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In Vitro Quality Control of Metronidazole Tablets From Different Supplier Available In Saudi Arabia; Comparative Study

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ABSTRACT : ***Five brands of film coated metronidazole 500 mg tablets have been evaluated using some quality control tests as uniformity of weight, friability, content uniformity, disintegration and dissolution with the aim to assess its quality. The results obtained have been discussed in some details using monograph in the United States Pharmacopeia (USP). The results were also subjected to statistical analysis. In particular, the dissolution test results where subjected to further tests to determine significance of ANOVA at (p < 0.05), the kinetic order of the drug release and the mechanism of reaction were investigated. The results revealed that the five brands included in the study complied with their quality control tests and showed good dissolution profile for the drug release.***

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I. INTRODUCTION

Metronidazole (MNZ) is **an antibiotic derived from synthetic** nitroimidazole. Usually used to treat human diseases, including parasitic infections, trichomoniasis, trichomoniasis and amebiasis. (1)

The antibacterial activity of metronidazole was **accidentally discovered** in 1962 when metronidazole cured **patients with trichomonas** vaginitis and bacterial gingivitis. However, it was not until the 1970s that metronidazole **became** popular for **the treatment** of infections caused by **Gram-negative** anaerob**ic bacteria** such as Bacteroides or **Clostridium gram-positive** anaerobes. (2) **At present,** metronidazole is **cheap,** has good tissue **permeability,** and **has** relatively mild side **effects. It is** u**sed by** most hospitals **to prevent** anaerobic **infections** after **intestinal** surgery, treat wound **abscesses,** and treat **antibiotic-related colitis. Caused** by Clostridium difficile. Metronidazole is an important part of **combined** therapy **for** Helicobacter **pylori. Helicobacter pylori is one of the main causes** of gastritis and a risk factor for **gastric cancer. (3)**

Tablets **come** in various sizes and shapes. The ingredients **in** the tablet play an important **role in** the formulation of the tablet. Particle size, uniformity and active ingredients also play a **vital** role.**(4)**

Metronidazole is **an antibiotic widely** used in **Saudi Arabia. The purpose** of this study **is** to **evaluate** the quality **of 500 mg metronidazole hydrochloride tablets of** different leading brands in the **market in Saudi Arabia.** (5)
It is **very important** to maintain **product** quality by **conducting** various quality control (QC) **tests** on **the product** to **ensure the safety of the product in the** public domain. At the same time, it maintains the efficiency and quality of the overall product. Q**uality control tests** also ensure that the drug **meets** the description and **details of the data** on the drug label. It involves checking the **purity** and impurities **of the** drug, **the effective** ingredients, **and the absorption of the drug by** the **human body.** The in vitro **tests** performed in this **study are based on the United States Pharmacopeia (USP) and** determine the quality, efficacy, and effectiveness of metronidazole **medications.** British **Pharmacopoeia metr12**

2. Materials and methods

2.1. Materials:

2.1.1. Metronidazole powder form Pharco Pharmaceuticals, Alexandria, Egypt. Hydrochloric acid from Avonchem Ltd**,** Mcclesfiled, UK.

2.1.2. Five commercial brand tablets containing 500 mg were purchased from pharmacies in Saudi Arabia (Riyadh). All tests were performed before the product expiration dates, which
were similar among brands. **metr 11**

Tablet (2): Detailed information of metronidazole hydrochloride 500 mg tablets from different supplier evaluated for quality

Brand Name	Manufacturer	Batch number	Manufacture date	Expiry date
Flagyl ® 500 mg	Sanafi Aventis France 1-13 romain Rolland	715	02-2014	02-2017
Negazole ® 500 mg	Julphar gulf pharmaceutical industries Ras Al Khaimah,U.A.E	0085	10-2014	10-2017
Flazol ® 500 mg	JPI, Al-jazerah Pharmaceutical industries Saudi Arabia	K0516	12-2013	12-2016
Anazol ® 500 mg	Tabuk Pharmaceutical industries Saudi Arabia	5029	07-2014	07-2017
Riazole ® 500 mg	Riyadh Pharma Medical & cosmetic products co. Ltd Saudi Arabia	K696	10-2014	10-2017

2.2. Apparatus and procedure:

2.2.1.instruments: ERWEKA disintegrator (Heusenstamm / Germany)**,**Friabilator apparatus (**Roch friabilator / china),** ERWKA dissolution Apparatus (Type II -paddle type): Heusenstamm / Germany**,**Spectrophotometer (UV/VIS) : Amersham biosciences, PH meter (Sartorius/Germany)**,** Electronic Balance (Sartorius/Germany)

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3. Results and discussion

Among five brands of metronidazole tablets included in this study, two brands were imported from foreign countries while three were manufactured locally. Furthermore, all metronidazole brands were subjected to different quality control tests in order to assess their dissolution profile along with other quality parameters like uniformity test, weight variation, friability, hardness, and disintegration.

