Comparative in-vitro quality evaluation of some brands of metronidazole tablet available in Bangladesh

Sadia Noor, Fayad Bin Abdus Salam, Habibun Nahar Hima, Md. Shahidul Islam Bhuiyan and Shaila Chowdhury

Abstract
Quality of pharmaceutical products is very important because drugs must be marketed as safe and therapeutically active formulations whose performance is consistent and predictable. The evaluation of the physical characteristics of the pharmaceutical products can ensure their quality as well as bioavailability and impart optimum therapeutic activity. Metronidazole was chosen for this comparative study because this drug is widely used worldwide in the treatment of amoebiasis and other microbial diseases. Studies on metronidazole revealed that it is a recommended treatment during pregnancy for infections with bacterial vaginitis and Trichomonas vaginalis. The purpose of this study was to compare the quality of metronidazole tablets of some brands and to evaluate whether all brands obey the USP protocols. There are many different brands and different types of dosage forms of metronidazole under various trade names manufactured by different pharmaceutical companies available in the market. For this current research work nine brands (brand codes M1, M2, M3, M4, M5, M6, M7, M8, M9) of metronidazole film coated tablets (400mg) commercially available in Bangladesh were collected and evaluation studies were conducted which includes diameter and thickness measurement, weight variation test, friability test, hardness test, disintegration time, dissolution profile, and potency determination. Tests were performed as per the method described in United States of Pharmacopoeia (USP). All brands were found to comply with the USP specifications. According to this analysis, minimum weight variation was found in brand M4. Brand M9 showed the highest average hardness of 298.33N with minimum disintegration time (2.32 minutes) and highest friability (0.42%) among other brands. The lowest friability was 0.02% with brand M1. The highest potency was 104.09% (brand M7) and all the brands showed active drug release within ±5% of label amount. Dissolution pattern and potency of the metronidazole tablets were determined by the UV spectroscopic method at 278nm in the acidic (0.1N HCl) medium. All brands showed satisfactory dissolution profile as they released more than 85% drug in 60 minutes. Among these brands M4 showed highest drug release at required time interval. Dissolution profile of brand M1, M5 and M6 were found similar to that of brand M4 by comparing difference factor (f1) and similarity factor (f2) values of all nine brands. For better therapeutic effects and safe use of drugs, quality parameters should be maintained strictly.

Keywords: Metronidazole, in vitro comparative study, bioavailability, disintegration time, dissolution profile, potency

1. Introduction
Metronidazole, a nitro-imidazole, is widely used throughout the world and available in many different brands and dosage forms in Bangladesh. It is the most common isomer of imidazole containing one nitro group. The term nitro-imidazole also refers to a class of antibiotics that share similar chemical structures. It is one of the rare examples of a drug developed against a parasite which has since gained broad use as an antibacterial agent. Metronidazole is an antiprotozoal and antibacterial medication used mainly in the treatment of infections caused by anaerobic bacteria and protozoa \([12]\). This study was performed to evaluate whether the sample brands of metronidazole tablet maintain the quality, to obtain a brief idea about quality parameters of those brands and to make a comparative analysis of different metronidazole brands available in Bangladesh market. The safety and therapeutic effects of a pharmaceutical dosage form can be ensured when it complies with the particular specifications.
The efficacy of pharmaceutical dosage forms generally depends on their formulation, manufacturing process, hence it is likely that the quality of dosage form may vary [8, 26]. There are many indicators of drug quality which can broadly be classified as (i) physical tests that includes visual inspection, (ii) chemical tests for content of active ingredients and impurities under normal and simulated storage conditions, (iii) in vitro disintegration and dissolution tests and (iv) in vivo bioavailability studies. Thus, physical tests may include tests performed on liquid, semi-solid and solid pharmaceutical dosage forms. For instance, for tablets, uniformity of weight, friability, hardness and so on, can all be carried out as part of the quality tests [3]. Among these tests Dissolution test is one of the in vitro tests usually employed to assess the quality of oral drug products such as tablets and capsules.

