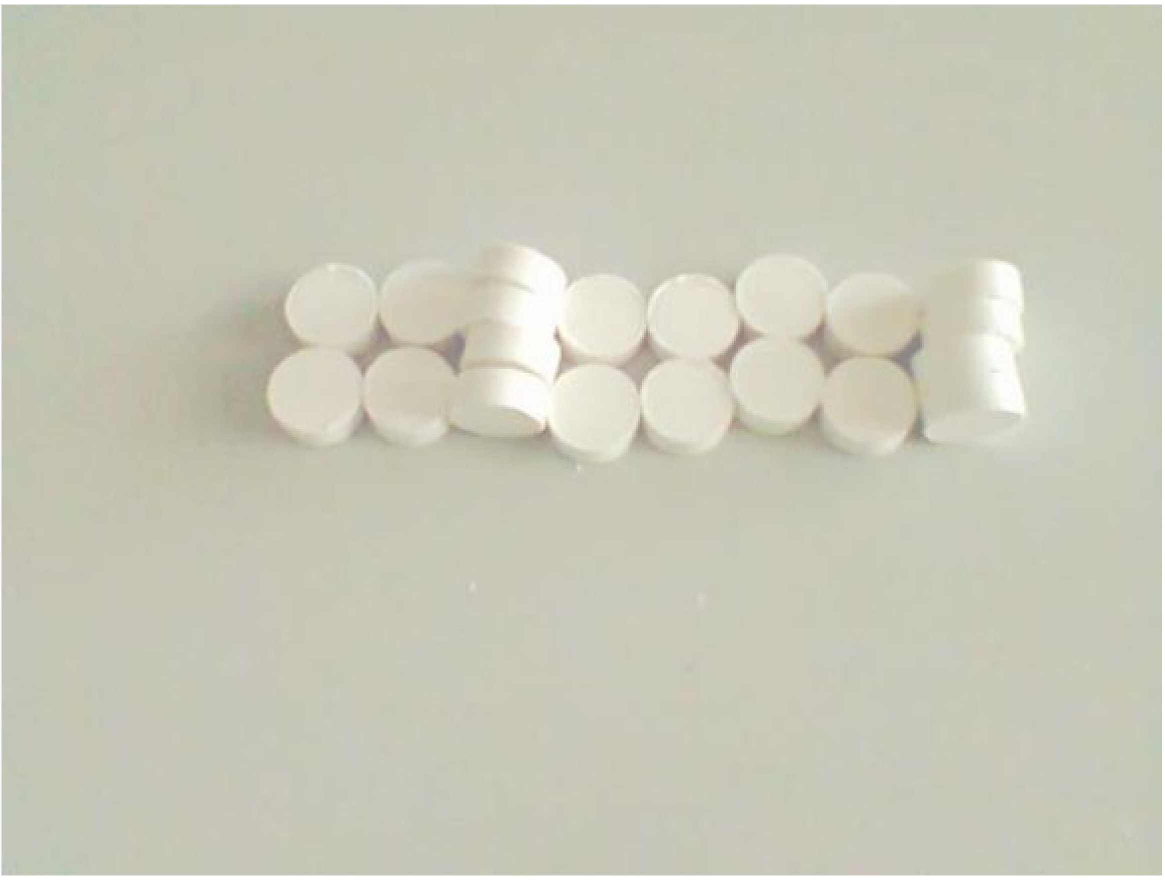


Figure 2:



