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Research Article

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Comparative quantitative analysis of different brands of 300mg aspirin tablet marketed in Maiduguri metropolitan council

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ABSTRACT

In the last few years, aspirin has become a life saver against cardiovascular accident. This study was carried out to determine possible dose variations in the amount of active constituent (acetylsalicylic acid) in the various brands of aspirin drugs marketed in Maiduguri metropolitan council. In this study, ten different brands of 300mg aspirin tablet were randomly sampled from different pharmacy shops; identification test was performed on each sample to confirm the presence of the active drug (acetylsalicylic acid), and each of these samples was subjected to a rigorous quantitative analysis using HPLC and UV-spectrophotometer to determine the amount of the active drug. From the analysis, out of the ten brands of aspirin worked on, only Bond aspirin(41.7%) has less than 90% of active drug in UV-spectroscopy and Odesprin(112%) has more than 110% while Biopharma(99.77%), Kp(90%), Kunimed(100%), Maxprin(105%), Michelleaspirin(95%), Nemeprin(100%),Propon(93%) and Stop-eke(105%) passes the USP specification. In HPLC analysis, both Bond aspirin(41%) and Propon(57%) have less than 90% while Odesprin(112.6%) still has more than 110% and Biopharma(99.9%), Kp(95.5%), Kunimed(100%), Maxprin(105%), Michelle(95.5%),Nemeprin(100%), and Stop-eke aspirin(105%) passes the official specification. At the end of the study, it is convincingly seen that quantitative variation often exists among drugs of different product. However, despite the variation most drug products are within the official limit

Keywords: Asprin, HPLC, UV Spectrophotometer.

INTRODUCTION

Pharmaceuticals are an integral component of health care system world wide. Thus regulating weakness in the governance of pharmaceutical system can negatively impact health outcome especially in developing countries [1] Nigeria is one of the number of countries whose pharmaceutical system has been impacted by corruption and has struggled to curtail the production and trafficking of substandard drugs [2]. In 2001 the national Agency for food and drug administration (NAFDAC) underwent organizational restructuring resulting in reforms to reduce counterfeit drugs and better regulate pharmaceutical [2].despite these changes there is still room for improvement.

The WHO defined counterfeit drugs as" medicine which is deliberately and fraudulently mislabeled with respect to identity and or source". According to WHO, counterfeiting can apply to both branded and generic product and counterfeit product may includes product with correct ingredient or with wrong ingredients, without active ingredient or with fake packaging. (WHO department of essential drugs and other medicine)

Substandard drugs are genuine drug product which does not meet quality specification set for them. The term substandard is used to describe the quality status of genuine drug produced by legitimate manufacturer. Normally, manufacturers used specifications laid down by official pharmacopoeias such as British pharmacopoeia (BP), united state pharmacopoeia (USP) and European pharmacopoeia (EP) for each drug that they produced, if a drug fails to meet the pharmacopoeias specifications used for its formulations, The drug is classified as substandard [3]

There are also cloned drug with some quantity of active ingredient as the original drug. Cloning is hiding behind a fast moving registered product to rake up profit with out the associated liabilities and it is solely driven by financial motives. For Example panadol by GSK containing 500mg of Paracetamol powder was cloned by some criminals to contain the same 500mg paracetamol powder as original. What this frauds stars fails to understand is that minimal effective blood concentration which determines the efficacy of drug, is not only dependent on the quantity of active ingredients but also on the quality, excipient and formulation technique [3]

The big question however is who take responsibility when there are adverse effects of cloned drugs, Drugs without full name and address of the manufacturer expired drugs or drugs without expiry dates, toxic herbal preparation mixed with or orthodox medicine etc.?

As such, it is the responsibility of the pharmacist to study various brands of drug in his care before dispensing them to their patient.

Aspirin /Acetyl salicylic acid is a derivative of salicylic acid, is a derivative of salicylic acid that is a mild, non-narcotic analgesic usefully in the relief of head ache and muscle and joint aches [4]

Salicylic acid was tough on stomach and a means of "buffering" the compound was searched for, the first person to do so was fredric Gerherdt. In 1853 Gerhardt neutralized salicylic acid by buffering it with sodium salicylate and acetyl chloride [5]. Since no structural theory existed at that time, Gerherdt called the compound he obtained "salicylic acetic anhydride" Gerherdt product worked but he had no desire to market it and abandoned his discovery. In 1859, Von Gilm obtained analytically pure acetyl salicylic acid (which he called acetylated salicylic acid) by a reaction of salicylic acid and acetyl chloride [6]. In 1869, Schroder, prinzhorn and kraut concluded that both reaction gave the some compound, "Acetyl salicylic acid." they were the first to assign to it the correct structure with the acetyl group connected to the phenolic oxygen. [7]

In 1899, a German chemist named Felix Hoffmann, rediscovered Gerhardt's formulary. Hoffmann made some of the formulae and gave it to his father who was suffering from the pain of arthritis, with good result. Hoffmann then convinced Bayer to market the new wonder drug. Aspirin was patented on February 27, 1900 [4].

The folk at Bayer came up with the name Aspirin, it comes from the "A" in Acetyl chloride, the "spir" in spiraea ulmaria (the plant from which salicylic acid was derived) and the "in" was a then familiar name ending for medicine [4].

Aspirin was first sold as a powder. In 1915, the first aspirin tablets were made. The popularity of aspirin grew over the first half of the 20^{th} century, spurred by it supposed effectiveness in the wake of the Spanish flu pandemic [8].

