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COMPARATIVE EVALUATION OF THE BIOPHARMACEUTICAL AND CHEMICAL EQUIVALENCE OF SOME COMMERCIALLY AVAILABLE BRANDS OF RANITDINE HYDROCHLORIDE TABLETS

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ABSTRACT

The study was undertaken with the objective of evaluating the biopharmaceutical equivalency of seven brands of Ranitidine hydrochloride tablets and the chemical equivalency with a method which is easy to use, accurate, reproducible and inexpensive. The biopharmaceutical and chemical equivalence of seven brands of Ranitidine hydrochloride tablets were assessed through the evaluation of Uniformity of Weight, Hardness, Disintegration test, Dissolution rate and U.V. spectroscopic method. All the brands complied with the official specifications for the uniformity of weight, Disintegration test, Dissolution test and U.V. spectroscopic method for the chemical equivalence. Seven brands evaluated in this study could be regarded as being biopharmaceutically and chemically equivalent and they passes the standard as per I.P. 1996 and 2007.

INTRODUCTION[1, 2, 3]

Drug substances most frequently are administered by means of solid dosage forms such as tablet and capsule. Additives are also included in the formulation to facilitate handling, enhance the appearance and improve stability. Tablets are the solid unit dosage forms containing medicament or medicaments, usually circular and may be flat or biconvex in shape. The compressed tablets are the most popular dosage form in use today. About, two-third of all the prescriptions is compressed tablets. A tablet can be formulated to deliver an accurate dosage to specific site. It is usually taken orally, but administered sublingually, rectally or intra-vaginally. The tablet is just one of the many dosage forms that an oral drug can take such as syrups, elixirs, suspensions and emulsions. Medicinal tablets were originally made in a shape of a disk of whatever their colours determined, but are now made in many shapes and colours to distinguish between different medicines that they take. Tablets are often stamped with symbols, letters and numbers which enable them to be identified. Sizes of tablets, to be swallowed, range from a few millimeters to about a centimeter. Some tablets are in shape of capsules and are called "caplets". Medicinal tablets and capsules are often called pills. This is technically incorrect, since tablets are made by compression, whereas pills are ancient solid dosage forms prepared by rolling a soft mass into a round shape. Other products are also manufactured in the form of tablets which are designed to dissolve or disintegrate e.g. cleaning and deodorizing products.

Equivalence studies[4]

❖ Equivalence

It is a relative term that compares drug products with respect to a specific characteristic or function or to a defined set of standards.

There are several types of equivalences

- **Chemical Equivalence**

It indicates that the two or more drug products contain the same labeled chemical substances as an active ingredient in the same amount.

- **Pharmaceutical Equivalence**

This term implies that two or more drug products are identical in strength, quality, purity, content uniformity and disintegration and dissolution characteristics. They may, however, differ in containing different excipients.

- **Bioequivalence**

It is a relative term which denotes that the drug substance in two or more identical dosage forms, reaches the systemic circulation at the same relative rate and to the same extent i.e. their plasma

concentration-time profiles will be identical without significant statistical differences. When statistically significant differences are observed in the bioavailability of two or more drug products, bio-inequivalence is indicated.

- **Therapeutic Equivalence**

This term indicates that two or more drug products that contain the same therapeutically active ingredient elicit identical pharmacological effects can control the disease to the same extent.

If a new product is intended to be a substitute or equivalent or alternative for an approved medicinal product, then the equivalence with this product should be justified. In order to ensure clinical assurance of such drug products, bioequivalence studies are performed.

The introduction of generic drug product from multiple sources into the health care delivery system of many developing countries was aimed at improving the overall healthcare delivery systems in such countries. However this has been accompanied by a variety of problems of which the most critical is the widespread distribution of fake and substandard drug products.

The need to select one product among several drug products of the same active ingredients during the course of therapy is a cause of concern to a healthcare practitioner. The first step in ascertaining the therapeutic equivalence of any drug product involves ascertaining the chemical and biopharmaceutical equivalence of such drug products.

Drug product that are chemically and biopharmaceutically equivalent must be identical in strength, quality, purity, as well as content uniformity, disintegration and dissolution rates. There are several brands of Ranitidine Hydrochloride tablets available in the market in India. The increasing level of use of Ranitidine hydrochloride tablets as result of its versatility in management of heartburn, dyspepsia and hyperacidity, which can be associated with reflux oesophagitis, functional dyspepsia and/or peptic ulcers.

