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Research Article

Exploring the Practice and Implications of Tablet Splitting in Pharmaceutical Care

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Abstract

Tablet splitting is a widely practised method for adjusting medication doses, reducing costs, and improving patient compliance. However, concerns regarding dose accuracy and content uniformity remain, especially for medications with a narrow therapeutic index, such as alprazolam. This study evaluates the weight variation, content uniformity, mechanical properties, and dissolution profiles of split alprazolam tablets. Scored and unscored alprazolam tablets were assessed using manual splitting and tablet cutters to determine the impact on dose accuracy. The results revealed significant variability in weight distribution and active pharmaceutical ingredient (API) content, particularly in unscored tablets. Additionally, the splitting method and tablet formulation affected the fragmentation and loss of mass. These findings underscore the need for caution when splitting alprazolam tablets, as inconsistent dosing may impact therapeutic efficacy and patient safety. The study emphasises the importance of regulatory guidelines and patient education to ensure safe and effective tablet splitting practices.

Keywords: Split tablets, Alprazolam, Scored and underscored.

1. INTRODUCTION:

Alprazolam is a short-acting drug of the benzodiazepine group used for the treatment of moderate-to-severe anxiety disorders and panic attacks. it is used as an adjunctive treatment for anxiety, sedative, hypnotic, anticonvulsant, and muscle relaxant properties [12]. The process of quality control is carried out to confirm the expected level of quality in a product. it includes the necessary actions a business conceives, essential to provide for the control and verification of certain characteristics of a product or service. There are certain quality parameters, like weight variation, friability, disintegration time, dissolution profile, etc., that demonstrate a significant effect on the drug product formulation. Therefore, the study was aimed at evaluating various in vitro quality control parameters of alprazolam tablet brands available in India[3–5].Tablet splitting is a known practice in both patient and outpatient settings. Several studies have examined the advantages of tablet splitting with regard to the health outcomes of patients, particularly with the gastric and psychiatric communities. These advantages include dose adjustment, ease of swallowing, and cost savings[6]. However, some studies revealed that splitting may results in the administration of an inaccurate dose, which can be of significant risk, especially if the split tablet formulation has a narrow therapeutic index[7]. Tablets are either hand split or split using a variety of tablet splitters for second or unscored tablets. with these devices, which are easy to use, the tablets are cut in half. studies have also reported increased patient adherence due to ease of splitting as well as cost benefit[8].

Some studies have found an impact of tablet splitting on the weight and content uniformity of the resulting tablet halves. Elderly patients performing splitting may be of particular concern because of their reduced compliance and dexterity[9]. i.e., the ability to properly split the tablets. Results from the absorption and dissolution of split tablets have also shown that this population may be disproportionate. Compared to hand splitting and tablet cutter procedures, a higher accuracy of tablet splitting was reported for tablet cutting devices versus hand splitting[10]. Alprazolam is a Neuronal hyperpolarisation drug with a half-life of 11-16hr.of renal excretion. It is used to treat anxiety, panic disorders or psychiatric disorders and depression. The purpose of our current

study is to investigate the difference in the weight variation of the Alprazolam split tablets (model drug) using two different tablet splitting methods and to analyse the impact of splitting Alprazolam tablets on certain physical parameters such as the friability, dissolution and disintegration.

2. MATERIALS

Alprazolam tablets (0.5 mg; Micro labs Ltd., India) were obtained from a local pharmacy (Basaveshwara Drug House, Davanagere, India). To split the tablets into equal half, we utilised a wolphin pill cutter from Amazon India. We procured potassium dihydrogen orthophosphate, phosphoric acid, potassium hydroxide, and sodium hydroxide of AR quality (SD Fine Chemicals Ltd.) From vasa scientific supplies. All of the trials utilized water that had been distilled twice.

3. METHODOLOGY

3.1. Sample preparation

Alprazolam tablets were purchased from Basaveshwara Drug House located at Davangere, Karnataka. The samples were properly checked for their manufacturing license numbers, batch numbers, and date of manufacture and expiry dates. The entire tablet brand contained a labelled shelf life of three years from the date of manufacture, and before two years of the labelled expiry date, it was taken for evaluation[11]. The labelled active ingredient was 0.5mg of alprazolam, and all were packaged in a strip. The reference standard of alprazolam (99.87%) was collected from Micro Labs Limited, Bangalore, India.

