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# Application of microcrystalline cellulose from *Saccharum officinarum* as dry binder in ciprofloxacin tablet formulation

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**Abstract**

This work was aimed at the application of microcrystalline cellulose (MCC) obtained from *Saccharum officinarum* stem pulp (coded *MCC-Sacc*) as a dry binder in the formulation of ciprofloxacin hydrochloride tablets. Formulations containing 250 mg ciprofloxacin hydrochloride powder and different ratios of *MCC-Sacc* were mixed dry and compressed into tablets. Some physical properties and dissolution studies of the ciprofloxacin tablets was done using the British Pharmacopoeia (BP) method. Avicel PH 102 was used as comparing standard. Results show tablets that conformed with BP specifications in terms of weight (300 mg ± 5 %), hardness (4.74 ± 1.41 to 6.00 ± 1.05 kg/F), friability of ≤ 1 %, and disintegration time (3.20 ± 0.01 to 3.79 ± 0.37 min). The drug dissolution studies for both MCCs showed more than 80 % release of ciprofloxacin within 60 min. Ciprofloxacin tablets containing *MCC-Sacc* compared favourably with those containing Avicel PH 102 in terms of uniformity of tablet weight and disintegration time. Tablets containing Avicel PH 102 were significantly ($p < 0.05$) harder and less friable than those containing *MCC-Sacc*. Thus, *MCC-Sacc* served as a good dry binder and has a good potential as a directly compressible excipient in the formulation of ciprofloxacin tablets.

*Keywords*: Microcrystalline cellulose; *Saccharum officinarum*; Dry binder; Avicel PH 102; British Pharmacopoeia

## INTRODUCTION

Microcrystalline cellulose is a partially depolymerized fine, white, odorless, crystalline powder obtained from the acid hydrolysis of α-cellulose derived mostly from wood fiber or cotton linters [1,2]. Its production from agricultural residues [3], bacterial cellulose [4], waste cotton fabrics [5] reed stalks [6], wheat and rice straws [7,8], jute [9], water hyacinth [10], sugar cane bagasse [11,12] coconut husk/shells [13], Indian bamboo [14], soybean husk [15], *Luffa cylindrica* fibers and flax straw [16], rice straw [17], groundnut husk [18], and orange mesocarp [19] have been reported. Microcrystalline cellulose that is commercially available is derived from both softwood and hardwood [20], and is synthesized on an industrial scale by hydrolysis of cellulose using dilute mineral acids. Microcrystalline cellulose is a biodegradable material, which makes it eco-friendly. This attribute combined with its natural abundance, accessibility, and ease of processing continues to make it an interesting research material for many researchers.

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*Saccharum officinarum* commonly called sugarcane is a perennial plant that grows in clumps. The stems whose colours range from green, purple or pink are jointed, with nodes present at bases of alternate leaves, are usually un-branched. New shoots sprout from a network of rhizomes under the soil near the primary stem, which may also be surrounded by secondary shoots [21]. The plant is cultivated because of its economic value, which is derived mainly from its sap or the modifications of the sap and includes sugar, cane syrup, molasses and rhum. Folk medicine claims that it is used as a remedy for arthritis, cough, dysentery, fever sores, tumours, inflammations, hiccups etc [21]. The bagasse (refuse cane) is mainly used as feed for cattle [21]. It is also used for the generation of heat and electricity [22]. The baggase is rich in cellulose and is bio-degradable and thus a cheap way of deriving cellulose and cellulosics such as MCC. Besides its use as a dry binder, MCC also has disintegrant and lubricant properties. These properties make it a desirable pharmaceutical tablet excipient. Tablet formulations containing MCC have good hardness/tensile strength and can also disintegrate rapidly in water due to the swelling of the MCC particles and destruction of the hydrogen bonding forces holding them together in the tablet.

