

## **Comparative Study of The Physicochemical Properties And Dissolution Profiles of Some Brands of Acetylsalicylic Acid Tablets Marketed In Benin City, Edo State, Nigeria.**

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**Abstract:** In this study, effort was made to assess the quality of some commercially available brands of Acetylsalicylic acid 300 mg tablets dispense in Benin City. Acetylsalicylic acid (ASA) tablet is one of the safest and most affordable over the counter (OTC) drug globally. It is used in the treatment of general pain, fever, and also to relieve mild to moderate pain from conditions such as muscle aches, toothaches, common cold and headache. Different parameters of quality control of pharmaceutical product that can guarantee the quality, bioavailability and optimal therapeutic activities were studied.

**Material and methods:** Seven (7) brands of Acetylsalicylic acid (300 mg) tablets were purchased from different pharmacy outlets in Benin City, Edo State, Nigeria. Benin City was chosen for this study because of its central location to the Southwestern, Southeastern and the Northern states of Nigeria and hence of significant importance in drug distribution net work. The organoleptic and physicochemical properties were determined. The British Pharmacopoeia (BP) and United States Pharmacopoeia (USP) Official standards (weight uniformity, content uniformity, disintegration time and dissolution rate) and unofficial standards as recommended by manufacturers (such as hardness, thickness and friability) were determined. The moisture absorption tendency of the various brands was studied for a period of 10 days.

**Results and discussion:** The organoleptic parameters revealed that the various brands had suitable appearances, smooth and evenly colored with distinct inscriptions. Two brands failed the disintegration test ASA 3 (20 min) and ASA 4 (24.6min). All the brands passed the weight uniformity test as per the BP and USP standard that not more than 2 of the samples should deviate from the average weight within  $\pm 5\%$ . All the brands passed the hardness test. ASA 1, 2, 3 and 7 had relatively high rate of moisture absorption tendencies. All brands showed high tensile strength values except ASA 5 (0.68) and ASA 6 (0.48) that were relatively low. Friability values were satisfactory except ASA 1 (1.6), a value slightly higher than the upper limit of 1. The BP dissolution requirement of  $\geq 70\%$  drug release within 45 min was met by all the brands.

**Conclusion:** Although the acetylsalicylic acid tablets marketed and dispensed in Benin City, Edo State, vary in their total pharmaceutical quality, they nevertheless satisfy the average BP, USP standards of quality and therefore safe for patients use.

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### **I. INTRODUCTION**

Acetylsalicylic acid tablet is a relatively safe, available and most affordable over the counter drug (OTC) amongst the Non-steroidal anti-inflammatory drugs (NSAIDS). Acetylsalicylic acid also known as Aspirin (ASA) is used often in the management of pain, fever, and inflammation in conditions such as arthritis. At low doses, aspirin is used long-term to help prevent heart attacks, strokes, and blood clot formation in people at high risk<sup>1</sup>. The quality of a pharmaceutical product is to ensure the safety of the patients and the effective delivery of the product to its site(s) of action and to optimally achieve its clinical response when administered. Aspirin is stable in dry air, but gradually hydrolyses in contact with moisture to acetic and salicylic acids<sup>2</sup>. This necessitates that appropriate and adequate packaging measures are put in place to forestall this breakdown of the drug. There is some evidence that acetylsalicylic acid tablet is effective at preventing colorectal cancer<sup>3</sup>. Aspirin is known to cause hemolytic anemia in people who have the genetic disease glycoase-6-phosphate dehydrogenase deficiency, particularly in large doses and depending on the severity of the disease<sup>4</sup>. People with kidney disease, hyperuricemia, or gout are cautioned not to take aspirin as this may inhibit the kidneys' ability to excrete uric acid; thus exacerbating these conditions<sup>5</sup>. The Pharmacopoeias and the formularies have defined standards which compressed tablets must meet known as Official tests (weight uniformity, content uniformity, disintegration time

and dissolution rate)<sup>6</sup>. These are however different from the “unofficial tests” which although not stated in the pharmacopoeias are undertaken by manufacturing companies in order to ensure uniformity and integrity of manufactured products (appearance, size and shape, friability, hardness, thickness). Various limits of variation from the standards are set for different drug monograph.

