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Comparative Dissolution Study of Different Brands of Amoxicillin Trihydrate Capsules Available in Bangladesh

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ABSTRACT

Commercially available twenty national and four multinational brands of Amoxicillin Trihydrate capsules were studied in water for 60 minutes using USP reference dissolution apparatus. All, except two national brands (Code: NB-8 and NB-15); complied with the USP *in vitro* dissolution specification for drug release (not less than 80% of the labelled amount of amoxicillin trihydrate should be dissolved in 60 minutes). Drug releases from those two brands were 75% and 67% respectively within the specified time period.

Key words: *In vitro* Dissolution, Market preparations, Amoxicillin Trihydrate, Capsule, National Brand, Multinational Brand.

INTRODUCTION

Antibiotics, being the wonder drugs, are widely prescribed in the developing countries. In reality, 25 to 40% prescriptions contain one or more antibiotics (Public Sector Studies, 1990-1993). Amoxicillin is one of the extensively prescribed drugs within the list in the antibiotic therapeutic class (Hossain *et al.*, 1982; Resi *et al.*, 2003). Amoxicillin is a β-lactam antibiotic that interferes with the synthesis of the bacterial cell wall peptidoglycan. After attachment to binding sites on bacteria they inhibit the transpeptidation enzyme that cross-links the peptide chains attached to the backbone of the peptidoglycan. The final bactericidal event is the inactivation of an inhibitor of the autolytic enzymes in the cell wall; this leads to lysis of the bacterium (Rang *et al.*, 2003).

Nowadays, antibiotic resistance by plasmid transfer has become a significant clinical problem, because an organism may become resistant to several antibiotics at the same time due to acquisition of a plasmid that encodes resistance to multiple agents (Lippincott's Illustrated Reviews: Pharmacology, 2008). Antibiotic resistance can be developed through its wide and inappropriate use without following any standard guidelines. This alarming situation has been addressed in several scientific journals (Glass *et al.*, 1980; Farrar, 1985; Saha *et al.*, 2003; Lina *et al.*, 2007; Hasan *et al.*, 2009)

Along with the inappropriate use of antibiotics, use of substandard antibiotic preparations may also contribute to the development of antibiotic resistance (Edelman *et al.*, 1999). To assess the standard of a product, in vitro dissolution test is widely used because, for any solid dosage forms, gastrointestinal absorption first requires dissolution of the tablet or capsule that liberates the drug into solution (Goodman & Gilman's - The Pharmacological basis of Therapeutics, 2006). The dissolution characteristic of a drug from the dosage form depends on many factors including its formulation and manufacturing process (Augsburger *et al.*, 1983). This study deals with the comparative *in vitro* dissolution characteristics of some most commonly available national and multinational brands of amoxicillin trihydrate capsules in Bangladesh in order to find out any out of compliance market preparation.

MATERIALS AND METHODS

Drug: Amoxicillin Trihydrate RS (Square Pharmaceuticals Limited, Bangladesh); **Equipments:** Tablet dissolution tester (Electrolab, India), UV spectrophotometer (Gamma, England), Electric balance (Mettler Toledo, Switzerland).

Dosage forms

Twenty national and four multinational brands of marketed (production date not more than three months ago from the time of purchase) amoxicillin trihydrate capsules were collected from various stores. The samples were properly checked for their manufacturing licence number, batch number, manufacturing and expiry dates before purchasing. The samples were randomly coded as NB-n for national brands, where n=1, 2, 3, 4, …… 19, 20 and MB-n for multinational brands, where n=1, 2, 3 and 4. The labelled active ingredient was Amoxicillin Trihydrate 500mg and packaged in strip or in blister packing. The strip or blister packs were stored at 25±2℃ for four weeks before the dissolution study in order to evaluate any change in organoleptic properties.

In vitro dissolution Study

These studies were conducted at 37±0.5℃ on an USP specification dissolution rate test type II apparatus (Paddle apparatus) with six sections assembly according to the USP 30 procedure (USP 30 and NF 25, 2007). For *in vitro* dissolution studies, water was used as dissolution media.