Ciprofloxacin hydrochloride is a fluoroquinolone compound with recognized anti-infective activity/antibacterial activity [23]. It has been applied in the treatment of susceptible bacterial infections in different parts of the body such as gastro-intestinal tract (GIT), eye, ear, nose, and throat. It has also been found useful in the treatment of dermatological infections, cystic fibrosis and HACEK endocarditis [24]. It has the versatility of application in terms of routes of administration. The parenteral, topical, eye and ear drops, and orally ingested tablets have been established. Of these routes, the oral tablet is the most popular. Tablets of 250, 500 and 1000 mg are commercially available [25]. It has an oral bioavailability of about 70 %, peak plasma concentrations of between 0.5 to 2 h after the ingestion of food and its biologic half-life is about 4.5 h [26]. Ciprofloxacin tablet is most popularly prepared through the wet granulation technology. However, the wet granulation technology is known to be disadvantaged by its high economical cost, tediousness, loss of therapeutic activity or degradation of the active pharmaceutical ingredient to heat and moisture sensitive drugs. This work aims at using *MCC-Sacc* as a dry binder in the manufacture of ciprofloxacin tablets using the direct compression technology.

## EXPERIMENTAL

**Materials.** Hydrochloric acid, Avicel PH 102, ciprofloxacin hydrochloride, talc, magnesium stearate (Sigma Chemical coy, USA), sodium hydroxide (Quaillikems Laboratory, India), corn starch (BDH, Poole, England).

**Derivatization of alpha and microcrystalline cellulose.** Matured stems of *Saccharum*. *officinarum* were cut into bits of about 2-4 cm after their bark had been peeled off. These chips were pressed to remove the sap and air dried for 5 days under ambient conditions until they were sufficiently dry [11]. Delignification to obtain alpha (α) cellulose involved successive heating of 1.5 kg of the chips in 2.0 % w/v of sodium hydroxide at 80 °C for 5 h, and later in 17.5 % w/v NaOH at the same temperature for 1 h. This was accompanied with intermittent bleaching with a 1:2 aqueous dilution of sodium hypochlorite and washing with distilled water until neutral to litmus. Microcrystalline cellulose was obtained by partially depolymerizing the α cellulose obtained using 2.5 N hydrochloric acid, with the mixture heated up to 105 ± 2˚C for 15 min in a liquid paraffin bath [11]. Washing of the resultant MCC was done with distilled water

until it became neutral to litmus and the resultant MCC hot air oven dried at 60 °C for 2 h and was coded *MCC-Sacc*.

**Characterization of microcrystalline cellulose.** Nwachukwu and Ugoeze [11] had earlier reported the physicochemical characterization of *MCC-Sacc* in terms of pH, solubility, ash content, swelling capacity, hydration capacity, moisture sorption, scanning electron microscopy (SEM), degree of polymerization, particle density, and porosity. The flow and compaction behavior of *MCC-Sacc* had also been reported [27]

**Formulation of ciprofloxacin tablets.** Formulation of ciprofloxacin tablets was done using the ingredients and in the quantities as shown in Table 1. Six batches of one hundred tablets per batch were prepared at target tablet weights of 300 mg each for batches MCS-1 and MCC-AV1, 305 mg for batches MCS-2 and MCC-AV2, and 310 mg for batches MCS-3 and MCC-AV3. Talc and magnesium stearate were added prior to compression. The powder blends were compressed into tablets using a single punch automated tablet press (Model EP-1, Erweka®, Germany) fitted with a set of concave faced punches of 8 mm diameter. Compression was done at a uniform compression pressure of 3 kg and dwell time of 20 sec for all the batches of tablets.

**Evaluation of ciprofloxacin tablets**

***Wholesomeness.*** Ciprofloxacin tablets containing both *MCC-Sacc* and Avicel PH 102 were physically inspected for wholesomeness. This included checks for chipping, cracking or breaking, physical abrasion, stains or any undesirable physical observation that depicts unwholesomeness.

***Uniformity of weight test.*** Twenty tablets randomly selected from each of the batches of the ciprofloxacin tablets were evaluated for variations in weight from the estimated target tablet weight. The tablets were individually weighed using an analytical balance and the mean, standard deviation and coefficients of variation determined for each batch.

