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The Influence of Splitting on Content Uniformity, Weight Uniformity of Marketed Ciprofloxacin Hydrochloride Tablets in Bangladesh

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Research Article

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Abstract

Splitted tablets provide dose flexibility, ease of swallowing and may reduce the costs of medication. Factors influencing the performance of splitting are shape, size, curvature and thickness of the tablet and the form and deepness of the score line. The uniformity of mass of divided tablets and loss of mass was calculated. It was observed that a notable amount of weight was loss and a wide verity was observed in fractioned tablets which were extended more than 2%. It is much higher than the pharmacopoeial limit which was not more than 1%.The weight uniformity and content uniformity test were performed to observe the variation of weight uniformity and content uniformity and it was observed that weight loss was more in splitting by hand than splitting by knife. 30% weight variation was observed between two half of the tablets. Drug content variation in half-tablets appeared to be attributable primarily to weight variation occurring when tablets powder or fragment during the splitting process.

Keywords: *Splitting, weight uniformity, content uniformity.*

Introduction

Dose-related adverse effects of medications are a major problem in modern medical practice. The "correct" dose, based on drug company guidelines in package inserts, may not be correct for many patients. Broad variation in drug response among patients is a common phenomenon in clinical practice [1]. The ability to match doses to patients depends on the availability of multiple dose sizes and adequate dose-response information. For many drugs, especially those with long half-lives and/or a wide therapeutic range, dose fluctuations are unlikely to be clinically significant [2]. Removing tablets from foil packaging or exposing uncoated tablet surfaces may increase the rate of degradation of the active substance. This has important ramifications as the patient may get lower than intended dose and adverse effects may be increased by degradation products [3]. The tablet dissolution rate and absorption properties may also be affected when tablets are split. Tablets can be split manually into two portions by breaking with the fingers along a scored line, cutting with a knife or using a specially designed tablet splitter. Uneven division of the tablet or a degree of wasting may occur as some tablets crumble or break into more than two parts. Irregularly shaped tablets may be difficult to load and may not easily be split into equal halves [4].

Materials and Methods

Collection of Samples

A good number of companies of Bangladesh manufacture Ciprofloxacin. From these we have randomly selected ten brands for this study. These brands were collected from retail medicine shop of different areas of Dhaka, Bangladesh.

Tablets of ten different brands were coded as C01 to C10. The samples were properly checked for their physical appearance, name of the manufacturer, batch number, and manufacturing date and expiry date, manufacturing license number, D.A.R. number and maximum retail price at the time of purchase. No

samples were bought and analyzed whom date of expiry had already been expired.

Materials

Materials used in this project work are Hydrochloric Acid Fuming (37%) (Merc, Germany) and Iron Chloride ($FeCl_3$) (Merc, Germany). All chemicals and reagents were analytical grade ,UV-Visible Spectrophotometer, Model:LUV-300 (Labnics Equipment, California, USA), Electronic Balance, Model: TX423L (Shimadzu Corporation, Japan) and Dissolution Test Unit, Model: Disso DS 14000 (Pharma Chem Machineries, Mumbai, India) were used [5].

Determination of Uniformity of Weight of Ciprofloxacin Tablets

10 tablets were weighed individually. The average weight and standard deviation was calculated.5 of the 10 tablets were individually weighed. Each tablet was split by hand, resulting in 10 half tablets. Each half tablet was weighed. The average weight loss was calculated. Again, remaining 5 of the 10 tablets were individually weighed. Each tablet was split by knife, resulting in 10 half tablets. Each half tablet was weighed. And again the average weight and loss was calculated [6, 7].

Determination of Content Uniformity of Ciprofloxacin Tablets

A solution of 1% w/v ferric chloride was freshly prepared as well as 100 mcg/ml of standard ciprofloxacin. 5 tablets from each brand were crushed and 100 mg of the powdered samples were weighed, dissolved in 100 ml 0.1N hydrochloric acid (HCl) and further dilution was made to obtain 100 mg/ml for each brand. To 5 ml of each sample and standard, 1 ml of ferric chloride was added and made up to 50 ml with 0.1N HCl. The absorbance of each sample was taken at 438 nm against the blank reagent (1 ml ferric chloride solution made up to 50 ml with 0.1N HCl) with an ultraviolet spectrophotometer (LUV-300). The percentage content was calculated for each sample [8].