3.1. Determination of `(ë max) of metronidazole HCl powder

Weight 10 mg of metronidazole HCl pure powder, dissolve it in 100 ml 0.1N HCl (pH=1) to obtain 100 mcg/mL (stock solution I). Take 1 mL from a stock solution I, dilute it with 10 mL of 0.1 N HCl to get 10 mcg/mL (stock solution II). The absorbance of 10 mcg/mL (stock solution II) was scaned by a UV/VIS spectrophotometer at different wave lengths (200-400 nm). The maximum absorbance (ë max) value obtained after scanning the stock solution II was at 277 nm.

3.2. Calibration curve preparation

From the stock solution II (10 mcg/ml) various dilutions were made and the absorbance were measured. Standard calibration curve was plotted by using absorbance values as Y-axis versus the concentration values as X-axis.

3.3. Quality control test of metronidazole products

A- Unofficial tests (according to USP Pharmacopeia)

1-Weight variation (uniformity of weight) test: select 20 tablets randomly from the batch provided, and then weigh the tablets individually, then weigh the 20 tablets together and calculate the average weight (W), Compare the average weight calculated to the previous table to determine the maximum % difference allowed finally Calculate the upper and lower limits at the % difference allowed:

Upper limit = W + [(%/100) (W)]
Lower limit = W – [(%/100) (W)]

Furthermore, calculate the upper and lower limits at double the % difference allowed:

Upper limit = W + [(2x %/100) (W)]
Lower limit = W – [(2x % /100) (W)]

Compare the individual weights of tablets to the upper and lower limits calculated at the % difference allowed and at double that percentage. **Limit:** For the batch to be accepted:
Not more than 2 tablets (out of the 20 tablets) differ from the average weight by the % difference listed, and no tablet differs from the average weight by double that percentage. (20)
2-Friability test: Select 20 tablets randomly, dedust and weigh (WO) and Place the tablets in the Roche friabilator apparatus adjusting the timer at 4 min. and the speed at 25 rpm, then at the end of this operation, remove the tablets from the friabilator, dedust and reweigh (W), (any tablet that breaks up should be rejected before reweighing). Friability is expressed as a percentage loss in weight according to the following equation:

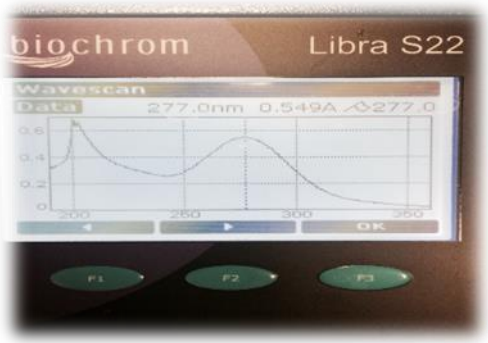
$$\% \text{ loss} = \frac{WO - W}{WO} \times 100$$

(if the value of friability (% loss) is less than or equal to 1%, the batch is accepted)

B-Official tests
1-Disintegration test: Place one tablet in each of the six tubes of the basket (tablets are selected randomly), The basket rack in 1 L beaker containing distilled water (as the disintegration medium) maintained at 37 ˚C. Start the apparatus (to move the basket assembly containing the tablets), and record the time required for all of the six tablets to break into particles and to pass to the disintegration medium. **Limit:** The tablets should disintegrate within 30 minutes (uncoated tablets), also if one tablet fails to disintegrate within 30 minutes, the disintegration test is repeated on 12 additional tablets. Not less than 16 out of the total 18 tablets tested disintegrate completely within 30 minutes.(20)

2-Dissolution test;
Preparation of the buffer system (0.1 N HCl, pH 1.2)
Take 8.5 mL of 36% hydrochloric acid solution and diluted to 1000 mL with distilled water, then measure the pH of resulting buffer. **Method:** The procedure is started by assembling and calibrating the apparatus at the above conditions, place the tested tablets, at specific time intervals (5-10-15-20-25-30) min withdraw 5mL sample from dissolution medium through a Millipore filter unit (polyethylene tube with cotton), and place the sample in a test tube. Replace the withdrawn sample with 5 mL fresh 0.1N HCl kept at 37±0.5 °C. Various dilutions were made to determine the appropriate dilution factor, mix well read the absorbance for the diluted samples at 277 nm against a blank of 0.1 N HCl. Calculate the concentrations of metronidazole released by using standard calibration curve. Plot the % dissolved curve of metronidazole verses time. Two tablets from each metronidazole product were tested by dissolution test and the average values were obtained. **Limit:** Not less than 80% of labeled amount metronidazole is dissolved in 30 minutes.

4.1. Determination of (ë max) of metronidazole powder
By scanning of stock solution II (10 mcg/mL) using a spectrophotometer between 200-400 nm.
It was found that the maximum absorbance of metronidazole was at 277 nm.