## II. MATERIALS AND METHODS

**Materials:** Seven (7) different brands of acetylsalicylic acid tablets (300mg) were purchased from different pharmacy outlets in Benin City, Edo state, Nigeria. Pure Acetylsalicylic acid (analytical grade) was purchased from Sigma, Aldrich, ChemieGmb H, Germany. The information on the various brands of acetylsalicylic acid tablets (300mg) is shown on Table 1 with ASA 6 (Chemo Pharm Laboratories) taken as the standard brand.

**Table 1: Information on the Various Brands of Aspirin 300mg Tablets**

COD E NO.	BRAND OF ASPIRIN	NAME OF MANUFACTURER	COUNTRY OF ORIGIN	NAFDA C NO.	BATC H NO.	MANUFACTURING DATE	EXPIRY DATE
ASA 1	Biopharma	Biopharma Ltd.	Nigeria	A4-2081	AO4AT	02/17	01/20
ASA 2	Emprin	Emzor Pharmaceutical	Nigeria	04-0264	4213T	08/16	10/19
ASA 3	Kunimed	Kunimed Pharmaceutical	Nigeria	04-3231	AK166	12/16	02/19
ASA 4	Disprin	ReckitBenckierer Pakistan Ltd.	Nigeria	000152	4017	11/16	10/19
ASA 5	Anacin	While Hall Laboratories	Nigeria	04-2225	A1523	09/17	05/20
ASA 6	Aspirin Caplet	Chemo Pharm Laboratories	Nigeria	04-3587	AC0031 5	10/16	10/19
ASA 7	Propron	Pharmchem Industries	Nigeria	04-1204	PP971	02/16	11/19

**Methods:** The parameters evaluated were based on standards of tablet properties as published in the various International Pharmacopoeias and Formularies (BP, USP/NF).

**Organoleptic properties:** the color, inscription on the tablet surface, finishing (dull/glossy) and coating type were examined. All the samples and differences in observations were handled objectively.

**Dimensions (thickness and diameter):** The dimensions of the tablets were measured using a Vernier caliper. The tablets were selected randomly from each brand and measured and the mean of triplicate readings were recorded in millimetres.

**Hardness tests:** the hardness of the tablets was measured using a Monsanto hardness tester. The force to break the tablet was applied diametrically, placing the tablet between the anvil and spindle of the tester, and the knurled knob turned until the tablet fits into space and adjusted to zero. The pressure was applied by turning the knurled knob until the tablet breaks. The force (kg) was read from the scale and the mean of triplicate determinations of each brand was recorded.

**Tensile strength:** the mean of dimension values of tablet thickness, diameter and hardness of each brand were used to calculate the tensile strength of the tablets using the formula:

$$\text{Tensile strength} = \frac{2F}{\pi DH}$$

Where

- F = breaking force (kg)
- D = tablet diameter (mm)
- H = tablet thickness (mm)
- $\pi$  = 3.143

**Weight uniformity test:** randomly selected tablets (20) from each brand were weighed individually and collectively using a digital weighing balance (Ohaus-Scout PRO) and values in (gm) recorded.

**Friability test:** tablets (10) were selected randomly from each brand, weighed, collectively and recorded ( $W_1$ ). The tablets were placed in an Erweka friability tester and rotated at a speed of 25 rpm, and after 100 revolutions (4 min), the machine was stopped and tablets dusted and re-weighed ( $W_2$ ). Friability (%) was calculated using the formula:

$$\text{Friability (\%)} = \frac{(w_1 - w_2)}{w_1} \times \frac{100}{1} \text{-----} 2$$

**Disintegration test:** The USP disintegration apparatus was used. It consists of 6 glass tubes that are 3 inches long, open at the top, and held against a 10-mesh screen at the bottom end of the basket rack assembly. One tablet was placed in each tube, and the basket rack positioned in distilled water maintained at a temperature of  $37 \pm 0.5^\circ\text{C}$ . This was done such that the tablet remained 2.5cm below the surface of the liquid on their upward movement and descent not closer than 2.5cm from the bottom of the beaker. A perforated plastic disc was placed on top of the tablets to impart an abrasive action to the tablets and also to prevent the tablets floating to the top. The apparatus was operated and the time it took all the particles to pass through the 10-mesh screen was recorded. The mean of the time for the six tablets of each brand to disintegrate was recorded<sup>7</sup>. For uncoated tablets the USP and BP specifies disintegration time of 15 min.