***Disintegration time test.*** Six tablets randomly selected from each of the six batches of the ciprofloxacin tablets were evaluated for the time they would completely break up or disintegrate in 500 mL of 0.1 N hydrochloric acid warmed up to a temperature of 37 ± 1°C using a model ZT-3 disintegration tester/equipment (Erweka®, Germany). The time taken for the tablets to break up and pass through the mesh was noted. Replicate determinations were conducted.

***Hardness test.*** The hardness of ten tablets randomly selected from each of the batches of the ciprofloxacin tablet formulations was ascertained using a model TBH 100 tablet hardness tester (Erweka®, Germany). The hardness values were taken when the tablet under test has split diametrically into two halves. The mean and standard deviation were calculated for each batch.

***Friability test.*** Ten tablets randomly selected were used for the test. They were dusted, weighed and placed inside the drum of the friability testing machine, model TAR 200 (Erweka®, Germany), and set to rotate at a speed of 25 revolutions per minute (rpm) for 4 min. The tablets were collected from the drum, de-dusted and reweighed. The friability was calculated from the equation:

$$\text{Friability (F)} = \frac{W_o - W_f}{W_o} \times 100 \qquad \ldots\ldots 1$$

where $w_o$ is the initial weight of the tablets and $w_f$ is the weight of the tablets after the test.

***Tensile strength test.*** The tensile strength of the tablets was a measure of the hardness of the tablet in comparison with the diameter and thickness of the tablet and is calculated using Equation 2:

$$\text{Tensile strength (TS)} = \frac{2P}{\pi dt} \qquad \ldots\ldots 2$$

where P is the breaking force, d is the tablet diameter, t is the tablet thickness.

**Determination of wavelength of maximum absorption & standard calibration curve.** A stock solution of the pure sample of ciprofloxacin powder was made by weighing 100 mg of the pure ciprofloxacin using a model AV 114 Adventurer analytical balance (OHAUS Adventurer®, USA). This was dissolved in 50 mL 0.1 N HCl in a 100 mL volumetric flask and the volume made up to the 100 mL mark with the same vehicle. Serial dilutions of the stock were made such that 0.20 mg %, 0.40 mg %, 0.60 mg %, 0.80 mg % and 1.00 mg % were obtained. Scanning of the 0.20 mg % filtrate was done in a JENWAY 6405 UV/Vis spectrophotometer (Jenway®, England) at wavelengths ranging from 220 nm to 400 nm. The wavelength of the maximum/peak absorbance ($\lambda_{max}$) was noted to be 278 nm. The serially diluted solutions of ciprofloxacin containing 0.20 mg %, 0.40 mg %, 0.60 mg %, 0.80 mg % and 1.00 mg % were scanned using the spectrophotometer at a wavelength of 278 nm. A plot of the concentration against absorbance readings was made and the slope determined.

**Assay of tablets.** Twenty tablets randomly selected from each ciprofloxacin tablet batch were collectively weighed, powdered in a porcelain mortar, and the equivalent mean mass of one tablet taken. A 100 mL dispersion of it was made in a volumetric flask using 0.1 N HCl. Filtrates of the stock solutions were appropriately diluted and scans of the different dilutions read using the JENWAY spectrophotometer at 278 nm. The absorbance readings obtained were used to calculate the concentrations of each the stock solutions of the tablets by fitting into the standard calibration curve equation.

**Dissolution studies.** The dissolution or drug release studies of the different batches of the ciprofloxacin tablets were carried out using a six station dissolution equipment model DT 600 (Erweka®, Germany) filled with 900 mL of 0.1 N HCl per beaker heated up to a temperature of 37 ± 0.5˚C, with the paddles set to rotate at 50 rpm. Each beaker contained one tablet and from each beaker 5 mL samples were withdrawn at 10 min intervals up to 1 h. An equal replacement with dissolution media maintained at a temperature of 37 ± 0.5˚C was done after each withdrawal. A portion of the filtrate from each of the withdrawn samples was scanned using a JENWAY 6405 spectrophotometer at a wavelength of 278 nm. The absorbance results were fitted into the standard calibration curve equation to determine the concentration of ciprofloxacin.

