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Evaluation of Ibuprofen Tablets Obtained from Prepared Microcrystalline Cellulose from *Gompherena serrata* (Batchelors Button) as Pharmaceutical Disintegrant

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Abstract

Acid hydrolysis of microcrystalline cellulose can improve its physicochemical properties such as solubility, swelling capacity and gelatinization which are very important for pharmaceutical application. The objectives of this study were to formulate Ibuprofen tablets using different microcrystalline cellulose such as prepared microcrystalline cellulose (PMCC) and commercial microcrystalline cellulose (CMCC) and to evaluate their efficacy as pharmaceutical excipient. Six batches of *Ibuprofen* 200 mg tablets were prepared by direct compression technique using cellulose as binders and disintegrants, with total of 100 tablets per batch. The tablets were produced using tableting machine and then subjected to routine pharmaceutical quality evaluations. All the formulated samples passed the uniformity of weight test, hardness test, disintegration test, and friability test. All the tablets formed using the prepared MCC obtained from *Gompherena serrata* Fiber were good and acceptable as none had a surface defect with all the pharmacopoeia test carried out on the tablets in compliance BP, 2012. As such, it can be concluded that MCC can be extracted from *Gompherena serrata* fiber; which can be used to produce ibuprofen tablets.

Keywords: Microcrystalline cellulose (MCC); Evaluation; *Gompherena serrata* (BATCHLOR'S BUTTON)

Introduction

Significant amount of waste is being produced each day which contain high quantities of organic matter. The agricultural wastes produced in a particular period of the year pose potential pollution problem. Therefore, an efficient utilization of such agricultural wastes is one of great importance not only for minimizing the environmental impact, but also for obtaining a higher profit [1]. Plants are rich sources of bioactive constituents with diverse pharmacological properties and medicinal values, therefore the extraction and characterization of phytochemicals from plants.

One of such plants resulted in the discovery of novel drug entities with high therapeutic value is *Gomphrena serrata* that belong to a family *Amaranthaceae* [2]. The family *Amaranthaceae* contains nearly 60-70 exotic species. All parts of the plant are widely used as a folklore medicine for the treatment of various ailments by Indian traditional healers, such respiratory diseases like asthma, gastrointestinal conditions like diarrhea, gastric disturbances, piles, skin diseases like dermatitis, as antimicrobial, anticancer, antimalarial, analgesic, as tonics and carminatives and allergic conditions like hay fever, etc.

Nowadays the focus of the researchers is on the use of the traditionally available plants because they are medicinally and pharmacologically important and they possess valuable bioactive molecules. From ancient times these medicinal plants have been used and their effectiveness has been increasing day by day in the world. The compounds available naturally are considered as environmentally friendly and also more effective than the synthetic drug. These medicinal Plants represent a foundation for many pharmaceutical treatments of many human diseases [3].

Microcrystalline Cellulose (MCC)

Microcrystalline cellulose (MCC) is a white crystalline powder that is recognized as one of the widely used cellulose derivatives in cosmetics, food, pharmaceuticals, and filler industries [4]. MCC is pure partially depolymerized cellulose synthesized from α-cellulose precursor. The MCC can be synthesized by different processes such as reactive extrusion, enzyme mediated, steam explosion and acid hydrolysis. It is valuable additive in pharmaceutical, food, cosmetic and other industries.

MCC is one of the most important tableting excipients due to its outstanding dry binding properties of tablets for direct compression [5]. Different properties of MCC such as particle size, density, compressibility index, angle of repose, powder porosity, hydration swelling capacity, moisture sorption capacity, moisture content, crystallinity index, crystallite size and mechanical properties such as hardness and tensile strength are measured to qualify its suitability for such utilization, Thermogravimetric analysis (TGA) and differential thermal analysis (DTA) or differential scanning calorimetry(DSC) are also important to

predict the thermal behavior of the MCC upon heat stresses [5].

Polysaccharides are very large biomolecules with high molecular weight and are made up of long chains of monosaccharide that are linked to each other by glycosidic bonds (-O-) [6]. They undergo hydrolysis in the presence of concentrated acids to give the constituent monosaccharides. Polysaccharides can be either linear or branched. They are produced by animals, microorganisms and plants. Plants produce about 90% of the overall natural polysaccharides [7]. Polysaccharides are broadly classified into Homopolysaccharides and Heteropolysaccharides. The homopolysaccharides are composed of the same sugar units (or monosaccharides). Examples of homopolysaccharides are starch, glycogen and cellulose. These are referred to as homoglycans because they are made up of a large number of glucose molecules. Another example of homopolysaccahrides is inulin which is made up only fructose as the only monomer units. The heteropolysaccharides contain more than one different type of sugar units and often contains other groups [8].