Since its market introduction under the trade mark aspirin in the year 1899, it has profitably led to fierce competition and proliferation of aspirin brands and products, especially after the American patent held by Bayer expired in 1917 [9].

The popularity of aspirin declined after the market release of paracetamol in 1956 and ibuprofen in 1969.

CHEMICAL PROPERTIES

Aspirin, an acetyl derivative of salicylic acid, is a white crystalline, weakly acidic substance, with a melting point of 150^{o}c (pharmaceutical codex 11th edition). Acetyl salicylic acid decomposed rapidly in solutions of ammonium acetate or of the acetates, carbonates citrates or hydroxides of metals [10]

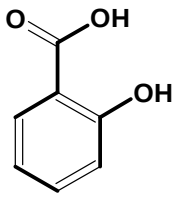
Acetylsalicylic acid is stable in dry air but in contact with moisture with the great degrades by hydrolysis to acetic acid and salicylic acid. Hydrolysis is catalyzed by H^+ and by OH^-.Sodium ions can also catalyze hydrolysis.

In aqueous suspensions, then PH of maximum stability is 2-3. Aqueous Suspensions shows appreciable decomposition after storing for only a few days. (Pharmaceutical codex 11th edition)

Degradation in tablet is increased in the presence of stearates used as lubricants (Pharmaceutical codex 11th edition), the acid dissociation constant (Pka) for aspirin is 3.5 at 25^{o}C (77^{o}F). [10].

CHEMISTRY

Aspirin also known as acetylsalicylic acid has chemical formula of $C_9H_8O_4$ and a chemical structure as [4].



salicylic acid

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There are various salt of aspirin developed i.e. the Calcium or Aluminum Salt (Soluble aspirin) hysine acetyl salicylate (Aspegic) and acetylsalicylic acid sodium glycerol phosphate (ivepirine). Aspirin slowly hydrolyses in the presence of moisture into acetic acid and salicylic ; Decomposition of aspirin is detected by the appearance of a violet color when the product is treated with ferric chlorides solutions, practically all salt of aspirin except those of calcium and aluminum are unstable for pharmaceutical use[11].

EXPERIMENTAL SECTION

Liquid Chromatography (LC) equipped with 280nm detector and 4.0mm X 30cm column packed with silica gel.
Plastic test tube
Distilled water

REAGENTS

Acetonitrile
Brand of 300mg of Aspirin tablet
Glacial acetic acid
Formic acid
Pure aspirin (USP) Tablet
Sodium -1- heptane sulfonate
0.1N HCL

IDENTIFICATION TEST

To 200mg of each of the powered drug sample, 4ml of dilute sodium hydroxide solutions was added, boil for 3minutes; cooled 5ml of dilute sulphuric acid was then added and filter; the residue, after washing with water and drying at 105^{o}C melt at about 158^{o}C. A portion of the residue was dissolved in water and ferric chloride solution was added; a purple colure was produced. This confirmed that all the brands contain the active drug (Acetyl salicylic acid).

The filtrate obtained produced an ethyl acetate odor on heating with 2ml of alcohol and 2 ml of sulphuric acid.

SAMPLE AND SAMPLE SIZE
Aspirin is used as a case study of this work; and the study is limited to ten different brands of aspirin [12].

SAMPLING METHOD
10 Different brands were randomly obtained from different pharmacy shop to ensure that each product or sample is obtained on the basis of chance [13].

UV METHODOLOGY
10 tablet of each brands of the 300mg aspirin were randomly weighed and there average weight was determined, 3 tablets from each of the brands were powered and an equivalents weight of 100mg aspirin tablet is weighed and dissolved in 100ml 0.1N GCL to give a solution equivalent to 1.0mg/ml, 1ml of this solution was pipetted and diluted with 99ml of 0.1N HCL to give a solution equivalent of 0.01 mg/ml.

The solution of each brand equivalent to 0.01mg/ml pure aspirin was then place in UV-spectrophotometer to determine their absorption at wave length of 229nm (E1%, 1cm= 434).

The Sample concentration, percentage content and the milligram content of each brand was obtained as followed.

$$C = \frac{A}{EL}$$

where
C = Sample Concentration
A = Absorbance
E = Molar Absorption
L= Path Length

$$\text{Percentage content (\%)} = \frac{\text{Sample Conc}}{\text{Working Conc.}} \times 100$$

$$\text{Milligram content (mg)} = \frac{\text{percentage content}}{100} \times 300\text{mg}$$

The USP 2007 official compendia of standard volume 2, stated that Aspirin Tablet should contain not less than 90.0% and not more than 110% of the labeled amount of aspirin ($C_9H_8O_4$).

CHROMATOGRAPHIC SYSTEM
The LC is equipped with a 280nm detector and a 4.0mm X 30cm column packed with silica gel. The flow rate is about 1ml/min. The tailing factor is not greater than 2.0 and the relative standard deviation is not more than 2.0% [14].

HPLC METHODOLOGY
MOBILE PHASE PREPARATION
2g of sodium -1- heptane sulfonate was dissolved in a mixture of 550ml of water and 150ml of acetonitrile, and adjusted with glacial acetic acid to a pH of 3.4.

DILUTING SOLUTION
A mixture of acetonitrile and formic acid was prepared at a ratio of 99:1.

STANDARD PREPARATION
100mg of pure aspirin (USP aspirin) was accurately weighed and dissolved in diluting solution to obtain a solution having a known concentration of 0.01mg/ml.