4.2. Calibration curve:

Concentration (mcg/mL)	Absorbance (nm)
5	0.199
10	0.398
15	0.555
20	0.769
25	0.968

Table (3) Standard calibration curve of metronidazole solution in different concentration

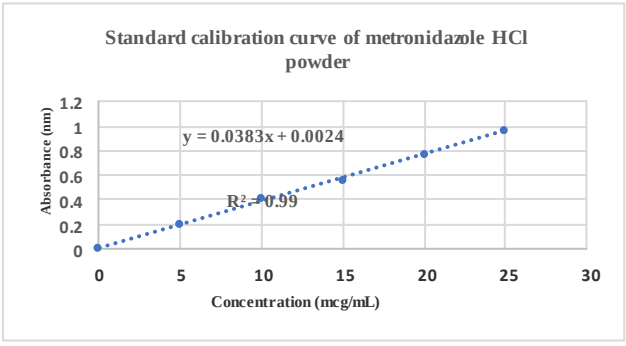


Figure (8): Standard calibration curve of metronidazole HCl in 0.1 N HCl.

4.3. Quality control tests of metronidazole
A- Unofficial tests
4.3.1. Weight variation (uniformity of weight) test
4.3.1.1. Weight variation of Flagyl® tablets
Average weight W=0.6887 g, so difference allowed is ±5%.
Upper limit=0.7276 g Lower limit=0.6543 g
Table (4): Weight variation of Flagyl® tablets

Tablet number	Weight 1 (gram)	Weight 2 (gram)	Weight 3 (gram)	Average weight (gram)±SD
1	0.691	0.677	0.682	0.683±0.007
2	0.701	0.671	0.707	0.693±0.019
3	0.671	0.682	0.682	0.678±0.006
4	0.676	0.682	0.701	0.686±0.013
5	0.701	0.696	0.701	0.699±0.002
6	0.690	0.695	0.689	0.691±0.003
7	0.692	0.689	0.671	0.684±0.011
8	0.690	0.690	0.701	0.693±0.006
9	0.701	0.707	0.677	0.695±0.016
10	0.689	0.690	0.685	0.688±0.003
11	0.682	0.701	0.690	0.691±0.009
12	0.695	0.671	0.696	0.687±0.014
13	0.696	0.685	0.676	0.686±0.010
14	0.677	0.701	0.692	0.690±0.012
15	0.685	0.685	0.690	0.687±0.003
16	0.685	0.701	0.682	0.689±0.010
17	0.682	0.685	0.685	0.684±0.002
18	0.685	0.691	0.684	0.687±0.004
19	0.685	0.692	0.685	0.687±0.004
20	0.707	0.694	0.684	0.695±0.012

As shown in table (5), no tablet has been out of the % difference allowed.

4.3.1.2. Wight variation test of Anazol® tablets
Average weight = 0.7402 g, so difference allowed is ±5%.
Upper limit=0.7772 g
Lower limit =0.7032 g

Table (5): Weight variation test of Anazol® tablets

Tablet Number	Weight 1 (gram)	Weight 2 (gram)	Weight 3 (gram)	Average weight (gram)±SD
1	0.753	0.749	0.748	0.750± 0.003
2	0.727	0.735	0.729	0.730± 0.004
3	0.749	0.737	0.727	0.738± 0.011
4	0.735	0.753	0.735	0.741± 0.010
5	0.729	0.735	0.748	0.737± 0.001
6	0.743	0.736	0.743	0.741± 004
7	0.735	0.740	0.749	0.741± 0.001
8	0.727	0.729	0.736	0.731± 0.005
9	0.749	0.749	0.727	0.742± 0.013
10	0.736	0.743	0.747	0.742± 0.006
11	0.735	0.753	0.729	0.739± 0.012
12	0.747	0.736	0.749	0.744± 0.007
13	0.744	0.735	0.735	0.738± 0.005
14	0.735	0.727	0.744	0.735± 0.009
15	0.748	0.748	0.737	0.744± 0.006
16	0.737	0.751	0.740	0.743± 0.007
17	0.740	0.735	0.735	0.737± 0.003
18	0.739	0.744	0.735	0.739± 0.005
19	0.751	0.747	0.747	0.748± 0.002
20	0.748	0.739	0.748	0.745± 0.005

As shown in table (6), no tablet has been out of the % difference allowed.

4.3.1.3. Weight variation test of Flazol® tablets

Average weight variation = 0.6508 g, so difference allowed is ±5%.

Upper limit=0.6833 g

Lower limit=0.6508 g

Table (6): Weight variation test of Flazol® tablets

Tablet number	Weight 1 (gram)	Weight 2 (gram)	Weight 3 (gram)	Average weight (gram)±SD
1	0.656	0.673	0.654	0.661±0.010
2	0.650	0.655	0.660	0.655±0.005
3	0.644	0.608	0.650	0.634±0.022
4	0.660	0.662	0.644	0.655±0.009
5	0.664	0.632	0.664	0.653±0.018
6	0.631	0.656	0.655	0.647±0.014
7	0.662	0.644	0.662	0.656±0.010
8	0.655	0.650	0.631	0.645±0.012
9	0.609	0.644	0.648	0.634±0.021
10	0.673	0.631	0.656	0.653±0.021
11	0.656	0.648	0.673	0.659±0.012
12	0.648	0.641	0.609	0.633±0.020
13	0.641	0.656	0.690	0.662±0.0251
14	0.676	0.650	0.663	0.663±0.013
15	0.690	0.690	0.650	0.677±0.023
16	0.650	0.676	0.641	0.656±0.018
17	0.663	0.650	0.670	0.661±0.010
18	0.670	0.654	0.663	0.662±0.008
19	0.650	0.670	0.654	0.658±0.011
20	0.654	0.670	0.650	0.658±0.011

As shown in table (6), no tablet has been out of the % difference allowed.