About 50% of the world's organic carbon is found in cellulose [9]. It is therefore, the most abundant polysaccharide in nature. Cellulose is the main constituents of natural fiber such as cotton and higher plants.

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Cellulose is the most abundant structural polysaccharide found in the plant kingdom [10]. Cellulose is a linear molecule and can lie side by side in a parallel series of rows. This is because all glucose molecules that make up cellulose have a beta-configuration at the C-1 atom, so all the glucose molecules are joined together by beta-glycosidic bonds. This differentiates cellulose from the other homoglycans (starch and glucose). The enzymes produced in humans cannot act on the beta- glycosidic bonds of cellulose as it will act on starch and glycogen. Therefore, the human gastrointestinal tract cannot digest cellulose [10].

Disintegrant

Disintegrating agents or disintegrants are important component of tablet dosage forms as they are added to a formulation to promote the drug release, they do so by increased water wicking into the plug, and also promote deaggregation of the plug particles [11]. For IR tablets disintegrants are essential, but for capsules, they are less important because the plug is less of a barrier to the drug release than a compressed tablet [12]. They are added to a tablet formulation to break apart (disintegrate) the compressed tablet when placed in an aqueous environment. This can happen due to the effervescence properties of granules, which can break the tablet matrix and cause the eventual disintegration of the tablet. Sodium starch

glycolate, croscarmellose, and pregelatinized starch work according to this mechanism [13].

Material and Methods

Material

Ibuprofen powder (98%), talc %purity not specify, magnesium stearate (97.5%), lactose (99.6%), maize starch (95.7%), and commercial microcrystalline cellulose (CMCC) (97.5%) were purchased from (BDH England), Riedel-haen China, Qualikens England, (BDH) England, A.G.M.P and ISO India respectively. Prepared microcrystalline cellulose was isolated and evaluated from *Gompherena serrata* (BATCHLORS BUTTON) in our laboratory at Usmanu Danfodiyo University Sokoto, Nigeria. Sodium hydroxides (98%), sodium hypochlorate (99%), hydrochloric acid 98%), hydrogen trioxonitrate (v) (98%) and hydrogen peroxides (99%), was purchased from LOBA chemicals India. Distilled water was produced in the laboratory house using QuickFit water still (QWS4), UK.

Method

Preparation of Tablets

Six (6) different batches of tablet were prepared using direct compression technique method. The composition of single tablet per batch is given in a Table 1.

Table 1: Formula for Ibuprofen Tablet Formulation

Materials (mg)	F1	F2	F3	F4	F5	F6
Ibuprofen	200	200	200	200	200	200
Lactose	40.24	34.50	40.24	34.50	40.24	34.50
P MCC	5.60	11.20	-	-	-	-
CMCC	-	-	5.60	11.20	-	-
Starch BP (powder)	-	-	-	-	5.60	11.20
Maize starch	28	28	28	28	28	28
Talcum (mg)	5.6	5.6	5.6	5.6	5.6	5.6
Magnesium stearate(mg)	0.56	0.56	0.56	0.56	0.56	0.56

Tablet weight=280mg, Lubricants=0.2%, Glidant=2%, Disintegrant=2%, and 4%, Binder=10%, API=200mg.

F1= Batch 1, F2= Bach 2, F3= Batch 3, F4= Batch 4, F5= Batch 5, F6= Batch 6.

The required amount of powder was weighed and compressed using tableting machine (single station). The compressed tablets of each batch were stored in air tight container at room temperature. A total of 100 tablets was produced per batch.

Parameters for Tablet Evaluation

Tablet Strength (Hardness Test)

Five tablets of each batch were randomly selected, placed between the spindle of the Erweka hardness tester machine and pressure was applied by turning the knurled knot just sufficient to hold the tablet in position. The pressure was uniformly increased until the tablet breaks and the pressure required to break the tablet was recorded [1].

Friability Test

Ten tablets each from batch were randomly selected and weighed on the analytical balance. These tablets were put in an automated friabilator that was spun at 100 rev/ 4 minutes to roll and fall

within the rotating apparatus. After spinning, the tablets were reweighed after all loose particles were excluded by blowing off gently with a hand fan [1]. The friability of the tablets was calculated using equation 1:

$$\text{Friability} = \frac{\text{Initial weight} - \text{final weight}}{\text{Initial weight}} \times 100 \quad \ldots (1)$$

Disintegration Test

The disintegration time of six randomly selected tablets from each batch was determined. The test was performed using a disintegration test apparatus (Erweka DT-700 germany) with the column that can contain six vessels and basket mashes where the tablets were inserted. The baskets were inserted in 700 ml. of 0.1 M HCl. The machine was operated was operated at 37 ^{O}C. The time when no granules of any tablets remained on the mesh was taken as the disintegrating time using a stop watch [5].

