

PHYSICO-CHEMICAL ANALYSES OF PARACETAMOL AND CIPROFLOXACIN TABLET BRANDS RETAILED IN DRUG OUTLETS IN AWKA AND ONITSHA, ANAMBRA STATE

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Abstract

The materials used for investigation, 5 brands of paracetamol 500mg and 5 brands of ciprofloxacin 500mg were bought from drug outlets. In-process tests for hardness, thickness, average weight, friability and disintegration were carried out using hardness tester, vernier caliper, digital electronic weighing balance, tablet friability test apparatus and digital tablet disintegration test apparatus. Assay was carried out using UV-visible spectrophotometer. The in-process tests and assay were performed using the methods described in the British Pharmacopoeia and P.D.Sethi. The results of assay (%) for the brands of paracetamol 500mg and ciprofloxacin 500mg showed Emzor (101.7), M&B (100.3), GSK Panadol, (101.3), Bonadol (97.0), Yef (80.0), Cipromaxforte (107.5), Cipxin (96.7), Cenox (96.9), Nuel (103.2), Wincip (97.4). The results of in-process tests and assay for all the brands evaluated were in conformity with specification, except one brand of paracetamol 500mg (YEF) that failed the assay. Since the results of in-process tests and assay obtained (for all the brands except one) are within the acceptable limit defined by British Pharmacopoeia and United States Pharmacopoeia, it is concluded that the method used be applied to the routine qualitative and quantitative analyses of paracetamol 500mg and ciprofloxacin 500mg in tablet drug formulation. It is recommended that each of the brands evaluated (except one brand of paracetamol that failed assay) is safe for its intended use. The brand of paracetamol (YEF) that failed the assay, with value far below the allowed limit, indicated deficiency in the process of quality control.

Introduction

The fear that some common analgesic and antibiotic formulations show poor therapeutic efficacy for pain and on susceptible micro-organisms due to inadequacy of active ingredients necessitated this research (Harold, 1992). The aim of this work is to investigate quantitatively the paracetamol and ciprofloxacin drug formulation of different brands using UV-vis spectrophotometer. Analgesics e.g. paracetamol, are medications designed to relieve the symptoms of pain (Strom, 1994). Antibiotics e.g. ciprofloxacin, are drugs used to treat bacterial infections (Umezawa, 1982). Before bacteria can multiply and cause symptoms, the body's immune system can usually destroy them (Sameer, et al., 2013). Human body has special white blood cells that attack harmful bacteria. Even if symptoms do occur, the body's immune system can usually cope and fight off the infection. There are occasions, however, when it is all too much and some help is needed from antibiotics (Davidand Joseph, 2000). Antibiotics have been around for a long time. There is concern worldwide that antibiotic resistance is being developed by bacteria (Marin and Victoria, 2001).

The European Centre for Disease Prevention and Control (ECDC) says that antibiotic resistance continues to be a serious public health threat worldwide. In a statement issued on 19th November 2012, the ECDC informs that an estimated 25,000 people die each year in the European Union from antibiotic resistant bacterial infections (Davidand Joseph, 2000). "Then there is danger that the ignorant man may easily under dose himself and by exposing his microbes to non-lethal quantities of the drug, make them resistant" said Alexander Flemin, speaking in his Nobel Prize acceptance speech in 1945. As predicted almost 70 years ago by the man who discovered the first antibiotic- pencillin, drug resistance is upon us (Umezawa et al., 1982).

Paracetamol (Pcm) or acetaminophen is a widely used over the counter (OTC) analgesic (Pain reliever) and antipyretic (fever reducer). It is commonly used for the relief of headaches and other minor aches and pains and is a major ingredient in numerous cold and flu remedies (Strom,

1994). In combination with opioid analgesics, pcm can also be used in the management of more severe pain such as postsurgical pain and providing palliative care in advanced cancer patients. The onset of analgesia is approximately 11 minutes after oral administration of pcm and its half-life is 1-4 hours. Though acetaminophen is used to treat inflammatory pain, it is not generally classified as nonsteroidal anti-inflammatory drugs (NSAID) because it exhibits only weak anti-inflammatory activity (Cheung *et al.*, 1994).