2

Figure 3: Vc = h?r 2

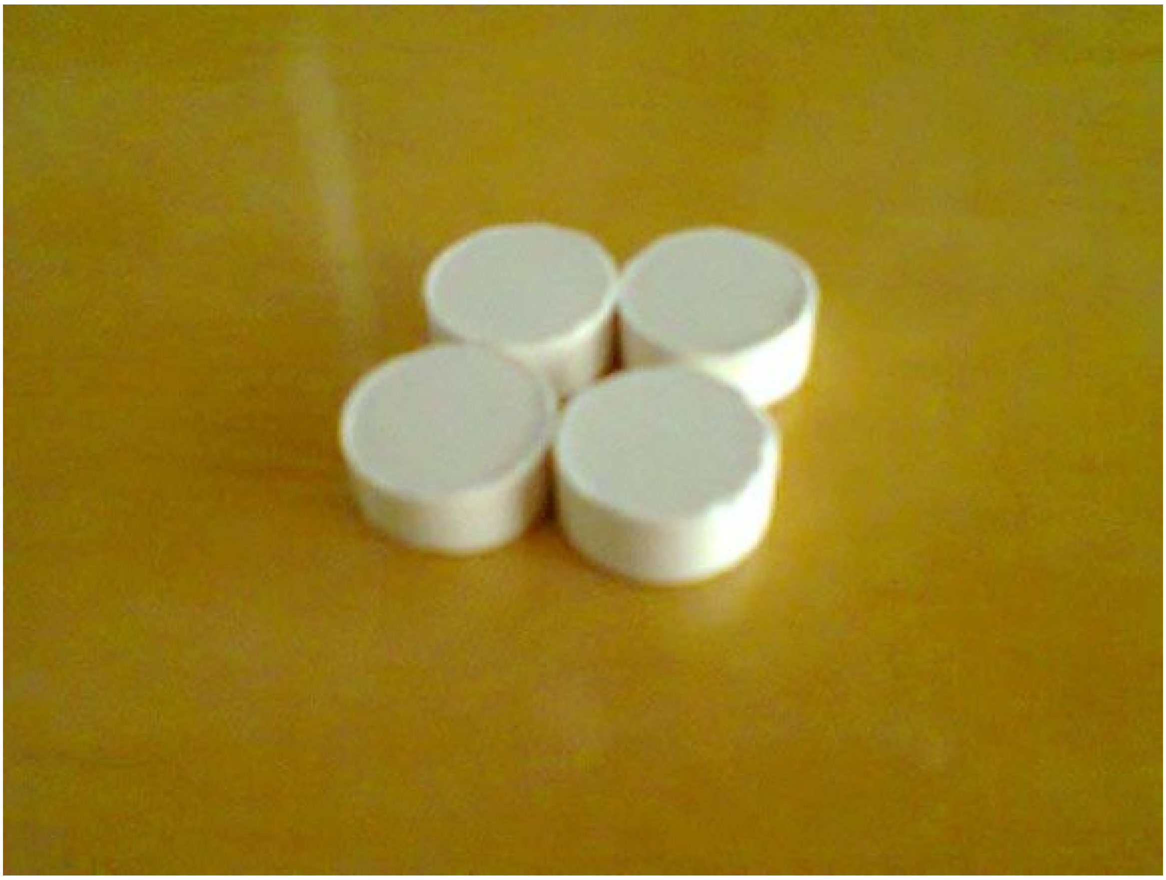


Figure 4:

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Figure 5: MSCLFigure 1 :Figure 2 :Figure 3 :

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Figure 6: Table 1 :

2

filler-binder

[Note: Y NB. MSCL, MCTS, NTS, LMH, and MCC represent: microcrystarcellac, microcrystalline tapioca starch, native tapioca starch, ?-lactose monohydrate, and microcrystalline cellulose. B2 and B3 represent batch 2 and batch 3. Batch 2 consist of MCTS, LMH, and MCC in ratio 40 %, 40 % and 20 % respectively; while batch 3 consist of MCTS, LMH, and MCC in ratio 35 %, 35 % and 30 % respectively. Ratio]

Figure 7: Table 2 :

3

Material	K	P Y (MNm -2)	A	e -A	D o	D A	D B
Microcrystarcellac (B2)	0.048	22.3	1.0	0.368	0.470	0.632	0.162
Starlac	0.007	143	1.7	0.183	0.413	0.817	0.404
Cellactose	0.041	24.2	0.6	0.545	0.298	0.455	0.157

[Note: NB: A and K represent: constants of Heckel equation. PY represent: mean yield value. Do, DA, and DB represent: initial rearrangement phase of densification, total degree of densification at zero pressure and rearrangement phase of particles in the early stages of compression respectively.]

Figure 8: Table 3 :

4

Material	a	1/a	D i =(1 -a)	1/b	P K (MNm -2)
Cellactose ®	0.526	1.9	0.474	17	17
Starlac ®	0.714	1.4	0.286	19.1	19.1
Microcrystarcellac B 2					

Figure 9: Table 4 :

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Figure 10:

4

Figure 11: Table 4 .

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