Uniformity of Weight

Twenty tablets from each of the nine batches were randomly selected, weighed together and average weight was determined. Each tablet was subsequently weighed individually on analytical weighing balance and percentage (%) deviation was determined. [1].

Standard calibration curve by ultraviolent visible assay

A standard stock solution of ibuprofen was prepared by dissolving 20 mg of pure ibuprofen powder with 0.1 M sodium hydroxide solution to get a 100 ml solution. Various standard concentrations ranging from 2 µg/ml to 200 µg/ml were prepared from further dilution of the stock solution with 0.1 M NaOH solution. The standard solutions were analyzed spectrophotometrically at 264 nm using a double-beam spectrophotometer, (model ATE 4331 ATICO, India). The mean absorbance of triplicate determinations was plotted against their corresponding concentrations to obtain a calibration curve.

Sample Preparation

Ten tablets were randomly selected from each batch and commercial microcrystalline cellulose (CMCC) product, weighed and then crushed in to powders. A powder equivalent to 20 mg of ibuprofen was weighed in to a volumetric flask and dissolved in 0.1 M NaOH to give a 100 Ml solution. The solution was filtered using whatman filter paper. The resulting solution was scanned at 264 nm. The average absorbance for the triplicate measurement of each batch and commercial microcrystalline cellulose product were extrapolated on the calibration curve derived from the pure ibuprofen powder to get the equivalent concentration, and then the percentage content was calculated.

Dissolution Test

Calibration curve was plotted for the drugs. This was done by serially diluting ibuprofen tablets (that is batch by batch from F1 to F6) in 0,1M HCl and absorbance was taken at 264 nm in UV spectrometer (SURGISPEC SM752S SURGIFIELD MEDICAL ENGLAND). The concentration obtained was plotted against absorbance to give the calibration curve. Using basket method, one tablet was placed in dry basket and lowered 50 mm from the bottom of the glass vessel into the dissolution medium 0.1 M HCl for the ibuprofen tablet before the rotation begin at the speed of 100 rev per min. 10ml of the sample was withdrawn from a distance of 40 mm between the surface of the dissolution medium and top of the rotating basket at 10 minutes interval for 1 hour. After every withdrawal, 10ml of the medium was replaced. A 1 in 10 dilution of the withdrawal of each tablet from F1 batch to F6 batch, with the dilution media was made before the absorbance of the sample was taken.

Results and Discussion

Summary of Evaluated Physicochemical Characteristics of Six (6) Batches of Ibuprofen Tablet

Table 2: Uniformity of weight of different sample of ibuprofen tablets for F1-F6.

Batches	Total weight (g) of 20 tablets	Mean weight (g) ± SD	No of tablets deviating by ± 7.5 %
F1	9.6	0.48	1
F2	9.34	0.467	2
F3	10.4	0.52	1
F4	9.4	0.47	1
F5	9.00	0.45	0
F6	9.8	0.49	1

Table 3: Results of hardness, disintegration, and friability tests of ibuprofen 200 mg tablets

Type of ibuprofen tablets	Hardness (kgf) ± SD	Mean disintegration time (min) ± S.D.	Friability (%)
F1	4.72	10.56	1.20
F2	5.27	8.3	0.88
F3	4.80	9.02	0.62
F4	5.26	11.45	0.60
F5	4.83	13.35	0.94
F6	4.93	14.30	0.60