**Statistical analysis.** Data obtained were statistically evaluated using ANOVA and the student's t-test (IBM SPSS 21) and were considered significant at $p < 0.05$.

## RESULTS AND DISCUSSION

**Wholesomeness.** The ciprofloxacin tablets were evaluated 24 h post compression. A physical inspection of the tablets showed that the tablets did not have any form of physical deformity, were not chipped nor capped, and there was no stain.

**Uniformity of weight.** The results of the uniformity of weight of the different brands of ciprofloxacin are shown in Table 2. All the batches of the tablets complied with the uniformity of weight test as specified by the BP. In any given batch, if the powders were accurately weighed and properly blended, and fed uniformly into the die cavity, the tablets compressed therefrom would not vary much in weight. A coefficient of variance reading of ± 5 % is stipulated for uncoated tablets weighing 250 mg and above [28].

**Hardness.** Table 2 shows the results of the hardness test of the ciprofloxacin tablets. The tablets containing *MCC-Sacc* were not as hard as those containing Avicel PH 102. The hardness was found to increase as the quantity of MCC contained in the tablet increased. The hardness also increased with increase in tablet

weight and thickness/height. However, the hardness values (4.37 ± 1.23 to 7.96 ± 1.51) obtained for all the tablets conformed with the BP 2012 set limits for uncoated tablets. Uncoated tablets with a hardness of ≥ 4 kg/F are considered hard enough to be able to withstand objectionable stresses of handling, packaging, and transportation, which the tablets may be subjected to before consumption [28].

**Disintegration time.** The disintegration time results of the ciprofloxacin tablets are shown in Table 2. The disintegration time is the time it takes the tablets to break up on hydration or contact with gastro-intestinal fluid to enable the release of the pharmaceutically active ingredient. Values obtained were within 5 min and these values are within both the United States Pharmacopoeia and BP upper set limits of 15 min for uncoated tablets [23,28]. Thus the tablets passed the disintegration time test and would predictably release their ciprofloxacin content for dissolution within 5 min of ingestion of the tablet.

**Friability.** The effect of attrition arising from the tablets rubbing against each other resulting in the wear and tear of the tablet is regarded as friability. The ciprofloxacin tablets showed percentage friability values that ranged from 0.13 ± 0.01 to 0.47 ± 0.01 for all batches. The USP and BP set a limit of ≤ 1 % friability for uncoated tablets [23, 28]. Since the friability values were below 1 %, all the batches of ciprofloxacin tablet can be considered as having passed the test. Thus, the tablets would be able to withstand abrasional forces that may be encountered during packaging, transportation and other forms of similar handling on the shelf or prior to usage.

**Height/ thickness.** The height/ thickness readings are shown in Table 2. There was a gradual increment in the thickness of the tablets as the quantity of binder incorporated into the tablet increased. Thus the larger the amount or weight of powder that is compressed, the thicker the tablet would be so long as a uniform compression pressure is applied. The ciprofloxacin tablets containing Avicel PH 102 were thicker than those containing *MCC-Sacc* at a similar batch size/weight.

**Tensile strength.** The tensile strength of the ciprofloxacin tablets is shown in Fig. 1. Tensile strength describes the mechanical strength that exists in a tablet in relation to the proportionality of its hardness to the surface area and thickness of such tablets. Batches MCC-AV2 and MCC-AV3 compared well with MCS-2 and MCS-3 although MCC-AV3 had the highest tensile strength. The tensile strength value took a similar trend like the results of hardness for tablets containing both MCCs.

**Drug assay.** Results of the total ciprofloxacin content per batch of tablets are shown in Fig. 2. The content of active ingredient for all batches of tablets complied with the BP 2012 specifications for ciprofloxacin, which is given in a range of 95 to 105 %. Thus, the formulations were good in terms of the content of active ingredient.

