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Research Article

COMPARATIVE QUANTITATIVE STUDY OF DIFFERENT BRANDS OF CIMETIDINE TABLET MARKETED IN MAIDUGURI METROPOLIS USING ULTRA VIOLET SPECTROPHOTOMETRY AND HIGH PERFORMANCE LIQUID CHROMATOGRAPHIC (HPLC) METHODS

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Abstract

The quantitative analysis of different brands of Cimetidine tablets was carried out (using HPLC and U.V spectrophotometric method) to determine if the drugs are of required standards. The results obtained from analysis of the various drugs were compared with that of the standard. The percentage content for each sample was calculated using the absorbance and peak areas of the samples of the samples and that of the standard to see if they are specified limit as stated by the official books. Cimetidine has a range of 98.0%-102% according to USP 2007 and the UV result shows that 4 samples passes and 3 failed while for HPLC, none of the samples passed.

Keywords: Cimetidine Tablets, UV, HPLC.

1.Introduction

The science of drug analysis is an extensively active one in terms of research and development of new, more reliable or more sensitive methods that have become of great importance in the analysis and quality control of drug and drug products at every stage of their life. A whole arsenal of chemical, physicochemical and automated analytical techniques is now available for determining the identity, purity, content, stability, safety and efficacy of drugs and their formulations. Thus in the development, formulation, marketing and pharmacokinetic assessment of a drug, the analyte is involved in several diverse areas including the following:

1. Determination of identity and purity of starting materials used in the manufacturing of the drug substance.
2. Test for identity and purity of the drug.
3. Isolation and identification of trace impurities of the drug.
4. Determination of degradation rates and degradation products of the drug.
5. Identification of the drug in a formulated product and its qualitative analysis.
6. Determination of any degradation within the formulated product and possible isolation of substance for toxicity test.
7. Evaluation of content uniformity for low dose formulations Ajibola, (2000)

1.1 CIMETIDINE

Cimetidine a H_2-receptor antagonists inhibit acid production by reversibly competing with histamine for binding to H_2 receptors on the basolateral membrane of parietal cells. cimetidine (TAGAMET), is less potent

than proton pump inhibitors but still suppress 24-hour gastric acid secretion by about 70%. Cimetidine predominantly inhibits basal acid secretion, which accounts for their efficacy in suppressing nocturnal acid secretion. Because the most important determinant of duodenal ulcer healing is the level of nocturnal acidity, evening dosing of cimetidine is adequate therapy in most instances. Cimetidine is available as prescription and over-the-counter formulations for oral administration, Intravenous and intramuscular preparations. When the oral or nasogastric routes are not an option, these drugs can be given in intermittent intravenous boluses or by continuous intravenous infusion Goodman and Gilman (2006).

1.2 LITERATURE REVIEW

In a study that was carried out on the Comparative Effects of Amlodipine and Cilnidipine on Sympathetic Nervous Modulation in Patients with Hypertension and showed the following in their Results: In patients with continuous amlodipine treatment, systolic and diastolic blood pressures (SBP, DBP) and heart rate (HR) remained unchanged. LF/HF and HF/TP ratios also remained unchanged (LF/HF 1.77±1.05 vs. 1.83±1.22, HF/TP 0.419±0.122 vs. 0.402±0.116). Plasma norepinephrine levels were comparable (370±88 pg/ml vs. 491±137 pg/ml). In patients switched to cilnidipine, SBP, DBP and HR were similar before and after switching. Interestingly, LF/HF ratio decreased significantly (p = 0.012) from 2.37±1.56 to 1.89±1.42, and HF/TP ratio increased significantly (p = 0.049) from 0.366±0.132 to 0.417±0.156, despite the comparable HR. Plasma norepinephrine concentrations decreased significantly (p = 0.009) from 359±65 pg/ml to 282±72 pg/ml. Ikai, et.al. (2010).