Figure 1: F1 - Ibuprofen Tablets obtained from *Gompherena serrata* fiber

Figure 2: F2 - Ibuprofen Tablets obtained from *Gompherena serrata* fiber

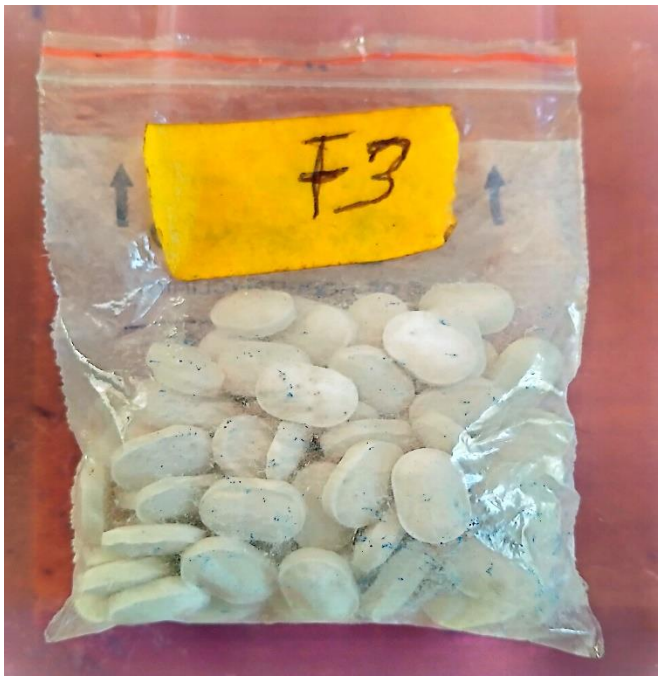

Figure 3: F3 - Ibuprofen Tablets obtained from *Gompherena serrata* fiber

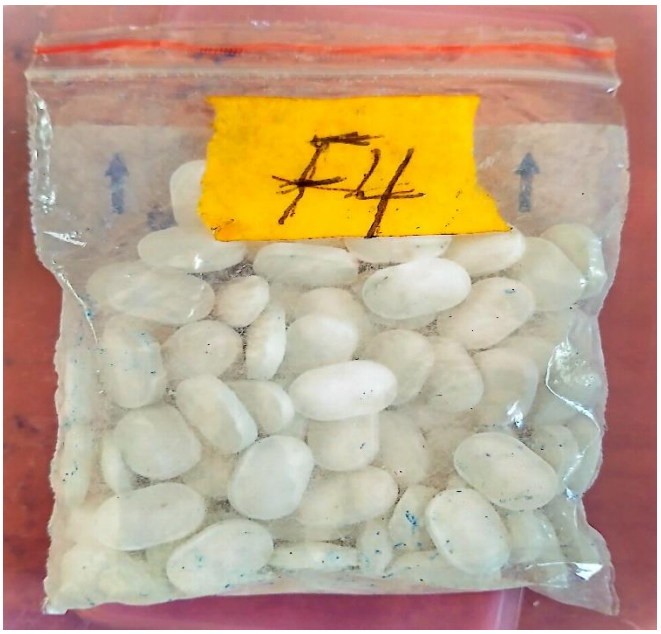

Figure 4: F4 - Ibuprofen Tablets obtained from *Gompherena serrata* fiber

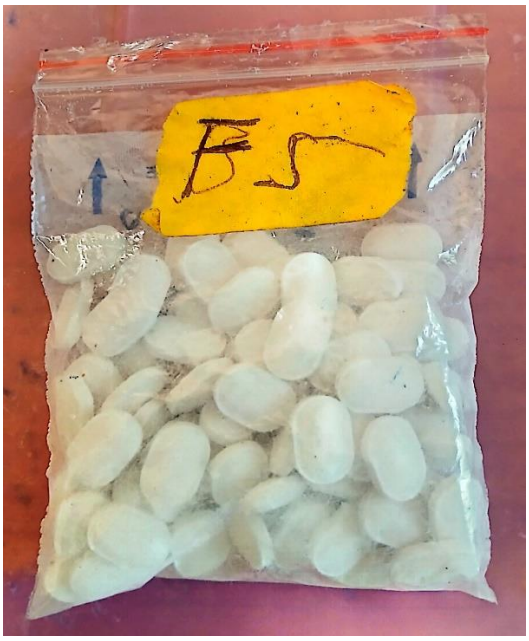

Figure 5: F5 - Ibuprofen Tablets obtained from *Gompherena serrata* fiber

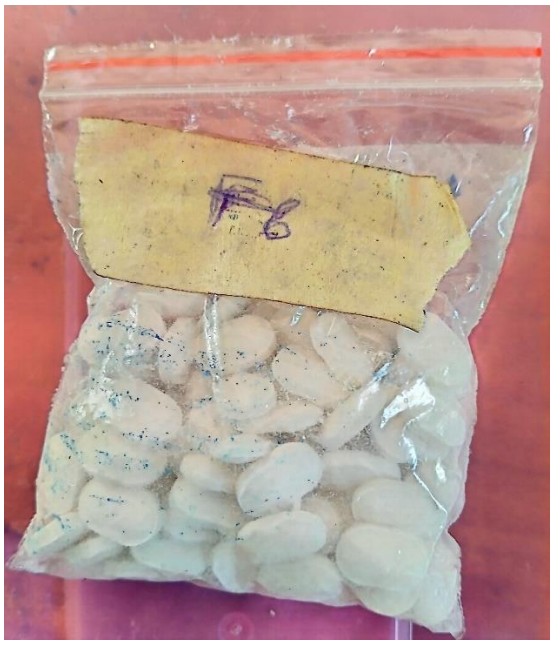

Figure 6: F6: Ibuprofen Tablets obtained from *Gompherena serrata* fiber

Discussion

One hundred Ibuprofen (200 mg) tablets were formulated each from prepared microcrystalline cellulose, commercial microcrystalline cellulose, starch BP powder, and maize starch. The tablets produced for each were found to have a good physical appearance. They appeared brown and are oblong in shape (figure). The tablets were stored in

air-tight containers and cool place (25 ^{O}C) before further analysis.

Uniformity of weight

Weight uniformity refers to the consistency of the tablet weight, ensuring that each tablet contains the correct amount of active pharmaceutical ingredients and excipients. It is critical quality attribute in tablet manufacturing, as it directly affects dose accuracy and consistency, potency and efficacy as well as patient safety and compliance. For tablets to pass the test, more than two of the individual weight of the tablets should deviate from the average weight by ± 7.5 % [5]. From the results obtained in table 3 showed that most of the tablets passed the test with percentage deviation less than ± 7.5 % which indicated that the tablets contained proper ingredients. The tablets also passed the British pharmacopoeia uniformity of weight test (< 2 tablets ± 5 % mean weight, n = 20) [2].

Friability

Friability of a formulated tablet refers to its ability to withstand mechanical stress and resistance to breaking or crumbling. It is a critical quality attribute, as excessive friability can lead to tablet breakage during handling and storage, loss of potency and efficacy as well as patient non-compliance due to tablet fragmentation. From Table 2 all the batches (F1 – F6) passed the friability test with values ranges from 0.60 – 0.94% except F1 with a value of 1.20%. According to BP standard, once the friability test of a tablet exceeds 1%, it considered to be failed test and thus, and thus shows that the tablets are not in good quality. An increase in cassava starch disintegrant concentration did not produce any sprcific effect on tablet friability [2].

Hardness