4.3.1.4. Weight variation of Negazole® tablets

Average weight = 0.94525 g, so difference allowed is ±5%.

Upper limit=0.9925 g Lower limit=0.8979 g

Table (7): Weight variation test of Negazole® tablets

Tablet number	Weight 1 (gram)	Weight 2 (gram)	Weight 3 (gram)	Average weight (gram)±SD
1	0.951	0.962	0.940	0.951±0.011
2	0.940	0.941	0.956	0.945±0.008
3	0.940	0.954	0.940	0.945±0.008
4	0.956	0.923	0.952	0.944±0.018
5	0.920	0.960	0.951	0.944±0.020
6	0.948	0.958	0.947	0.951±0.006
7	0.947	0.937	0.948	0.944±0.006
8	0.951	0.934	0.919	0.935±0.016
9	0.947	0.941	0.954	0.947±0.007
10	0.940	0.954	0.941	0.945±0.008
11	0.941	0.947	0.947	0.945±0.003
12	0.954	0.943	0.940	0.946±0.007
13	0.934	0.947	0.960	0.947±0.013
14	0.937	0.951	0.957	0.948±0.010
15	0.958	0.948	0.937	0.948±0.010
16	0.960	0.920	0.934	0.938±0.020
17	0.954	0.956	0.962	0.957±0.004
18	0.923	0.941	0.941	0.935±0.010
19	0.962	0.940	0.954	0.952±0.011
20	0.941	0.951	0.923	0.938±0.014

In the table (7) there is no tablet has out the % difference allowed.

4.3.1.5. Weight variation of Riazole® tablets

Average weight = 0.65802 g, so difference allowed is ±5%.

Upper limit= 0.6909 g

Lower limit= 0.6251g

Table (8): Weight variation test of Riazole® tablets

Tablet number	Weight 1 (gram)	Weight 2 (gram)	Weight 3 (gram)	Average weight (gm)±SD
1	0.658	0.664	0.656	0.659±0.004
2	0.663	0.655	0.663	0.661±0.005
3	0.655	0.656	0.658	0.656±0.001
4	0.657	0.663	0.663	0.661±0.004
5	0.656	0.655	0.655	0.655±0.000
6	0.663	0.657	0.657	0.659±0.004
7	0.656	0.658	0.656	0.657±0.000
8	0.654	0.663	0.655	0.658±0.005
9	0.662	0.655	0.657	0.658±0.004
10	0.657	0.657	0.656	0.657±0.000
11	0.656	0.656	0.655	0.656±0.000
12	0.658	0.663	0.655	0.658±0.004
13	0.664	0.658	0.657	0.659±0.003
14	0.655	0.663	0.658	0.658±0.004
15	0.657	0.656	0.657	0.656±0.000
16	0.662	0.654	0.658	0.658±0.004
17	0.655	0.662	0.663	0.660±0.004
18	0.656	0.657	0.655	0.656±0.001
19	0.663	0.656	0.657	0.658±0.004
20	0.658	0.656	0.656	0.657±0.000

In the table (8) there is no tablet has out the % difference allowed.

4.3.2. Friability test

Table (9): Friability test of different metronidazole brands.

Name of Brand	Weight before the test (gram)	Weight after the test (gram)	% loss
Flagyl®	13.816	13.800	0.1158
Negazole®	19.093	18.986	0.5604
Flazol®	13.174	13.060	0.8653
Anazol®	14.893	14.885	0.0537
Riazole®	14.821	14.811	0.0674

There is no tablet more than 1% of loss, so the batch is accepted.

B-official test

4.3.3. Drug content (uniformity) test

Table (10): Drug content of different metronidazole brands

Brand Name	% of drug content (1)	% of drug content (2)	% of drug content (3)	% of mean drug content ±SD
Flagyl®	104.50	103.74	103.60	99.687±0.4842
Negazole®	96.987	103.94	100.74	100.555±3.480
Flazol®	103.617	104.40	99.800	102.605±2.461
Anazol®	100.550	97.144	98.070	98.588±1.761
Riazole®	104.460	101.00	100.03	100.787±2.329

The results in table (10) show that all the brands of metronidazole tablet complied with USP specification for assay (90-110%).

4.3.4. Disintegration test

Table (11): Disintegration test of different metronidazole brands

Brand name	Disintegration time 1 (min)	Disintegration time 2 (min)	Disintegration time 3 (min)	Mean Disintegration time±SD (min)
Flagyl®	7.07	6.45	6.49	6.53±0.008
Anazol®	3.03	2.47	2.54	2.68±0.006
Ngazole®	4.33	4.40	4.25	4.32±0.005
Flazol®	1.42	1.27	1.43	1.37±0.006
Riazole®	1.18	1.11	1.20	1.16±0.003

The results in table (11) show that all the brands of metronidazole tablets complied With the USP specification for disintegration. The USP specification is that film coated tablet should disintegrate within 30 min.

