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Research Article


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# Comparative analysis of different brands of metronidazole infusion available in Karachi, Pakistan.

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## Abstract

**Background:** The aim of the research is to evaluate comparative assay details of metronidazole infusions of different brands.
**Objective:** The purpose of this work is to establish similarity and improved understanding regarding the efficacy of metronidazole infusion of different brands.
**Methodology:** Samples of infusions of different brand were taken from local pharmacies of Karachi, Pakistan. The assay was determined by measuring the absorbance of standard solution and comparing with the absorbance of available brands of metronidazole at the wavelength of 277 nm by spectrophotometer. Statistical tests One way Anova and Post Hoc Tukey test were applied.
**Result:** Percent assay is calculated and according to statistical tests, the hypothesis is accepted that assay of all three brands are within limit because P values are less than 0.05 and there is no significant difference between their means. All of the samples show percent assay within the normal range.
**Conclusion:** Metronidazole is an antibiotic and our study revealed that all the brands were equal in efficacy, so they are equal in their therapeutic action.

**Keywords:** analysis, brands, metronidazole infusion

## Introduction

Metronidazole (MTZ, 1-[2-hydroxyethyl]-2-methyl-5-nitroimidazole) [1], is a cream-colored [2] or colorless to light yellow crystals or crystalline powder, odorless [3], melting point is 158-160 °C [2]. Intravenous metronidazole has recently been permitted by the U.S. Food and Drug Administration for the management of serious anaerobic bacterial infections diseases. It is usually bactericidal at small concentrations, and its range of activity embraces almost all anaerobic bacteria and some capnophilic organisms [4].

Generally use as an Antiprotozoal (Trichomonas); antiamebic; antibacterial agent [5].

The success of metronidazole in treating human protozoal infection or giardiasis, vaginal and oral trichomoniasis, and hepatic and intestinal amoebiasis has direct to investigation of its potential use against certain protozoan diseases of domestic animals. [6]. It is also used in the management of periodontitis caused by Bacteroides. Various studies show that metronidazole may be efficient, in combination

with bismuth subsalicylate or colloidal bismuth subcitrate, and other oral antibiotic treatment, such as ampicillin or amoxicillin, intented for Helicobacter pylori-related gastritis and duodenal ulcer. Conversely, metronidazole resistance may develop, particularly in patients who have been earlier exposed with metronidazole.

Intravenous metronidazole is indicated for the prophylaxis of preoperative infections during colorectal surgery. Metronidazole is indicated in the treatment of female pelvic infections, and postsurgical vaginal cuff infections and intra-abdominal infections, including peritonitis, intra-abdominal abscess, and liver abscess.

Orally, it is well absorbed and bioavailability is at least 80%, disseminated to saliva, bile, seminal fluid, breast milk, bone, liver and liver abscesses, lungs, and vaginal secretions; passes the placenta and blood-brain barrier [7].

Following IV administration of 1,2-(14)C-metronidazole to mice, activity was observe in liver and kidney, and in heart, brain, salivary gland, GI tract, spleen, and skeletal muscle and observed to cross placenta to fetus. In rats it was complexes in liver and eliminate in bile and urine [8].

Approximately 30-60% of an oral or IV dose of metronidazole is metabolized by hydroxylation, side-chain oxidation, and glucuronide conjugation in the liver. The main metabolite has some antibacterial and antiprotozoal activity that is 2-hydroxy metronidazole. [9].

Indian Pharmacopoeia describes the assay of metronidazole by non-aqueous titration method using Perchloric acid as titrant and malachite green as indicator. British Pharmacopoeia reported potentiometric and non-aqueous procedures using perchloric acid as titrant. United States Pharmacopoeia explained HPLC and non-aqueous titration methods for the assay of metronidazole. Some methods have been described for the determination of metronidazole including Spectrophotometry, Polarography [10]. Dissolution tests are used for many purposes in the pharmaceutical industry: in the development of new pharmaceuticals, for quality control and also assistance the determination of bioequivalence. Current regulatory evolutions such as the Biopharmaceutics Classification Scheme have highlighted the significance of dissolution in the regulation of post-approval variations and introduced the possibility of substituting dissolution tests for clinical studies in various cases. As a result, there is a requirement to develop dissolution tests that better predict the *in vivo* behavior of drug products. This could be accomplished if the conditions in the gastrointestinal tract were successfully reconstructed *in vitro* [11].

## Materials and Methods

### Instruments:

**Analytical Balance:** Analytical balance of used Schimadzu AUX 220 for weighing of working standard of Metronidazole.

**UV Spectrophotometer and wavelength selection:** UV Visible 1602 Schimadzu double beam spectrophotometer was used for measurement of spectra at UV region of 200 to 400nm. The maximum wave length was observed at 277nm and was adopted for the measurement of absorbance of standard and samples [12, 13].