**Preparation of standard drug solution:** Pure acetylsalicylic acid powder (0.1g) was dissolved in 50 ml of 0.1N HCl, stirred for 5min and the volume made upto 100ml with same solvent to get stock solution of  $20\mu\text{g/ml}$ . This was serially diluted to concentrations of 2, 4, 6, 8 and  $10\mu\text{g/ml}$  respectively. The absorbance of these solutions was determined respectively, using the UV Spectrophotometer at maximum wavelength of 284nm and plotted against concentration.

**Determination of dissolution rate:** The dissolution medium (800 ml of 0.1N HCl) was maintained at a temperature of  $37 \pm 0.5^\circ\text{C}$  with a thermometer and a thermostat. The USP dissolution apparatus (rotating basket) was used<sup>8</sup>. This consists of a cylindrical vessel with a hemispherical bottom made of glass and covered, a motor, a metallic drive shaft, and a cylindrical basket. The vessel was partially immersed in a suitable water bath maintained at a temperature of  $37 \pm 0.5^\circ\text{C}$  during the test whilst keeping the bath fluid in constant smooth motion<sup>8</sup>. One tablet of Aspirin 300mg was placed in the apparatus, and care was taken to exclude airbubbles from the surface of the tablet and the apparatus was operated at the specified rate. At time intervals of 5, 10, 15, 30, 45 and 60 min, 5ml aliquot samples were withdrawn from the flask into appropriately labeled test tubes. A 5ml of fresh dissolution medium at same temperature was added to the flask after each withdrawal to maintain sink condition. These samples were then filtered to remove any particle and the absorbance of the solutions was measured at a maximum wavelength of 284 nm. The amount of drug dissolved was calculated using the standard calibration curve. The same procedure was repeated for the different brands of tablets. The percentage drug dissolved at the different time intervals was calculated and recorded using the formula below:

$$\% \text{ drug dissolved} = \frac{\text{Conc. dilution factor} \times \text{vol. of dissolution medium}}{\text{Actual content of active ingredient}} \times \frac{100}{1} \text{-----} 3$$

**Humidity sorption of acetylsalicylic acid tablets:** The method previously adopted by Shendeet *al.*, 2009 was employed<sup>9</sup>. The tablets were stored for 10 days in a controlled environment of 75% relative humidity and temperature of  $25^\circ\text{C}$ . Saturated solution of Sodium Chloride was used to obtain the above conditions using laboratory desiccators. The Petri dish containing the tablets was then placed in the 75% RH Chamber to observe the moisture uptake. The weight increase due to moisture absorption was measured by taking weight at different intervals of 24 h and 48 h; followed by consecutive weighing at every 72 h for a period of 10 days.

### III. RESULTS AND DISCUSSION

**Table 2: Organoleptic parameters of the brands of aspirin tablets**

CODE NO.	BRAND NAME	COLOUR	COATING	INSCRIPTION	FINISHING
ASA 1	BIOPHARMA	WHITE	COATED	NONE	ROUGH
ASA 2	EMPRIN	OFF WHITIE	UNCOATED	EMZOR	SMOOTH
ASA 3	KUNIMED	WHITE	UNCOATED	KUNIMED	ROUGH
ASA 4	DISPRIN	WHITE	UNCOATED	DISPRIN	SMOOTH
ASA 5	CHEMOPHARMA	LIGHT BLUE	UNCOATED	CHEMOPHARMA	SMOOTH

<b>ASA 6</b>	ANACIN	LIGHT BROWN	UNCOATED	NONE	SMOOTH
<b>ASA 7</b>	PROPON	PINK	UNCOATED	PIL	SMOOTH

**Organoleptic properties:** Table 2 shows the organoleptic properties of the different brands of Aspirin tablets. All the samples have suitable appearance. They were smooth and evenly coloured with the inscription marking clearly distinct. Dates of manufacture and expiry dates were clearly written along with the manufacturers identities.