4.3.5. Dissolution test

4.3.5.1. Flagyl®

Table (12): Dissolution profile of Flagyl® tablet (1)

Time (min)	Absorbance	Amount (mg)	% Released
5	0.225	264.26	52.85
10	0.273	320.63	64.00
20	0.347	407.10	81.14
30	0.396	465.55	93.11
45	0.4200	493.29	98.65
60	0.443	520.30	104.06

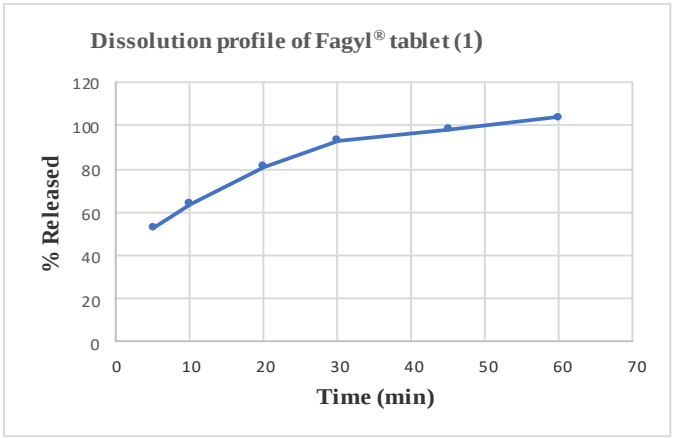


Figure (9): Dissolution profile of Flagyl® tablet (1).

Table (13): Dissolution profile of Flagyl® tablet (2).

Time (min)	Absorbance	Amount (mg)	% Released
5	0.224	234.9	46.980
10	0.282	286.58	57.316
20	0.354	411.07	82.210
30	0.400	469.80	93.960
45	0.4190	492.12	98.423
60	0.441	517.90	103.59

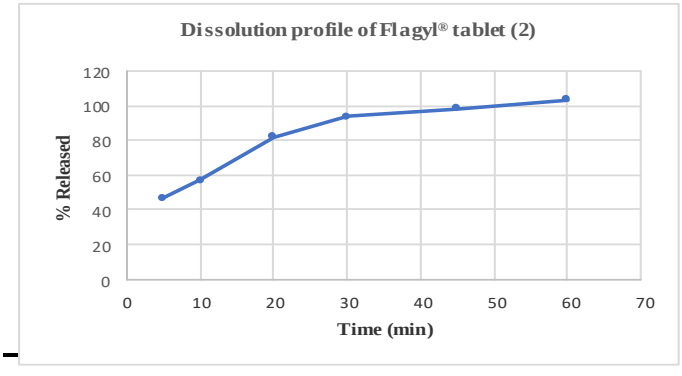


Figure (10): Dissolution profile of Flagyl® tablet (2).

Table (14): The Mean % released of metronidazole ±SD from Flagyl® tablet.

Time (min)	Mean amount (mg)	Mean % Released ±SD
5	263.000	49.795±0.398
10	325.919	61.770±6.310
20	411.436	82.684±0.663
30	467.675	93.535±0.601
45	492.702	98.536±0.160
60	519.100	103.82±0.332

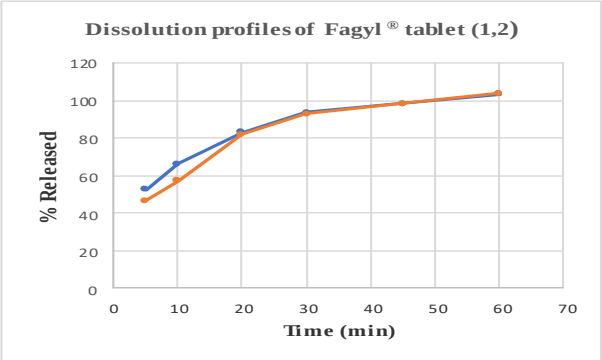


Figure (11): Comparative dissolution profiles of Flagyl® ablets (1, 2).

4.3.5.2. Negazole®

Table (15): Dissolution profile of Negazole® tablet (1)

Time (min)	Absorbance	Amount (mg)	% Released
5	0.241	283.05	56.60
10	0.320	375.84	76.00
20	0.360	425.166	85.00
30	0.419	492.11	98.42
45	0.439	515.60	103.12
60	0.439	515.60	103.12

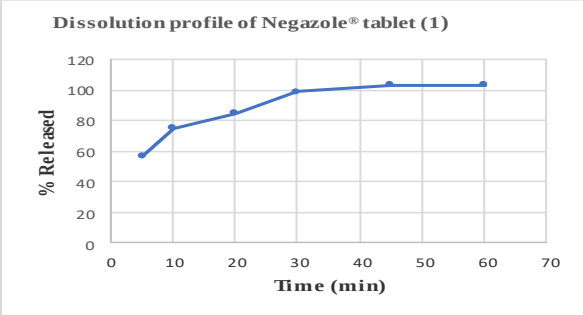


Table (16): Dissolution profile of Negazole® tablet (2).