Hardness of a formulated tablet refers to its resistance to crushing or breaking, which is critical for tablet integrity and durability, patient convenience and compliance as well as product stability and shelf-life. On the other hand, too-hard tablets cannot disintegrate quickly, and the bioavailability of the API from the tablets can be significantly affected [4]. A 4 kgf crushing force is considered the minimum force for a good tablet. From the result obtained in table 3 all the batches passed the hardness test as their crushing force were within the range of British Pharmacopeia (BP) specification of 4-6 kgf, which makes them have ability to withstand fracture. According to Aminu N. *et al.*, 2024, the ibuprofen tablets prepared with native and acetylated starches passed the test, as their crushing force were within the range of British Pharmacopeia (BP) specification of 4-6 kgf while that of that of maize and marketed ibuprofen failed the test with hardness value of 6.07 kgf and 6.441 kgf.

Disintegration Time

The disintegration time for tablets determines whether tablets disintegrate within a prescribed time when placed in a liquid medium under the

prescribed experimental conditions. From Table 3 all the batches passed the test with all the tablets disintegrating in less than 15 minutes which compliance with the [7]. The disintegration time of a tablet can be affected by the pore and bonding structure withing tablet. A high porosity and the presence of large pores facilitate rapid water penetration into tablet with a subsequent rupture of bonds, followed by disintegration of tablet. The fastest disintegrating ibuprofen tablets were F2 (8.3 mins), and F3 (9.02 mins). While the slowest ones were F5 and F6 with disintegrating time of (13.35 mins) and (14.30 mins). Adjei *et al.*, (2017) also found that all the tablets formulated with cassava and maize starches passed the official disintegration test for uncoated tablets with disintegration time of ≤ 15 mins [2].

Conclusion:

This research has shown that, the MCC prepared from *Gompherena serrata* Fiber gives the optimum yield. The Prepared MCC was determined and the result obtained for evaluated physicochemical characteristics of six (6) batches of ibuprofen tablet. This indicates significance evidence *Gompherena serrata* can be used to prepared MCC for pharmaceutical excipient

The tablets obtained from the prepared microcrystalline cellulose were good and acceptable as none had a surface defect, with all the physical parameters test carried out on the tablets.

Conflict of interest:

There is no conflict of interest to declare.

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