POTENCY AND STABILITY STUDIES OF MARKETED PARACETAMOL AND RANITIDINE HCl PREPARATIONS IN BANGLADESH

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Abstract: A number of marketed pharmaceutical preparations of paracetamol and ranitidine were analyzed. Potency of the selected products was assayed spectrophotometrically and their various physical parameters (color variation, thickness, weight variation, hardness, friability, disintegration time, dissolution rate) were analyzed according to the official (BP/USP) pharmacopoeial methods. It is evident from the study that most of the brands tested showed satisfactory results but a few of them failed to meet the specification.

Key words: Potency, stability, paracetamol, ranitidine, Bangladesh

Introduction

Paracetamol is an effective analgesic and antipyretic drug but has a weak anti-inflammatory effect. It is available as tablet, syrup, suspension and also as suppository dosage forms in Bangladesh. Ranitidine is a H2 receptor antagonist and is indicated for the short term treatment of duodenal ulcer, gastric ulcer and the management of hypersecretory conditions such as Zollinger-Ellison syndrome (a pathological condition in which a non-beta-cell tumor of the pancreatic islets may produce gastrin in a quantity sufficient to stimulate gastric secretion to life threatening levels, Hardman and Limbird, 1996) and systemic mastocytosis, (Gennaro, 1990). Ranitidine is available as tablet (film coated), injection, and suspension and also as large volume parental (250 ml).

Because of the increasing complexity of modern pharmaceutical manufacture arising from a variety of unique drugs and dosage forms, complex ethical, legal and economic responsibilities have been placed on those concerned with the manufacture of modern pharmaceuticals. Substandard or spurious drugs could endanger patient’s life. This realization influenced to evaluate some of the pharmaceutical preparations available in the market. The main purpose of this study was to investigate the overall quality of the marketed paracetamol (tablet, syrup and suspension) and ranitidine (tablet and injection) preparations available in Bangladesh. The investigation was performed during February 2002 to August 2002.

Materials and Methods

Collection of Sample: About 120 brands of paracetamol (tablet, syrup and suspension) and 80 brands of ranitidine are available in Bangladesh. These were arranged alphabetically and every forth was selected for the analysis. Thus 30 brands of paracetamol and 20 brands of ranitidine were collected from retail medicine shop of different areas of Bangladesh. About 40-50 tablets of each brand were collected for the analysis of tablets and 3 unit files of syrup, suspension and injection of each brand were collected for that purpose. The collected paracetamol tablets were coded as PT01 to PT20, syrups were coded as PSp1 to PSp7 and the suspensions as PSn1 to PSn3. Ranitidine tablets were coded as RT01 to RT17 and the injections were coded as RI01 to RI03. All the collected samples were properly checked for their physical appearance, name of the manufacturer, batch number, manufacturing date, expiry date, manufacturing license number, D.A.R. number and maximum retail price at the time of purchase. No samples were bought and analyzed whose date of expiry had already been passed.

Weight variation test of tablets: Twenty tablets were taken and weighed individually with an analytical balance and the average weight of the tablets was calculated. Then % of weight variation was calculated by using the following formula.

\[ \text{% of weight variation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100 \]

Hardness test of tablets: Tablet hardness is defined as the load required to crush or fracture of a tablet placed on its edge. Sometimes it is also termed as tablet crushing strength. In this study Monsanto Hardness Tester was used.
Disintegration time test of tablets: Disintegration time is the length of time required for causing disintegration of tablet, that directly influences the onset of action. This test not only evaluates the quality but also the bioavailability and effectiveness of tablets. Disintegration time for tablets was determined according to the USP method by using a suitable USP disintegration apparatus (USP, 2000).

Dissolution rate test of tablets: Dissolution is the property or tendency of a drug to undergo solution, which affects the rate of drug absorption. Dissolution rate of tablets was determined according to the USP method by using a suitable USP dissolution apparatus (USP, 2000).