Time (min)	Absorbance	Amount (mg)	% Released
5	0.239	280.70	60.00
10	0.301	353.52	70.70
20	0.370	434.56	86.91
30	0.400	496.80	93.96
45	0.435	510.90	102.18
60	0.438	514.431	102.10

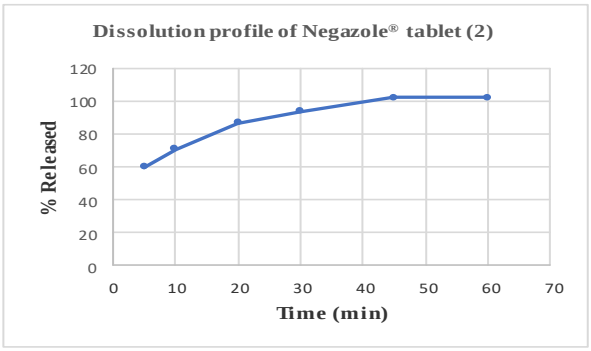


Figure (13): Dissolution profile of Negazole® tablet (2).

Table (17): The Mean % released of metronidazole ±SD from Negazole® tablet.

Time (min)	Mean amount (mg)	Mean % released ±SD
5	281.875	56.37±0.325
10	375.250	75.046±0.160
20	422.783	84.545±0.643
30	492.700	93.96±0.450
45	513.250	102.65±0.664
60	515.015	102.65±0.222

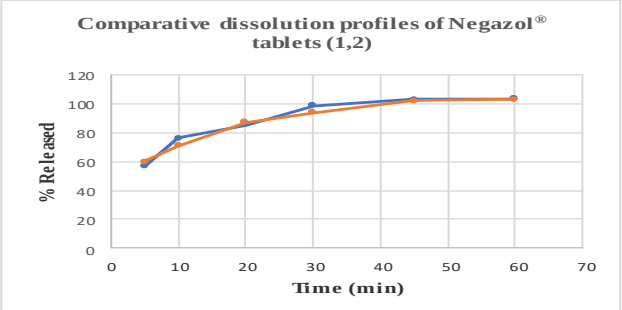


Figure (14): Comparative dissolution profiles of Negazole® tablets (1,2).

4.3.5.3. Flazol®

Table (18): Dissolution profile of Flazol® tablet (1)

Time (min)	Absorbance	Amount (mg)	% Released
5	0.230	270.135	54.00
10	0.311	365.260	73.05
20	0.390	458.005	91.16
30	0.420	493.290	98.66
45	0.423	496.813	99.36
60	0.423	496.813	99.36

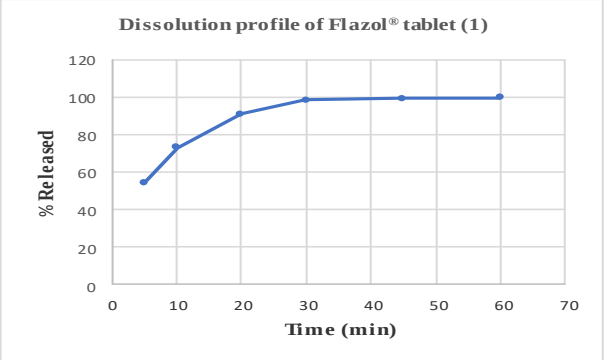


Figure (15): Dissolution profile of Flazol® tablet (1).

Table (19): Dissolution profile of Flazol® tablet (2).

Time (min)	Absorbance	Amount (mg)	% Released
5	0.235	276.00	55.200
10	0.250	293.62	58.720
20	0.385	452.18	90.430
30	0.2890	493.29	98.650
45	0.2890	496.81	99.362
60	0.2899	496.81	99.362

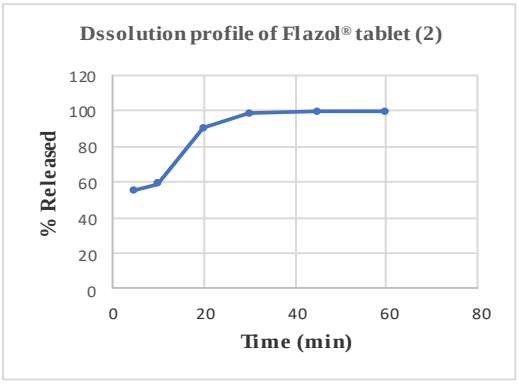


Figure (16): Dissolution profile of Flazol® tablet (2).