**Chemicals:** The standard along with three different brands of Metronidazole Infusion 500mg/100ml were provided by CDL (Central Drugs Laboratory, Government of Pakistan), Karachi.

The reagent used was 0.1M HCl standardized solution for sample and standard preparation and Distilled water was used throughout the experiment.

### Standard solution:

Reference standard of Metronidazole taken equivalent to 20mg Metronidazole base in a 100ml volumetric flask and makeup volume with reagent solution. The solution is sonicated, shaked to dissolve and volume with reagent solution. Then 10ml of above solution is taken in a 100ml volumetric flask and volume with reagent solution. The standard stock solution is of 10mcg.

### Working Standard:

Working Standard of Metronidazole Base (99%) equivalent to 20 mg Metronidazole.

### Sample solution preparation:

Three different brands of Infusions are taken namely: MTZIF.1, MTZIF.2& MTZIF.3 of strength 500mg/100ml were taken. A quantity of 2ml

containing 10mg of sample were withdrawn from each sample Infusion and transferred into 100ml of volumetric flask. The volume was makeup with reagent solution, followed by a 10ml dilution in another 100ml volumetric flask with same reagent of 0.1M HCl.

The sample and standard prepared were measured at absorbance maximum of 277 nm using the reagent solution as blank.

## Results and Discussion

The purpose of this study was to compare the efficacy of different brands of metronidazole infusion available in Karachi. This proposed method for assay of commercially available metronidazole is very simple, economical, accurate, least time consuming and rapid.

**Table: 1 Percent Assay**

| Sample | Absorbance of sample | Absorbance of standard | % assay |
|---|---|---|---|
| | | | |
| MTZIF.1 | 0.382 | 0.401 | 95.26% |
| MTZIF.2 | 0.396 | 0.401 | 98.753% |
| MTZIF.3 | 0.412 | 0.401 | 102% |

Table 1 shows the absorbance of sample and standard taken through spectrophotometer and the calculated % assay. According to figure 1, the percentage assays of all three samples are within normal range but the sample MTZIF.3 has highest percent content than MTZIF.2 and least content in MTZIF.1.

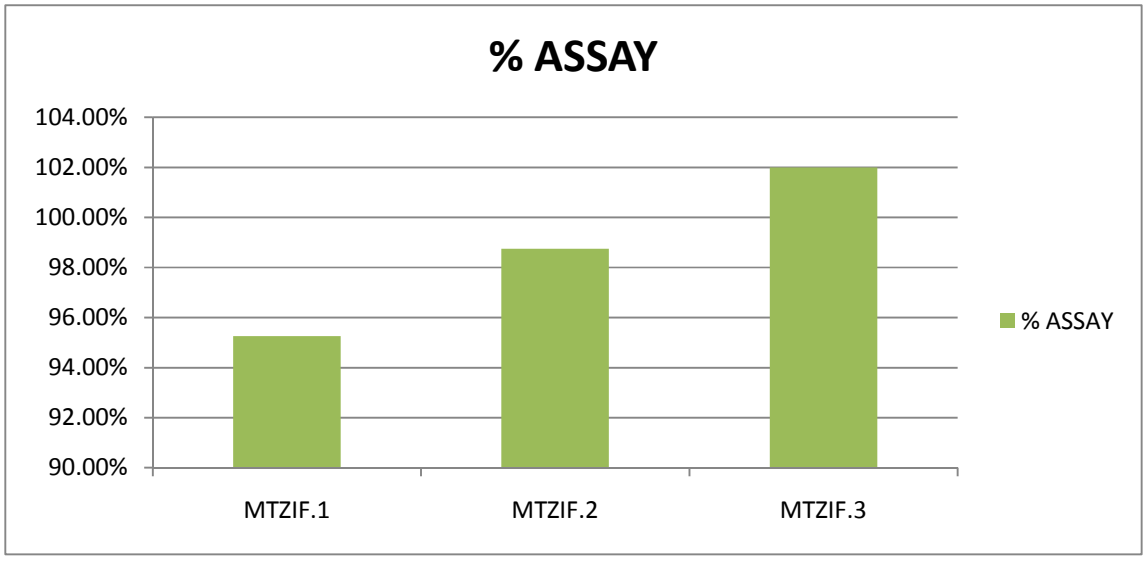


**Figure 1 % ASSAY**

Statistical analysis is conducted by using the test of one way analysis of variance to investigate that is there any difference between the means of the three samples in order to evaluate the difference between the absorbance of three samples at mean levels.