Potency determination of tablets: Preparation of standard solution: 25 mg of standard paracetamol and 20 mg of standard ranitidine were weighed and dissolved in 100ml of 0.1N NaOH and distilled water, respectively. 1 ml of each of the above solutions was diluted to 100 ml with the same solvent. Preparation of assay solution: 20 tablets from each brand of paracetamol and ranitidine were weighed and powdered. An amount of powder equivalent to 25 mg of paracetamol and 20 mg of ranitidine were taken in 2 separate volumetric flask (100 ml) and volume was adjusted by using 0.1 N NaOH and distilled water, respectively. 1 ml of the filtered solution was diluted to 100 ml with the same solvent. Calculation: Potency of paracetamol and ranitidine tablets was determined by a suitable UV-VIS spectrophotometer at 257 and 315 nm, respectively. Potency of sample = \[ \frac{\text{Absorbance of sample} \times \text{Weight of standard}}{\text{Absorbance of standard} \times \text{Weight of sample}} \times \text{Purity of standard} \]

Potency determination of syrup, suspension and injection: Preparation of standard solution: Standard solution was prepared according to the procedure described for the potency determination of tablets. Preparation of sample solution: An amount of sample equivalent to 25 mg of paracetamol and 20 mg of ranitidine was taken in separate volumetric flask (100 ml) and the volume was adjusted with 0.1N NaOH and distilled water, respectively. Then 5 ml of the above solutions were taken and diluted to 100 ml by adding the same solvents.

Results and Discussion

Weight variation test of tablets: Table 1 shows the results of weight variations of paracetamol and ranitidine tablets.

Table 1. Weight variations of tablets

| Sample code | Av. wt. of tablets | No. of tablets outside the range | Sample code | Av. wt. of tablets | No. of tablets outside the range |
|-------------|-------------------|---------------------------------|-------------|-------------------|---------------------------------|
| PT01        | 559.84            | 0                               | RT01        | 283.72            | 2                               |
| PT02        | 612.90            | 0                               | RT02        | 260.1             | 1                               |
| PT03        | 569.21            | 0                               | RT03        | 287.49            | 4                               |
| PT04        | 653.73            | 0                               | RT04        | 239.86            | 0                               |
| PT05        | 570.98            | 2                               | RT05        | 285.61            | 2                               |
| PT06        | 536.54            | 4                               | RT06        | 291.30            | 0                               |
| PT07        | 609.84            | 0                               | RT07        | 307.11            | 0                               |
| PT08        | 556.41            | 5                               | RT08        | 355.5             | 2                               |
| PT09        | 582.45            | 0                               | RT09        | 391.60            | 1                               |
| PT10        | 595.72            | 0                               | RT10        | 273.5             | 1                               |
| PT11        | 578.58            | 1                               | RT11        | 270.11            | 5                               |
| PT12        | 618.51            | 2                               | RT12        | 252.53            | 0                               |
| PT13        | 554.32            | 0                               | RT13        | 286.82            | 0                               |
| PT14        | 604.52            | 1                               | RT14        | 301.68            | 1                               |
| PT15        | 561.77            | 0                               | RT15        | 277.64            | 0                               |
| PT16        | 613.48            | 1                               | RT16        | 290.45            | 1                               |
| PT17        | 602.53            | 0                               | RT17        | 287.68            | 0                               |
| PT18        | 597.65            | 1                               |             |                   |                                 |
| PT19        | 610.42            | 0                               |             |                   |                                 |
| PT20        | 608.62            | 0                               |             |                   |                                 |

Av.= average; wt.= weight

The BP/USP specification of weight variation is ± 5% (w/w). It is observed from the above result that same samples 2 brands of paracetamol (PT06, PT08) and 2 of ranitidine (RT03, RT11) did not comply with the specification. The rest of the brands complied with the specification.
Hardness test of Tablets: Table 2 shows the observed values of the hardness test of tablets. The BP / USP specification of hardness is, not more than 7.0 kg / cm. It is seen from the results that none of the samples exceeded the specification for hardness.