In another study a work was carried out to check the Reduction of metformin renal tubular secretion by cimetidine in man. To determine whether cimetidine altered the renal handling of metformin, seven subjects took 0.25 g metformin daily with and without cimetidine 0.4 g twice daily. Blood and urine samples were collected and assayed for metformin, cimetidine and creatinine by HPLC. Cimetidine significantly increased the area under the plasma metformin concentration-time curve by an average of 50% and reduced its renal clearance over 24 h by 27% (P less than 0.008). There was no alteration in the total urinary recovery of metformin when cimetidine was co-administered. The effect of cimetidine on the renal clearance of metformin was time dependent, being significantly reduced up to 6 h following cimetidine. These results appeared to be consistent with competitive inhibition of renal tubular secretion. Cimetidine had no effect on the renal clearance of creatinine, but time-dependent variations in both metformin and creatinine renal clearances were observed. Metformin had no effect on cimetidine disposition. It is concluded that cimetidine inhibits the renal tubular secretion of metformin in man, resulting in higher circulating plasma concentrations. Because of its propensity for causing dose and concentration-dependent adverse effects, the dose of metformin should be reduced when cimetidine is co-prescribed. Somogyi, et.al. (1987).

Some researchers studied the use of cimetidine to reduce dapsone-dependent methaemoglobinaemia in dermatitis herpetiformis patients; they attempted to reduce dapsone-dependent methaemoglobinaemia formation in six dermatitis herpetiformis patients stabilised on dapsone by the co-administration of cimetidine. In comparison with control, i.e. dapsone alone, methaemoglobinaemia due to dapsone fell by 27.3 +/- 6.7% and 26.6 +/- 5.6% the first and second weeks after commencement of cimetidine administration. The normally cyanotic appearance of the patient on the highest dose of dapsone (350 mg day-1), underwent marked improvement. There was a significant increase in the trough plasma concentration of dapsone (2.8 +/- 0.8 x 10(-5)% dose ml-1) at day 21 in the presence of cimetidine compared with control (day 7, 1.9 +/- 0.6 x 10(-5)% dose ml-1, P less than 0.01). During the period of the study, dapsone-mediated control of the dermatitis herpetiformis in all six patients was unchanged. 4. Trough plasma concentrations of monoacetyl dapsone were significantly increased (P less than 0.05) at day 21 (1.9 +/- 1.0 x 10(-5)% dose ml-1) compared with day 7 (1.6 +/- 0.9 x 10(-5)% dose ml-1:control). 5. Over a 12 h period, 20.6 +/- 8.9% (day 0) of a dose of dapsone was detectable in urine as dapsone hydroxylamine. Significantly less dapsone hydroxylamine was recovered from urine at day 14 (15.0 +/- 8.4) in the presence of cimetidine, compared with day 0 (control: P less than 0.05). 6. The co-administration of cimetidine may be of value in increasing patient tolerance to dapsone, a widely used, effective, but comparatively toxic drug. Coleman, et.al. (1992).

The major therapeutic indications are to promote healing of gastric and duodenal ulcers, to treat uncomplicated GERD, and to prevent the occurrence of stress ulcers. Goodman and Gilman (2006).

2.Materials and Methods

- seven(7) brands of Cimetidine were used for the study
- Pure sample of the drugs were obtained from NAFDAC which serve as standard
- Writing and labeling materials
- Measuring cylinder, Beakers, 1000ml volumetric flask, 100ml volumetric flask, 50ml volumetric

flask, Sonicator, Filter paper, Spatula, High performance liquid chromatography set up, UV Visible spectrophotometer (Beckman), Analytical weighing balance, Pestle and mortar, Distilled water

- All reagents used were obtained from NAFDAC office, Maiduguri. Sani et.al. (2012):

2.1 PRACTICAL METHOD

The methods employed for the purpose of this study are the UV visible spectrophotometer and high performance liquid chromatographic methods. Sani et.al. (2011):

2.2 UV PROCEDURE FOR CIMETIDINE

The tablets were assayed spectrophotometrically using the following procedures

- The average weight of the tablets from each sample was determined by weighing ten(10) tablets and dividing the results gotten by seven to obtain the average weight

- From the value gotten the equivalent weight of each brand was weighed accurately and transferred into 250ml volumetric flasks. All the seven samples were labelled using pen and masking tape.