Results and Discussion

Weight Loss of Ciprofloxacin Tablets

The average weight of whole tablet were determined for all 10 collected brands and % of weight losses were calculated after tablets were halved by hand and knives. All the calculated data were tabulated below:

Table 1: Weight Loss of Ciprofloxacin Tablets due to Tablet Splitting by Hand

Average Weight (gm)				
Sample Code	Whole Tablet	Left Half	Right Half	%Weight loss
C01	0.738	0.369	0.363	0.81
C02	0.746	0.382	0.361	0.40
C03	0.794	0.425	0.366	0.38
C04	0.734	0.360	0.369	0.68
C05	0.846	0.428	0.415	0.35
C06	0.843	0.432	0.409	0.24
C07	0.727	0.369	0.356	0.28
C08	0.681	0.341	0.338	0.29
C09	0.792	0.338	0.449	0.63
C10	0.733	0.390	0.341	0.27

Figure- 1: % Weight Loss with respect to average weight of whole tablet due to tablet splitting by hand

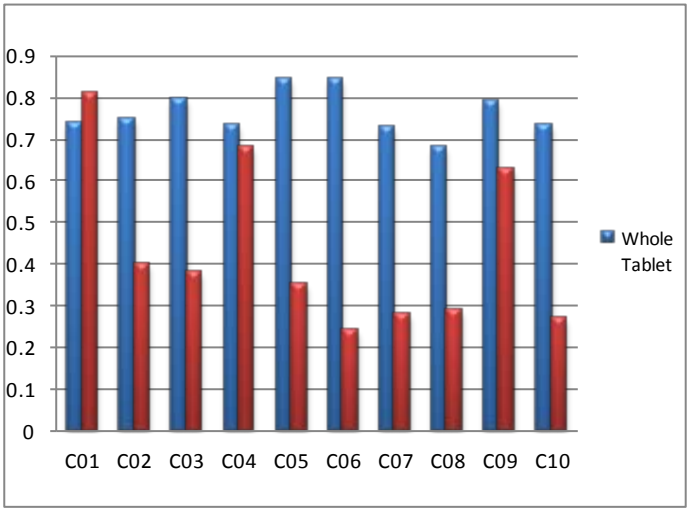


Table 2: Weight Loss Ciprofloxacin Tablets due to Tablet Splitting by Knife

Average Weight (gm)				
Sample Code	Whole Tablet	Left Half	Right Half	% Weight loss
C01	0.738	0.355	0.381	0.27
C02	0.746	0.370	0.372	0.54
C03	0.794	0.406	0.378	1.26
C04	0.734	0.345	0.375	1.91
C05	0.846	0.420	0.411	1.77
C06	0.843	0.435	0.391	2.02
C07	0.727	0.378	0.344	0.69
C08	0.681	0.334	0.343	0.59
C09	0.792	0.370	0.420	0.25
C10	0.733	0.375	0.342	2.18

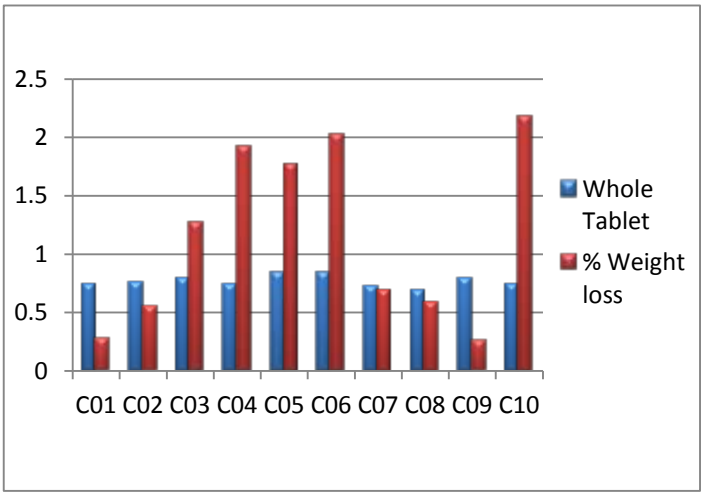


Figure- 2: % Weight Loss with respect to average weight of whole tablet due to tablet splitting by Knife

Table 1 & 2 and figure 1 & 2 showed that a substantial amount of drugs were lost even after a careful split of a tablet.