The systematic name for paracetamol is N- (4- hydroxyphenyl) acetamide. Pcm is part of the class of drugs known as “aniline analgesics”; it is the only such drug still in use today. It is the active metabolite of phenacetin, once popular as an analgesic and antipyretic in its own rights, but unlike phenacetin and its combinations, pcm is not considered carcinogenic at the therapeutic doses (Bosch, 2006). The word acetaminophen (used in the US, Canada, South Korea, Hong Kong, Iran) and paracetamol (used elsewhere) both come from a chemical name for the compound; paraacetylaminophenol. In some contexts, it is simply abbreviated as APAP, for acetyl-paraaminophenol. While generally safe for use at recommended doses (1,000mg per single dose and up to 4,000mg per day for adults), acute overdoses of pcm can cause potentially fatal liver damage and, in rare individuals, a normal dose can do the same; the risk is heightened by alcohol consumption (Larson *et al.*, 2005). PCM toxicity is the foremost cause of acute liver failure in the Western World and accounts for most drug overdoses in the United States, the United Kingdom, Australia, and New Zealand (Bonkovsky, 1995).

On the other hand, CIPRO (ciprofloxacin hydrochloride) tablet is synthetic broad spectrum antimicrobial agent for oral administration. Ciprofloxacin hydrochloride, a fluoroquinolone, is the monohydrochloride monohydrate salt of 1-cylopropyl -6- fluoro- 1, 4-dihydro – 4- oxo -7- (1-piperazinyl) -3- quinoline carboxylic acid. It is a faintly yellowish to light yellow crystalline substance with a molecular weight of 331.4 g/mol, its empirical formula is $C_{17}H_{18}FN_3O_3 \cdot HCl \cdot H_2O$ (David and Joseph, 2000). CIPRO film-coated tablets are available in 250mg and 500mg (ciprofloxacin equivalent) strengths. Ciprofloxacin tablets are white to slightly yellowish in colour. The inactive ingredients are cornstarch, microcrystalline cellulose, silicon dioxide, crospovidone, magnesium stearate, hypromellose, titanium dioxide and polyethylene glycol (Chris, 2015). Signs of an allergic reaction include difficult breathing, swelling of face, lips, tongue or throat. Side effects include severe dizziness, fainting, fast or pounding heartbeat, sudden pain or loss of movement in any of the joints, diarrhea that is watery or bloody, hallucinations, depression (David and Joseph, 2000). The need for safety, efficacy, quality and consistency in drug production and usage can only be guaranteed with proper drug formulation. Equally, the prevention of prevalent drug resistance by organisms and drug adverse effects on patients can be achieved through proper drug formulation as well as obtaining treatment guidance from an approved source (Ajibola, 2005).

Materials and Methods Materials

Materials and Reagents for Paracetamol: Paracetamol reference standard, Brands of paracetamol tablets containing 500mg paracetamol and inactive ingredient used in drug matrix, Hydrochloric acid (IN), Sodium nitrite solution (10% w/v) in water- freshly prepared, Ammonium sulphamate solution in water (10% w/v), Sodium hydroxide solution in water (20% w/v)

Materials and Reagents for Ciprofloxacin: Ciprofloxacin reference standard, Brands of ciprofloxacin tablets containing 500mg ciprofloxacin and inactive ingredients used in drug matrix, Hydrochloric acid (0.1N), Ferric chloride solution (1% w/v) in water (freshly prepared)

Apparatus and Equipment for Paracetamol and Ciprofloxacin: Volumetric flasks (50mL, 100mL, 250mL), pipettes, measuring cylinders, mortar and pestle, filter paper/aluminum foils, beakers, magnetic stirrer and pellet, cotton wool, electronic weighing balance, tablet hardness

tester, digital vernier caliper, tablet friability test apparatus, digital tablet disintegration test apparatus, curvettes, spectrophotometer

Methods

Material Collection and Preparation

Paracetamol reference standard and ciprofloxacin reference standard were supplied by Qwality Pharmaceuticals Pvt Ltd. India.

Drug samples used, 5 brands of paracetamol and 5 brands of ciprofloxacin tablets containing 500mg paracetamol and 500mg ciprofloxacin were obtained from markets in Awka and Onitsha, Anambra State, Nigeria. Analytical grade hydrochloric acid, ferric chloride and ammonium sulphamate in water were manufactured by Qualikems Fine Chemicals PVT Ltd. India. Sodium nitrite was manufactured by BDH Chemicals Ltd., Poole England. Sodium hydroxide pellets used was manufactured by Burgoyne Urbidges & Co. (India) Mumbai.