- To each volumetric flask, 50ml of Methanol water was poured and sonicated for few minutes to dissolve the drug molecule.

- The mixture in each flask was mixed well and filtered through a filter paper into clean beakers.
- 1ml of the solution was taken and diluted with 9 ml of 50ml of methanol water
- The UV spectrophotometer was put at zero by running a base line using diluent as blank.
- The absorbance of each sample was determined at the peak wavelength by putting small amount of the sample into a cuvette, and the cuvette was put back into the machine.
- The same procedure was repeated for the standard using 200mg of the powdered standard and the absorbance determined and from which the % content and mg content was determined as

$$\% \text{ content} = \frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times 100$$

$$\text{Mg content} = \frac{\% \text{ content} \times \text{Manufactures claim}}{100}$$

United States Pharmacopeia, 2007,

2.3 HPLC PROCEDURE FOR CIMETIDINE

2.3.1 Mobile phase

Transfer 200ml of methanol and 0.3ml of Phosphoric acid to a 1000ml volumetric flask, dilute with water to mix and filter. Make adjustment if necessary.

2.3.2 Standard's Preparation

Dissolve accurately weighed quantity of USP cimetidine RS in a mixture of water and methanol (4:1) to obtain a stock solution having a known concentration of about 0.4mg/ml by initially dissolving the reference standard in one part of methanol and diluting the methanolic solution quantitatively with about 4 part of water to volume in volumetric flask. Transfer 5.0ml of this stock solution to a 200ml volumetric flask, dilute with mobile phase to and mix to obtain a solution having a known concentration of about 10mg/ml

Assay Preparation

Weigh the finely powder not fewer than 10 tablet, transfer an accurately weighed portion of the powder, equivalent to about 100mg of cimetidine, to a 250ml volumetric flask. Add 50ml of methanol, shake for 2mins add 40ml of water, sonicate for 15minutes, dilute with water and mix. **ALI et.al (2015)**

2.3.3 Procedure

Separately inject equal volume (about 50ml) of the standard preparation and the assay preparation into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity in mg of cimetidine in the partion of tablets taken by the formular **ALI et.al (2015)**

2.3.4 Chromatographic system

The liquid chromatograph is equipped with a 220nm detector and a 150 cm x 4.6mm column that contains packing L1. The flow rate is about 2.0ml/minute. Chromatograph the standard preparation and record the peak responses as directed for procedure. The capacity factor K1 is not less than 0.6; the column efficiency determined from the analyte peak is not less than 1000 theoretical plate and the relative standard deviation of the response for replicate injections is not more than 2.0%.

3.Results

Table 1: Samples Name and Code

Brand Name	Brand Code
Cetilab	J
Sabydine	K
Bisotidine	L
Shegment	M
Paucodine	N
Taximet	O
Cimebios	P

The data below shows the result of UV spectrophotometer which is used to calculate the percentage and milligram content of the drugs.

The results are as follows:

3.1 CIMETIDINE

J

%content = 6447.8 x 100 = 99.7%
6466.9

Mg content = 99.7 x 200 = 199.4mg
100

K

%content = 6371 x 100 = 98.53%
6466.9

Mg content = 98.53 x 200 = 197.06mg
100

L

%content = 6741.2 x 100 = 104.24
6466.9

Mg content = 104.24 x 200 = 208.4mg
100

M

%content = 6937.9 x 100 = 107.3%
6466.9

Mg content = 10.3 x 200 = 214.6mg
100

N

%content = 6332.2 x 100 = 97.9%
6466.9

Mg content = 97.9 x 200 = 195.8mg
100

O

%content = 6880.5 x 100 = 106.39%
6466.9

Mg content = 106.39 x 200 = 212.78mg
100

P

%content = 6527.4 x 100 = 100.9%
6466.9

Mg content = 100.9 x 200 = 201.8mg
100

TABLE 2: UV ABSORBANCE FOR CIMETIDINE AT A WAVELENGHT OF 220nm

Sample	Absorbance (A)
J	6447.8
K	6371.9
L	6741.2
M	6937.9
N	6332.2
O	6880.5
P	6527.4