Metronidazole (C6H9N3O3) is a white or yellowish crystalline powder, bitter and saline in taste, slightly soluble in water [5, 22, 15]. Metronidazole is commonly available as film coated tablet along with other dosage forms. Tablet is one of the most preferred solid dosage forms of medicaments all over the world, with or without suitable diluents and prepared by molding or by compression. They may be disc shaped or convex surface but also may be round, oval and oblong, cylindrical [10]. Almost all drug molecules can be formulated in a tablet and process of manufacturing of tablets is very simple and flexible [2]. It is very easy to mask the taste of bitter active ingredients thus make convenience for patient [20]. Metronidazole was first synthesized by France's Rhone-Poulenc laboratories and introduced in the mid-1950s under the brand name Flagyl. It began to be commercially used in 1960 in France. It initially was approved by the FDA in 1963. The antibacterial activity of metronidazole was discovered by accident in 1962 when metronidazole cured a patient of both trichomonas vaginitis and bacterial gingivitis [21]. Metronidazole was shown to be efficacious against Entamoeba histolytica, the cause of amoebic dysentery and liver abscess, in 1966 [19]. Giardia lamblia (also known as G. duodenalis) was treated with metronidazole after this luminal parasite was recognized as a cause of malabsorption and epigastric pain in the 1970s [28]. It was also the first drug to have a cure rate approaching 100 % with systemic treatment [9]. However, it was not until the 1970s that metronidazole was popularized for treatment of infections caused by gram-negative anaerobes such as bacteroides or gram-positive anaerobes such as clostridia [17]. A study on in vitro dissolution pattern of metronidazole film coated tablet in presence of fruit juice showed that all brands got reasonably higher dissolution release specifically in presence of mango juice; therefore, concluded that mango juice assists to enhance the therapeutic response of metronidazole on set of quick response [4]. Following oral administration, metronidazole is well absorbed, with peak plasma concentrations occurring between one and two hours after administration as well as more than 80% bioavailability. Plasma concentrations of metronidazole are proportional to the administered dose [7, 24]. Metronidazole is widely distributed in body tissues and fluids. It is the major component appearing in the plasma, with lesser quantities of metabolites also being present. Less than 20% of the circulating metronidazole is bound to plasma proteins. Metronidazole appears in cerebrospinal fluid, saliva, and breast milk in concentrations similar to those found in plasma. Bactericidal concentrations of metronidazole have also been detected in pus from hepatic abscesses [6]. The major route of elimination of metronidazole and its metabolites is via the urine (60% to 80% of the dose), with fecal excretion accounting for 6% to 15% of the dose. The metabolites that appear in the urine result primarily from side-chain oxidation [1-(ß-hydroxyethyl)-2-hydroxymethyl-5-nitroimidazole and 2-methyl-5-nitroimidazole-1-ylacetic acid] and glucuronide conjugation, with unchanged metronidazole accounting for approximately 20% of the total. Both the parent compound and the hydroxyl metabolite possess in vitro antimicrobial activity. Renal clearance of metronidazole is approximately 10 ml/min/1.73 m2. The average elimination half-life of metronidazole in healthy subjects is eight hours.

Metronidazole is a pro-drug. Unionized metronidazole is selectively taken up by anaerobic bacteria and sensitive protozoal organisms because of the ability of these organisms to intracellularly reduce metronidazole to its active form. This reduced metronidazole then covalently binds to DNA, disrupt its helical structure, inhibiting bacterial nucleic acid synthesis and resulting in bacterial cell death. Presence of oxygen prevent reduction of metronidazole and so reduces its cytotoxicity. Presently, metronidazole which is inexpensive has good penetration and produces relatively few side effects, is on the formulary at most hospitals for prophylaxis against anaerobic infection after bowel surgery, for treatment of wound abscesses and for treatment of antibiotic associated colitis caused by Clostridium difficile [21]. Despite some common side effects the most serious adverse reactions reported during treatment with metronidazole have been convulsive seizures, encephalopathy and aseptic meningitis. In addition, patients have reported headache, syncope, and dizziness, vertigo, in coordination, ataxia, confusion, dysarthria, irritability, depression, weakness, and insomnia. Very rare cases such as reversible abnormal liver function tests, cholestatic hepatitis, reversible neutropenia, reversible thrombocytopenia and hypersensitivity reactions have also been reported [14].