In-Process Tests

- (i) **Thickness:** Digital vernier caliper was used for testing.
- (ii) **Procedure:** Hand gloves were put on, then the tablet was placed in a horizontal position in the vernier caliper. The knob was screwed until it made contact with the tablet. The reading in mm was taken.

- (ii) **Average Weight:** Electronic weighing balance was used for checking the average weight. Procedure: Weighing of 20 tablets selected at random, each one individually $x_1, x_2, x_3, \dots, x_n$ using electronic weighing balance and determining the average weight. $X = (x_1 + x_2 + x_3 \dots + x_n) / 20$, the value was taken as average weight (g).
- (iii) **Hardness:** Tablet hardness tester was used for testing.

Procedure: Safety goggles and hand gloves were put on. The tablet for testing was placed in a vertical position in the space provided in the tablet hardness tester. The knob of the tester was screwed until it made contact with the tablet, then initial reading was taken. The hardness tester knob was tightened further until the tablet broke, then the final reading was taken. The hardness reading (kgcm^{-2}) was obtained by subtracting the initial reading from the final reading.

- (iv) **Friability:** Tablet friability test apparatus was used for testing.

Procedure: The equipment was connected to the electric mains with the power cord and switched on. The 'START' button was pressed and the LCD screen displays 'LEFT INITIAL WEIGHT'. Left initial weight of ten tablets weighed was put then 'ENTER' key pressed to continue. The LCD displayed 'ADD TABLETS' and the tablets added and 'ENTER' key pressed to continue. The LCD displayed "RIGHT INITIAL WEIGHT" and the right initial weight of the ten tablets weighed entered. 'ENTER' key was pressed to continue. The LCD displayed 'ADD TABLETS' and the tablets were added and 'ENTER' key pressed to continue. Then LCD displayed 'PRESS O TO PROG' the revolution (Note: 100 revolution is programmed on the apparatus). After a hundred revolutions, the equipment stopped and offloaded the tablets on both sides (LEFT and RIGHT sides). The LCD displayed 'LEFT FINAL WEIGHT' and the new 'LEFT FINAL WEIGHT' of the weighed tablets was typed and 'ENTER' key pressed to continue. The LCD then displayed 'RIGHT FINAL WEIGHT' and the 'RIGHT FINAL WEIGHT' of the weighed tablets typed and 'ENTER' key was pressed to continue.

The apparatus calculated and displayed the percentage friability of the inputted values for the 'LEFT'. The 'ENTER' key was pressed to obtain the percentage friability for the 'RIGHT'. The ENTER was pressed to 'EXIT' and the apparatus switched off.

The friability (%) = (percentage friability for the LEFT + percentage friability for the RIGHT)/2

(v) **Disintegration:** Digital tablets disintegration test apparatus was used for testing.

Procedure: After ensuring that the apparatus was clean, the 'WATER CHAMBER' was filled to the required water level and the equipment was connected to the electric mains with the power cord and the 'ON' switch engaged. The equipment was allowed to test-run itself, thereafter, the heater was switched on, and the required temperature of 37.5⁰C was selected. On pressing 'ENTER' the LCD displayed 'Heating in Progress'. On pressing 'ENTER' the LCD displayed 'START TEST'. The 'START MENU' was selected with the keypad, and the LCD displayed 'Test, validation, clock setting, product setting, Data printing', then 'Test' was selected. The 'ENTER' button was engaged until the LCD displayed 'INSERT SAMPLE'. The tablet samples were inserted after which the 'ENTER' button is pressed to continue, and the LCD displayed 'TEST STARTED'. The disintegration time (mins) of the inserted tablet samples displayed by the equipment was recorded. The apparatus was switched off and disconnected from the mains.

Preparation of Standard Solution of Paracetamol

Paracetamol Powder equivalent to 25mg(reference standard) was accurately weighed and put into 250mL of volumetric flask, then 200mL of hydrochloric acid (IN) was added and shaken vigorously for 15 minutes to dissolve and was made up to volume (100mcg/mL)

Preparation of Sample solution of Paracetamol

Tablets (20) were weighed and powdered. Powdered tablets equivalent to 25mg of paracetamol was accurately weighed and put into 250mL volumetric flask, then 200mL of hydrochloric acid (IN) was added and shaken vigorously for 15 minutes to dissolve and was made up to volume (100mcg/mL).