3.2. Evaluation studies

The evaluation studies of the whole tablet of alprazolam were carried out. Then the 20 tablets were split by hand, knife, and a commercially available tablet cutter (Wolpin 1 Pc Pill cutter). The weights of individual cut tablets were checked by an analytical balance (scale tech). the individual tablet parts are obtained from the right or left part of the operator's hand, knife, or cutter. Split tablets were tested for weight variation and loss of weight. The content uniformity of the split tablets was tested[12].

3.3. Thickness and diameter

A vernier calliper was used to measure the thickness of alprazolam tablets. A random sample of tablets was measured, and the average thickness was reported.

3.4. Weight variation test

A weight variation test was conducted on twenty individual alprazolam tablets to evaluate the consistency of dosage form mass. Each tablet was weighed separately using a calibrated analytical balance, and the mean tablet weight was calculated. The deviation of each tablet from the mean weight was assessed, and the percentage variation was determined according to pharmacopeial standards.

The tablets were then bisected into left and right halves using a pill cutter, and weight variation was assessed independently for each half-tablet. Each half-tablet was weighed, and the mean weight and percentage deviation were calculated to evaluate weight uniformity following subdivision. All measurements were performed under controlled laboratory conditions, and the analytical balance was calibrated prior to use to ensure the accuracy and reliability of the results.

3.5. Hardness test

The hardness of alprazolam tablets was evaluated using a Monsanto hardness tester. Tablets were randomly selected and placed between the anvils of the instrument, where diametric force was applied until the tablets fractured. Hardness was recorded in kg/cm^2 for each tablet, and the mean value was calculated. The instrument was calibrated prior to analysis, and all measurements were performed under controlled laboratory conditions.

3.6. Friability test

Alprazolam tablet friability was assessed using Yamato Friabilator. Tablets were weighed prior to testing, placed in the friabilator, and rotated at 25 rpm for 4 minutes, equivalent to 100 revolutions. Following the test, tablets were de-dusted and reweighed. the percentage weight loss, representing friability, was calculated to evaluate tablet mechanical strength. the procedure followed pharmacopeial standards, and all measurements were conducted under controlled laboratory conditions.

The percentage friability was calculated using the following formula:

$$Friability(\%) = \frac{(Initial\ weight - Final\ weight)}{initial\ weight} \times 100$$

3.7. Drug content

Both whole and divided(half) tablets were analysed using a double-beam UV-Visible spectrophotometer (Shimadzu UV-1800). Twenty alprazolam tablets (0.5 mg each) were accurately weighed and ground into a fine powder with a mortar and pestle. A quantity equivalent to 0.5 mg of alprazolam was measured from the powder, transferred to a 100 ml volumetric flask, dissolved in methanol, and diluted to obtain a final concentration of 0.5 mg/ml.

The solution was thoroughly mixed and sonicated for 5 minutes at room temperature to ensure complete dissolution of the drug. After sonication, the solution was filtered through a 0.22 µm polypropylene membrane filter under vacuum. Serial dilutions were prepared using methanol as the solvent, and absorbance was measured at 260 nm against an appropriate blank. The same procedure was applied to split tablets to evaluate drug content uniformity after subdivision.

3.8. Disintegration test

The disintegration test for Whole and split tablets was performed using 500 ml of phosphate buffer at pH 7.4, maintained at 37 ± 0.5°C to simulate physiological conditions. Each divided tablet was placed in the basket-rack assembly of the disintegration apparatus (LAB INDIA, Model No.2678R37) located in the instrumentation room. The basket was immersed in the buffer medium, and the apparatus was operated according to standard protocol. Disintegration time was

recorded as the point at which no visible residue of the tablet remained on the mesh screen, indicating complete disintegration in accordance with pharmacopeial standards.

3.9. Dissolution test

A phosphate buffer solution with a pH of 6.0 ± 0.1 was prepared for the dissolving testing of both whole and split tablets. The buffer was prepared by dissolving 80 g of potassium dihydrogen orthophosphate in 1 litre of water, followed by the addition of 20 g of dibasic potassium phosphate. The pH was adjusted to 6.0 ± 0.1 by gradually adding phosphoric acid or potassium hydroxide solution under continuous agitation, with pH monitored throughout. This buffer solution served as the dissolution medium for evaluating split and whole tablets, ensuring consistent and controlled conditions during dissolution testing.