| Sample code | Av. hardness (kg/cm) | Av. D.T. (min) | Sample code | Av. hardness (kg/cm) | Av. D.T. (min) |
|-------------|----------------------|----------------|-------------|----------------------|----------------|
| PT01        | 5.1                  | 11             | RT01        | 4.5                  | 16             |
| PT02        | 4.4                  | 10             | RT02        | 4.8                  | 12             |
| PT03        | 6.2                  | 06             | RT03        | 3.9                  | 25             |
| PT04        | 4.7                  | 11             | RT04        | 3.5                  | 07             |
| PT05        | 3.9                  | 07             | RT05        | 4.25                 | 11             |
| PT06        | 4.3                  | 18             | RT06        | 3.7                  | 13             |
| PT07        | 5.2                  | 14             | RT07        | 3.5                  | 17             |
| PT08        | 6.3                  | 08             | RT08        | 4.5                  | 11             |
| PT09        | 4.7                  | 12             | RT09        | 6.2                  | 23             |
| PT10        | 3.9                  | 06             | RT10        | 3.8                  | 13             |
| PT11        | 4.8                  | 15             | RT11        | 4.3                  | 07             |
| PT12        | 4.2                  | 16             | RT12        | 4.5                  | 09             |
| PT13        | 4.6                  | 12             | RT13        | 3.25                 | 16             |
| PT14        | 5.0                  | 08             | RT14        | 4.2                  | 21             |
| PT15        | 4.3                  | 17             | RT15        | 3.9                  | 11             |
| PT16        | 3.9                  | 16             | RT16        | 4.51                 | 19             |
| PT17        | 5.2                  | 12             | RT17        | 4.26                 | 11             |
| PT18        | 4.6                  | 14             |             |                      |                |
| PT19        | 5.3                  | 15             |             |                      |                |
| PT20        | 5.5                  | 13             |             |                      |                |

Av.= average; D.T.= disintegration time

Disintegration time test of Tablets: Table 2 also shows the observed values of the disintegration time for tablets. It is evident from the above results (Table 2) that none of the samples exceeded the specification for disintegration time. The BP /USP specification of disintegration time is 5 – 30 min.

Dissolution rate test of tablets: Table 3 shows the results for the dissolution rate of tablets. It is seen from the results that 2 brands of paracetamol (PT06, PT12) and 3 of ranitidine (RT03, RT09, RT14) failed to fulfill the USP specification. According to the BP/USP specification, not less than 75% paracetamol should be dissolved in 30 min and not less than 80% ranitidine should be available in 45 min.

| Sample code | Drug release (%) | Sample code | Drug release (%) |
|-------------|------------------|-------------|------------------|
|             | After 30 min.    | After 45 min. | After 30 min.    | After 45 min. |
| PT01        | 85.65            | 93.20       | RT01             | 71.71          | 80.20          |
| PT02        | 88.83            | 90.37       | RT02             | 78.21          | 86.61          |
| PT03        | 82.95            | 89.49       | RT03             | 68.53          | 77.03          |
| PT04        | 91.54            | 98.87       | RT04             | 82.53          | 95.32          |
| PT05        | 88.22            | 92.99       | RT05             | 78.01          | 87.75          |
| PT06        | 70.45            | 75.53       | RT06             | 77.58          | 87.19          |
| PT07        | 94.79            | 98.43       | RT07             | 71.54          | 81.93          |
| PT08        | 86.75            | 90.83       | RT08             | 76.15          | 85.87          |
| PT09        | 93.76            | 97.78       | RT09             | 69.73          | 79.01          |
| PT10        | 87.48            | 94.54       | RT10             | 75.24          | 86.54          |
| PT11        | 91.34            | 98.45       | RT11             | 81.99          | 91.70          |
| PT12        | 74.59            | 79.77       | RT12             | 78.74          | 89.32          |
| PT13        | 89.64            | 95.65       | RT13             | 76.82          | 88.20          |
| PT14        | 87.46            | 93.38       | RT14             | 65.50          | 76.03          |
| PT15        | 90.57            | 97.45       | RT15             | 76.75          | 86.65          |
| PT16        | 84.25            | 90.12       | RT16             | 77.09          | 86.01          |
| PT17        | 86.70            | 92.50       | RT17             | 80.20          | 86.77          |
| PT18        | 84.26            | 89.78       |                  |                |                |
| PT19        | 85.75            | 91.45       |                  |                |                |
| PT20        | 90.40            | 96.60       |                  |                |                |
Potency determination of Tablets: Table 4 shows the potency of paracetamol and ranitidine tablets. The BP specification for potency is 95 – 105 % (w/w). From the results it is evident that 3 brands of paracetamol (PT05, PT06, PT12) and 5 of ranitidine (RT01, RT03, RT07, RT08, RT12) were below the specified limit for drug content. This may be due to the degradation of active ingredient or due to the addition of either poor quality raw material or less amount of active ingredient at the time of manufacture.