Methodology of UV-visible Spectrophotometer for Paracetamol

Each of the sample and standard solutions (5mL) was taken into two different 50mL volumetric flasks. To each of the 50mL volumetric flasks was added 5mL of 1N HCl acid and 5mL of sodium nitrite solution. It was allowed to stand for 5 minutes with intermittent shaking. To neutralize excess of nitrous acid, 5mL of freshly prepared ammonium sulphamate solution was added to each of the volumetric flasks. The flasks were shaken vigorously and allowed to stand for 5 minutes, followed by addition of 5mL of sodium hydroxide solution. The volume was made up to the mark and the absorbance of 5 sets of sample solution and standard solution was measured at 430nm against reagent blank. Results were deduced by comparison.

Preparation of Standard Solution of Ciprofloxacin

Ciprofloxacin Powder (reference standard) equivalent to 100mg was accurately weighted into 250mL of volumetric flask, then 70mL of 0.1N hydrochloric acid was added and shaken for 10 minutes and made up to 100mL with the acid. Further dilution was done with the acid to get to final concentration of 100mcg/mL.

Preparation of Sample Solution of Ciprofloxacin

Tablet sample equivalent to 100mg of the substance was accurately weighed and powdered, then 70mL of 0.1N hydrochloric acid was added and shaken for 10 minutes and made up to 100mL with the acid. Further dilution was done with the acid to get final concentration of 100mcg/mL.

Methodology of UV-visible Spectrophotometer for Ciprofloxacin

Each of the sample and standard solutions was taken into two different 50mL volumetric flasks. To each of the 50mL volumetric flasks was added 1mL of freshly prepared ferric chloride solution and made up to 50mL with 0.1N hydrochloric acid. The absorbance of 3 sets of sample solution and standard solution was measured at 438nm against reagent blank (1mL of ferric chloride solution diluted to 50mL with the acid). The percentage content of paracetamol and ciprofloxacin in the tablets was deduced by comparison using the formula:

$$\frac{\text{Absorbance of test}}{\text{Absorbance of standard}} \times \frac{\text{Weight of standard}}{\text{Weight of test}} \times \frac{\text{Average weight of tablets} \times 1000}{1} \times \frac{100}{500\text{mg} \times 1}$$

Results and Discussions

In-Process Tests

Paracetamol brands

Result of In-process tests for Paracetamol

S/n	Paracetamol test sample	Thickness (mm)	Average weight (g)	Hardness (kgcm ⁻²)	Friability (%)	Disintegration (mins)
1	EMZOR	4.000	0.546	4.000	0.199	2.000
2	M & B	4.000	0.561	7.000	0.226	0.550
3	GSK PANADOL	6.000	0.658	5.000	0.123	1.467
4	BONADOL	4.000	0.551	7.000	0.357	5.001
5	YEF	4.000	0.533	5.000	0.469	0.917

In-process tests for the brands of paracetamol 500mg indicate that for Thickness (mm) Gsk Panadol has the highest value of 6mm and the rest of the brands with 4mm each. Thickness has to do with the shape of the drug. Gsk Panadol is caplet while the rest of the brands are circular and flat in shape.

Average weight (g): The highest value of 0.658g for GSK Panadol is not surprising since average weight has direct relationship with thickness.

Hardness (Kgc^m-²): The highest value of 7.0kgcm⁻² for M & B and Bonadol indicates that the brands can withstand mechanical pressure better than the rest of the brands. Emzor has the lowest value of 4.0kgcm⁻² showing it breaks up with little mechanical pressure. Hardness has to do with drug formulation and binding agent used. It is in order for tablet drugs to be hard enough, provided the hardness does not affect disintegration time adversely.

Friability (%): Friability has direct relationship with hardness. Gsk Panadol with friability of 0.123% followed by Emzor with 0.199% is the best in terms of keeping the tablets intact over a long period of time. Friability shall not exceed 1% (BP and USP standard).

Disintegration (mins): M & B with disintegration value of 0.55mins has the best disintegration property. The lower the disintegration value, the better, since lower value indicates that the drug can easily dissolve and go into solution and rapidly be absorbed into the blood stream. Bonadol

has highest value of 5.00mins thus poorest in terms of disintegration property comparably with the other brands. The disintegration time shall not exceed 15mins by BP and USP specification.

