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PHARMACEUTICAL EVALUATION OF DIRECT COMPRESSIBLE ACETYLSALICYLIC ACID TABLETS CONTAINING SAWDUST MICROCRYSTALLINE CELLULOSE

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ABSTRACT

The objective of this work was to evaluate the in-vitro formulation properties of sawdust microcrystalline cellulose with a poorly compressible active pharmaceutical ingredient, by direct compression. All the tablets produced by direct compression, show acceptable pharmacopeia standard and a superior tableting properties when compare to aspirin® available commercially in Nigeria pharmaceutical market. The accelerate stability studies reveals, that the formulation under consideration is very stable as the percentage decrease in acetylsalicylic acid content after six months was less than 0.1% w/w while other tested parameter remain the same. Therefore sawdust microcrystalline cellulose can be developed locally (Nigeria) in commercial quantity for use as direct compressible excipients in pharmaceutical tableting.

Keywords: Acetylsalicylic acid (ASA), Sawdust Microcrystalline cellulose, Direct Compression

INTRODUCTION

Acetylsalicylic acid today is one of the poorly compressible pharmaceutical active ingredients. Acetylsalicylic acid powder is also high hydro-labile and as such, judicious selection of both the pharmaceutical excipients and tableting method cannot be overemphasized, in order to ensure stability of acetylsalicylic acid tablet, dry granulation (i.e. slugging) is mostly preferred method of production. Acetylsalicylic acid belong to class of drug referred to as Non-steroidal anti-inflammatory drugs, it's clinically useful as analgesics, anti-inflammation, antipyretic, anti-thrombolytic and anti-rheumatic **[1]**. Acetylsalicylic acid act by inhibiting the cyclooxygenase (Cox) activity resulting in decrease synthesis of prostaglandin, leukotriene and thromboxane precursors which is the ubiquitous enzyme that catalyze the initial step in the synthesis of prostanoids **[2]**.

Acetylsalicylic acid was first isolated in 1928 from willow bark by Johann Buchner, it is still clinically relevant drug. It is useful in the treatment of pain, inflammation, and rheumatics' conditions. Its also useful in preventing formation of thrombus in certain cardiovascular diseases **[3]**.

Microcrystalline cellulose is a naturally occurring polymer, useful pharmaceutically as tableting excipient; microcrystalline cellulose has been proven to be stable, safe and physiologically inert **[4]**. The introduction of microcrystalline cellulose as tableting excipient had revolutionized tableting technology because of it's unique compressibility and carry capacity and sawdust microcrystalline cellulose had been show to posses similar physicochemical properties to avicel® **[4]**. There is therefore a need to evaluate the tableting properties of sawdust microcrystalline cellulose with a poorly compressible active pharmaceutical ingredient like acetylsalicylic acid with the view of assessing the suitability of locally process sawdust microcrystalline cellulose in tablet production by direct compression.

Direct compression is the simplest and most economical method of producing pharmaceutical tablets, since it require less processing steps than other techniques of tableting, such as wet granulation and roller compaction **[5]**. Direct compression involve the mixing of active pharmaceutical ingredient with other excipients and then compressed without the granulation step,

thereby providing an excellent technique of tableting heat or moisture sensitive pharmaceutical ingredients **[5]**.

Figure 1: Chemical Structure of Aspirin

MATERIALS AND METHODS

Materials

Acetylsalicylic acid powder (Cadilar Pharmaceutical, India), Sawdust microcrystalline cellulose (60µm) (A.B.U. Zaria), Cafenol® tablet (Lifecare Pharmacy and stores, Kano).

Direct Compression Production of Acetylsalicylic Acid Tablets

To produce hundred tablets of acetylsalicylic acid tablets by direct compression, the formula in **Table 1** was used. 30g of acetylsalicylic acid powder was accurately weighed into a mortal, this was however followed by weighing, addition and mixing of sawdust microcrystalline cellulose. The two powders were thoroughly mixed for about 20 minutes. 1.12g of the dry disintegrants, (starch) was weighed and added to the mixture, and mixing was continued for another 10 minutes. The admixture was adequately lubricated with appropriate quantities of talc and magnesium stearate before compression in a tableting machine (Erweka apparatus GmbH AR 400) fitted with 12mm flat-faced punch and die set. The compressing pressure was % metric tone. The tablets produced were kept in desiccators for 24 hours before the tableting properties were evaluated.

Table 1: Formula for Acetylsalicylic Acid Production Tablets by Direct Compression

MATERIAL	QTY/ TABLET (In mg)	QTY/100 TABLETS (In gm)
ASA	300	30
SDMCC	80	8
STARCH	11.2	1.12
MAGNESIUM STEARATE	0.8	0.08
TALC	8	0.8
TOTAL	400	40

Evaluation of Tablets Properties

A. Uniformity of Tablet Weight Test

Ten tablets from the batch were randomly selected, individual weight of the selected representative was determined using a digital electronic balance [Denvar Instrument xp 300, England]. The average tablet weight and the standard deviation from the mean were calculated.

