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A Review of In Vitro Dissolution Study of Metronidazole Tablet

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Abstract: *The plot of this study is to obtain a deep knowledge regarding the effect of different fluids (Gastric medium, simulated gastric fluid without enzyme, ORS solution, rice water, lentil soup, watermelon juice, apple juice, mango juice, pomegranate juice, black and green tea) on dissolution of metronidazole tablet by alteration of different medium.*

Study had been focused on the in vitro dissolution study of metronidazole in the presence of different fluids (Gastric medium, simulated gastric fluid without enzyme, ORS solution, rice water, lentil soup, watermelon juice, apple juice, mango juice, black and green tea) which has been commonly used in diarrheal condition. Dissolution study was performed as per mentioned in Indian pharmacopoeia.

Other general quality assessment tests of these tablets like weight variation, hardness, friability, disintegration time and assay were also determined according to established methods.

Also in the study,bio-equivalence of three metronidazole brand was assessed and studied in three different dissolution media by in vitro dissolution study. Several methods for dissolution of metronidazole comes with the limitation,so most economic,rapid UV-Visible method of analysis was used for assessment

Keywords: Metronidazole, Dissolution, In-vitro, Enzymes, Different fluids

I. INTRODUCTION

Metronidazole capsules and tablets are used to treat infections of the reproductive system, gastrointestinal (GI) tract, skin, heart, bone, joint, lung, blood, nervous system, and other areas of the body. Metronidazole capsules and tablets are also used to treat sexually transmitted diseases (STDs). Metronidazole extended-release (long-acting) tablets are used to treat bacterial vaginosis (an infection caused by too much of certain types of harmful bacteria in the vagina) in women. Metronidazole is in a class of medications called nitroimidazole antimicrobials. It works by stopping the growth of bacteria.

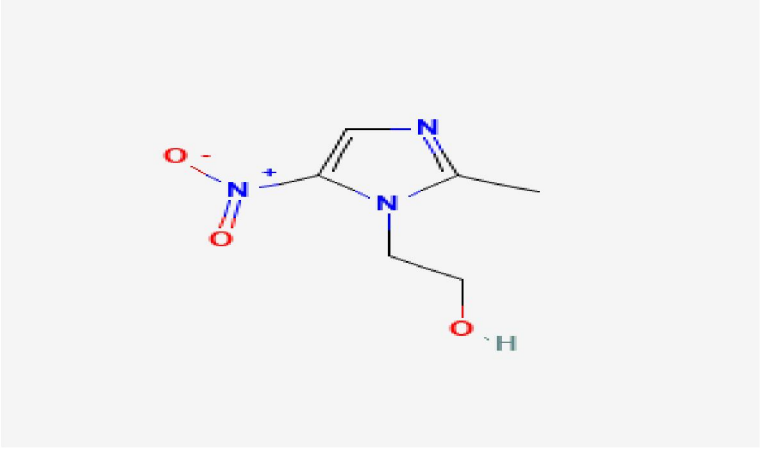

Figure 1: Structure of Metronidazole

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Metronidazole comes as a tablet, an extended-release tablet, and as a capsule to take by mouth. Metronidazole capsules and tablets are usually taken as a one-time dose (or divided into two doses on 1 day) or two to four times daily for up to 10 days or longer. Metronidazole extended-release tablets are usually taken once daily at least 1 hour before or 2 hours after a meal for 7 days.

Metronidazole tablet (400 mg) is included in essential medicine list of Nepal. It is an antiprotozoal anti-parasitic agent used in the treatment of amoebiasis, trichomoniasis, giardiasis, and other parasitic diseases. Since 1960 it has been extensively used as systemic trichomonacide and also shown activity against anaerobic microorganisms including bacteria and protozoa [1]. It is the drug of choice for the treatment of various parasitic infections, Anaerobic infections, Pseudomembranous colitis, Helicobacter pylori and Crohn's disease.

The process of dissolution plays a vital role in liberation a drug from its dosage form and making it available for subsequent gastrointestinal absorption. Therefore, dissolution analysis of pharmaceutical solid dosage forms is a very important test of product quality and it can be used as a sensitive method for differentiating between formulations of the same therapeutic agent [2].

Tablet Dissolution is a standardized method for measuring the rate of drug release from a dosage form. Actually in vitro dissolution of the drug from the tablet matrix relies on many factors, which includes physiochemical properties, nature of formulation and process manufacturing of drugs. Several studies shows that the percentage drug release varies when *in vitro* studies has been conducted in presence of different juices.