4. RESULTS

4.1. Weight variation test

The weight variation of twenty whole alprazolam tablets was assessed to determine dose consistency. The mean tablet weight was 0.1407g, the average percentage deviation from the mean was 1.23%, indicating minimal variability among individual tablets. The standard deviation expressed as a percentage was 1.53% further demonstrating strong weight consistency. All intact tablets complied with United States Pharmacopoeia (USP) weight variation standards for tablets more than 130 mg, thereby confirming consistency in the manufacturing process.

The mean percentage difference for the left half tablets was 7.25%, with a standard deviation of 6.41% and a relative standard deviation (RSD) of 88.50%,

indicating substantial variability following tablet subdivision. The right half-tablets exhibited a mean percentage difference of 7.18%, a standard deviation of 6.76%, and an RSD of 94.13%. The elevated variability observed in both left-and right-half tablets demonstrates that tablet splitting significantly affects weight consistency compared with whole tablets.

Table 1: Statistical analysis of weight variation and precision for left-half, right-half, and whole tablets.

	Left half tablets	Right half tablets	Whole tablets
Mean difference	7.25%	7.18%	1.23%
Standard deviation	6.41%	6.76%	1.53%
Relative standard deviation (RSD)	88.50%	94.13%	95.96%

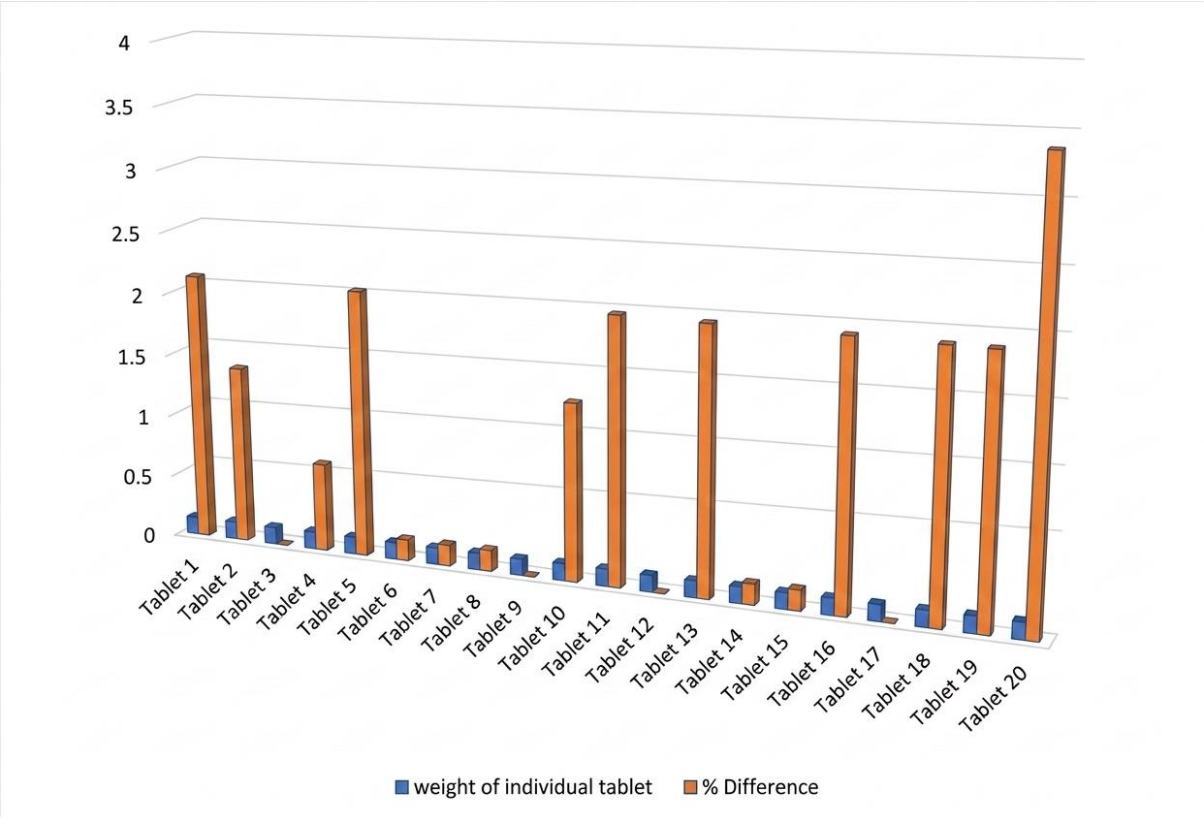

Figure 1: Tablet Weight Uniformity and Deviation Analysis.