2. Materials and methods
2.1. Collection of samples
Metronidazole tablets (400 mg) of 09 different brands (20 tablets from each brand) of were purchased from different local medicine shops located in Dhaka, Bangladesh. The samples were properly checked for their visual appearance, manufacturing company, manufacturing date, expiry date, manufacturing license number, batch number and DAR number at the time of purchase. Standard metronidazole was a gift from Square Pharmaceutical Ltd., Bangladesh.

2.2. Identification of sample
The brands were randomly coded as M1, M2, M3… & M9, so that the identity of the manufacturers can be blinded. All brands were labeled with a shelf life of two years and claimed to contain 400 mg of metronidazole per tablet. All the tablets were found packaged in strip or in blister with a good condition. The shape, size and color of different branded tablets were subjected to visual inspection at the very beginning of the research work. The label information of 09 different brands of metronidazole tablet (400 mg) is represented in Table 1.
Table 1: Label information of nine different brands of metronidazole tablets (400 mg)

<table>
<thead>
<tr>
<th>Brand code</th>
<th>Shape of the tablets</th>
<th>Mfg. date</th>
<th>Exp. date</th>
<th>Pack size</th>
<th>Price of pack found (BDT)</th>
<th>Price per unit (BDT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>oval</td>
<td>June 2016</td>
<td>June 2018</td>
<td>250</td>
<td>315</td>
<td>1.26</td>
</tr>
<tr>
<td>M2</td>
<td>capsule</td>
<td>August 2016</td>
<td>August 2018</td>
<td>200</td>
<td>254</td>
<td>1.27</td>
</tr>
<tr>
<td>M3</td>
<td>capsule</td>
<td>March 2016</td>
<td>March 2018</td>
<td>150</td>
<td>199.5</td>
<td>1.33</td>
</tr>
<tr>
<td>M4</td>
<td>capsule</td>
<td>June 2016</td>
<td>June 2018</td>
<td>100</td>
<td>114</td>
<td>1.14</td>
</tr>
<tr>
<td>M5</td>
<td>capsule</td>
<td>April 2016</td>
<td>April 2018</td>
<td>100</td>
<td>115</td>
<td>1.15</td>
</tr>
<tr>
<td>M6</td>
<td>capsule</td>
<td>January 2016</td>
<td>January 2018</td>
<td>200</td>
<td>220</td>
<td>1.10</td>
</tr>
<tr>
<td>M7</td>
<td>Round</td>
<td>July 2016</td>
<td>July 2018</td>
<td>100</td>
<td>114</td>
<td>1.14</td>
</tr>
<tr>
<td>M8</td>
<td>Round</td>
<td>April 2016</td>
<td>April 2018</td>
<td>100</td>
<td>102</td>
<td>1.02</td>
</tr>
<tr>
<td>M9</td>
<td>Round</td>
<td>August 2016</td>
<td>August 2018</td>
<td>100</td>
<td>127</td>
<td>1.27</td>
</tr>
</tbody>
</table>

2.3. Diameter and thickness measurement
Selected 20 tablets from each brand were subjected to diameter and thickness measurement individually using a digital slide calipers (Shanghai, China). The values were reported in millimeter (mm). Mean diameter, thickness and their standard deviation (SD) were calculated.

2.4. Weight variation test
Individual weights of selected 20 tablets of each brand were measured in milligram using electronic analytical balance (ELB 3000, Shimadzu Corporation, Japan) and from these data mean weight with standard deviation (SD) were calculated.

2.5. Hardness test
Crushing strength (N) of 03 tablets from each brand was determined with an automatic hardness tester (Dr. Schleuniger, Switzerland). Mean hardness with standard deviation (SD) were calculated.

2.6. Friability test
07 tablets from each brand were weighed and subjected to rotation by employing a Roche friabilator (VEEGO, India) which was operated at 25 RPM for 4 minutes and then all tablets were re-weighted after removing from friabilator.

2.7. Disintegration test
Three tablets from each brand were employed for the disintegration test in distilled water at 37 °C using a tablet disintegration tester (VDT-2, Veego, India) as per condition described by United State Pharmacopeia, 2013 [24]. The disintegration time (DT) was noted down and it’s the time taken for the entire tablet to disintegrate completely.