SAMPLE PREPARATION
Not fewer than 10tablet of each brand is weighed and powered. An accurately weighed quantity of the powder equipment to about 100mg of aspirin tablet is then transferred into a 100ml volumetric flask, 20ml of diluting

solution was added and shaken for 10minutes and centrifuge (Stock solution). 1ml of the stock solution is measured and diluted with 9ml of the diluting solution (Assay preparation) [13].

PROCEDURE

Equal volume (about 10uL) of the standard preparation and the sample preparation were separately injected into the chromatograph. The chromatogram is recorded and the major peak responses were measured.

The percentage content and the milligram content of aspirin in each brand are obtained as followed.

$$\text{Percentage Content (\%)} = \frac{\text{Area peak of Sample}}{\text{Area peak of standard}} \times 100$$

$$\text{Milligram Content (mg)} = \frac{\text{Percentage content}}{100} \times 300\text{mg}$$

The USP 2007 official compendia of standard volume 2, stated that: Aspirin tablet should contains not less than 90.0% and not more than 110% of the labeled amount of Aspirin ($C_9H_8O_4$).

RESULTS

INFORMATION ABOUT THE SAMPLES

TABLE1: SHOWING INFORMATION ABOUT THE VARIOUS SAMPLE

Manufacturer	BRANDS	BATCH NUMBER	EXPIRY DATE	NAFDAC NUMBER	SRENGTH	MANUFACTURE ADDRESS	MANUFACTURY DATE
Bond chemical industrial ltd	Bond aspirin	1100a	04/14	04-1619	300mg	Adesakin layout, Awe, oyo state, Nigeria	04/2011
Biopharma Nigeria ltd	Biopharma aspirin	A28AI	08/14	A4-2081	300mg	10,palace road,odogunyan,ikorodu,lagos state	09/2011
Kingsize pharmaceutical ltd	KP aspirin	29AS	06/15	04-8441	300mg	Off KM 15 Enugu road Ogidi Anambara	07/2010
Kunimed pharmchem ltd	Kunimed aspirin	AK94	08/14	04-3231	300mg	1,Adelanwa street, valley Estate, Dopemu, ikeja, lagos Nigeria	08/2011
Michelle laboratory ltd	Michelle aspirin	A134	11/13	A4-2081	300mg	Plot 23,Block 2,Thinkers corner industrial layout, Enugu, Nigeria	11/2011
Charzmax pharmaceutical ltd	Maxprin	CAS927	11/13	04-1204	300mg	Odume layout, off km2 Nkapor/obosi road, obosi Anambara state, Nigeria	12/2009
Nemel pharmaceutical ltd	Nemelprin	01	09/13	04-5037	300mg	No 4a/4b medical road, phase vi,Trans Ekulu Enugu, Nigeria	09/2010
Odesco pharmaceutical ltd	Odesprin	AO291	01/15	A4-3530	300mg	88 school road lyiowa layout ogbaru L.G.A Anambara	02/2011
Pharmchem industrial ltd	Propon	PP762	10/13	04-1204	300mg	Plot J. industries street, ilupeju PMB 21211 ikeja Lagos, Nigeria	10/2010
Richy gold international ltd	Stop-eke	1114	05/14	04-6620	300mg	103,Amuwo-odofin,industrial scheme, oshodi-Apapa expressway, Lagos, Nigeria	06/2011

TABLE 2: SHOWING MINIMUM, MAXIMUM AND AVERAGE WEIGHT

S/No	SAMPLE	MINIMUM WEIGHT	MAXIMUM WEIGHT	AVERAGE WEIGHT
1	Bond	290	300	295
2	Biopharma	310	320	321
3	Kp	320	330	323
4	Kunimed	340	360	350
5	Michelle	370	373	372
6	Maxiprin	340	420	398
7	Nemeprin	330	350	336
8	Odesprin	340	360	357
9	Propon	600	610	608
10	Stop-eke	420	440	428

