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Original Article

Comparative study of Metronidazole formulations

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Abstract

The aim of this study is to check pharmaceutical equivalence of the different brands of metronidazole tablets available in Karachi, Pakistan. Three different brands of metronidazole tablets (400 mg) were included in the study. Four QC quality control parameters: weight variation test, hardness test, thickness, friability test were carried out specified by BP/USP (British and United state Pharmacopoeia).The results showed that all parameters (weight-variation, thickness, hardness, friability of metronidazole tablets are in accordance with the BP/USP limits.

Keywords: metronidazole, thickness, weight variation, hardness and friability.

Introduction

Metronidazole (MTR), is 2-(2-methyl-5-nitro-1H-imidazol-1- yl) ethanol (Figure 1). [1]. Metronidazole is metabolized by oxidation and by conjugation with glucuronic acid to 2–hydroxymethyl metronidazole and 2–methyl–5–nitroimidazol–1–acetic acid. About 70 to 80% of a dose is excreted in the urine in 48 hr with less than 10% of the dose as unchanged drug, up to 10% as conjugated MTR, about 27% as 2–hydroxymethylmetronidazole, 10% as the conjugated 2–hydroxymethyl metabolite, and 20% as the acid metabolite [2].

Metronidazole is a commonly used antibiotic agent. It is used for various conditions such as protozoal infections (for example, giardiasis) anaerobic bacterial infections,, *Helicobacter* associated gastritis, and hepatoencephalopathy. According to Previous reports metronidazole toxicity may induce several neurologic side effects, including ataxic gait, peripheral neuropathy, dysarthria, encephalopathy and convulsive seizures. [3-6]

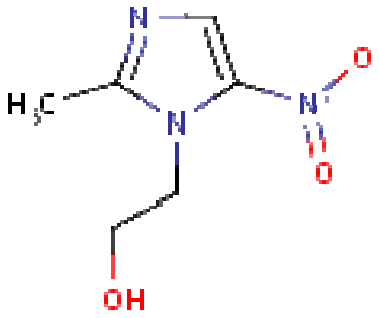

Figure 1: Metronidazole

EXPERIMENTAL

Tablet specifications

All parameters (wt. variation, thickness, hardness and friability) of different brands of metronidazole were carried out and results showed that they are in accordance with BP/USP limits.

Weight variation test: Weight variation test of above mentioned tablets proved strictly that all the tablets were in accordance to the BP/USP requirements that not more than two tablets out of 20 tablets should cross ±7.5 % deviation. Similarly their statistical control chart(shewart chart)shows that metronidazol tablets were in range of the upper and lower limits.

Thickness test: Thickness of metronidazol including average , standard deviation, upper and lower limits are in accordance with BP/USP.

Hardness: Hardness test of metronidazol tablets was found to be in conjunction with the stated guidelines as given in BP/USP. Similarly the official range of hardness stated in BP/USP is not less than 4.00 Kg of pressure is required to break a tablet and we found all the samples were in accordance with the limit.

Friability test: This test is intended to determine the friability of uncoated tablets, the phenomenon where by tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition.(British Pharmacopoeia 2000).Friability of tablets was not less than 1%. Therefore it is not compliance with the BP/USP standard.

Results and Discussions

WEIGHT VARIATION TEST: Weight variation test of metronidazole tablets proved statistically that all the tablets were in accordance to the BP/USP requirements (Table-1, 2 & 3).

TABLE 1: Weight of 20 tablets (randomly selected) of different brands

Tablets	Gramex	Flagyl	Metrozine
1	748	512	759
2	755	516	768
3	754	508	754
4	750	505	755
5	782	519	759
6	776	520	730
7	764	528	756
8	763	516	756
9	766	512	731
10	750	506	764
11	758	510	727
12	743	510	749
13	754	508	755
14	750	505	759
15	782	519	730
16	776	528	730
17	754	510	756
18	756	512	756
19	748	510	750
20	750	506	750

TABLE 2: STATISTICAL WEIGHT VARIATIONS

Tablets	Average (Gm)	Standard deviation	Upper limit (X+3S)	Lower limit (X-3S)
Gramex	0.75895	0.011808	0.794374	0.723536
Flagyl	0.513	0.006898	0.53369	0.49231
metrozine	0.7497	0.012695	0.78779	0.71162

TABLE 3: WEIGHT VARIATION TEST

tablets	Result (Gm)	BP/USP Specification	Deviation from BP/USP Specification
Gramex Flagyl metrozine	0.75895 0.513 0.7497	Deviation should be ±7.5%	Within specified limit

THICKNESS TEST: Thickness of all tablets of metronidazole including standard deviation, average weight, upper & lower limits are in accordance with BP/USP (Table-4 & 5).

TABLE 4: Thickness of 10 tablets (mm)

	Gramex	Flagyl	Metrozine
1	6.5	5.1	6.6
2	6.6	5.1	6.6
3	6.5	5.1	6.8
4	6.5	5.1	6.7
5	6.5	5.1	6.6
6	6.6	5.1	6.6
7	6.5	5.2	6.6
8	6.6	5.5	6.7
9	6.6	5.1	6.8
10	6.5	5.1	6.6

TABLE 5: STATISTICAL THICKNESS

No. of tablets	Average Thickness (mm)	Standard deviation	Upper limit (X+3S)	Lower limit (X-3S)
Gramex	6.54	0.05164	6.69492	6.385
Flagyl	5.15	0.12693	5.5307	4.7692
metrozine	6.66	0.08433	6.91298	6.407

HARDNESS TEST: Hardness test of metronidazole was found to not be in conjunction with the stated guidelines as given in BP/USP **(**Table-6&7).

TABLE 6: Hardness of 10 tablets from the optimised formulation.

	Gramex	Flagyl	Metrozine
1	20.39796	11.15306	9.897959
2	16.02041	8.193878	13.16327
3	12.95918	12.39796	11.22449
4	17.1	11.05102	13.21429
5	17.2449	11.11224	14.03061
6	17.7551	11.56122	14.10204
7	13.26531	10.30612	13.46939
8	18.26531	9.94898	13.06122
9	15.5102	8.183673	13.46939
10	20.30612	8.928571	10.40816

TABLE 7: STATISTICAL HARDNESS

no. of tablets	Average (Kg)	Standard deviation	Upper limit (X+3S)	Lower limit (X-3S)
Gramex	16.88245	2.539352	24.5005	9.264393
Flagyl	10.28367	1.447588	14.62644	5.940909
metrozine	12.60408	1.517265	17.15588	8.052288

FRIABILTY TEST: Friability of metronidazole tablets was less than 1%. Therefore it is compliance with the BP/USP standards. It's data is given in (Table-8).

TABLE 8: FRIABILITY TEST

No of tablets	Result (%)	BP/USP Specification	Deviation from BP/USP Specification
Gramex Flagyl metrozine	0.0525 0.077 0.0797	Not more than1%	In specified limit

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