Null hypothesis was that standard and all the three samples are same and equal. The results evaluate that p value is less than 0.05 which indicates that there is no significant mean difference between all of the three groups, further post hoc tukeys test is applied to observe the differences between the means of the three samples in comparison, taking into account three groups separately one by one, the table shows the significant mean difference of absorption between MTZIF1, MTZIF2 and MTZIF3 , between Standard, MTZIF2 and MTZIF3, between standard, MTZIF1 and MTZIF3, also between standard, MTZIF1 and MTZIF2 . Thus the hypothesis is accepted that assay of all three brands are same because p values are less than 0.05 and there is no significant difference between their means, if the p value was greater than 0.05 the null hypothesis will be rejected.

The ANOVA method assesses the relative size of variance among group means (between group variance) compared to the average variance within groups (within group variance).

Tukey's HSD, Schaffe method, and Duncan multiple range test are more frequently preferred methods for the multiple comparison procedures. [14, 15].

Table 2 shows the descriptive statistic of drugs with standard deviation and standard error. Test of hypothesis i.e. ANOVA (table: 3) and multiple comparison of different brands of metronidazole are given in Table 4. It shows F value is 9.904 of all brands with df 3, 8 between and within groups.

Table: 5 shows the means for groups in homogenous subsets, MTZIF.1 and MTZIF.2 has same subset 1 of alpha=0.05, whereas MTZIF.2 and STD has same subset 2 of alpha =0.05

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**Table: 2 Descriptive statistics**

Absorbance

| | N | Mean | Std. Deviation | Std. Error | 95% Confidence Interval for Mean | | Minimum | Maximum |
|---|---|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound | | |
| STD | 3 | .4010 | .00000 | .00000 | .4010 | .4010 | .40 | .40 |
| MTZIF.1 | 3 | .3837 | .00569 | .00328 | .3695 | .3978 | .38 | .39 |
| MTZIF.2 | 3 | .3960 | .00400 | .00231 | .3861 | .4059 | .39 | .40 |
| MTZIF.3 | 3 | .4040 | .00700 | .00404 | .3866 | .4214 | .40 | .41 |
| Total | 12 | .3962 | .00913 | .00264 | .3904 | .4020 | .38 | .41 |

**Table: 3 ANOVA**

**ANOVA**

ABSORBANCE

| | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Between Groups | .001 | 3 | .000 | 9.904 | .005 |
| Within Groups | .000 | 8 | .000 | | |
| Total | .001 | 11 | | | |

**Table: 4 Multiple comparison between brands Multiple Comparisons**

ABSORBANCE

Tukey HSD

| (I) S.No | (J) S.No | Mean Difference (I-J) | Std. Error | 95% Confidence Interval | |
|---|---|---|---|---|---|
| | | | | Lower Bound | Upper Bound |
| STD | MTZIF.1 | .01733* | .00403 | .0044 | .0302 |
| | MTZIF.2 | .00500 | .00403 | -.0079 | .0179 |
| | MTZIF.3 | -.00300 | .00403 | -.0159 | .0099 |
| MTZIF.1 | STD | -.01733* | .00403 | -.0302 | -.0044 |
| | MTZIF.2 | -.01233 | .00403 | -.0252 | .0006 |
| | MTZIF.3 | -.02033* | .00403 | -.0332 | -.0074 |
| MTZIF.2 | STD | -.00500 | .00403 | -.0179 | .0079 |
| | MTZIF.1 | .01233 | .00403 | -.0006 | .0252 |
| | MTZIF.3 | -.00800 | .00403 | -.0209 | .0049 |
| MTZIF.3 | STD | .00300 | .00403 | -.0099 | .0159 |
| | MTZIF.1 | .02033* | .00403 | .0074 | .0332 |
| | MTZIF.2 | .00800 | .00403 | -.0049 | .0209 |

**Table: 5 Homogenous Subsets**

**ABSORBANCE**

Tukey HSD[a]

| S.No | N | Subset for alpha = 0.05 | |
|---|---|---|---|
| | | 1 | 2 |
| MTZIF.1 | 3 | .3837 | |
| MTZIF.2 | 3 | .3960 | .3960 |
| STD | 3 | | .4010 |
| MTZIF.3 | 3 | | .4040 |
| Sig. | | .061 | .269 |
| Means for groups in homogeneous subsets are displayed. | | | |
| a. Uses Harmonic Mean Sample Size = 3.000. | | | |

## Conclusion

The UV spectrophotometric method is planned for the determination of metronidazole in infusions, this technique is employed effectively for analysis; as it is particular, rapid, basic, precise, economic and do not require any sophisticated instruments. This technique is quick and efficient as contrasted with different techniques, that's why it is efficient, effective and helpfully established practice for routine QC testing or investigation in research centers. Our study revealed that all the brands have nearly same absorbance and %assay which means there is no significant difference in their efficacy and therapeutic action. So they are interchangeable where compliance issue occurs in terms of cost and other factors.

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