UV-SPECTROPHOTOMETRY CALCULATION OF PERCENTAGE AND MILLIGRAM CONTENT

Bond Aspirin

% content=$\frac{0.181}{0.434}\times 100=41.7\%$

Mg content=$\frac{41.7}{100}\times 300mg=125mg$

Biopharma Aspirin

% content=$\frac{0.433}{0.434}\times 100=99.8\%$

Mg content=$\frac{99.8}{100}\times 300mg=299mg$

Kp Aspirin

% content=$\frac{0.391}{0.434}\times 100=90\%$

Mg content=$\frac{90}{100}\times 300mg=270mg$

Kunimed aspiri

% content=$\frac{0.434}{0.434}\times 100=100\%$

Mg content=$\frac{100}{100}\times 300=300mg$

Maxiprin

% content=$\frac{0.456}{0.434}\times 100=105\%$

Mg content=$\frac{105}{100}\times 300mg=315mg$

Nemepirin

% content=$\frac{0.434}{0.434}\times 100=100\%$

Mg content=$\frac{100}{100}\times 300mg=300mg$

Odesprin

% content=$\frac{0.486}{0.434}\times 100=125\%$

Mg content=$\frac{125}{100}\times 300mg=376mg$

Propon

% content=$\frac{0.404}{0.434}\times 100=93\%$

Mg content=$\frac{93}{100}\times 300mg=279mg$

Stop-eke

% content=$\frac{0.456}{0.434}\times 100=105$

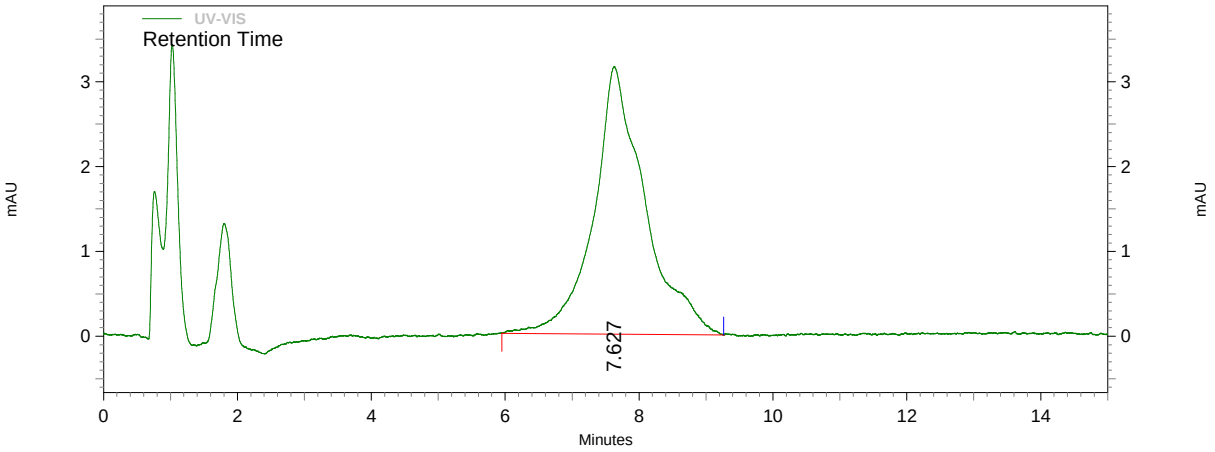
Mg content=$\frac{105}{100}\times 300mg=315$

TABLE 3: SHOWING UV-SPECTROMETRY RESULT

SAMPLES	ABSORBANCE(A)	PERCETAGE CONTENT (%)	MILLIGRAM CONTENT(Mg)
Bond aspirin	0.181	41.7	125
Biopharma aspirin	0.433	99.77	299.31
KP aspirin	0.391	90	270
Kunimed	0.434	100	300
Michelle aspirin	0.413	95	285
Maxprin	0.456	105	315
Nemepirin	0.434	100	300
Odesprin	0.486	112	336
Propon	0.404	93	279
Stop-eke	0.456	105	315

HPLC GRAPHICAL PRESSENTATION

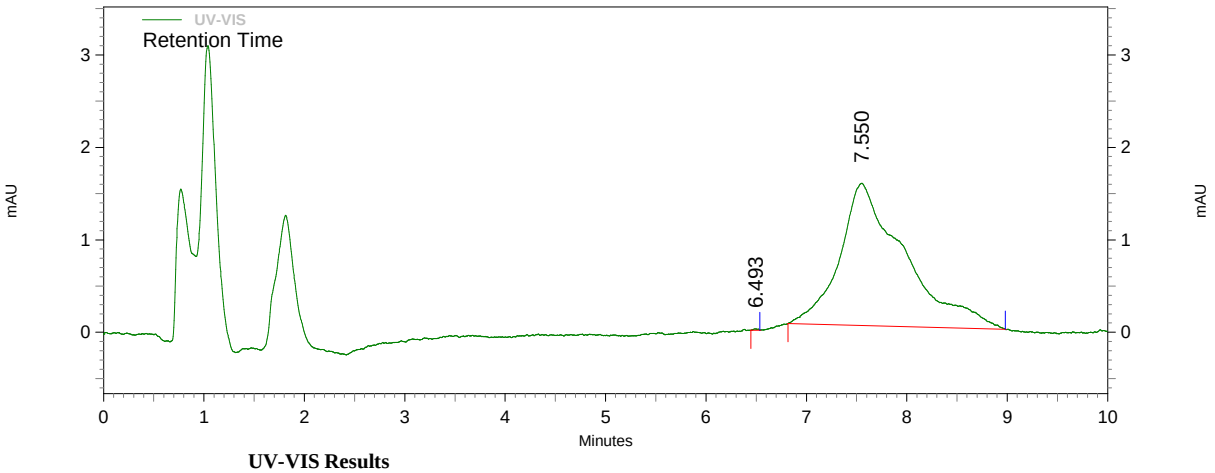
Analyst: LAB MANAGER
Sample ID: ASPIRIN STD 0.05 151211 **Vial: 200** **Injection Volume: 20**



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
ASPIRIN	7.627	668702	100.000	MM
Totals		668702	100.000	