In the quality control parameter of tablet various parameters was taken under consideration and was studied thoroughly.

Table 1: Physical parameters of tablets

Weight			**Length (mm)**	**Thickness** (mm)	**Hardness (Kg/mm)**	**Friability %**	DT (min)	Assay%
Mean(mg)	%Maximum deviation	%Minimum deviation						
920.17	3.03	2.61	19.28 ± 0.1	6.37 ± 0.3	5.75 ± 1.3	0.021	7.45	101.37

On the research conducted on the dissolution of various commercially available metronidazole tablet in India. The quantitation of metronidazole dissolution samples was carried by HPLC chromatographic condition: Mobile phase consists of water:methanol mixture (85:15), which was pumped at flow rate of 1 ml/min through Luna C8 column. The UV detector was maintained at an absorption wavelength of 319 nm. HPLC method was validated for the suitability in all three-dissolution media for accuracy, precision, and recovery studies according to USP.

The linear range was selected based on an expected lowest release concentration of about 3.7% and highest of 120% of drug content dissolved in 900 ml of each medium at pH 1.2, 4.5, 6.8[3].

Table 2. Metronidazole Products Tested

Country	**Company**	**Product**	**Dosage form**	**Batch**	**Expiry date**	**Excipients**
INDIA	Sun Life Sciences	Metro sun 400	Tabs	T110244	01/2013	Sunset yellow FCF and Titanium dioxide
	Abbot	Flagyl® 400	Tabs	VC0017	05/2015	Tartrazine and titanium dioxide
	Medi best Pharma	Metronidazole 400	Tabs	MFF1001	06/2012	NA
	JB Chemicals	Metrogyl® 400	Tabs	TM81167	03/2015	Sunset yellow FCF
	Quest lab	Metgyl 400	Tabs	09	02/2013	Titanium dioxide
	Martin &Brown	Metronidazole 400	Tabs	MTZ24	10/2012	Sunset yellow

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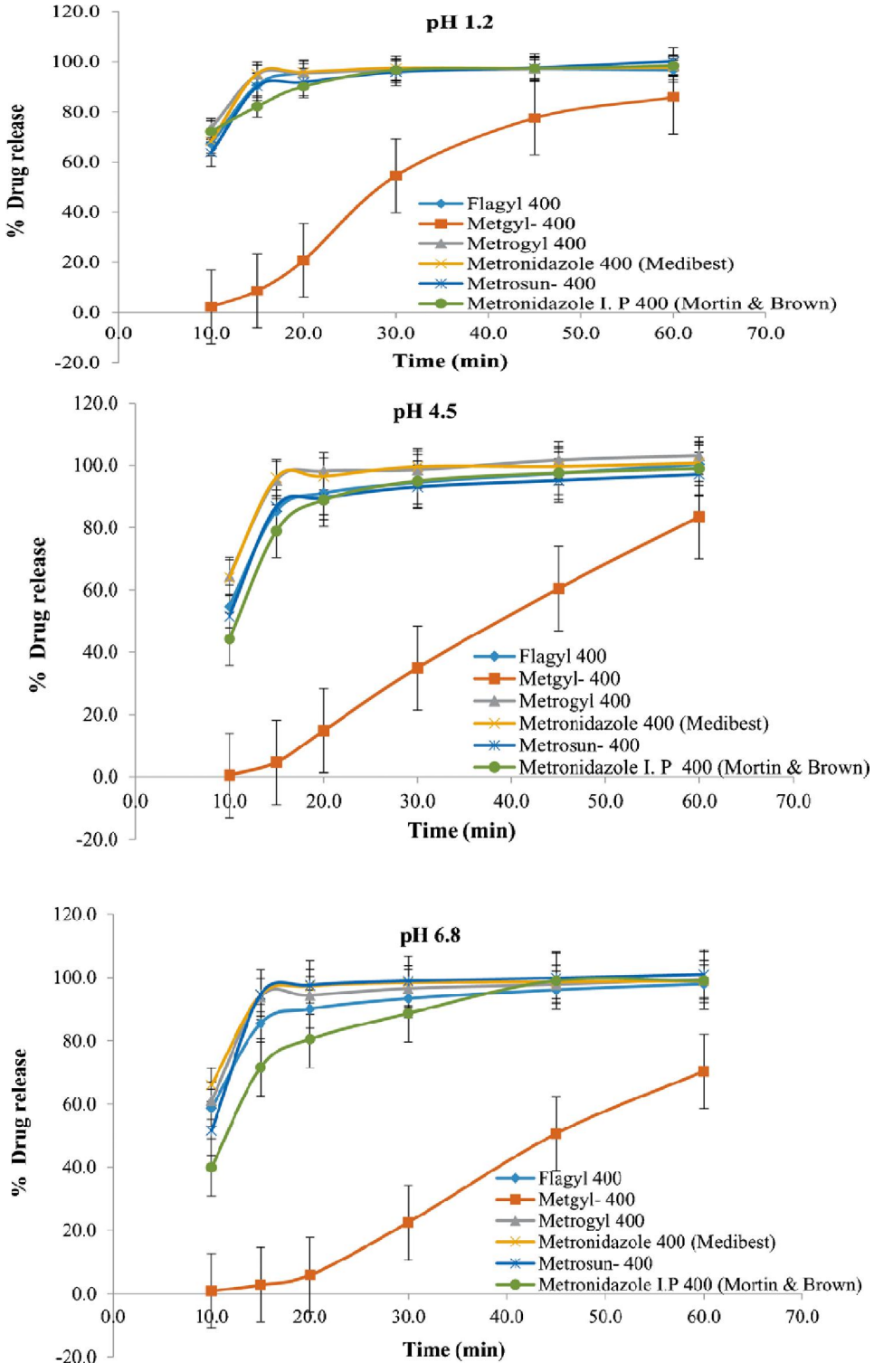
Dissolution profiles of the CPP and metronidazole products marketed in India