Table (20): The Mean % released of metronidazole ±SD from Flazol® tablet

Time (min)	Mean amount (mg)	Mean % released ±SD
5	273.00	54.60±0.848
10	370.55	74.105±1.491
20	455.09	90.795±0.516
30	493.29	98.654±0.005
45	496.81	99.361±0.001
60	496.81	99.546±0.260

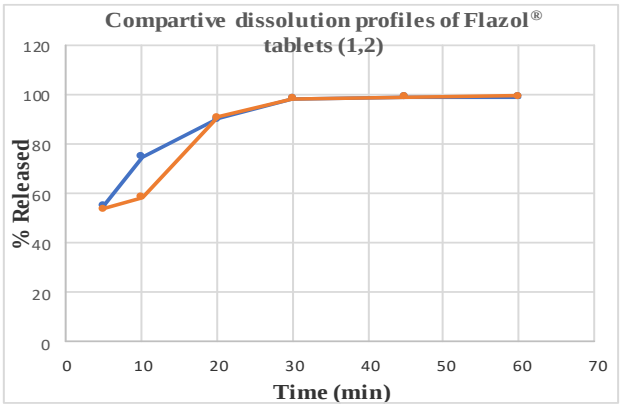


Figure (17): Comparative dissolution profiles of Flazol® tablets (1, 2).

4.3.5.4. Riazole®

Table (21): Dissolution profile of Riazole® tablet (1)

Time (min)	Absorbance	Amount (mg)	% Released
5	0.249	292.450	58.49
10	0.402	472.149	94.42
20	0.425	499.420	99.83
30	0.425	499.420	99.83
45	0.425	499.420	99.83
60	0.425	499.420	99.83

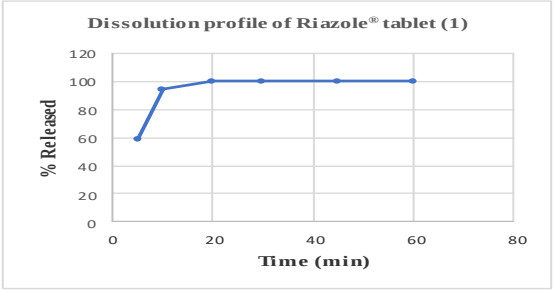


Figure (18): Dissolution profile of Riazole® tablet (1).

Table (22): Dissolution profile of Riazole® tablet (2)

Time (min)	Absorbance	Amount (mg)	% Released
5	0.319	373.491	74.69
10	0.410	481.545	96.30
20	0.425	499.420	99.83
30	0.425	499.420	99.83
45	0.425	499.420	99.83
60	0.425	499.420	99.83

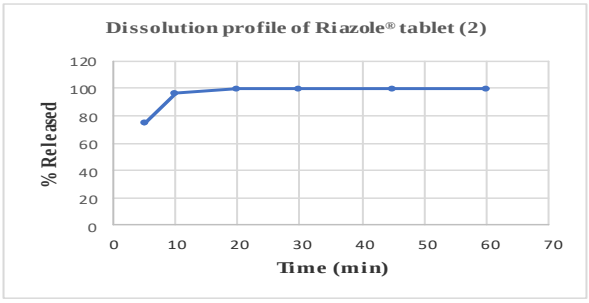


Figure (19): Dissolution profile of Riazole® tablet (2).

Table (23): The Mean % released of metronidazole ±SD from Riazole® tablets

Time (min)	Mean amount (mg)	Mean % released ±SD
5	332.97	66.594±1.460
10	476.84	95.360±1.329
20	499.42	99.830±0.000
30	499.42	99.830±0.000
45	499.42	99.830±0.000
60	499.42	99.830±0.000

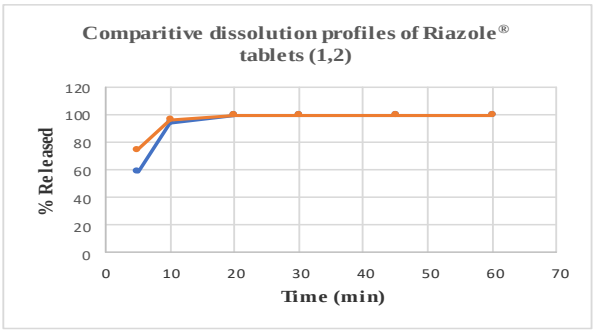


Figure (20): Comparative dissolution profiles of Riazole® tablets (1, 2).

4.3.5.5. Anazol®

Table (24): Dissolution profile of Anazol® tablet (1)

Time (min)	Absorbance	Amount (mg)	% Released
5	0.239	280.70	56.14
10	0.385	452.18	90.44
20	0.396	465.10	93.02
30	0.419	492.11	98.42
45	0.423	496.81	99.36
60	0.423	496.81	99.36

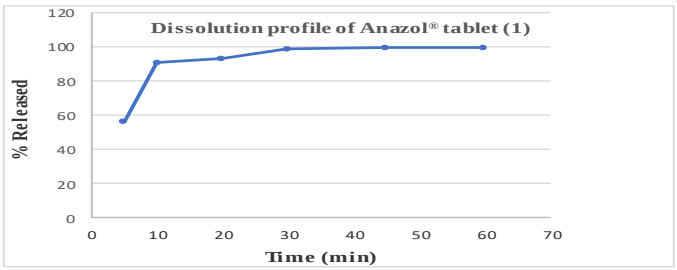


Figure (21): Dissolution profile of Anzol® tablet (1).