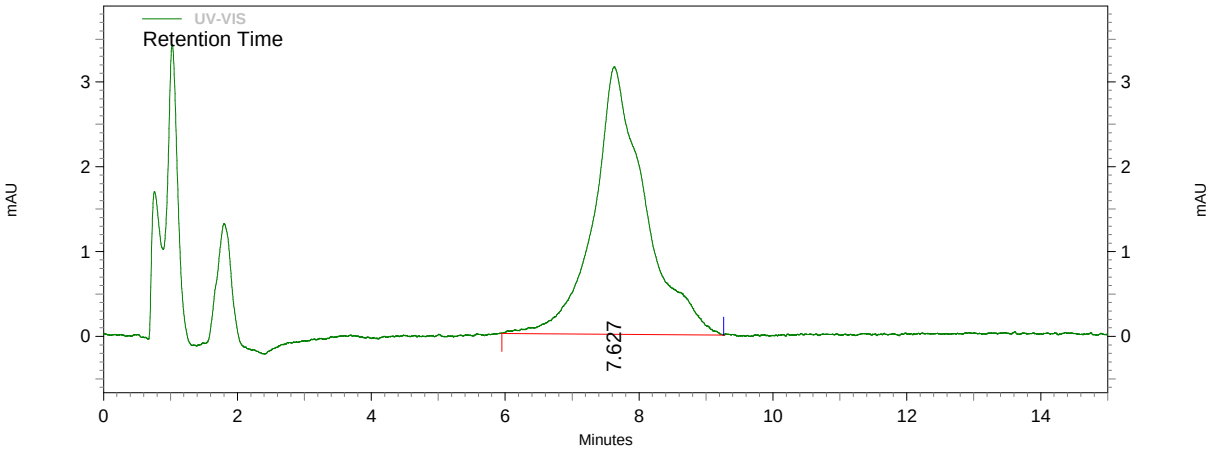
Analyst: LAB MANAGER
Sample ID: BOND 0.05 151211 **Vial: 190** **Injection Volume: 20**



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
ASPIRIN	6.493	200	0.072	IB
	7.550	276663	99.928	MM
Totals		276863	100.000	

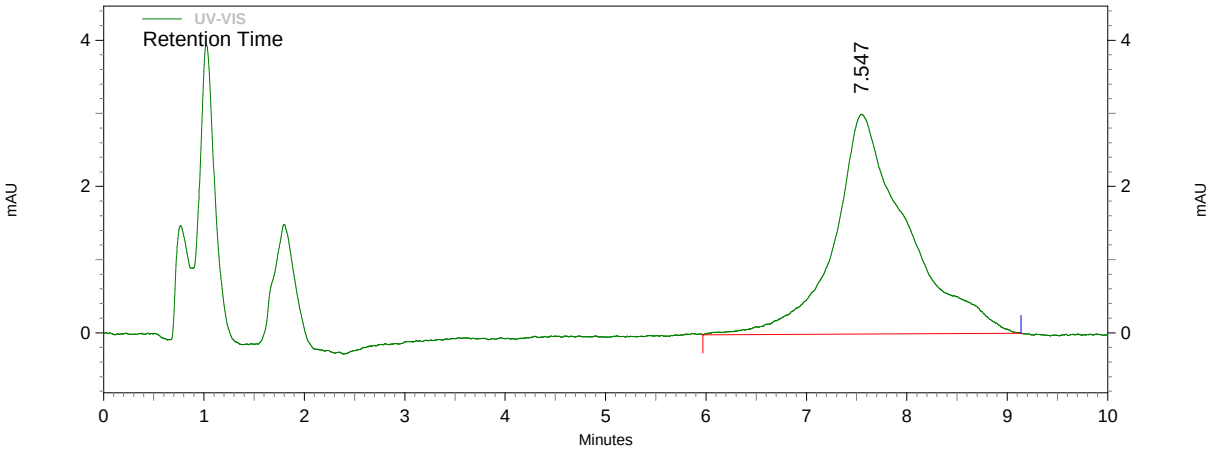
Analyst: LAB MANAGER
Sample ID: BIOPHARMA ASPIRIN 0.05 151211 **Vial: 200**
Injection Volume: 20



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
ASPIRIN				
	7.626	668701	100.000	MM
Totals		668701	100.000	

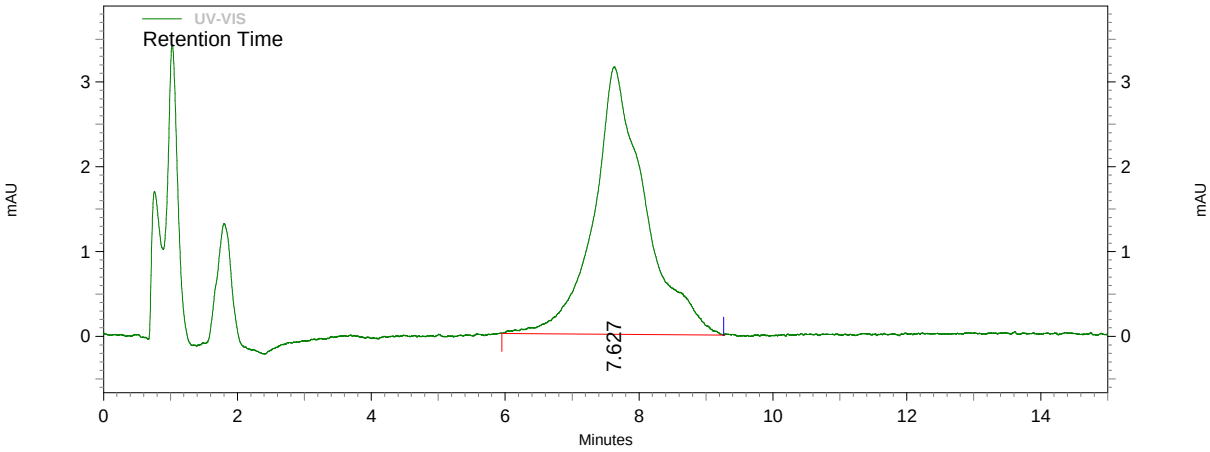
Analyst : LAB MANAGER
Sample ID: KP ASPIRIN 0.05 151211 **Vial: 190** **Injection Volume: 20**