2.8. Standard curve preparation
The powder equivalent to 10 mg of standard metronidazole was taken and dissolved in 0.1 N HCl. Then it was diluted to produce a final concentration of 15μg/ml for working solution. Absorbance values were then measured at the maximum wavelength (λmax) of metronidazole of the serially diluted concentrations (0, 1.5, 3, 4.5, 6, 7.5, 9, 10.5, 12, 13.5 & 15 μg/ml) using a UV-VIS spectrophotometer (UV-1700, Shimadzu, Japan). Maximum wavelength was obtained by scanning sample of diluted standard metronidazole from 200 to 400 nm wavelengths and it was found to be 278 nm.

2.9. Measurement of potency
Sample was prepared by weighing and crushing 04 tablets, transferring amount of drug powder equivalent to 10 mg in 0.1 N HCl solution and placing it in sonicator (Hwashin Technology, Seoul, Korea). The portion of solution was filtered and the filtrate was suitably diluted. Absorbance was taken at 278 nm by using UV- visible spectrophotometer. Finally the potency of different brands was calculated using the following equation:

Potency = \( \frac{\text{Drug present in a single tablet \times 100}}{\text{Strength (mg)}} \)

2.10. Dissolution test
The dissolution test was undertaken for 03 randomly selected tablets using USP dissolution apparatus I (Electrolab). The dissolution medium was 900 ml of 0.1 N HCl which was maintained at 37±0.5 °C. Rotations were 100 RPM. Each time 10 ml sample was withdrawn after 5 min, 15 min, 30 min, 45 min & 60 min, and was then filtered. The filtrates were then suitably diluted with 0.1 N HCl. Absorbance was measured at 278 nm. Using the \( y = mx + c \) equation derived from the standard curve of API, concentrations of sample at different above mentioned times were calculated. From these data Cumulative amount release and then % Drug release were calculated using the following equation:

\% Drug release = \( \frac{\text{Cumulative amount release (mg) \times 100}}{\text{Strength (mg)}} \)

3. Results and discussion
3.1. Price fluctuation
There is minor price variation among the brands. Brand M3 had the maximum price of 1.33 taka per tablet and brand M8 had the minimum price of 1.02 taka per tablet while there was no major variation in the quality of the tested drugs (Table 1).
3.2. Diameter and thickness test
The diameter and thickness of tablets depend on the die and punches selected for making the tablets. The thickness of various tablets may be prepared without any change of their weights. Variations in diameter and thickness are generally due to the difference in density of granules, pressure applied for compression and the speed of compression.

Among nine brands, brand M3 had the highest average diameter (18.15 mm) having capsule shape whereas brand M8 had the lowest average diameter (10.16 mm) having round shape. The average thickness was found to be between the ranges of (4.71-6.20) mm (Table 2).

3.3. Test of uniformity of weight
The objective of the weight variation test is to ensure - good manufacturing practices (GMP), appropriate size of the tablets and the content uniformity of the formulation [27]. The United States Pharmacopoeia (USP) provides criteria for tablet weight variation test of intact dosage forms which states that the percent weight variation should be within ±5% for tablets having average weight more than 324mg. The tablets met the USP test if there are not more than 2 tablets outside the percentage limit and if no tablets deviate twice of the percentage limit [16, 25].

All the brands complied with the compendia specification for uniformity of weight as the percent deviations from average weight of all the tablets were within the acceptable range of ±5%. Minimum percent deviation from average weight was found in brand M4 (Table 2).

3.4. Hardness test
Tablet hardness testing is a laboratory technique used by the pharmaceutical industry to test the breaking point and structural integrity of a tablet under conditions of storage, transportation, and handling before usage [14]. The hardness of the tablet depends on the materials used, amount of binder, space between the upper and lower punches at the time of compression and pressure applied during the process of compression [5]. Hardness influences many tablet properties including disintegration, dissolution and friability. High hardness values may result in increased disintegration times and decreased dissolution times. As opposed to this situation, high friability values may be observed in case of low hardness values [16, 11].

Brand M9 had the highest average hardness (298.33 N) whereas brand M8 had the lowest average hardness (65.33 N) (Table 2). A force of about 40 N is the minimum requirement for a satisfactory tablet [1]. Hence the tablets of all the brands comply with this requirement.

