Original article

In vitro evaluation of the quality of different trade brands of Co-Trimoxazole tablet formulation by qualitative assay methods

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Abstract

Objectives : In vitro evaluation of different trade brands of co-trimoxazole tablet formulation was done in this study by conducting assay of different quality control parameters like average weight, friability, disintegration & hardness test.

Methods : This was a cross sectional analytic study done from July, 2007 to June, 2008. A total sixty tablets from each batch of different trade brands were collected from the local market & evaluated by the qualitative assay methods.

Result : Quality control parameters of most of the brands were within normal limits of BP standard (Disintegration time-15 mins, Hardness-4-10 kg, Friability <1 % weight loss, Average weight 444 –516 mg for single strength & 888-1032 mg for double strength formulations except excipients). Four batches of different trade brands (Code U,O,S,N) did not comply with BP standard. Disintegration time of Code U (37.50 mins.) exceeded the normal limit & the Code O just reached the upper limit (14.58 mins) of normal. Hardness of Code O (4.02 kg) was at the lower limit of normal. Code O completely failed in friability test and Code S (10.65% weight loss) exceeded the normal limit. Average weight of Code N (821.26 mg) was below the normal limit of BP specification.

Conclusion : This study included only 17 trade brands which are not sufficient to generalize widespread existence of substandard preparations of co-trimoxazole. It needs further similar studies by taking more number of samples.

Key words: In vitro, evaluation, quality, co-trimoxazole, qualitative assay

Introduction

The use of ineffective and poor quality drugs may lead to serious health hazards including treatment failure, adverse drug reactions, development of drug resistance, increased morbidity and mortality. Drug quality is a great concern worldwide, particularly in many developing countries. Recent reports indicate that the availability of substandard drugs has reached in a disturbing proportion in resource -poor settings, such as in most Asian countries. The reported percentage of substandard drugs range from 2% to >60%[1]. Quality assessment study of some of the marketed drug product could give an insight into the quality of the products[2]. Co-trimoxazole is a combination of sulfa methoxazole (SMZ) & trimethoprim (TMP).

During the last three decades co-trimoxazole had occupied a central role in the treatment of various infections & has also been particularly useful for several other specific clinical conditions. However, changing resistance patterns and the introduction of newer broad-spectrum antibiotic have led to the need to carefully redefine the appropriate use of this agent in clinical practice[3].

Suspicion and concern about the quality of co-trimoxazole in the market are due to its;

- easy availability and
- popularity in our country as a broad spectrum agent against a variety of infections
- high consumption rate
- inclusion in essential drug list
- previous reports of being substandard.

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Our government has limited manpower and facilities to cope with the country's fast expanding pharmaceutical sector. There are only two drug testing laboratories and 37 drug supervisors for entire country, which account for the poor supervision in this sector.

Quality test of drug can be performed in any medical college laboratory. This may reduce the burden on central drug testing laboratory which is always overburdened with sample testing from all over the country. So drug administration of Bangladesh will be able to utilize the medical college laboratories (pharmacology and biochemistry) for random testing of alleged and suspicious samples from the market in a cost effective way.

So, this study was done to ascertain the general standard of quality of different trade brands of Co-trimoxazole tablet formulation in our country and to suggest means for detection of substandard drugs in a cost effective way.

Materials and methods

This cross sectional analytic study was done in the Department of Pharmacology & Therapeutics, Sher-E-Bangla Medical College and the Chemist Laboratories Limited, Barisal during the period of one calander year from July, 2007 to June, 2008.

Samples : A total of 21 batches of co-trimoxazole tablet formulations from 17 trade brands, of which 8 batches were of single strength & rest 13 batches were of double strength formulations were collected from the local market by convenient sampling. Coding was done to avoid bias. Decoding was not done as it was not the objective of investigator to identify any alleged manufacturers. Sixty tablets from each batch were taken for evaluation of drug quality. All the samples were within their expiry dates.

Tests of some physical parameters such as average weight, friability, hardness and disintegration were done in the qualitative assay. The results were analyzed manually and were presented in tables.

Apparatus : (1) Metler Balance 2) Tablet Disintrigration Test Apparatus (3) Tablet Friability Test Apparatus (4) Manual Hardness Tester.

Methodology

Average weight : Ten tablets from each batch of different co-trimoxazole tablet formulation were taken. Each tablet was weighted individually on metler balance & average weight of ten tablets was determined.

Hardness test : Five sample tablets from each batch of different co-trimoxazole tablet formulation were taken. One sample tablet was mounted on the edge of the hardness tester and piston was screwed until the tablet was held lightly in the extreme end of the tester. The weight mark of this point was recorded as the 1st weight. Then the piston was screwed up to the point at which the tablet breaks up and the weight at this broken point was recorded as 2nd wt. The hardness of the tablet was calculated by subtracting the 1st wt from the 2nd wt. In this way hardness of other 4 sample tablets was calculated and the mean hardness was recorded. That was the hardness of that specific batch of specific trade brand.

Friability test : Ten sample tablets from each batch of different co-trimoxazole tablet formulation were taken. The total weight of 10 tablets was taken by metler balance (1st wt), then these 10 tablets were placed in the drum of the friability tester. The drum must be cleaned before. The drum was rotated 100 times and tablets were removed from the drum. Any loose dust was removed from the tablets and again weighed the tablets (2nd wt).

Then the friability of those tablets was calculated by using following formula;

$$\text{Friability weight loss} = \frac{\text{1st wt} - \text{2nd wt}}{\text{1st wt}} \times 100\ \%$$

Disintegration time test : Five sample tablets from each batch of different co-trimoxazole tablet formulation were taken & placed in five tubes of disintegration time tester, a disc was added to each tube. The assembly was suspended in the beaker containing distilled water inside the tester, then the tester was started and the state of the tablet was observed. The time was noted at which the first and the fifth tablet were completely disintegrated. This time range was taken as disintegration time for specific batch of specific trade brand. All samples were assayed according to methods outlined in the individual drug monographs of the BP 2007, except for dissolution test which used USP-32[4].