**Table 1**: Formula for ciprofloxacin tablets

| Batch/ingredient | *MCC-Sacc* | | | Avicel PH 102 | | |
|---|---|---|---|---|---|---|
| | MCS-1 | MCS-2 | MCS-3 | MCC-AV1 | MCC-AV2 | MCC-AV3 |
| Ciprofloxacin (mg) | 250 | 250 | 250 | 250 | 250 | 250 |
| Magnesium stearate (mg) | 3 | 3 | 3 | 3 | 3 | 3 |
| Talc (mg) | 3 | 3 | 3 | 3 | 3 | 3 |
| Corn Starch (mg) | 14 | 14 | 14 | 14 | 14 | 14 |
| *Binder (mg) | 30 | 35 | 40 | 30 | 35 | 40 |
| Total tablet weight (mg) | 300 | 305 | 310 | 300 | 305 | 310 |

*Binder (*MCC-Sacc* or Avicel PH 102).

**Table 2:** Some physical parameters of ciprofloxacin tablets

| Batch/Parameter | *MCC-Sacc* | | | Avicel PH 102 | | |
|---|---|---|---|---|---|---|
| | MCS-1 | MCS-2 | MCS-3 | MCC-AV1 | MCC-AV2 | MCC-AV3 |
| Uniformity of weight* | 300.50 (1.75) | 303.10 (3.59) | 312.20 (1.14) | 302.20 (1.85) | 305.00 (2.24) | 307.40 (3.45) |
| Hardness (kg/F) | 4.74 ± 1.41 | 4.37 ± 1.23 | 6.00 ± 1.05 | 6.08 ± 1.59 | 6.52 ± 0.79 | 7.96 ± 1.51 |
| Disintegration (min) | 3.79 ± 0.37 | 3.77 ± 0.25 | 3.20 ± 0.01 | 3.10 ± 0.07 | 3.42 ± 0.08 | 3.32 ± 0.08 |
| Friability (%) | 0.37 ± 0.01 | 0.47 ± 0.01 | 0.35 ± 0.05 | 0.23 ± 0.03 | 0.25 ± 0.02 | 0.13 ± 0.01 |
| Height/Thickness (mm) | 4.48 ± 0.05 | 4.60 ± 1.04 | 5.07 ± 0.93 | 5.17 ± 0.65 | 5.25 ± 0.22 | 5.38 ± 0.33 |

*represents % coefficiency of variation.