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
ASPIRIN				
	7.547	605036	100.000	MM
Totals		605036	100.000	

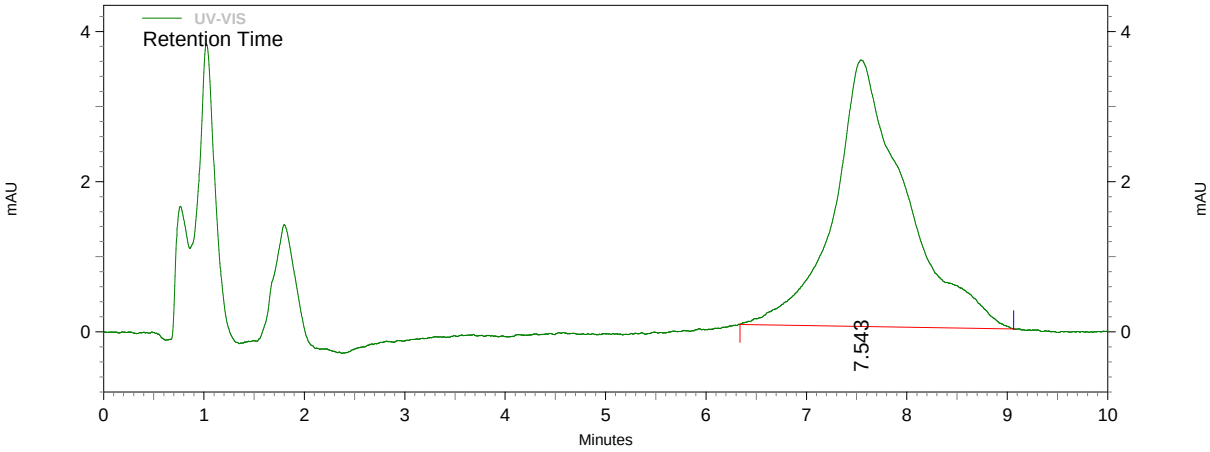
Analyst: LAB MANAGER
Sample ID: KUNIMED 0.05 151211 **Vial: 200** **Injection Volume: 20**



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
ASPIRIN				
	7.627	668702	100.000	MM
Totals		668702	100.000	

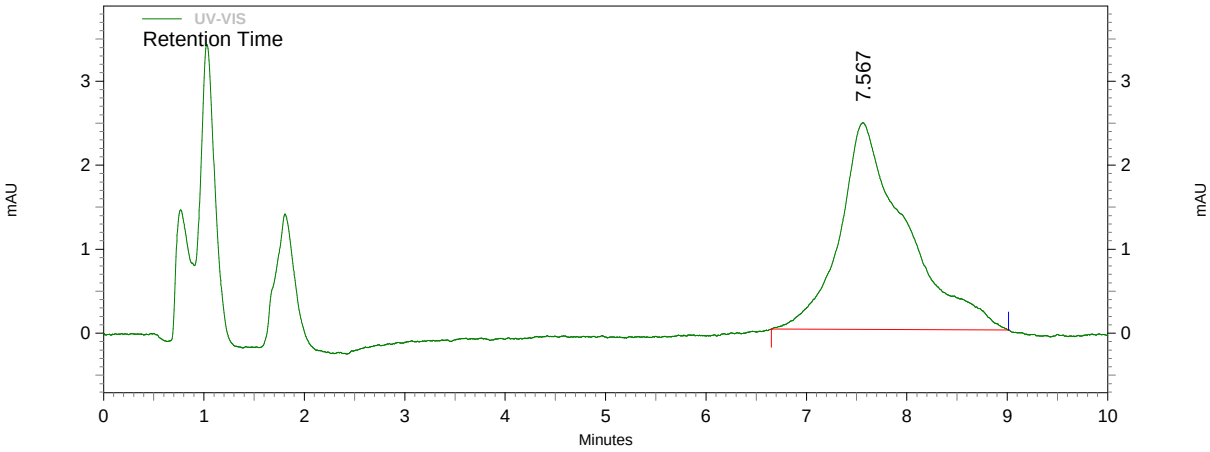
Analyst: LAB MANAGER
Sample ID: MAXPRIN 0.05 **Vial: 197** **Injection Volume: 20**



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
ASPIRIN				
	7.543	702661	100.000	MM
Totals		702661	100.000	

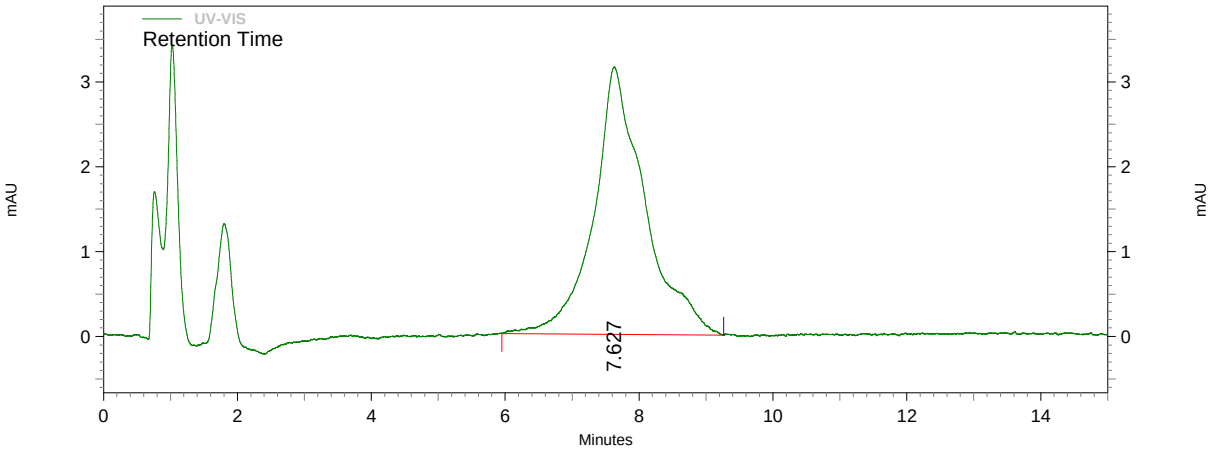
Analyst: LAB MANAGER
Sample ID: MICHELLE ASPIRIN 0.05 151211 **Vial: 200**
Injection Volume: 20