**Table 3: Summary of results on the various tests carried out on the brands of aspirin tablets.**

CODE	Means weight (gm)	Mean diameter (mm)	Mean thickness (mm)	Mean Hardness (kg)	Tensile Strength (h)	Friability (%)	Moisture Absorbance (%)	Disintegration Time (min)
ASA 1	0.31	9.18	4.31	7.9	1.30	1.6	3.23	19.20
ASA 2	0.35	10.21	4.53	8.4	1.33	0.5	6.94	13.01
ASA 3	0.34	11.05	4.20	12.5	1.68	0.6	3.03	20.1
ASA 4	0.45	12.20	2.17	7.1	1.67	0.2	1.06	24.6
ASA 5	0.43	10.38	4.28	4.84	0.68	0.2	0.0	2.33
ASA 6	0.58	9.45	16.02	11.34	0.48	0.5	0.83	1.80
ASA 7	0.54	12.22	4.15	9.1	1.12	0.2	3.70	1.50

Table 3 shows the mean values of the parameters evaluated for all the brands of Aspirin tablets. Tablet thickness specification is characteristic to each product and values must be within  $\pm 5\%$  of the specified value. The results showed that the various brands passed the test by not deviating from the mean by more than  $\pm 5\%$ . Factors such as the density of the granules, the applied compression pressure can influence the variation of tablet thickness. None conformity to thickness specification may cause packaging and transportation problems. The uniformity of tablet diameter depends on the diameter of the punch and die used for the compression process. The standard deviation permitted is  $\pm 5\%$  of the mean diameter. The result of the evaluation shows that all the brands complied with the test. The various brands of Aspirin tablets were sufficiently hard enough to withstand packaging and transportation hazards. Their values complied with the BPC specification of  $\geq 4$ kg. Tablet hardness depends on particle size distribution, moisture content of granules, compression pressure and the types and concentration of binders used in the formulation<sup>10</sup>. All the brands passed the weight uniformity test as specified by the BP and USP standard that not more than 2 of the tablets in the sample batch should deviate from the average weight within  $\pm 5\%$ . Flow properties and lubrication of the granules are factors that can affect the weight uniformity of tablets within a batch<sup>11</sup>. Tensile strength provides a more fundamental measure of the mechanical strength of the compressed material, and takes into account the geometry of the tablet. From the results of the 7 brands evaluated, all were found to be sufficiently strong except ASA 5 (0.68) and ASA 6 (0.48) respectively. However, the seven brands passed the hardness range of  $\geq 4$  kg. All samples passed the friability test of BPC which specifies values ranging within  $0 \leq 1$  except ASA 1 (1.6). Thus all the tablet brands were sufficiently strong enough to withstand the mechanical stress and abrasion as they are packaged and transported from one location to another. The BP and USP specify that the disintegration time of uncoated tablets should not exceed 15min. The result shows that the disintegration time of ASA brands 7, 6, 5 and 2 fall within the time of 15 min, while ASA brands 1, 3 and 4 exceeded 15min but within 30min. ASA 1 which is coated passed the time of within 30min for coated tablets. ASA brands 3 (20min) and 4 (24.6 min) fall short of the standard; their values however, did not affect the dissolution rate profile of the brands.

**Moisture absorption:** The results showed that the percentage of moisture absorbed by ASA 1, 2, 3 and 7 were high with values ranging from 3.03 to 6.94%. ASA brands 4, 5 and 6 have values ranging from 0.0 to 1.06%. The brands of Acetylsalicylic acid tablets ASA 2 (6.94%), ASA 7 (3.70%), ASA 1(3.23%) and ASA 3 (3.03%) with high propensity to absorb atmospheric moisture need to be adequately packaged with the inclusion of bags of silica gels or other agents to create a relatively dry environment within the package<sup>12</sup>. Moisture facilitates the rapid and premature degradation of acetylsalicylic acid thereby creating stability problems<sup>13</sup>.