Table 4. Potency of paracetamol and ranitidine tablets

| Paracetamol | Ranitidine |
|-------------|------------|
| Sample code | Potency (% w/w) | Sample code | Potency (% w/w) |
| PT01        | 99.94      | RT01        | 83.54      |
| PT02        | 97.77      | RT02        | 97.99      |
| PT03        | 98.55      | RT03        | 85.92      |
| PT04        | 97.50      | RT04        | 95.79      |
| PT05        | 86.16      | RT05        | 96.96      |
| PT06        | 91.07      | RT06        | 97.68      |
| PT07        | 101.19     | RT07        | 89.62      |
| PT08        | 99.04      | RT08        | 81.96      |
| PT09        | 98.74      | RT09        | 98.73      |
| PT10        | 95.69      | RT10        | 96.02      |
| PT11        | 97.34      | RT11        | 98.08      |
| PT12        | 86.48      | RT12        | 93.20      |
| PT13        | 101.79     | RT13        | 96.87      |
| PT14        | 98.54      | RT14        | 97.92      |
| PT15        | 99.67      | RT15        | 98.01      |
| PT16        | 97.62      | RT16        | 97.45      |
| PT17        | 98.25      | RT17        | 97.47      |
| PT18        | 98.64      |             |            |
| PT19        | 99.32      |             |            |
| PT20        | 98.54      |             |            |

Potency determination of syrup, suspension and injection: Table 5 shows the potency of syrup, suspension and injection. From the above results it is observed that all of the preparations complied with the specification.

Table 5. Potency of syrup, suspension and injection

| Paracetamol syrup & suspension | Ranitidine injection |
|-------------------------------|---------------------|
| Sample code                  | Potency (% w/w)     | Sample code | Potency (% w/w) |
| PSp1                          | 102.51              | Rl01        | 98.64          |
| PSp2                          | 99.12               | Rl02        | 100.03         |
| PSp3                          | 101.26              | Rl03        | 101.02         |
| PSp4                          | 100.84              |             |                |
| PSp5                          | 100.54              |             |                |
| PSp6                          | 101.24              |             |                |
| PSp7                          | 104.79              |             |                |
| PSn1                          | 99.56               |             |                |
| PSn2                          | 100.89              |             |                |
| PSn3                          | 102.54              |             |                |

Conclusion

At present about 95% of the essential drugs are being produced in Bangladesh. In 2000, only 5% drugs were imported which include different types of vaccines and drugs that require high technology for manufacturing and quality control operations. The overall quality of the drug is usually satisfactory but some spurious and substandard drugs are also available in the market. Substandard drugs cause not only wastage of money but also create many health hazards. The present study, although performed on a limited scale, the data reported in this study can help us to get an idea about the quality status of the marketed paracetamol and ranitidine preparations in Bangladesh. The study emphasizes the need of constant surveillance and continuous evaluation of marketed drug products by the governments, manufacturers and independent research groups to ensure proper supply and availability of quality medicines.
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References
Gennaro A.R. 1990. Remington’s Pharmaceutical Sciences, Easton, Pennsylvania, 18th edition, 781 p.
Hardman, J.G. and L.E. Limbird 1996. In: Goodman and Gilman’s-The Pharmacological Basis of Therapeutics, 9th edition, 906 p.
USP 2000. United States Pharmacopoeial Convention Inc., Rockville, MD 20852, Asian edition, pp. 1941-43.