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Comparative study of in-vitro parameters of branded, generic and in-house formulation containing selected drugs

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Abstract:

The combination of Ornidazole and Ofloxacin as tablet is an oral antiprotozoal and has marked antibacterial and antimicrobial properties. The aim of the present study was to formulate the above combination and study the post compression and evaluation parameters with that of branded and generic tablet combination. Tablets of ornidazole and ofloxacin were prepared by wet granulation method. Starch, lactose, magnesium stearate and talc were utilized as excipients for the preparation. After constructing calibration curve, the *in vitro* drug release studies were carried out using USP type II apparatus at 50 rpm. All the tablets formulations were evaluated for post compression parameters like friability, hardness, weight variation, *in vitro* disintegration. All the test results were found to be within the prescribed limits. The drug release from the branded, generic, and self-prepared formulations were found to be 103.5±0.10 %, 100.12±0.10 %, 99.56±0.19 % and 99.71±0.08 %, 101.76±0.08 %, 102.78±.0.12 % for ornidazole and ofloxacin respectively. *In vitro* dissolution study results reveals that there was no significant difference between the drug release profiles of all the formulation. In conclusion, all tablet formulations had good hardness. All the tablet formulations could immediate release for over 30 minutes.

Keywords:

Ornidazole, Ofloxacin, brand, generic, *in vitro* drug release.

1. Introduction:

Brand name medicine is originally discovered and developed by a pharmaceutical company brand name medicine is approved by FDA by submitting a new drug application along with data regarding proof of characteristics of dosage form, manufacturing, chemistry, stability, efficacy, safety, labeling, and packaging. A generic drug is a medication created to be the same as an existing approved brand-name drug in the dosage form, safety, strength, route of administration, quality, performance and intended use. Generics work in the same way and provide the same clinical benefit as its brand name version. A drug that has a trade name and is protected by a patent (can be produced and sold only by the company holding patent) proprietary drug.

Fixed dose combination formulations have unique advantages such as complementary mechanism of action, synergistic effects, better tolerability, elongated product life-cycle management, and cost savings. Use of fixed dose combinations is a rational approach for achieving optimal therapeutic benefits while minimizing pill-burden. Greater convenience with decreased pill-burden leads to improved adherence, resulting in superior clinical outcomes and greater cost-effectiveness. Regulatory approval of fixed dose combinations is based on bioavailability data, similar to the way generic medications are approved.

The present work is aimed to formulate and compare the various physicochemical characteristics like weight variation, friability, hardness, disintegration time and drug content of branded, generic and self-prepared product containing fixed dose combination of Ornidazole and Ofloxacin.

2. Materials:

Oflomac® OZ is a brand product obtained from local market shimoga, relevant generic for ornidazole and ofloxacin was also obtained from local market Ornidazole was procured from Aurz pharmaceuticals Private Limited, Bengaluru. Ofloxacin, a gift sample from Holid Pharmaceuticals Pvt Ltd, Starch, Lactose, and Magnesium Stearate were procured from SD Fine Chemicals, Mumbai.

3. Methods:

3.1. Preparation of 0.1M hydrochloric acid (pH 1.2)[4]:

Preparation of 0.1 M hydrochloric acid was done by adding 8.3 ml of concentrated hydrochloric acid into 1000 ml volumetric flask and volume was made up to mark with water by maintaining the acid

3.2. Calibration curve of ornidazole in 0.1 M hydrochloric acid solution (pH 1.2):

Accurately weighed ornidazole (50 mg) was transferred into a 50 ml volumetric flask, dissolved and adjusted the volume up to 50 ml with 0.1M hydrochloric acid solution (pH 1.2) to get stock solution A. From the stock solution A, 10 ml was pipetted out into a 100 ml volumetric flask and volume was made up to mark with 0.1M Hydrochloric acid solution (pH 1.2) to get stock solution B. From the stock solution B, known volume were pipetted out and made up to 10 ml with 0.1M hydrochloric acid solution (pH 1.2) in 10 ml volumetric flask to get 1-10 µg/ml concentration solutions and absorbance was recorded at 277 nm by UV-visible spectrophotometer (UV-1601, Shimadzu, Japan).