3.5. Friability test
Friability (the condition of being friable) testing is a method, which is also employed to determine physical strength of compressed and uncoated tablets upon exposure to mechanical shock and attrition. In simple words, friability test tells how much mechanical stress tablets are able to withstand during their manufacturing, distribution and handling by the customer. Throughout pharmaceutical industry, friability testing has become an accepted technology [22].

It is a compendial test and met the USP specification if friability is not more than 1% [16, 25]. The friability was found to be between the ranges of (0.02-0.42) %, thus all the brands met the friability specification (Table 2).

3.6. Disintegration test
Disintegration test is performed to find out that within how much time the tablet disintegrates. Disintegration test is very important for all coated & uncoated tablet because the dissolution rate of drug depends on the disintegration time, which ultimately affect the rate of absorption and subsequent bioavailability of drug [13].

According to BP/USP specification, film coated tablets should disintegrate within 30 min [16, 25]. Here film coated metronidazole tablets of all the brands met the requirement as the disintegration time (DT) was found to be between the ranges of (2.32-14.84) minutes (Table 2).

3.7. Potency test
Potency is a measure of drug activity expressed in terms of the amount of API (in percentage) required to produce an effect of given intensity. This test is done for determining the toxic and therapeutic effect of the drug. The potency of the tablet should comply with the specification because very highly potent drug may give toxic effect & very less potent drug may give sub-therapeutic effect.

All the brands showed potency within the range of (95-105) % of labeled amount of drug and complied according to USP [16, 25] (Table 2).
Table 3: Dissolution profile of nine brands of metronidazole tablets

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Brand M1*</th>
<th>Brand M2*</th>
<th>Brand M3*</th>
<th>Brand M4*</th>
<th>Brand M5*</th>
<th>Brand M6*</th>
<th>Brand M7*</th>
<th>Brand M8*</th>
<th>Brand M9*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>5</td>
<td>7.76 ± 1.79</td>
<td>24.97 ± 1.26</td>
<td>35.90 ± 1.74</td>
<td>12.81 ± 1.31</td>
<td>11.21 ± 1.52</td>
<td>10.73 ± 1.25</td>
<td>49.39 ± 0.23</td>
<td>47.47 ± 2.06</td>
<td>48.21 ± 2.47</td>
</tr>
<tr>
<td>15</td>
<td>47.16 ± 1.29</td>
<td>34.55 ± 4.34</td>
<td>48.71 ± 2.04</td>
<td>39.44 ± 2.00</td>
<td>35.43 ± 1.59</td>
<td>35.02 ± 2.58</td>
<td>53.98 ± 2.85</td>
<td>53.03 ± 4.36</td>
<td>50.81 ± 2.17</td>
</tr>
<tr>
<td>30</td>
<td>77.18 ± 0.96</td>
<td>56.04 ± 2.40</td>
<td>61.96 ± 1.67</td>
<td>60.53 ± 3.01</td>
<td>54.95 ± 1.95</td>
<td>56.69 ± 3.09</td>
<td>63.79 ± 5.61</td>
<td>61.42 ± 7.99</td>
<td>59.19 ± 2.45</td>
</tr>
<tr>
<td>45</td>
<td>81.41 ± 1.03</td>
<td>71.56 ± 7.79</td>
<td>74.09 ± 1.83</td>
<td>83.73 ± 3.67</td>
<td>85.44 ± 2.48</td>
<td>85.27 ± 1.45</td>
<td>74.45 ± 2.47</td>
<td>75.81 ± 2.57</td>
<td>73.63 ± 2.73</td>
</tr>
<tr>
<td>60</td>
<td>88.34 ± 0.79</td>
<td>85.34 ± 0.21</td>
<td>86.90 ± 0.65</td>
<td>99.56 ± 2.67</td>
<td>98.50 ± 3.37</td>
<td>96.06 ± 7.48</td>
<td>97.76 ± 2.34</td>
<td>98.87 ± 0.38</td>
<td>98.41 ± 2.61</td>
</tr>
</tbody>
</table>

* Values are expressed as average ± SD

3.8. Dissolution Test

The transfer of a drug from its solid dosage form into the solution of GI fluid as dissolved form is called dissolution. This is the slowest step in a series of kinetic processes of drug and called the rate-limiting step. Dissolution study measures the rate and extent of drug release from any dosage form. The test usually reports the % of drug released at a specific period of time. Dissolution tests are determining factors affecting drug bioavailability. For film coated metronidazole tablets, drug release should not be less than 85% of labeled amount in 60 minutes\[16, 25\].