Table (25): Dissolution profile of Anazol® tablet (2)

Time (min)	Absorbance	Amount (mg)	% Released
5	0.285	334.73	66.990
10	0.413	485.00	97.010
20	0.423	496.81	99.632
30	0.423	496.81	99.632
45	0.423	496.81	99.632
60	0.423	496.81	99.632

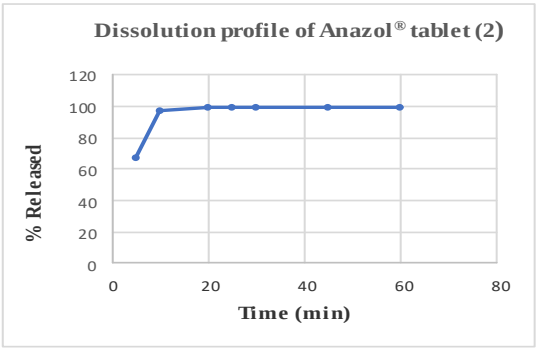


Figure (22): Dissolution profile of Anazol® tablet (2).

Table (26): The Mean % released of metronidazole ±SD from Anazol® tablets

Time (min)	Mean amount (mg)	Mean % released ±SD
5	140.492	61.565±0.672
10	226.296	93.723 ±0.648
20	232.762	96.191±0.484
30	246.266	98.891±0.000
45	248.616	98.891±0.001
60	248.616	98.891±0.001

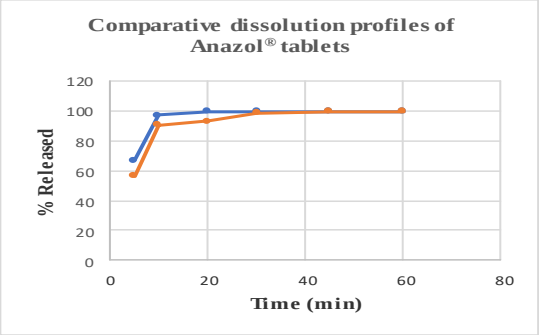


Figure (23): Comparative dissolution profiles of Anazol® tablets (1, 2).

Statistical analysis

Using one – way ANOVA (analysis of variance) with $p < 0.05$ for level of significance, statical comparisons of the mean dissolution data at each dissolution time point are performed. One – way ANOVA is equivalent to the t-test in the case where the dissolution profile data of two formulations is compared. This method takes the variability in the dissolution profile data into account while comparing each time point.

Table (27): The ANOVA test result of % released of five brands of metronidazole at 5 minutes.

ANOVA: Single Factor

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Column 1	2	99.83	49.915	17.22845
Column 2	2	116.6	58.3	5.78
Column 3	2	109.2	54.6	0.72
Column 4	2	133.18	66.59	131.22
Column 5	2	123.13	61.565	58.86125

ANOVA

Source of Variation	*SS*	*Df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	326.6527	4	81.66319	1.909717	0.247172	5.192168
Within Groups	213.8097	5	42.76194			
Total	540.4624	9				

According to the Table (27) which describes the ANOVA test results of % released of five brands of metronidazole at 5 minutes F value (cal) is less than F critical that means no significant difference in the % released results of the five brands at 5 minutes according to ANOVA test.

Table (28): The ANOVA test result of % released of five brands of metronidazole at 30 minutes.

ANOVA: Single Factor

SUMMARY

Groups	Count	Sum	Average	Variance
Column 1	2	187.07	93.535	0.36125
Column 2	2	192.38	96.19	9.9458
Column 3	2	197.31	98.655	5E-05
Column 4	2	199.66	99.83	0
Column 5	2	198.052	99.026	0.73447

ANOVA

Source of Variation	SS	Df	MS	F	P-value	F crit
Between Groups	53.02997	4	13.25749	6.003445	0.037839	5.192168
Within Groups	11.04157	5	2.208314			
Total	64.07155	9				

According to the table (28) which describes the ANOVA test results of % released of five brands of metronidazole at 30minutes F value (cal) is not less than F critical that mean there is significant difference in the % released results of the five brands at 30 minutes according to ANOVA test.

Table (29): The ANOVA test result of % released of five brands of metronidazole at 60 minutes.

ANOVA: Single Factor

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Column 1	2	207.65	103.825	0.11045
Column 2	2	205.22	102.61	0.5202
Column 3	2	198.72	99.361	2E-06
Column 4	2	199.66	99.83	0
Column 5	2	198.99	99.496	0.03699

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	33.77397	4	8.443493	63.23349	0.000181	5.192168
Within Groups	0.667644	5	0.133529			
Total	34.44161	9				

According to the table (29) which describes the ANOVA test result of % released of five brands of metronidazole at 60 minutes F value (cal) is not less than F critical but also higher than F critical that mean there is a significant difference in the % release results of the five brands at 60 minutes according to ANOVA test.

5.Conclusion

Five brands of film coated metronidazole 500 mg tablets have been evaluated using some quality control tests as uniformity of weight and friability as unofficial test we found no significance difference between five brands its within acceptable limit, then perform content uniformity, disintegration and dissolution as official test we found no significance difference between five brand regarding disintegration and content uniformity but for the dissolution test according to ANOVA there is significance difference between them at 30 and 60 minutes with the aim to assess its quality.

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