3.3. Calibration curve of ofloxacin in 0.1M hydrochloric acid solution (pH 1.2):

Accurately weighed Ofloxacin (50 mg) was transferred into a 50 ml volumetric flask, dissolved and adjusted the volume up to 50 ml with 0.1 M hydrochloric acid solution (pH 1.2) to get stock solution A. From the stock solution A, 10 ml was pipetted out into a 100 ml volumetric flask and volume was made up to mark with 0.1M Hydrochloric acid solution (pH 1.2) to get stock solution B. From the stock solution B, known volume were pipetted out and made up to 10 ml with 0.1M hydrochloric acid solution (pH 1.2) in 10 ml volumetric flask to get 1-10 µg/ml concentration solutions and absorbance was recorded at 294 nm by UV-visible spectrophotometer (UV-1601, Shimadzu, Japan).

3.4. Preparation of tablet[5]:

The tablets are prepared by wet granulation method. Calculated amount of drug, binder, and diluents were mixed using mortar and pestle and granules were prepared. Calculated amount of lubricants were added to the granules and then granules were compressed into tablet using tablet punching machine with 12 mm punched sets.

4. Evaluation of tablets[6, 7, 8]:

4.1. Hardness:

The hardness of the tablet was determined by using Monsanto hardness tester. The tester consists of barrel containing a compressible spring held between two plungers. The lower plunger was placed in contact with the tablet, and a zero reading is taken. The upper plunger was forced against a spring by turning a threaded bolt until the tablet fractures. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of fracture is recorded and the zero reading is deducted from it. The test was performed on three tablets and the average value was recorded. It is expressed in Kg/cm^2.

4.2. Friability:

The friability of tablet was performed in a Roche Friabilator. It consists of a plastic chamber that revolves at 25 rpm. Ten tablets were weighed together and then placed in the chamber. The friabilator was operated for 100 revolutions and the tablets were subjected to the combined effects of abrasions and shock because the plastic chamber carrying the tablets drops them at a distance of six inches with every revolution. The tablets are then dusted and reweighed.

Percentage friability is calculated by using following formula

$$\% \text{ Friability} = \frac{(W1 - W2)}{W1} * 100$$

Where,

W1= Weight of the tablets before test.

W2 =Weight of the tablets after test.

4.3. Weight variation test:

Weight variation was determined by weighing 20 tablets individually in an electronic balance. The average weight was calculated and the percentage variation of each tablet from the average weight of tablet was calculated.

$$\text{Percentage deviation} = \frac{(\text{Individual weight of tablet} - \text{Average weight of 20 tablets})}{\text{Average weight of 20 tablets}} * 100$$

4.4. Drug content determination:

The drug content was determined by crushing the tablets in glass mortar and pestle and shaking the crushed powder with 20 ml of 0.1M hydrochloric acid for 48 hours. The volume was made up 100 ml by using 0.1M hydrochloric acid and filtered using Whatman filter paper. The

extracted drug in solution was determined by analysing and aliquoting UV spectrophotometer (1601, Shimadzu, Kyoto, Japan) using suitable blank at 277 nm and 294 nm.

4.5. In-vitro dissolution studies:

In vitro dissolution was studied by using the USP apparatus II (paddle type). Tablets were placed into the 900 ml 0.1M hydrochloric acid pH 1.2. The temperature was maintained at 37±0.5 °C and stirred at a speed of 50 rpm. An aliquot of 5 ml was withdrawn at specified time intervals and replaced with fresh dissolution medium. The samples were filtered with 0.45 µ Whatman membrane filter. Amount of drug in each aliquot was assayed on a UV-Spectrophotometer (UV-1601, Shimadzu, Japan) at 277 nm and 294 nm. All the trials were conducted in triplicate and the average (±S.D) reading was noted.

4.6. In-vitro disintegration studies:

One tablet was placed in each of the 6 tubes of the basket in a disintegration testing apparatus (Rupa Industries, New Delhi). Disc was added to each tube and operated the apparatus using 0.1M hydrochloric acid (pH 1.2) maintained at 37˚C± 2˚C as the immersion liquid. Time taken to disintegrate the tablet was visually noted.