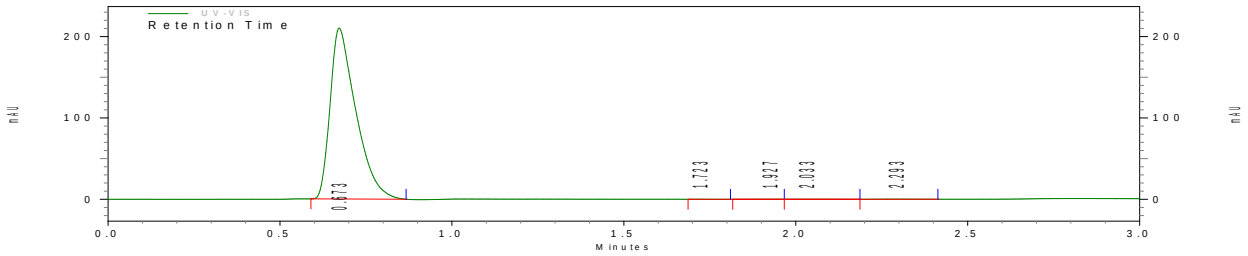
TABLE 3: Percentage content and mg content of different brands of Cimetidine using UV.

Sample	%content	Mg content
J	99.7	199.4
K	98.53	197.06
L	104.24	208.4
M	107.3	214.6
N	97.9	195.8
O	106.39	212.78
P	100.9	201.8

3.2 HPLC FOR CIMETIDINE

FIGURE 1:

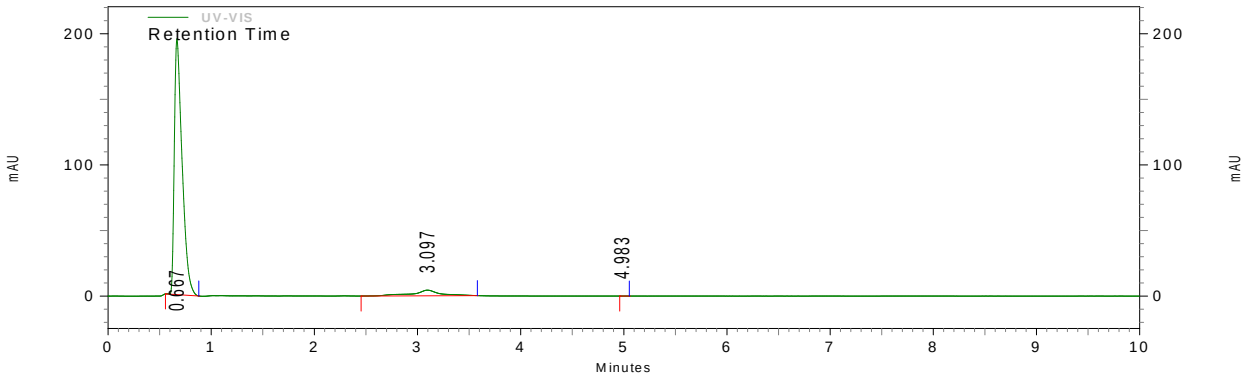
Analyst: manager
Sample ID: CIMETIDINE TABLETS STD 190313 Vial: 160 Injection Volume: 20



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
	0.673	4369272	99.880	MM
	1.723	226	0.005	IB
	1.927	789	0.018	BV
	2.033	879	0.020	VB
	2.293	3374	0.077	BB
Totals		4374540	100.000	