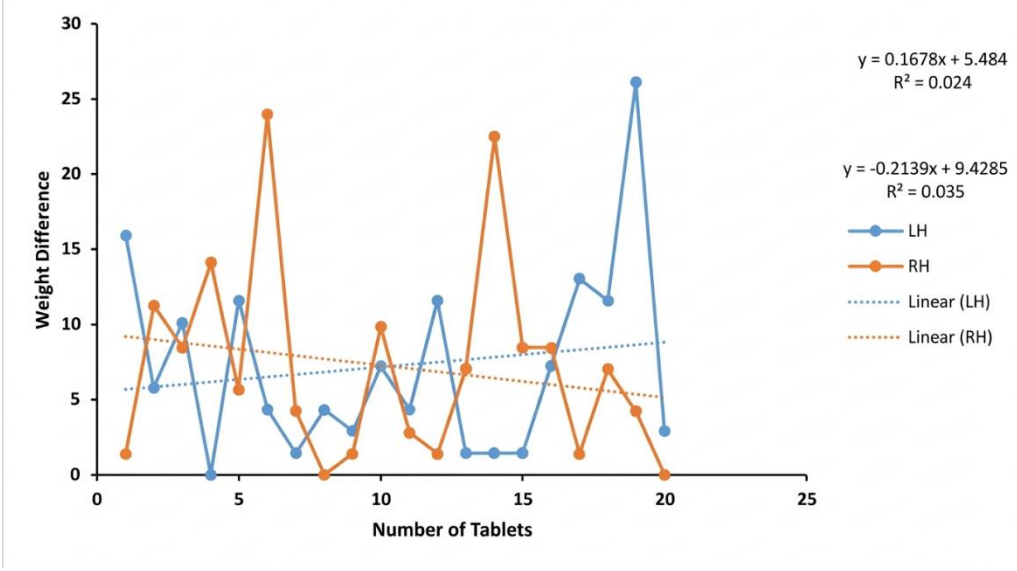

Figure 2: Weight Variability Analysis of Split Alprazolam Half-Tablets

4.2. Hardness test

Table 2: Summary of statistical analysis (Mean Difference, SD, and RSD) comparing weight variation between left-half, right-half, and whole tablets.

Average weight	Difference in weight (g)	% Difference
0.0692 g	-0.011	15.942
0.0692 g	0.004	5.7997
0.0692 g	-0.007	10.144
0.0692 g	0	0
0.0692 g	0.008	11.595
0.0692 g	-0.003	4.347
0.0692 g	0.001	1.449
0.0692 g	0.003	4.347
0.0692 g	-0.002	2.898
0.0692 g	-0.005	7.246
0.0692 g	0.003	4.347
0.0692 g	0.008	11.594
0.0692 g	0.001	1.449
0.0692 g	0.001	1.449
0.0692 g	0.001	1.449
0.0692 g	0.005	7.246
0.0692 g	0.009	13.043
0.0692 g	0.008	11.594
0.0692 g	-0.018	26.086
0.0692 g	-0.002	2.898
		Average difference 7.24

4.3. Disintegration test:

A disintegration test was performed on six whole alprazolam tablets (0.5 mg) and six half tablets, using pure water as the disintegrating medium at 37±2°C. All whole alprazolam tablets disintegrated completely within 92 seconds, which is well below the pharmacopeial limit of 15 minutes for uncoated tablets. These results demonstrated that the formulation possesses adequate disintegration characteristics, enabling rapid tablet breakdown in the dissolution medium.

The split tablets exhibited a significantly reduced disintegration time of 32 seconds. This accelerated disintegration is attributed to the increased surface area and exposure of the tablet core following subdivision, which facilitates rapid penetration of the disintegration medium. Despite the shorter disintegration time, the divided tablets also complied with pharmacopeial standards.

These findings indicate that both whole and split alprazolam tablets meet pharmacopeial disintegration standards, with tablet splitting significantly reducing disintegration time. This observation is relevant to immediate-release formulation, as accelerated disintegration may influence the onset of drug release, particularly in low-dose tablets.