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Comparison of the various Indian generic metronidazole products

Product	pH 1.2	pH 4.5	pH 6.8
Flagyl® 400- Reference	++	++	++
Metgyl- 400	-	-	-
Metrogyl® 400	++	++	++
Metronidazole 400 (Medibest)	++	++	++
Metrosun- 400	++	++	++
Metronidazole I.P 400 (Mortin & Brown)	+	+	+*

(++) At least 85% released within 15 minutes or less (Very rapidly dissolving)
(+) At least 85% is released within 30 minutes or less (Rapidly dissolving)
(-) Less than 85% released in more than 30 min
(*) Fails f_2

The dissolution profiles of the metronidazole products in India are shown in Fig. 1.

Metgyl 400 required 60 min to release 85% in all three-pH media and thus did not meet the biowaiver requirements. Metro sun 400, metronidazole 400 (Medibest), Metrogyl® 400, and metronidazole I.P. 400 (Mortin & Brown) dissolved very rapidly in pH 1.2 and in pH 4.5 buffers and thus met the requirement exceeding a release of 85% in 15 min.

In pH 6.8, Metrosun 400, metronidazole 400 (Medibest), and Metrogyl® 400 dissolved very rapidly and passed the f2 requireelement of ≥50. However, metronidazole I.P. 400 (Mortin & Brown) dissolved rapidly but did not meet the f2 requirements [3].

Metronidazole I.P. 400 (India) were very rapidly dissolving in pH 1.2 but were only rapidly dissolving in pHs 4.5 and 6.8

IN VITRO DISSOLUTION STUDY OF METRONIDAZOLE TABLET IN DIIFERENT FLUIDS: -

The dissolution of metronidazole tablet was performed in various types of fluids mention in **Table3.** The mean % drug release was determined from 6 tablets.

According to IP, the limit of % drug release should not be less than 85% of labelled amount in 60 mins at 100 rpm. Dissolution percentage of all 6 samples of metronidazole tablets in different fluids were shown in **Table3.**

The mean % drug release of metronidazole tablet in 0.1 N HCl was found to be 101 ± 2.22 which is within the IP specifications. In simulated gastric fluid without enzyme, the % drug release was found to be 101.28 ± 2.51 which is within the limit range. When dissolution study was performed in ORS solution the % drug release is 100.38 ± 2.52 which passed the test. Dissolution of metronidazole tablet was done in rice water which also pass the specification i.e., 95.16 ±

2.00. Lentil soup was also used as dissolution medium, in this medium the % drug release of metronidazole tablet is decrease to 78.69 ± 1.89. In lentil soup, the dissolution of metronidazole tablet doesn't compile with IP specification. The dissolution of Metronidazole was also performed in watermelon juice and % drug release was found to be 92.42 ± 4.72 which passed the limit. Percentage drug release when evaluated in apple juice, the dissolution of metronidazole tablet was within the limit i.e.,102.78 ± 2.10 which is higher % drug release among all other used mediums. For evaluation of metronidazole dissolution profile black and green tea medium were also used. Both medium shows dissolution profile within the limit. The average % drug release was found to be 86.89 ± 0.63 and 91.69 ± 1.06 in black tea and green tea respectively.