5. Results:

Calibration curves of Ornidazole and Ofloxacin

Table. 1: Calibration data for Ornidazole in 0.1M hydrochloric acid

SL. NO	Concentration(µg/ml)	Absorbance (at 277nm)
1	0	0
2	1	0.035
3	2	0.074
4	3	0.089
5	4	0.130
6	5	0.161
7	6	0.208

8	7	0.225
9	8	0.260
10	9	0.296
11	10	0.327

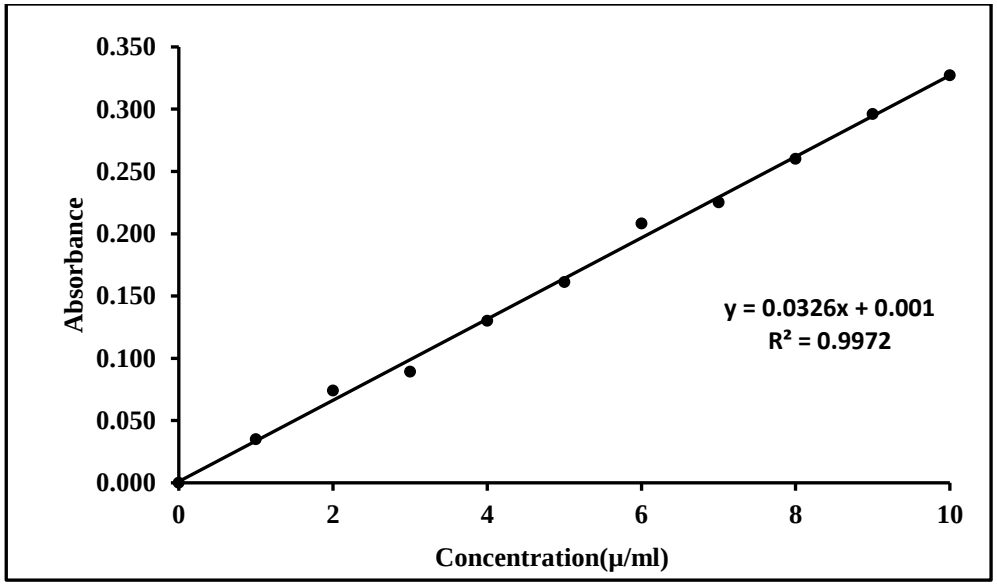

Figure. 1: Calibration curve of Ornidazole

Table. 2: Calibration data for Ofloxacin in 0.1M hydrochloric acid

SL. NO	Concentration(µg/ml)	Absorbance (at 294nm)
1	0	0
2	1	0.118
3	2	0.218
4	3	0.277
5	4	0.353
6	5	0.461
7	6	0.553
8	7	0.639