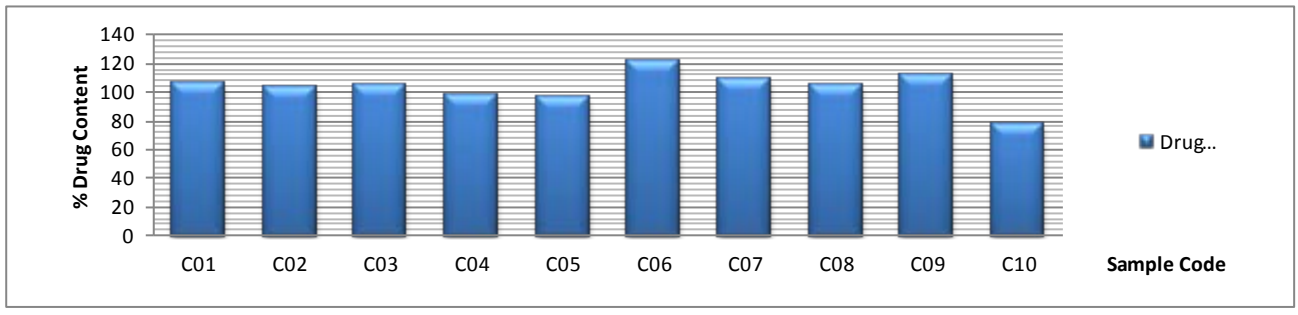
Content Uniformity of Ciprofloxacin Tablets

For all whole tablets studied, measured drug content expressed as a percent of target drug content and was tabulated in table 3 and presented in figure 3.

Table 3: Content Uniformity of Whole Ciprofloxacin Tablets

Sample	Drug Content (%)	Remarks
C01	106.62	Do not comply with BP Specification
C02	103.12	Comply with BP Specification
C03	105.17	Comply with BP Specification
C04	98.14	Comply with BP Specification
C05	96.62	Comply with BP Specification
C06	122.30	Do not comply with BP Specification
C07	108.90	Do not comply with BP Specification
C08	104.60	Comply with BP Specification
C09	111.60	Do not comply with BP Specification
C10	76.69	Do not comply with BP Specification

Figure- 3: Content Uniformity of Whole Tablets



It was found from the above table and figure that 05 (five) samples fail to comply USP specification, where 04 (four) contain more than the USP range and 01 (one) falls in short. All whole tablets also met the proxy USP specification for %RSD.

Conclusion

Tablets with single or multiple score lines allow the administration of a proportion of the tablet. In general, pharmacopoeial mass or weight uniformity compliance criteria do not consider the specific broken-tablet situation and consequently the general unit dose criteria are generally believed to be applicable to half-tablets and quarter-tablets as well. Only recently, there is the explicit addition that the subdivided parts of a tablet should indeed also comply with the content or mass uniformity requirements. In literature showed mass variations of broken tablets to be higher than whole or intact tablets [9].

From this study, it was found that a substantial portion of weight loss occurred during splitting of a tablet which can make a standard preparation into a sub-standard one. Weight loss was observed more in splitting by hand than splitting by knife. 30% weight variation was observed between two half of the tablets. Drug content variation in half-tablets appeared to be attributable primarily to weight variation occurring when tablets powder or fragment during the splitting process.

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

PEER REVIEW

Not commissioned; externally peer reviewed

CONFLICTS OF INTEREST

The authors declare that they have no competing interests