Statistical significance was determined between the dissolution on different mediums to investigate the difference between the mean dissolution in all mediums.

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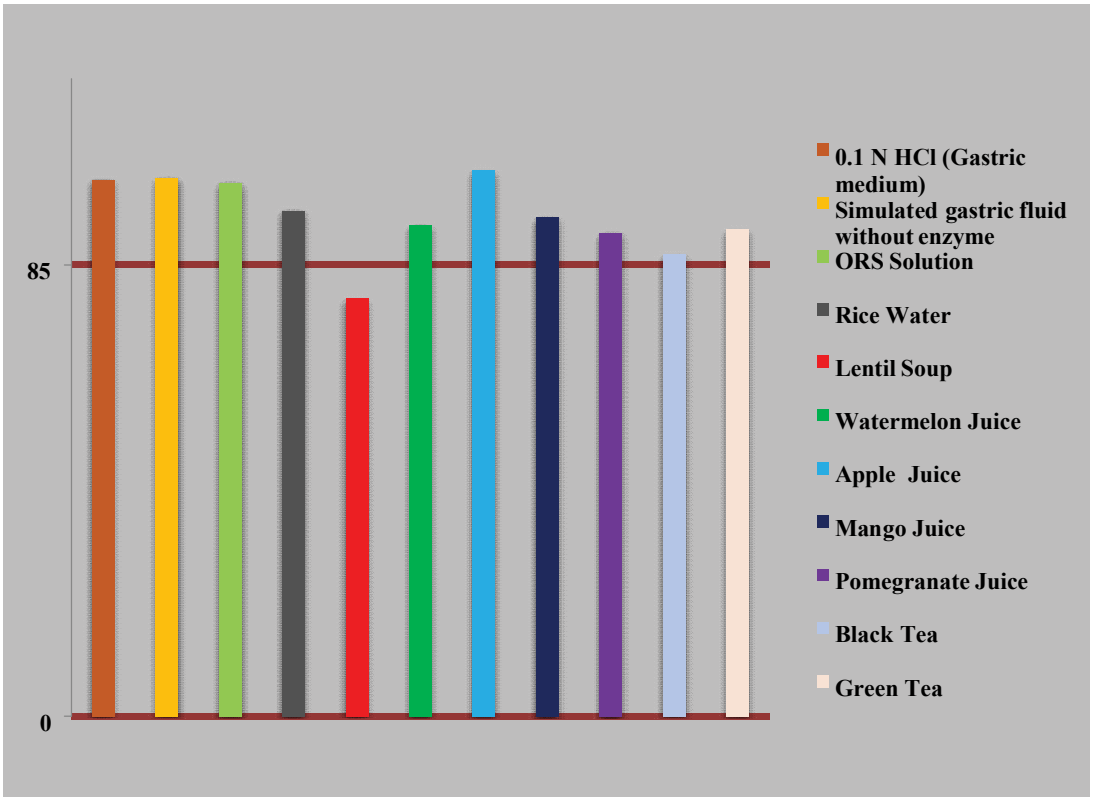
Sr. No	Dissolution Medium	% Drug release					
		S1	S2	S3	S4	S5	S6
1.	0.1 N HCl (Gastric medium)	98.97	103.9	97.90	101.1	101.8	102.1
2.	Simulated gastric fluid without enzyme	98.25	104.6	103.04	99.53	99.53	102.7
3.	ORS Solution	97.97	101.2	97.97	100.39	104.6	100.3
4.	Rice Water	95.79	95.50	96.37	95.50	96.66	91.18
5.	Lentil soup	77.56	76.68	76.90	79.75	81.29	79.97
6.	Watermelon juice	85.51	91.51	88.39	95.88	96.74	96.45
7.	Apple juice	102.90	104.7	104	103.5	98.74	102.83
8.	Mango juice	96.20	95.95	92.2	89.52	93.97	95.95
9.	Black tea	86.56	87.51	86.54	86.22	86.70	87.84
10.	Green tea	91.56	91.73	92.24	93.43	90.53	90.70

Table 3. %Drug release of Metronidazole samples



II. CONCLUSION

This review article provides an in-depth exploration of dissolution of metronidazole tablet invarious pH ranges and in different fluids. The drug food interaction can decrease the absorption of drug. Thus, undertaken dissolution testing in dissolution apparatus need to be able to deliver precise and consistent results. Metronidazole I.P. 400 (India) were very rapidly dissolving in pH 1.2 but were only rapidly dissolving in pHs 4.5 and 6.8

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The metronidazole tablet shows higher release in apple juice whereas in presence of lentil soup the % release of metronidazole decreases. Conclusively, the study suggests that metronidazole tablet should not be administered with lentil soup.