Procedures for qualitative assay are given in the appendix.

Result

In the present study qualitative analysis of different trade brands of co-trimoxazole tablet formulations was done.

Table-1 : Distribution of table according to average weight, Disintegration Time, Friability and Hardness of co-trimoxazole tablet formulation of different trade brands (single strength formulation):

Sample Code	Avg. wt. (mg)	Disintegration Time (secs)		Friability (%wt loss)	Hardness (kg)
		Range	Avg		
A	619.69	7-12	10	0.69%	7.90
B	607.81	95-120	112	0.33%	7.66
C	562.82	51-90	40	0.79%	4.40
D	619.36	12-18	15	0.44%	7.05
E	613.94	32-52	42	0.55%	8.10
F	520.72	246-315	280	0.42%	5.85
G	595.64	18-30	24	0.95%	6.85
H	550.55	76-132	104	0.96%	5.80

Table-2 : Distribution of table according to average weight, Disintegration Time, Friability and Hardness of Co-trimoxazole tablet formulation of different trade brands (double strength formulation):

Sample Code	Average wt (mg)	Disintegration Time (secs)		Friability (%wt loss)	Hardness (kg)
		Range	Avg		
I	1061.07	35-45	40	0.12%	10.00
J	1008.16	58-65	62	0.22%	10.05
K	1007.73	183-415	299	0.39%	10.15
L	1007.54	30-130	80	0.50%	10.00
M	1014.94	75-126	100	0.51%	10.15
N	821.26	400-480	440	0.94%	6.75
O	919.95	850-900	875	Failed	4.02
P	1080.54	60-480	270	0.31%	10.15
Q	1005.27	74-106	90	1.06%	10.15
R	992.29	20-55	37	1.01%	10.00
S	1058.37	15-45	30	10.65%	8.10
T	1058.15	215-270	242	0.43%	10.05
U	1064.58	2223	2223	0.48%	10.15

According to British Pharmacopoeia Disintegration Time limit up to 15 minutes for uncoated tablet formulation, Friability <1% weight loss, Hardness 4-10 kg & the limits for Average weight varies from 444 - 516 mg (excepting exipients) which correspond to quantity of active ingredients of Sulfamethoxazole and Trimethoprim (92.5 to 107.5 %). Table-1 showing the average weight, disintegration time, friability and hardness of single strength of co-trimoxazole tablet formulations in which average weight varied from 520.72 - 619.69 mg (including exipients), disintegration time varied from 10-280 seconds, hardness varied from 4.40 - 8.10 kg, friability varied from 0.33- 0.96 % weight loss.

Table-2 showing the average weight, disintegration time, friability and hardness of double strength formulation of co-trimoxazole tablet in which average weight varied from 821.26-1080.54 mg, disintegration time varied from 30 sec to 2223 sec (37.05 min), hardness varied from 4.02-10.15 kg, friability varied from 0.12-10.65 % weight loss & average weight varied from 821.26 mg -1080 mg.

Discussion

In this study, researcher analyzed the quality of different trade brands of Co-trimoxazole tablet formulations available in the local market. For this, different quality control parameters, such as Disintegration time, Friability, Hardness & Average weight were assayed by using methods given in British Pharmacopoeia.

Two batches of two trade brands did not comply regarding disintegration time. Disintegration time of one batch (code U - 2223 sec/37.05 min) exceeded the normal limit & another batch (code O - 875 sec) just reached the upper limit of normal. A study done in Nigeria in 2010 showed that 1 out of five(20%) co-trimoxazole tablet formulations was failed in disintegration time test[5]. This finding is not in agreement with the finding of the present study. This inconsistency may be due to very small number of samples in their study which gave increased percentage of disintegration time test failure.

In friability test most of the samples were within normal range of British Pharmacopoeial specification (<1% weight loss) except for two batches of two trade brands. One batch failed in friability test (code O - double strength formulation) and friability of another batch (code S-10.65% weight loss) exceeded the normal range of <1% weight loss according to British Pharmacopoeia. In a study 2 out of 11 co-trimoxazole tablet formulations

(18.18%) failed in friability test[4]. This finding is not similar with the finding of present study. This inconsistency may be due to less number of samples used in their study which gave increased failure rate in friability test.

Only one sample Code no O, had a hardness of 4.02 which is just around the lower limit of normal (4-10 kg). Average weight of most formulations was within normal range exceptone batch (code N -821.26) which is below the normal range. Hardness & average weight could not be compared with other studies because of the unavailability of concrete data from existing literature.

No attempt was made to find out the cause of poor quality of the drug. The co-trimoxazole trade brand that failed in quality test might be due to poor manufacturing practice, inadequate quality assurance or control, or possible decomposition of the raw materials. The decomposition is possible when drugs are stored under conditions conducive to chemical degradation of the active ingredients particularly in tropical countries.

This study included only 17 trade brands which are not sufficient to generalize widespread existence of substandard preparations of co-trimoxazole. This needs to be confirmed by further similar studies by taking more number of samples. Moreover bioequivalence study of various brands of co-trimoxazole may also reveal the existence of substandard preparations. So bioequivalence study may be conducted in future such study. As our drug administration has limited facilities to cope with the detection of suspicious samples from the market, the medical colleges can be utilized for detection of substandard drugs. The department of pharmacology and biochemistry can help sample analysis and reduce the burden on drug testing laboratories.

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