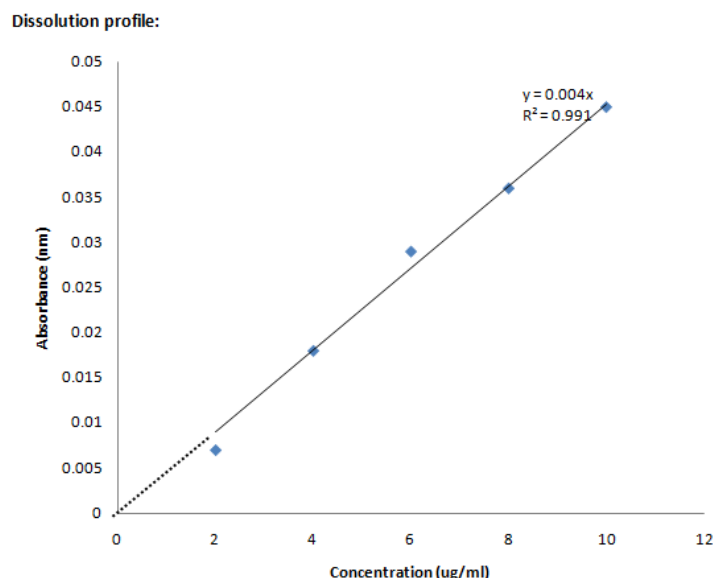


Figure 1: Standard calibration curve of pure acetylsalicylic acid powder

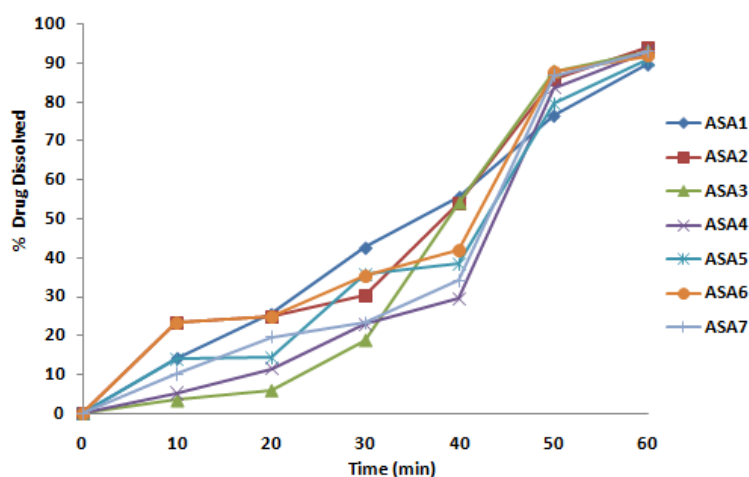


Fig2: Dissolution Profiles of 7 brands of aspirin 300 mg tablets.

All the brands of acetylsalicylic acid tablets (ASA 1 to ASA 7) passed the dissolution test, as 70% of the drug was dissolved within 45 min. Dissolution test gives an indication of assessing the bioavailability of drugs as the rate and extent of the drug absorbed depends in part on the dissolution rate of drug particles<sup>14</sup>.

#### IV. CONCLUSION

The seven (7) brands of Acetylsalicylic acid 300mg tablets evaluated had suitable appearances. Their colors were uniform with absence of visible cracks or chips and their marking were distinct. All brands passed the thickness, friability and weight uniformity tests and the tablets were sufficiently strong enough to withstand possible packaging and transportation hazards. There is the need therefore, for regular and strict regulatory control to be enforced both by the Regulatory agencies and the various Pharmaceutical companies. The synergistic efforts of these bodies will promote the total well being of users of these drugs and also help to easily identify products that are substandard in the market. It is recommended that regular assessments of quality of these drugs be carried out in the market places periodically.

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