Brand M4 had maximum drug release within the 60 minutes (99.56%) of the in vitro dissolution test, while brand M2 had minimum drug release (85.34%) within the same time interval. Intra-brand comparison of the drug release profile of all the brands indicated an increase in drug release with increasing time although this rate varied from brand to brand (Figure 1). Since all the brands met the USP specification, it can be assumed that all the brands possessed satisfactory dissolution profile although the brands were manufactured by different companies using different excipients in different ratio (Table 3).

Fig 1: Comparative average % drug release of metronidazole tablet of nine brands

3.9. Comparison of dissolution data

To compare the dissolution profile, difference factor ($f_1$) and similarity factor ($f_2$) were calculated using the following equations:

$$f_1 = \left( \frac{\sum_{i=1}^{n}[R_{t,i} - T_{t,i}]}{\sum_{i=1}^{n} R_{t,i}} \right) \times 100$$

$$f_2 = 50 \log \left\{ \left[ 1 + \frac{1}{n} \sum_{t=1}^{n}\left(R_t - T_t\right)^2 \right]^{-0.5} \times 100 \right\}$$

Where $n$ is the number of time points, $R_t$ is the dissolution value of reference product at time $t$ and $T_t$ is the dissolution value for the test product at time $t$. Similarity factor ($f_2$) has been adopted by FDA and the European Agency for the evaluation of medicinal products (CPMP) to compare dissolution profile. According to the FDA guidance \[29\], dissolution profiles are similar if $f_1$ values are between 0 and 15 while $f_2$ values are between 50 and 100.

The $f_1$ and $f_2$ values of different brands were calculated considering brand M4 as reference brand due to its highest drug release (%) in desired time interval. Brand M1, M5 and M6 showed $f_1$ and $f_2$ values within the above requirements thus it can be said that brand M1, M5 and M6 are similar to brand M4 in respect of drug release pattern (Table 4).

Table 4: Comparison of dissolution profile of nine brands of metronidazole tablets

<table>
<thead>
<tr>
<th>Brand comparison pair</th>
<th>Difference factor ($f_1$)</th>
<th>Similarity factor ($f_2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1 vs. M4</td>
<td>14.51</td>
<td>50.03</td>
</tr>
<tr>
<td>M2 vs. M4</td>
<td>16.19</td>
<td>49.02</td>
</tr>
<tr>
<td>M3 vs. M4</td>
<td>18.94</td>
<td>43.87</td>
</tr>
<tr>
<td>M5 vs. M4</td>
<td>4.72</td>
<td>73.24</td>
</tr>
<tr>
<td>M6 vs. M4</td>
<td>5.20</td>
<td>73.35</td>
</tr>
<tr>
<td>M7 vs. M4</td>
<td>22.11</td>
<td>37.01</td>
</tr>
<tr>
<td>M8 vs. M4</td>
<td>19.51</td>
<td>38.40</td>
</tr>
<tr>
<td>M9 vs. M4</td>
<td>20.05</td>
<td>38.13</td>
</tr>
</tbody>
</table>

4. Conclusion

The present study was undertaken with an aim to evaluate nine different brands of metronidazole market preparations available in Bangladesh. Metronidazole is a poorly water soluble drug. Due to its poor solubility it is very difficult to achieve desired bioavailability. The life of a patient relies on the drug he/she is taking needs to be safe and have good efficacy. So we did various official and non-official and in-vitro studies like weight variation, friability, hardness, disintegration, dissolution and potency tests. According to our analysis, almost all brands of metronidazole contain...
good quality and good efficacy by passing all the pharmacopoeia requirements. Bioavailability and therapeutic effect depends on these quality control tests. So, it is necessary to evaluate different tablet parameters properly before marketing. These types of studies should be conducted more frequently not only to build public awareness about the quality of marketed pharmaceutical products but also because these type of studies are very helpful for the betterment of pharmaceutical sector.

5. References