REFERENCES

[1] Deepti Piya Baniya, Kiran Bikram Bohara, Dr. Dharma Pd. Khanal, Saroj Bashyal, Priyanka Shahi . In Vitro Dissolution Study of Metronidazole Tablet in Different Fluids, Pharm Anal Acta, Vol.12 Iss. 4 No: 626

[2]Ahmed EM, Ibrahim ME and Magbool FF. Comparative *In-vitro* Dissolution Study of Some Metronidazole Generic Tablets Under Bio-waiver Conditions by UV-Visible Spectrophotometry. Austin J Anal Pharm Chem. 2019; 6(1): 1114.

[3] Nallagundla H. S. Reddy, Srinivas Patnala, Raimar Löbenberg, and Isadore Kanfer.In Vitro Dissolution of Generic Immediate-Release Solid Oral Dosage Forms Containing BCS Class I Drugs: Comparative Assessment of Metronidazole, Zidovudine, and Amoxicillin Versus Relevant Comparator Pharmaceutical Products in South Africa and India ,AAPS PharmSciTech, Vol. 15, No. 5, October 2014 (# 2014) DOI: 10.1208/s12249-014-0135-6

[4] Qonita Kurnia Anjani, Akmal Hidayat Bin Sabri, Juan Domínguez-Robles, Natalia Moreno-Castellanos, Emilia Utomo , Luki Ahmadi Hari Wardoyo, Eneko Larra˜neta, Ryan. Donnelly. Metronidazole nanosuspension loaded dissolving microarray patches: An engineered composite pharmaceutical system for the treatment of skin and soft tissue infection, Biomaterials Advances 140 (2022) 213073

[5] Daniel Preisig, Felipe Varum, Roberto Bravo, Claudia Hartig, Johannes Spleiss, Sonia Abbes, Federico Caobelli, Damian Wild, Maxim Puchkov, J¨org Huwyler, Manuel Haschke. Colonic delivery of metronidazole-loaded capsules for local treatment of bacterial infections: A clinical pharmacoscintigraphy study, European Journal of Pharmaceutics and Biopharmaceutics 165 (2021) 22–30

[6] Faisal A, Sultana T, Sohel MD, Sumon MH, Kawsar MH et al. In vitro dissolution pattern of metronidazole film coate d tablet in presence of fruit juice. Am J Pharmacol Sci. 2014; 2:32-36.

[7] Noor S, Salam FB, Hima HN, Bhuiyan MS, Chowdhury S. Comparative in-vitro quality evaluation of some brands of metronidazole tablet available in Bangladesh. Int J Appl Res. 2017; 3:753-758.

[8] A.H. Lau, N.P. Lam, S.C. Piscitelli, L. Wilkes, L.H. Danziger, Clinical pharmacokinetics of Metronidazole and other nitroimidazole anti-infectives, Clin. Pharmacokinetic. 23 (1992) 328–364,

[9] G.W. Houghton, H.K. Hundt, F.O. Muller, R. Templeton, A comparison of the pharmacokinetics of metronidazole in man after oral administration of single doses of benzoyl metronidazole and metronidazole, Br. J. Clin. Pharmacol. 14 (1982) 201–206

[10] Caro-Patón T, Carvajal A, Martín de Diego I, Martín-Arias LH, Alvarez Requejo A, et al. Is metronidazole teratogenic? A meta-analysis. Br J Clin Pharmacol. 1997;44:179-182.

[11] Thulasamma P, Venkateswarlu P. Spectrophotometric method for the determination of metronidazole in pharmaceutical pure and dosage forms. J Chem. 2009; 2:865-868.

[12] Musa H, Sule YZ, Gwarzo MS. Assessment of physicochemical properties of metronidazole tablets marketed in Zaria, Nigeria. Int J Pharm Pharm Sci. 2011; 3:27-29.

[13] Nawab A, Alam S, Shoukat N. In-vitro dissolution study of metronidazole film coated tablet 400 mg (flagyl) in the presence of different tea. World J Pharm Sci. 2015:102-115.