Ascertaining the quality of drug product involves the use of various procedures which includes both biopharmaceutical and chemical assay techniques. Various methods have been reported for chemical equivalence of Ranitidine Tablets. The Indian Pharmacopoeia (2007, Vol-3) suggests thin layer chromatographic method for the tablets as well as pure drug.

The objectives of this study was to evaluate biopharmaceutical and chemical equivalence of seven commercially available brands of Ranitidine hydrochloride tablets through the use of analytical method which will be easy to use, simple and inexpensive; and to compare the results obtained with the established official methods.

MATERIAL AND METHODS

Material

Following brands of Ranitidine hydrochloride tablets were used for the evaluation

Table no.1: List of brands of Ranitidine used for evaluation

Sample No.	Brand Name	Manufacturer
1.	Histac 150	Ranbaxy
2.	Zinetac	Glaxosmith
3.	Aciloc 150	CADILA
4.	Rantac	J.B. Chemicals & Pharmaceuticals
5.	Ranitin	Torrent
6.	R-Loc 150	Zydus Alidac
7.	Rdin	Helios

Methods

Tablet Description[1, 9]

All the brands of Ranitidine hydrochloride were examined for the color, shape and size by visual observation.

Hardness test[1]

The tablet to be tested was placed between the spindle and the anvil of hardness tester. The desired pressure needed to hold the tablet in the position was applied by moving the screw knob in the clockwise direction. The scale was moved so that the indicator is fixed at zero. The pressure was then applied till the tablet breaks. The reading was noted which indicates the pressure needed to break the tablet.

Disintegration test[1, 5, 6]

The disintegration test apparatus as per I.P. specification was used. The apparatus consists of six glass tubes that are three inches long, open at the top and held against a ten mesh screen at the bottom end of the basket rack assembly. The assembly should be raised or lowered between 28-32 times per minute in liquid maintained at 37^{o}C.

- **Disintegration test for coated tablet:**

One tablet was placed in each of the six tubes of the basket, and if the tablet had soluble external coating, the basket was immersed in water at room temperature for 5 minutes. Then a disc was added to each tube and the assembly was suspended in the disintegration medium maintained at 37 ± 2^{o}C and the apparatus was operated for 60 minutes or as indicated in monograph.

Dissolution test[1, 5, 6]

The in vitro dissolution test was carried using USP XXIV type-II paddle apparatus and 900 ml of dissolution medium, at paddle rotation of 50 rpm. The temperature of the dissolution medium was maintained at 37±0.5^{o}C. 1ml of sample was withdrawn at 10 minutes interval for 30 minutes and

exactly 1ml of fresh medium was added to the dissolution vessel to maintain the sink condition after each withdrawal. The samples were diluted to 10 ml using dissolution medium, filtered and were analyzed at 313 nm using a double beam UV-Visible spectrophotometer.

Uniformity of Weight[5, 6]

20 tablets were selected at random and weighed. Their average weight was determined. Not more than 2 of the individual weights may deviate from the average weight by more than percentage deviation as given in following table (Table 2) and none should deviate by more than twice that percentage.

Table 2: Average weight of tablet and percent deviation allowed as per I.P.

Sr. no.	Average weight of tablet (mg)	Percent deviation (%)
1.	130 mg or less	10
2.	More than 130 mg to 324 mg	7.5
3.	More than 324 mg	5

Estimation of Ranitidine tablet by UV spectrophotometric method (Use of Standard Absorptivity value) [8]

Accurately weighed 20 tablets were powdered. The powder equivalent to 150 mg of Ranitidine was transferred to 100ml volumetric flask and 20ml distilled water was added to dissolve the Ranitidine in it and then the volume was made to the mark with the same. This mixture was sonicated for 15 minutes and filtered through Whatmann filter paper. Further 1ml of sample was removed from the filtrate and was diluted to 100ml to obtain the strength of 15µg/ml (as theoretical concentration) and the respective absorbance was determined at λ max 313nm.

RESULT AND DISCUSSION

Tablet Description

All the brands of Ranitidine hydrochloride were examined for the color, shape and size by visual observation and it was observed that all seven brands comply with standards.