9	8	0.773
10	9	0.801
11	10	0.881

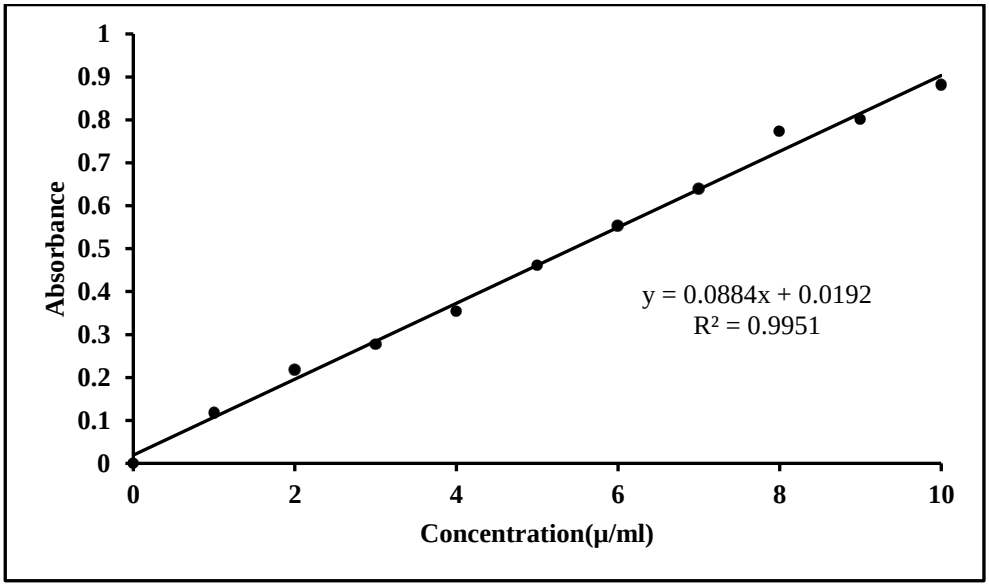

Figure. 2: Calibration curve of Ofloxacin

Physical properties of tablets:

Table. 3: Evaluation of tablets

Formulation	Hardness (kg/cm^2)	Friability (%)	% Deviation	Drug content (mg)	
				Ornidazole	Ofloxacin
Brand product	9.8±0.2	0.012	2.5±0.12%	505.5±0.43	207.95±0.24
Generic product	8.8±0.5	0.102	3.8±0.2%	503.125±0.80	203.40±0.13
Self-prepared	9.2±0.3	0.09	2.9±0.32%	515.125±0.12	197.72±0.84

Values are mean ±SD

In vitro drug release studies

Table. 4: In vitro drug release of brand, generic and in-house product in 0.1M hydrochloric acid (pH 1.2)

Time (min)	%CDR (Brand)		%CDR (Generic)		%CDR (In-house product)	
	Ornidazole	Ofloxacin	Ornidazole	Ofloxacin	Ornidazole	Ofloxacin
0	0	0	0	0	0	0
5	10.40±0.46	12.27±0.41	27.95±0.12	24.49±0.26	31.10±0.42	31.09±0.42
10	37.125±0.40	45.81±0.38	45.56±0.20	52.67±0.14	48.37±0.38	52.67±0.34
15	72±0.37	71.07±0.31	71.43±0.18	77.21±0.16	70.31±0.33	79.26±0.28
20	91.68±0.28	80.30±0.28	88.31±0.15	86.93±0.32	77.06±0.28	92.04±0.23
25	96.18±0.16	90±0.14	90.56±0.24	95.62±0.18	87.75±0.21	98.69±0.18
30	103.5±0.10	99.71±0.08	100.12±0.10	101.76±0.08	99.56±0.19	102.78±0.12

