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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 H_2- 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.

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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 ranidine tablets was determined by a suitable UV-VIS spectrophotometer at 257 and 315 nm, respectively.

$$\text{Potency of sample} = \frac{\text{Absorbance of sample} \times \text{Weight of standard}}{\text{Absorbance of standard} \times \text{Weight of sample}} \times \text{Purity of standard}$$

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 flasks (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

Paracetamol			Ranitidine		
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 ranitidin (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.

Table 2. Hardness and disintegration time of tablets

Paracetamol			Ranitidine		
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.

Table 3. Dissolution rate of tablets

Paracetamol			Ranitidine		
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 ranitidin (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	RI01	98.64
PSp2	99.12	RI02	100.03
PSp3	101.26	RI03	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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