FIGURE 2:
Analyst: manager
Sample ID: P 190313 Vial: 200 Injection Volume: 20



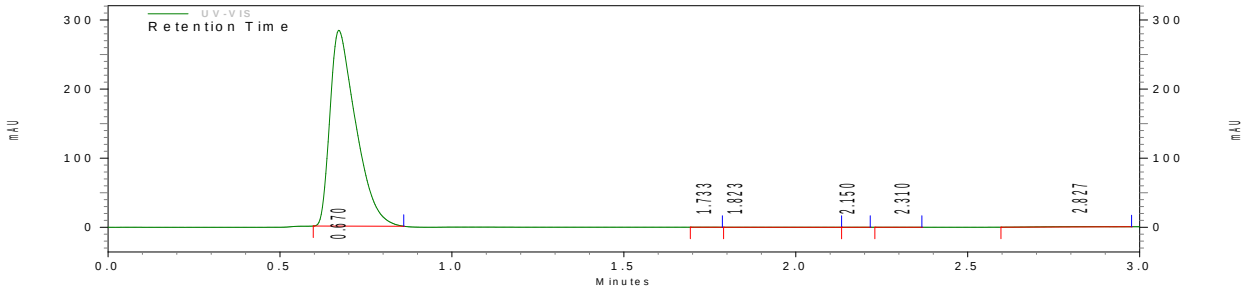
UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
	0.667	4084550	92.743	MM
	3.097	319548	7.256	MM
	4.983	70	0.002	II
Totals		4404168	100.000	

% content = 4084550 x 100 = 93.5%
4369272

Mg content = 93.5 x 200 = 187mg
100

FIGURE 3:
Analyst: manager
Sample ID: O 190313 **Vial: 199** **Injection Volume: 20**



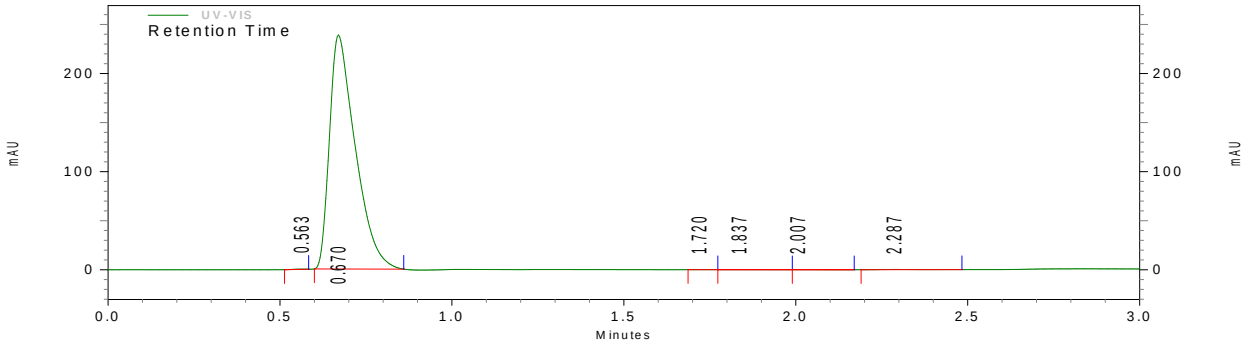
UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
	0.670	5917964	99.666	MM
	1.733	212	0.004	BB
	1.823	978	0.016	BB
	2.150	123	0.002	BB
	2.310	378	0.006	BB
	2.827	18144	0.306	MM
Totals		5937799	100.000	

% content = 5917964 x 100 = 135.5%
4369272

Mg content = 135.5 x 200 = 270.9mg
100

FIGURE 4:
Analyst: manager
Sample ID: N 190313 **Vial: 198** **Injection Volume: 20**