***Cumulative % drug released**

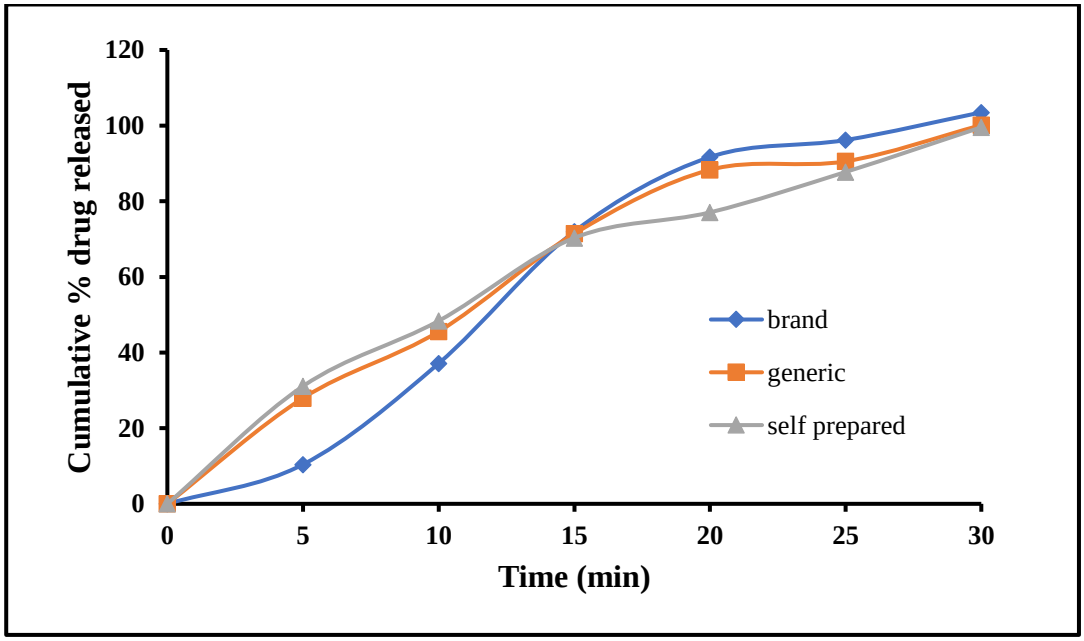

Figure. 3: In vitro dissolution comparison profile of brand, generic and self-prepared products (Ornidazole) in 0.1M hydrochloric acid

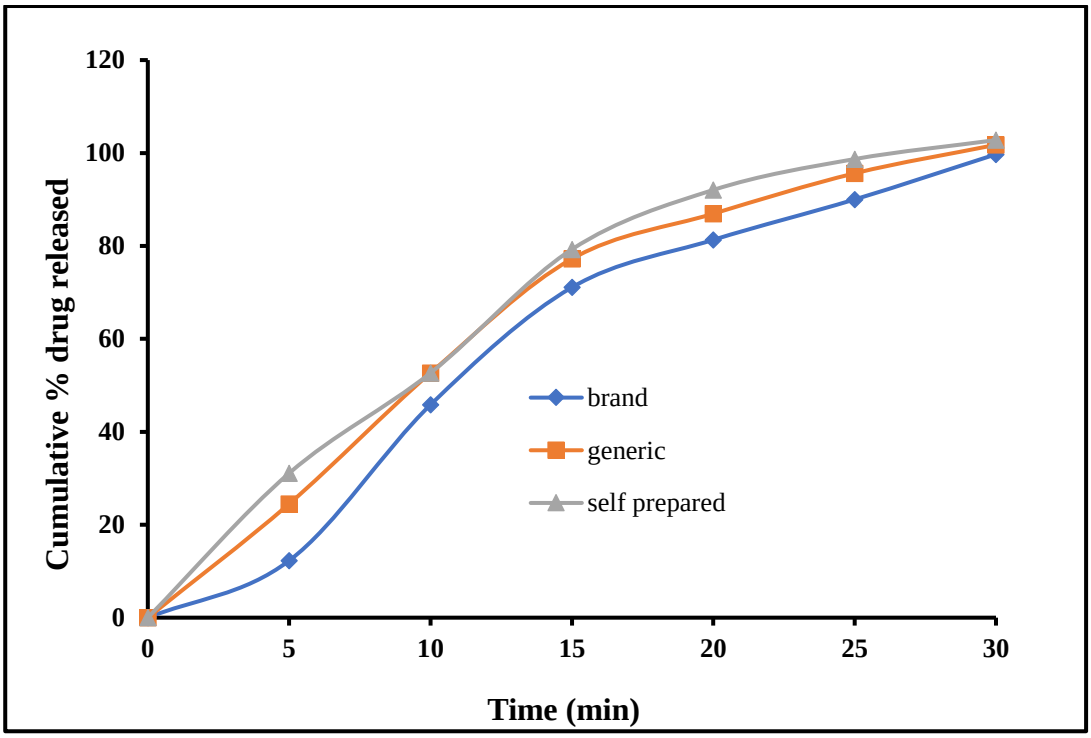

Figure. 4: In vitro dissolution comparison profile of brand, generic and self-prepared products (Ofloxacin) in 0.1M hydrochloric acid