B. Tablet Crushing Strength/ Tensile Strength

Using a Monsanto hardness tester, ten tablets were randomly selected, the instrument was set to zero reading, after which one tablet was placed in the mouth of the instrument which was operated by screwing clockwise until the tablet break. The reading at the breaking point was noted and the procedure repeated for the remaining nine tablets. The tensile strength was however calculated using the equation below.

Tensile strength = $2P/\pi dt$

Where P = Tablet crushing strength, d=Tablet diameter, t=tablet thickness

C. Tablet Friability Test

Roche friability (Erweka type TA3R) was employed for the friability test. The initial weight of all ten tablets together was noted before the tablets were placed in the friabilator which was then operated for four minutes at 25rmp. The tablets were dusted individually after the revolution and their finial weight determined by re-weighing all the ten tablets together.

$$\text{Friability or \% Lost in Weight} = \left[\frac{W_1 - Wf}{W_1}\right] \times 100$$

Where W_1 = initial weight of all the ten tablets

F_1 = finial weight of all the ten tablets after dusting

D. Tablet disintegration Test

Six tablets randomly selected were introduced into the six baskets of the Manesty disintegration testing apparatus (Manesty Ltd, U.K). The disintegrating medium was de ionized water maintained at $37\ ^0c \pm 1^0c$. The time taken for each tablet to break up into a smaller units and passes through the screen mesh orifices at the bottom of the basket was recorded.

E. Assay of Acetylsalicylic Acid Tablet.

Twenty tablets randomly selected were powdered with a mortar and a pestle, the amount of powder tablets equivalent to about 1.5g of acetylsalicylic acid was measured and added to 50ml of 0.5m of sodium hydroxide. Back titration was carryout with 0.25m of sulphuric acid using 3 drops of phenolphthalein as indicator.

Each ml of 0.5m sodium hydroxide is equivalent to 45.04mg of acetylsalicylic acid. The amount of acetylsalicylic acid content in the sample was then calculated

F. Dissolution Test for Acetylsalicylic acid Tablets.

Calibration Curve; Standard solutions of acetylsalicylic acid were prepared by weighing 100mg of Acetylsalicylic acid pure powder and dissolving in 100ml of 0.05M acetate buffer solution. Appropriate serial dilutions were made with 0.05M acetate buffer solution and the absorbance was determined at wave length of 296 nm. A graph of absorbance against concentration was plotted. The slopes and intercepts were calculated.

Procedure for Dissolution Test

The U.S.P (2010) basket method was employed.

The dissolution medium was acetate Buffer solution maintained at 37^0C, one tablet of acetylsalicylic acid tablet was added to the mesh cylindrical baskets and the baskets were lowered in the vessels and rotated at 100rmp. Aliquots of dissolution medium (acetate buffer) were withdrawn at 10 minutes intervals. This was filtered and diluted appropriately in a volumetric flack. Equal volume of acetate buffer was used to replace the volume withdrawn at each interval. Absorbance of each sample was taken and recorded at 296nm.

RESULT

Table 2 below shows the physical properties including mean tablet weight (mg), tablet hardness/crushing strength (kg/f), tensile strength (kg/fm^{-2}), friability (%), Disintegration time (min), thickness, diameter of the ASA tablet produced by direct compression. All the tablets produced were spherical in shape, and all are free from any tableting defects.

Table 2: Some Physical Properties of Acetylsalicylic Acid Tablets, Produced by Direct Compression

Tableting Properties	D/C	ASPIRIN®
Mean tablet weight (mg)	400 ± 0.8	400 ± 0.8
Tablet hardness/crushing strength (kg/f)	7.5	9.0
Tensile strength (kg/fm^{-2})	0.121	0.145
Friability (%)	0.32	0.33
Disintegration time (min)	2	10.0
Thickness	3.3 mm	3.3
Diameter	12 mm	12 mm

Table 3: % ASA Content with Time

Time point	%ASA	Disintegration	Friability
0 month	99.1%.89	2.6 min	0.32
1 month	99.1%	2.6 min	0.32
2 months	99.0%	2.6 min	0.32
3 months	99.0%	2.6 min	0.32
4 months	99.0%	2.6 min	0.32
5 months	99.0%	2.6 min	0.32
6 months	98.8%	2.6 min	0.32