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
ASPIRIN				
	7.567	638610	100.000	MM
Totals		638610	100.000	

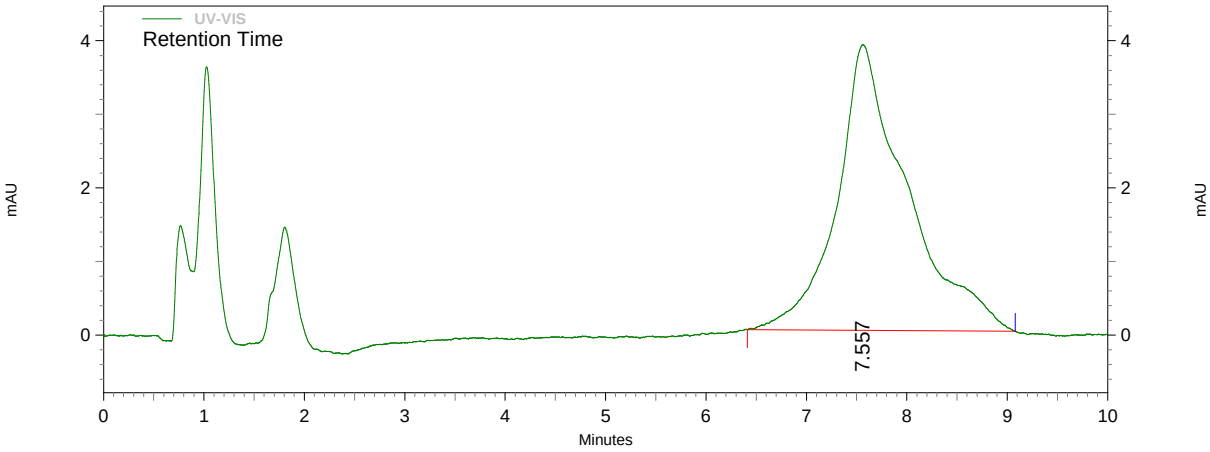
Analyst: LAB MANAGER
Sample ID: NEMEPRIN 0.05 151211 **Vial: 200** **Injection Volume: 20**



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
ASPIRIN				
	7.627	668702	100.000	MM
Totals		668702	100.000	

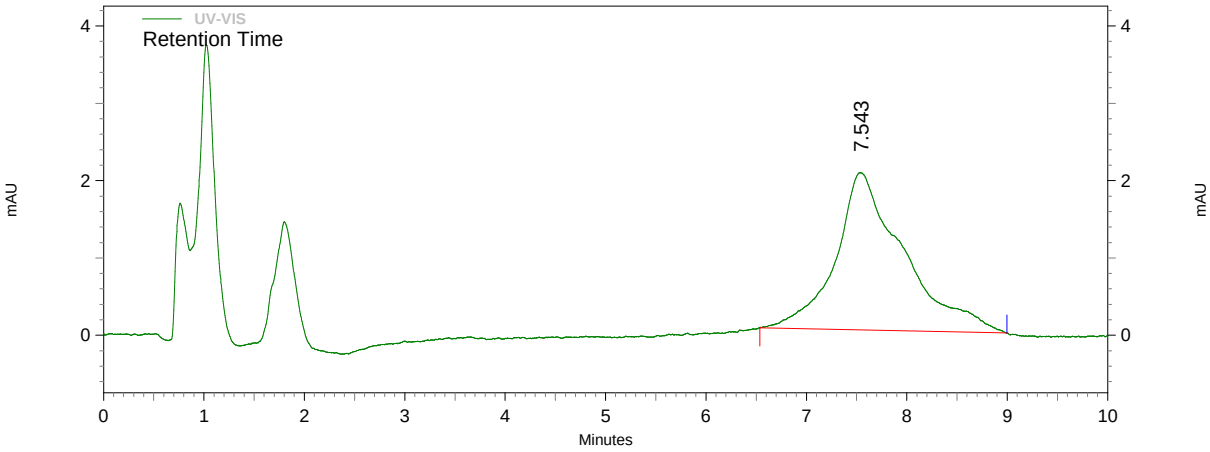
Analyst: LAB MANAGER
Sample ID: ODESPRIN 0.05151211 **Vial: 140** **Injection**
Volume: 20



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
ASPIRIN				
	7.557	753587	100.000	MM
Totals		753587	100.000	