The water-bath temperature was fixed & confirmed to be 37±0.5℃ before starting the experiment. The medium was preheated to 37℃ and then a quantity of 900 ml was added to each vessel. The apparatus was then assembled and paddle rotation was started and adjusted at 75 rpm and the system was allowed to equilibrate for 15 minutes. After that the paddle rotation was stopped and six capsules from same code were placed in the vessels (one capsule per vessel) and allowed to sink to the bottom. The apparatus was immediately operated at 75 rpm. Each vessel, vessel position and corresponding sample result were assigned the same code. The duration of the experiment was 60 minutes for each set of sample. At the end of the experiment, 10 ml of sample solution was withdrawn, filtered, diluted and analyzed at 272 nm for amoxicillin trihydrate by UV spectrophotometer. The amount of drug present in the samples was calculated from calibration curve constructed from the standard solution of USP reference standard test drug (Fig. 1).

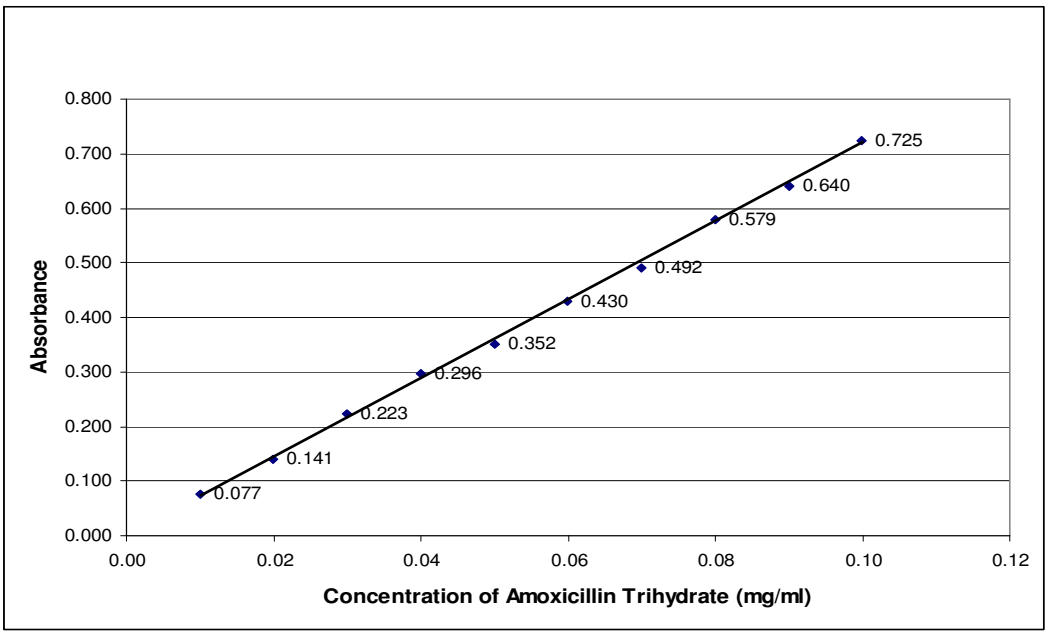

Figure 1: Calibration curve of Amoxicillin Trihydrate.

RESULTS AND DISCUSSION

According to USP, not less than 80% of the labeled amount of amoxicillin trihydrate should be dissolved in 60 minutes. The following table shows the dissolution data for each sub sample of each brand. Except two national brands (Code: NB-8 and NB-15), all the brands met the official

standard. These two brands were tested again according to BP (British Pharmacopoeia, 2003); however the results remained identical to the first one.