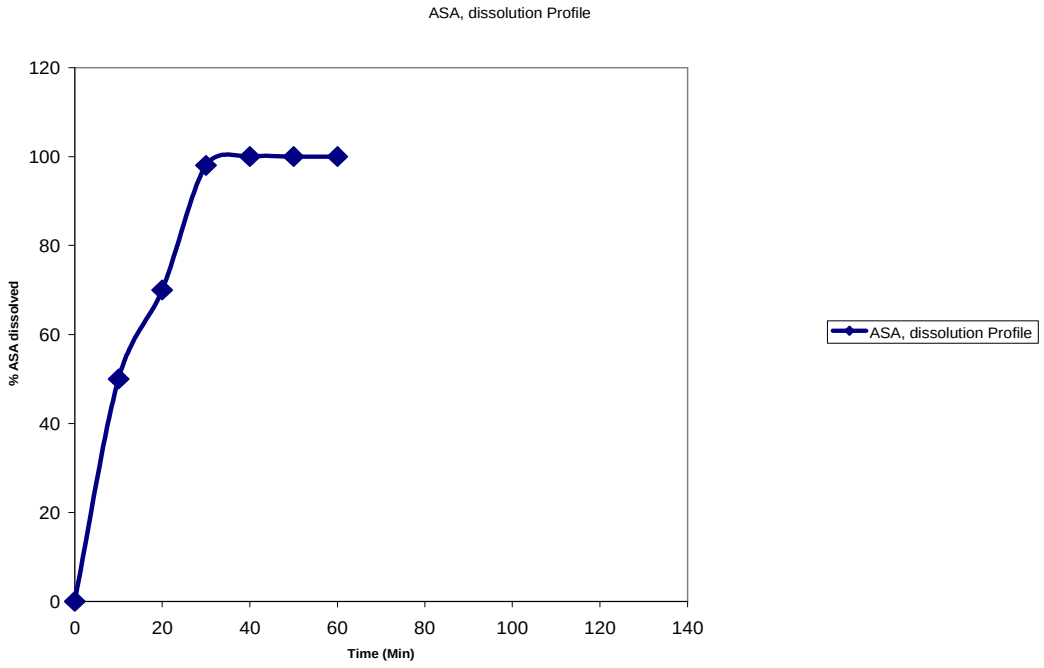

Figure 2: Dissolution Profile of Acetylsalicylic Acid Tablets

DISCUSSION

Direct compression acetylsalicylic acid tablets produced and evaluated in this study sow acceptable pharmacopeia standard and all are free from physical tableting defects. The average weight of the tablet was 400mg, and a standard deviation of 0.8% from the mean. The British pharmacopeia 2002 stated that no single tablet in a batch must deviate from the mean by value above 5% for pharmaceutical tablets to be acceptable and satisfactory.

The variation of the weight of individual tablet is a valid indication of the corresponding variation in the uniformity of drug content **[5]**. Also a good uniform weight tablet indicates a good uniform flow of powder mass from the hopper to the die wall.

The crushing strength of 6 kgf is considered adequate for tablet produced by direct compression. The crushing strength is a measure of the compressional strength of tablets which depends on binding ability of the binder used **[6]**. The higher the crushing strength the stronger the tablet. It has been reported that microcrystalline cellulose is the most compressible filler/binder known **[7]**.

Tablet Tensile Strength follow similar trend with the tablet crushing strength since there is established relationship between the two parameters.

The friability of 0.32% is considered very satisfactory and acetylsalicylic acid tablets produced is capable of withstanding any normal handling and transportation stress. Friability value above 1% is generally considered unsatisfactory and the batch of tablets is normally rejected.

The dissolution profile of acetylsalicylic acid tablets produce by direct compression show that total dissolution of the active drug in about 40 minutes.

Also the acetylsalicylic acid tablets disintegrate very rapidly and were well within the official limits of 15 minutes, and in actual fact the direct compression formulation disintegrate faster when compare to commercial aspirin tablets produced by slugging. The faster disintegration and dissolution of acetylsalicylic acid tablets produced under this study is an added advantage as this will provide faster therapeutic activities.

[8] suggested that direct compression is able to produce tablets at a lower cost than either wet granulation or dry granulation. This is due to a fewer manufacturing equipments and fewer processing steps. It was also confirmed during the studies that tablets produced by direct compression were similar in physical properties to those produced by wet/dry granulation method.

CONCLUSION

Direct compression method can be used alternatively to produce pharmaceutical tablets that will comply with official standards, most especially heat and water sensitive pharmaceutical products. Acetylsalicylic acid tablets formulation, contain 20% sawdust microcrystalline cellulose produced and evaluated in this study, complied with pharmacopeia standard and posses superior disintegrating properties when compare to commercial grade aspirin sold in Nigeria pharmaceutical market. The formulation was also shown to be pharmaceutically stable and fit for clinical use.

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