Ciprofloxacin

Result of the in-process tests for Ciprofloxacin

S/n	Ciprofloxacin test sample	Thickness (mm)	Average weight (g)	Hardness (kgcm ⁻²)	Friability (%)	Disintegration (mins)
1	CIPROMAXFORTE	6.000	0.800	8.000	0.038	3.750
2	CIPXIN	6.000	0.800	8.000	0.046	14.002
3	CENOX	7.000	0.789	7.000	0.064	5.483
4	NUEL	6.000	0.751	7.000	0.040	12.733
5	WINCIP	6.000	0.747	7.000	0.054	3.517

Result of in-process tests of ciprofloxacin 500mg brands shows that Thickness (mm): Cenox has the highest value of 7.000mm while other brands have 6mm each, indicating that Cenox has bigger shape.

Average weight (g): Cipromaxforte and Cipxin have the highest value of 0.8g each whereas Wincip has the lowest value of 0.747g. Average weight is a function of actives and excipients used in the drug formulation. Average weight, thickness and hardness parameters are in-house specification.

Hardness (kgcm⁻²): Cipromaxforte and Cipxin with 8.000kgcm⁻² each, have highest ability to withstand mechanical pressure or breakage. Other brands have 7kgcm⁻² each.

Friability (%): Cipromaxforte has the best value of 0.038% showing highest ability to retain the drug intact over a long period of time. Cenox with value 0.064kgcm⁻² has the least ability to retain the drug intact over time when compared with other brands.

Disintegration (mins): Wincip and Cipromaxforte with values 3.517mins and 3.750mins respectively, are best in terms of disintegration time, indicating the ease with which they dissolve and are absorbed into the blood stream. Cipxin with disintegration value of 14.002mins is poorest in terms of disintegration property, even though it falls within the range of not more than 15mins (by BP and USP standard).

UV-visible spectrophotometer Result for the Paracetamol Brands

Operator: Cynthia, D.O.A., G.O.E

Date & Time: January 2017: 07:46 2016

Memo:

Batch No: 4015U; A151655; 022W

Mfd Date: 08/15; 10/2015; 03/2015; 07/15; 05/15

Exp Date: 08/2020; 09/2020; 03/2018; 06/18; 04/19

Weight of Standard Sample: 0.025g

Weight of EMZOR: 0.027g; M & B: 0.028g; PANADOL: 0.033g, BONADOL: 0.027g, YEF: 0.028g.

Test sample			
Sample Name	430.0nm	Abs (eff)	Mg/L
EMZOR-1	0.2847	0.2847	3.8042
EMZOR-2	0.2851	0.2851	3.8070
EMZOR -3	0.2842	0.2842	3.8010
STD PMOL -1	0.2823	0.2823	3.7962
STD PMOL -2	0.2829	0.2829	3.7980
STD PMOL -3	0.2832	0.2832	3.8001
M & B -1	0.2818	0.2818	3.7857
M & B -2	0.2832	0.2832	3.7950
M & B -3	0.2836	0.2836	3.7971
GSK PANADOL -1	0.2874	0.2874	3.8782
GSK PANADOL -2	0.2872	0.2872	3.8774
GSK PANADOL -3	0.2879	0.2879	3.8808
BONADOL -1	0.2700	0.2700	3.7103
BONADOL -2	0.2704	0.2704	3.7132
BONADOL -3	0.2705	0.2705	3.7136
YEF – 1	0.2366	0.2366	3.4977
YEF – 2	0.2365	0.2365	3.4973
YEF – 3	0.2387	0.2387	3.5111

Assay of drugs**Paracetamol brands****Result of assay for the Paracetamol**

S/N	Paracetamol Test Sample	Assay (%)
1	EMZOR	101.7%
2	M & B	100.3%
3	GSK PANADOL	101.3%
4	BONADOL	97%
5	YEF	80%

Assay (%) for paracetamol 500mg brands indicates that Emzor BP, with value 101.7% has the highest percentage of active ingredient, whereas YEF USP with value 80% has the lowest percentage of active ingredient in terms of drug formulation. The brands Emzor BP (101.7%), M & B BP (100.3), Gsk Panadol BP (101.3%), and Bonadol BP (97%) all passed the assay test, while YEF USP (80%) failed the assay test (i.e. 95% to 105% for BP and 90% to 110% for USP