Table 1: Dissolution percentages for Amoxicillin Trihydrate samples

Code	Dissolution of Sub-samples (%)						%RSD	USP Standard
	1	2	3	4	5	6		
NB-1	89	89	90	89	90	90	0.61	Complies
NB-2	87	88	89	89	89	87	1.12	Complies
NB-3	90	90	91	91	91	90	0.61	Complies
NB-4	83	87	88	88	83	85	2.73	Complies
NB-5	88	87	88	88	88	88	0.46	Complies
NB-6	84	86	86	86	85	85	0.96	Complies
NB-7	89	90	90	90	90	90	0.45	Complies
NB-8	70	71	75	70	70	71	2.73	Does not comply
NB-9	85	84	85	85	85	84	0.61	Complies
NB-10	83	83	84	84	84	83	0.66	Complies
NB-11	90	90	93	91	93	92	1.51	Complies
NB-12	90	91	90	92	92	90	1.08	Complies
NB-13	86	86	86	85	86	86	0.48	Complies
NB-14	85	85	87	87	87	85	1.27	Complies
NB-15	63	64	66	67	66	67	2.51	Does not comply
NB-16	89	89	90	90	89	90	0.61	Complies
NB-17	90	92	95	93	95	93	2.04	Complies
NB-18	91	92	93	93	91	92	0.97	Complies
NB-19	86	87	89	88	88	87	1.20	Complies
NB-20	87	87	87	87	88	88	0.59	Complies
MB-1	93	94	93	95	94	94	0.80	Complies
MB-2	90	90	91	90	91	91	0.61	Complies
MB-3	95	95	95	92	95	92	1.65	Complies
MB-4	86	88	86	88	87	86	1.13	Complies

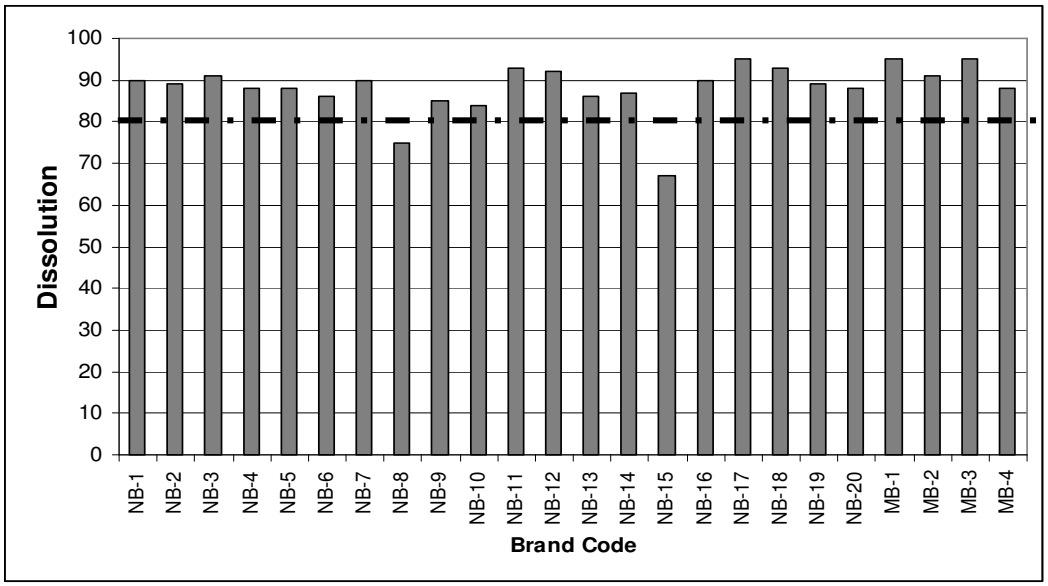

Figure 2: Comparison of dissolution percentages among different brands of Amoxicillin Trihydrate.

For ease of perception, the highest values from the six sub-samples of all the brands are taken to compare the values across different brands. The following figure (Fig. 2) clearly shows the failure of two brands to comply with the USP standard of 80% drug release within 60 minutes (this has been marked with the dot-dash line). The potency of each brand under investigation was also determined by spectrophotometric method and it was found that all the brands met the official standard, although few of them were at lower region within the specified standard. Along with the

formulation defects, this may contribute significantly towards the substandard dissolution characteristic of the above discussed samples.

CONCLUSION

From this study it has been revealed that most of the commercially available brands of amoxicillin trihydrate capsule in Bangladesh fulfilled the official specification of dissolution test, although few of them failed which might be explained by poor formulation and/or lower content of the active ingredient. To fight the challenge of antibiotic resistance effectively, first the pharmaceutical companies have to supply efficacious drug to the market.

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