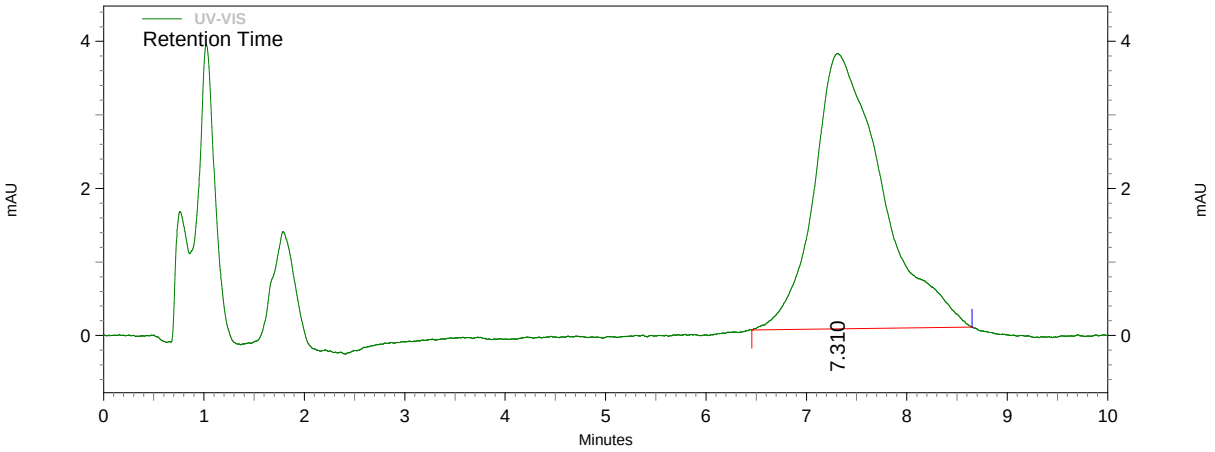
Analyst: LAB MANAGER
Sample ID: PROPON 0.05 151211 **Vial: 170** **Injection**
Volume: 20



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
ASPIRIN				
	7.543	383423	100.000	MM
Totals		383423	100.000	

Analyst: LAB MANAGER
Sample ID: STOP-EKE 0.05 151211 **Vial: 180** **Injection Volume: 20**



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
ASPIRIN	7.310	708841	100.000	MM
Totals		708841	100.000	

HPLC CALCULATION

Bond aspirin

% content = $\frac{276863}{668702} \times 100 = 41.4\%$

Mg content = $\frac{41.5}{100} \times 300 = 124\text{mg}$

Biopharma aspirin

% content = $\frac{668701}{668702} \times 100 = 99.9\%$

Mg content = $\frac{99.9}{100} \times 300 = 299.7\text{mg}$

Kp aspirin

% content = $\frac{605036}{668702} \times 100 = 90.5\%$

Mg content = $\frac{90.5}{100} \times 300 = 271.5\text{mg}$

Kunimed aspirin

% content = $\frac{668702}{668702} \times 100 = 100\%$

Mg content = $\frac{100}{100} \times 300 = 300\text{mg}$

Maxprin

% content = $\frac{702661}{668702} \times 100 = 105\%$

Mg content = $\frac{105}{100} \times 300 = 315\text{mg}$

Michelle aspirin
%content = 665358× 100=95.5%
668702
Mg content=95.5×300=286.5mg
100

Nemeprin
%content = 668702 × 100=100%
668702
Mg content=100×300=300mg
100

Odesprin
% content= 753587 × 100=112.6%
668702
Mg content=112.6×300mg=337.8mg
100

Propon
%content = 383423× 100=57%
668702
Mg content=57×300mg=171mg
100

Stop-eke
% content= 708841 × 100=105%
668702
Mg content =105×300mg=315mg
100

TABLE4: SHOWING HPLC RESULT

SAMPLE	PEAK AREA	PERCENTAGE CONTENT (%)	MILLIGRAM CONTENT(mg)
Bond aspirin	276863	41	124
Biopharm aspirin	668701	99.9	299.6
Kp aspirin	605036	95.5	271.5
Kunimed aspirin	668702	100	300
Michelle aspirin	638610	95.5	286.5
Maxprin	702661	105	315
Nemeprin	668702	100	300
Odesprin	753587	112.6	337.8
Propon	383423	57	172
Stop-eke	702661	105	315

DISCUSSION

To ensure that drugs produce the require therapeutic effect as well as avoiding toxicities due to overdose, it is very important that the content of the drugs meet the specification limit as stated in the monograph

According to USP, the percentage content of aspirin should fall within the range of 90%-110%. Out of the ten brands of aspirin analyzed, only BOND(41.7%) aspirin has less than 90% of the active drug [acetylsalicylic acid] in UV-spectroscopy while ODESPRIN(112%) has more than 110%, and the remaining brands pass the USP specification. In HPLC analysis, both BOND aspirin (41%) and PROPON (57%) have less than 90% while ODESPRIN (112.6%) has more than 110% and the remaining brands pass USP specification.

The failure to meet the specification could be due to poor preparation techniques during formulation and subsequent manufacturing, incorrect weighing and incorrect storage condition

In summary ten different product of 300mg aspirin tablet were randomly sampled from different pharmacy shop, identification test was perform to confirm the presence of aspirin (acetylsalicylic acid) in each sample and each of the sample were rigorously subjected to quantitative analysis using HPLC and UV-spectroscopy and the result were instantly recorded.

CONCLUSION

In conclusion quantitative variation often exists among drugs of different product and these variation can have significant influence on the drug activity; low level of active drug below the official recommendation often result in treatment failure, while high level of the active drug may predispose patient to drug toxicity.

However, despite the quantitative variation, most drug products are within the official specification.

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