Trends of paracetamol brands with respect to assay conducted indicate:

Emzor> Gsk> M&B> Bonadol> YEF

UV-visible spectrophotometer Result for the Ciprofloxacin Brands

Operator: DOA & GOE
Date & Time: December 16 16:12:59 2015

Memo:

Batch No: 143121021; CPN 031; CNXH 0165; NR 5005; WC 4015

Mfd Date: 09/2014; 04/2015; May 2014; 02/2015; 12/2014;

Exp Date: 09/2017; 03/2019; April 2017; 01/2018; 11/2017;

Weight of Standard Sample: STD CIPRO: 0.026g

Weight of CIPROMAXFORT: 0.038g; CIPXIN: 0.039g; CENOX: 0.038g; NUEL CIPRO: 0.038g; WINCIP: 0.040g.

Test sample

Sample Name	438.0nm	Abs (eff)	Mg/L
CIPROMAX FORTE -1	0.1345	0.1345	2.8616
CIPROMAX FORTE -2	0.1342	0.1342	2.8612
CIPROMAX FORTE -3	0.1340	0.1340	2.8609
STD CIPRO -1	0.1377	0.1377	2.8671
STD CIPRO -2	0.1370	0.1370	2.8627
STD CIPRO -3	0.1358	0.1358	2.8551
CIPXIN -1	0.1242	0.1242	2.7555
CIPXIN -2	0.1240	0.1240	2.7575
CIPXIN -3	0.1239	0.1239	2.7579
CENOX -1	0.1228	0.1228	2.7655
CENOX -2	0.1227	0.1227	2.7675
CENOX -3	0.1229	0.1229	2.7679
NUEL CIPRO -1	0.1363	0.1363	2.7768
NUEL CIPRO -2	0.1378	0.1378	2.7752
NUEL CIPRO -3	0.1379	0.1379	2.7749
WINCIP -1	0.1365	0.1365	2.7774
WINCIP -2	0.1375	0.1375	2.7798
WINCIP -3	0.1377	0.1377	2.7758

Ciprofloxacin Brands**Result of assay of the Ciprofloxacin**

S/N	CIPROFLOXACIN TEST SAMPLE	ASSAY (%)
1	CIPROMAXFORTE	107.5%
2	CIPXIN	96.7%
3	CENOX	96.9%
4	NUEL	103.2%
5	WINCIP	97.4%

Assay (%) for Ciprofloxacin 500mg brands indicates that CIPROMAXFORTE USP (107.5%) has the highest percentage of active ingredient whereas CIPXIN BP (96.7%) has the lowest percentage of active ingredient of all the brands investigated. CIPROMAXFORTE USP (107.5%), CIPXIN BP (96.7%), CENOX USP (96.9%), NUEL USP (103.2%) and WINCIP USP (97.4%) passed the assay test conducted. All the brands conformed to BP and USP standards of 95% to 105% and 90% to 110% respectively.

Trends of ciprofloxacin brands with respect to assay conducted show: cipromaxforte> Nuel> Wincip> Cenox> Cipxin.

Conclusions and Recommendations**Conclusions**

Trends of paracetamol brands with respect to assay conducted indicate:

Emzor> Gsk> M&B> Bonadol> YEF

Trends of ciprofloxacin brands with respect to assay conducted show: cipromaxforte> Nuel> Wincip> Cenox> Cipxin.

The assay for paracetamol and ciprofloxacin tablets in this research was determined by measuring absorbance of standard solutions against the solvent blank and comparing with the

absorbance of various brands sampled at 430nm and 438nm for paracetamol and ciprofloxacin respectively by spectrophotometer. The results of assay (%) obtained (for all the brands except one) are within the acceptable limit defined by BP and USP. It is concluded that the brand of paracetamol that failed the assay (with value far below the allowed limit) indicates deficiency in the process of quality control.

Recommendations

From the results obtained, it is recommended that each of the brands of paracetamol and ciprofloxacin evaluated (except one brand of paracetamol that failed assay) is safe for its intended use. It is recommended that the UV-visible spectrophotometer method used be applied to the routine quantitative analysis of paracetamol and ciprofloxacin in drug formulation.

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