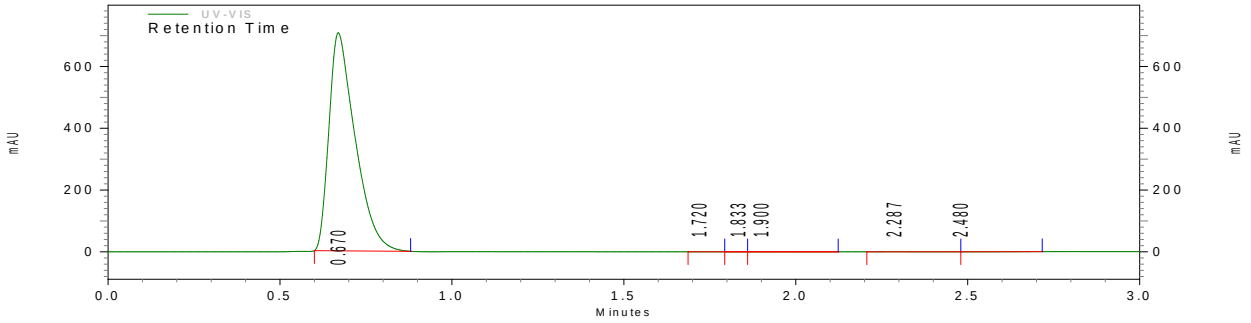
UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
	0.563	2154	0.043	MM
	0.670	4971490	99.794	MM
	1.720	429	0.009	IB
	1.837	938	0.019	BV
	2.007	707	0.014	VB
	2.287	6015	0.121	BB
Totals		4981733	100.000	

% content = $\frac{4971490}{4369272}$ x 100 = 113.8%

Mg content = $\frac{113.8}{100}$ x 200 = 227.6mg

FIGURE 5:
Analyst: manager
Sample ID: M 190313 **Vial: 197** **Injection Volume: 20**



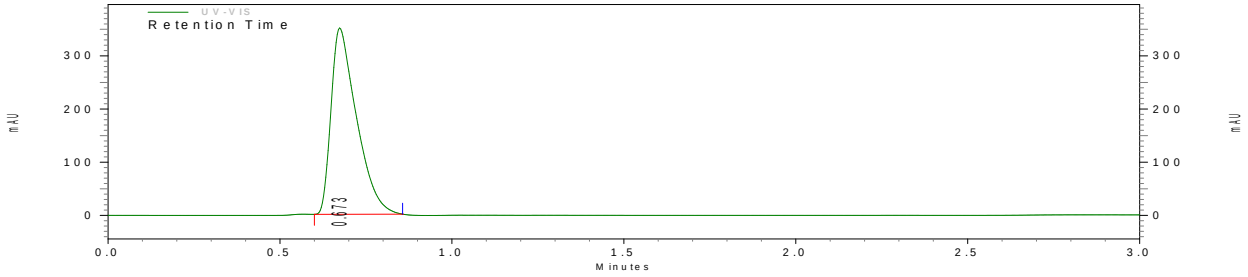
UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
	0.670	14937421	99.926	MM
	1.720	433	0.003	IB
	1.833	164	0.001	BV
	1.900	1653	0.011	VB
	2.287	2951	0.020	BB
	2.480	5873	0.039	BI
Totals		14948495	100.000	

% content = 14937421 x 100 = 341.9%
4369272

Mg content = 341.9 x 200 = 682.8mg
100

FIGURE 6:
Analyst: manager
Sample ID: L 190313 **Vial: 170** **Injection Volume: 20**



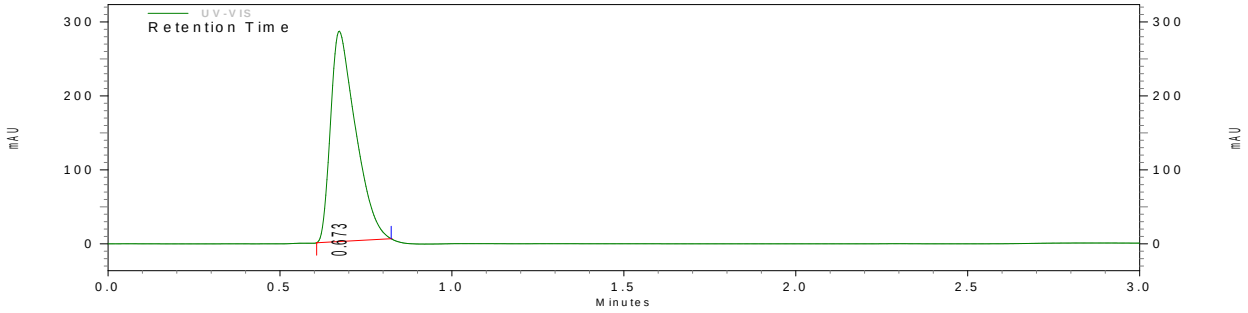
UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
	0.673	7210071	100.000	MM
Totals		7210071	100.000	