Table. 5: Disintegration of tablets

Formulations	Time (sec)
Brand	890
Generic	850
Self-prepared	800

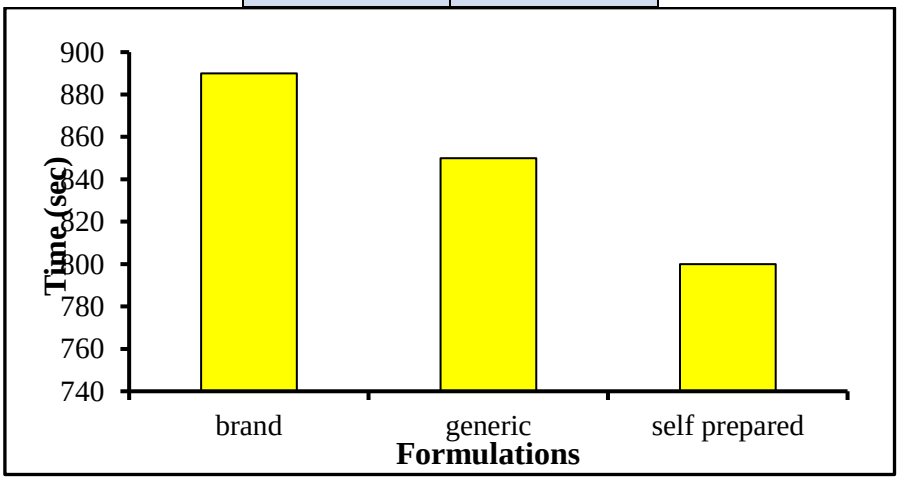

Figure. 5: In vitro disintegration comparison profile of brand, generic,self-prepared products in 0.1M hydrochloric acid (pH 1.2)

6. Discussion:

6.1. Determination of λ_{max}:

The standard solution of ofloxacin and ornidazole was scanned for absorption maxima blank between 200-400 nm using UV-visible spectrophotometer (UV-Shimadzu, Japan). The maximum absorption was found at 294 nm and 277 nm respectively.

6.2. Calibration curve of ornidazole and ofloxacin:

The calibration curve of ornidazole was developed in the range of 1-10 µg/ml (Table 1) at wavelength 277 nm. Good linearity with regression coefficient of 0.9972 (r^2 value) was observed. The calibration curve of ofloxacin was also developed in the range of 1-10 µg/ml (Table 2) at wavelength 294 nm. Good linearity with regression coefficient of 0.9951 (r^2 value) was observed

6.3. Post compression parameters:

Tablets of every batch were subjected to weight variation test, difference in weight and percentage deviation was calculated for each batch. The results of the test showed that weight of the tablet were in permissible limit. Brand product is having less variation in weight compared to generic and self-prepared product. (Table. 4). Hardness of three tablets of each batch was checked by using Monsanto hardness tester. The results showed that the hardness of the tablet. 8.8±0.5- 9.8±0.2 kg/cm^2. 10 tablets of each batch were subjected to friability and it was found in the range of 0.09 - 0.102%. The results suggest that the friability of prepared formulation was within the acceptable limits. Brand product showed less friability compared to generic and self-prepared product. The *in vitro* disintegration time is the very important parameter for immediate release dosage form. The disintegrating ability of all formulation was evaluated. For all the formulations, disintegration time was found to be within the range of 800 to 890seconds (Table. 5, fig. 5).

6.4. In vitro dissolution test:

Ofloxacin and Ornidazole tablets were evaluated for *in vitro* drug release for 30 minutes. The drug release from the branded, generic, self-prepared were found to be 103.5±0.10 %, 100.12±0.10 %, 99.56±0.19 % and 99.71±0.08 %, 101.76±0.08 %, 102.78±0.12 %, for ornidazole and ofloxacin respectively. Comparative study on drug release from all the formulation is given in (fig. 3 and fig. 4). There is no significant change in the drug release profile of brand, generic and self-prepared product.

7. Conclusion:

In the present study we have taken the branded and generic tablets of Ornidazole and Ofloxacin combination and compared the physical and other evaluation parameter tests with the best of formulated product. The physical parameters of all the branded, generic, and self-prepared tablets were found to be satisfactory and as per the pharmacopoeia specifications. All the formulations were evaluated for post compression parameters like hardness, friability, weight variation, etc. There is no significant variation seen among physical parameters. The self-prepared product exhibited more similarity with respect to hardness, friability of branded tablets. In-vitro dissolution study for all the formulations was conducted and there is no significant difference between the drug releases of all formulations

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