Hardness test

The Pharmacopoeia has not fixed any standard for the mechanical strength or hardness of the tablets. The manufacturer has employed their own test to ensure that their tablets will withstand the normal risk of handling and transportation. The hardness of the all seven brands of Ranitidine hydrochloride was found to be in the range of 2.5-4.5 Kg/cm^2 (Table 3)

Disintegration Test

Disintegration of a tablet means to break a tablet into smaller particles after swallowing. The time required to disintegrate the tablet is called “Disintegration time”. The rate of Disintegration depends upon the type of tablet. The tablets which are dissolved by slow solution in the mouth or

chewed or are to be dissolved in water before administration do not need a disintegration test. The test of disintegration is required in tablets which are swallowed.

The disintegration time of all the seven brands was determined (in minutes), as given in table (Table 3). It was found that all the seven brands passed the disintegration test for coated tablets as per IP 1996 and 2007 i.e. all the brands showed disintegration of tablets within 10 minutes.

Dissolution test

Dissolution testing is the most important way to study under in vitro conditions, the release of a drug from a solid dosage form and thus represents an important tool to assess the factors that affects the bioavailability of a drug from a solid preparation. During the dissolution of the drug the cumulative amount of the drug that passes in the solution is measured as a function of time.

Not less than 80% of the labeled amount of the Ranitidine to be released in 45 minutes as per USP specification. It was seen from the result (Table 3) that all the brands showed drug release ranging from a minimum of 82.97% to a maximum of 100.2% within 30 minutes, and hence all the brands passes the dissolution test.

Uniformity of Weight

It is desirable that every individual tablet in the batch should be uniform in weight, but a small variation in the weight of the tablet is liable to occur. Therefore a little variation is allowed in the weight of the tablet by the Pharmacopoeia.

The weight variation test was carried out for the seven brands. The average weight was determined and corresponding percent deviation was calculated. It was found that the weight of the individual tablet was within the limits. This indicates that all the brands complied with the weight variation test as per IP 1996 and 2007.

Estimation of Ranitidine tablet by UV spectrophotometric method (Use of Standard Absorptivity value)

The assay of an absorbing substance may be quickly carried out by preparing a solution in a transparent solvent and measuring its absorbance at a suitable wavelength. The wavelength normally selected is a wavelength of maximum absorption i.e. λmax. As per IP standards; Ranitidine HCl tablet contains not less than 90% and not more than 110% of the stated amount of Ranitidine.

It was observed from the result (Table 3) that the percent purity of all the brands was found within the range of 91.79% to 110%. Hence all the seven brands complies with IP standards.

Table 3: Biopharmaceutical and Chemical Equivalence of the seven brands of Ranitidine hydrochloride tablets.

Sample No.	Hardness (kg/cm^2)	Disintegration time (minutes)	Dissolution Profile (%CDR at the end of 30 mins.)	Uniformity of weight (gm)	Percent purity
1.	4.5±0.35	4±0.70	94.56%	0.308±0.0154	91.79%
2.	3.5±0.71	10±1.41	89.04%	0.307±0.0153	98.94%
3.	2.5±0.35	7±0.7	82.97%	0.256±0.0127	109.83%
4.	2.5±0.35	8±1.4	92.23%	0.230±0.0172	105.5%
5.	3±0.7	5±0.6	96.78%	0.300±0.015	109.6%3
6.	4.5±0.3	5±1.35	100.2%	0.225±0.017	110%
7.	3±2.12	10±2.2	96.96%	0.320±0.0160	106.49%

CONCLUSION

The ultimate objective of this research study was to analyze the quality status of Ranitidine HCl tablets with respect to the Biopharmaceutical and Chemical equivalence. For this purpose, the marketed samples of seven brands of Ranitidine HCl tablets were analyzed using established method and apparatus.

All the brands tested showed a good result for hardness, weight variation, disintegration and dissolution tests, and the U.V. analysis. The U.V. spectrophotometric method used for the assay of Ranitidine HCl was simple, inexpensive and reproducible.

The present study, although performed on a limited scale yet on the basis of professional judgment, the data reported in this study can help the Drug Control Authority to get an idea about the quality status of the marketed Ranitidine HCl tablet preparation.

This study emphasizes the need of constant surveillance and continuous evaluation of marketed drug products by Governments, Manufacturers and independent Research groups to ensure proper supply and availability of quality medicines.

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