% content = 7210071 x 100 = 165.0%
4369272

Mg content = 165.0 x 200 = 330mg
100

FIGURE 7:
Analyst: manager
Sample ID: J 190313 **Vial: 190** **Injection Volume: 20**



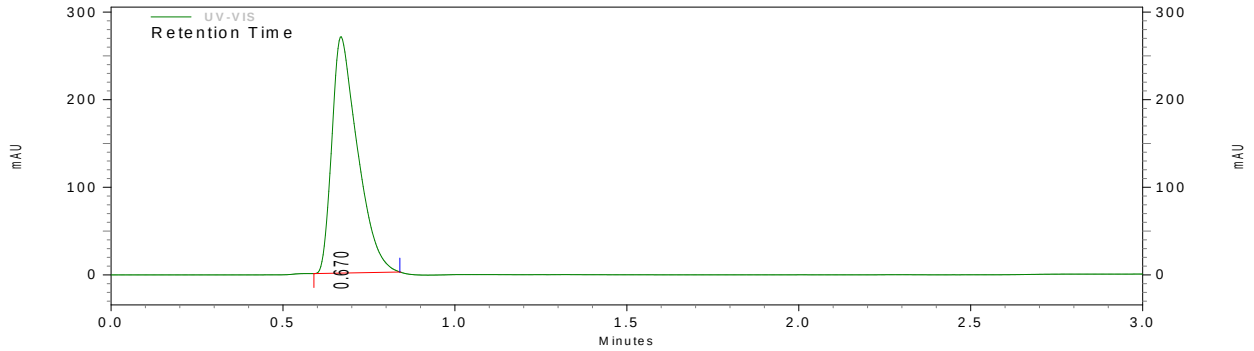
UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
	0.673	5753376	100.000	MM
Totals		5753376	100.000	

% content = 5753376 x 100 = 131.7%
4369272

Mg content = 131.7 x 200 = 263.4mg
100

FIGURE 8:
Analyst: manager
Sample ID: K 190313 **Vial: 180** **Injection Volume: 20**



UV-VIS Results

Name	Retention Time	Area	Area Percent	Integration Codes
	0.670	5595975	100.000	MM
Totals		5595975	100.000	

% content = 5595975 x 100 = 128.1%
4369272

Mg content = 128.1 x 200 = 256.2mg
100

TABLE 4: PERCENTAGE CONTENT AND Mg CONTENT OF CIMETIDINE USING HPLC ANALYSIS.

Sample	%content	mg content
J	131.7	263.4
K	128.1	256.2
L	165.9	330
M	341.9	682.8
N	113.8	227.6
O	135.5	270.9
P	93.5	187

4.Discussion

According to the United States Pharmacopoeia (USP, 2007), a cimetidine tablet should contain not less than 98.0% and not more than 102.0% of cimetidine. The standard cimetidine has an absorbance of 6466.9 at a wavelength of 220nm. From the result obtain using UV – Spectrophotometer, J (99.7%), K (98.53%), P (100.9%) and N (97.9%) are all within the U.S.P specified limit but L (104.24%), M(107.3%), O (106.39%) are said to be above the specified limit.

From the result obtained using HPLC, P (93.5%) is below the specified limit while O (135.5%), N (113.8%), M(341.9), L (165.0%), J (131.7%) and K (128.1) are said to be above the USP specified limit.

5.Conclusion

It can be concluded that the analysis of Cimetidine using UV spectrophotometry, 4 brands of the drug passed and 3 brands failed while for HPLC analysis all the Brands failed the test.

6.Recommendation

Pharmaceutical analysis should always be carried out on Drugs by regulatory bodies to ensure that drugs that are being marketed are of the required standard to eradicate the problems of fake and counterfeit drugs and also guilty companies should be queried or penalized appropriately.

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