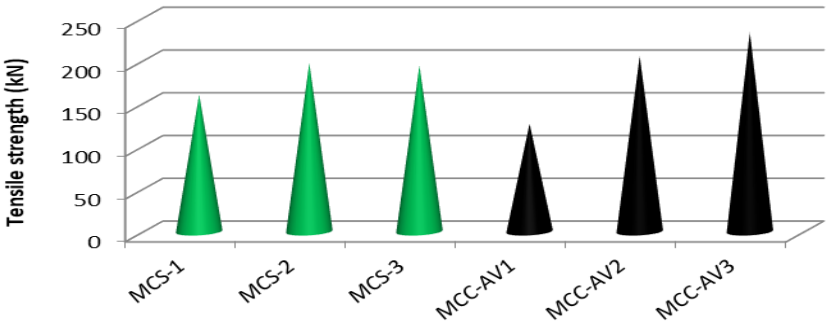


**Fig. 1: Tensile strength of ciprofloxacin tablets containing MCC-Sacc and Avicel PH 102**

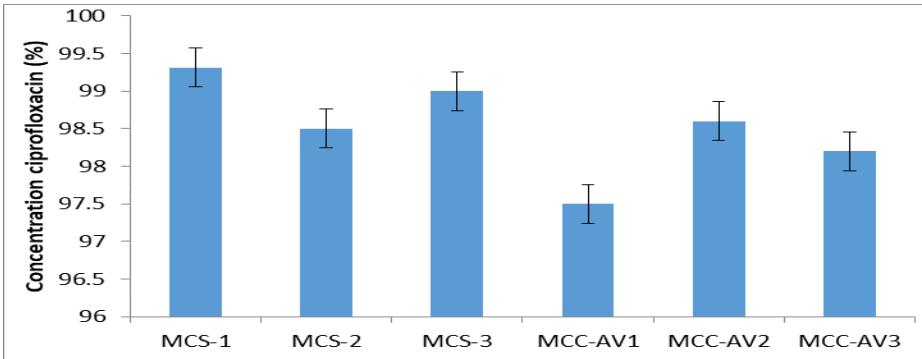


**Fig.2: Drug assay of ciprofloxacin tablets containing MCC-Sacc and Avicel PH 102**

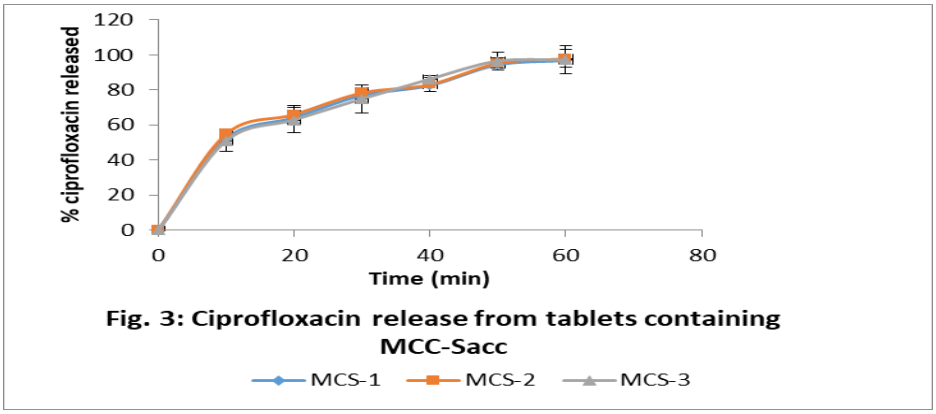


**Fig. 3: Ciprofloxacin release from tablets containing MCC-Sacc**

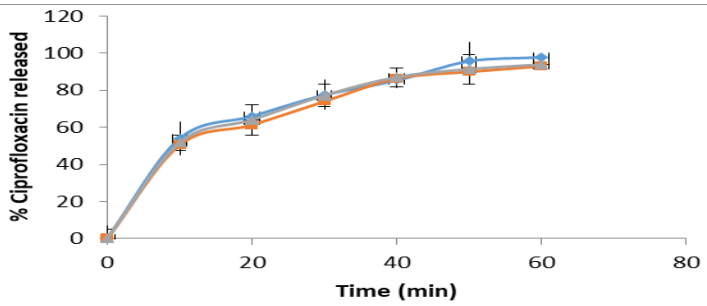


**Fig. 4: Ciprofloxacin release from tablets containing Avicel PH 102**

MCC-AV1 MCC-AV2 MCC-AV3

**Dissolution/drug release profile.** Figures 3 and 4 show ciprofloxacin release from tablets containing *MCC-Sacc* and Avicel PH 102. There was a steady incremental release of ciprofloxacin from the tablets as the dissolution time increased. This was consistent from batch to batch irrespective of the type of MCC. However, at $T_{45}$ more than 80 % of the ciprofloxacin content of each batch of tablets had been released. The ciprofloxacin release was found to increase as the amount of MCC contained per tablet increased. Formulations containing both MCCs in equal amounts compared well in their ciprofloxacin release/dissolution profile.

**Conclusion.** The ciprofloxacin tablets formulated with microcrystalline cellulose obtained from *Saccharum officinarum* were wholesome and did not exhibit any visual physical defects such as capping, lamination or chipping. The tablets had weights with minimum variation. The hardness, tensile strength, and friability showed that the tablets had good mechanical properties that are desirable in uncoated tablets. The disintegration time was within 5 min which would permit a fast release of the ciprofloxacin from the matrix thereby enhancing dissolution and bioavailability. The drug release was equally good for all the batches. All these parameters were comparable with the tablets containing Avicel PH 102 and conform to specifications of both the British Pharmacopoeia and United States Pharmacopoeia. Thus MCC obtained from *Saccharum officinarum* can be effectively applied as a dry binder in the formulation of ciprofloxacin tablets using the direct compression method.

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