Table 3: Comparative disintegration times for right-half and left-half tablet segments.

Number of tablets	Time of disintegration
6 tablets (right half)	22 min
6 tablets (left half)	20 min

4.4. Dissolution test

The dissolution test was conducted on six whole alprazolam tablets and their respective split halves using a USP Apparatus II (paddle method) with the dissolution

medium maintained at 37 ± 0.5 °C. The paddle rotation speed and medium composition were set in accordance with specified pharmacopeial requirements for alprazolam tablets. The whole tablets achieved complete dissolution within, while the split tablet analysis revealed dissolution times of for the right half and for the left half. These findings are well within the pharmacopeial acceptance criteria specifically the USP requirement of not less than release in confirming satisfactory and consistent in-vitro drug release characteristics for both full and split tablets within this batch.

4.5. Friability test

The friability test was conducted on a batch of twenty 0.5mg alprazolam tablets to evaluate mechanical resistance to abrasion and breakage. For the whole tablets, the initial total weight of 2.36g was reduced to 2.25g after testing, representing a total weight loss of 0.11g. Individual whole tablet friability values ranged drastically from 0% to 23.07%, resulting in a mean friability of 8.94% (± 8.33%SD), which significantly exceeds the accepted pharmacopeial limit of 1%.

In comparison, the split tablet analysis yielded lower mean weight differences of 0.348% for the left halves and 0.270% for the right halves. However, these split halves exhibited very high Relative Standard Deviations of 66.58% and 72.32% respectively, echoing the high RSD of 93.15% found in the whole tablets. Collectively, these results indicate poor mechanical strength and high variability throughout the batch, necessitating urgent optimization of the formulation or manufacturing process to ensure structural integrity.

Table 4: Individual and average friability results for tablets, showing weight loss and percentage friability.

Weight of tablet before test (w1) in g	Weight of tablet after test (w2) in g	Difference in weight (W1-W2) in g	% Friability
0.13	0.12	0.01	7.692
0.13	0.11	0.02	15.38
0.13	0.13	0.0	0
0.13	0.12	0.0	0
0.13	0.13	0.02	13.33
0.13	0.12	0.02	14.28
0.13	0.12	0.0	0
0.13	0.10	0.03	23.07
0.13	0.13	0.0	0
0.13	0.12	0.01	7.692
2.36 g		**0.11**	**Avg, % friability 4.66**

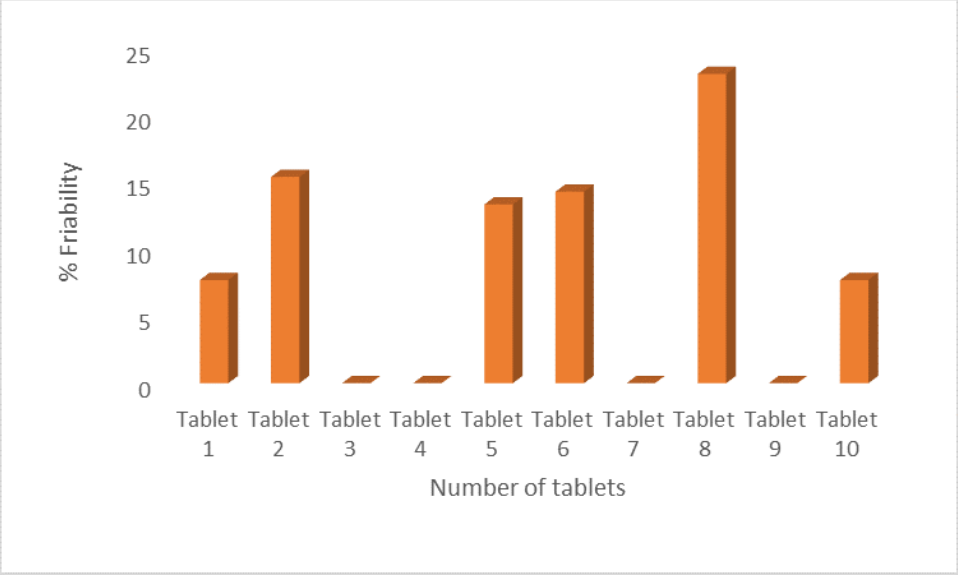

Figure 3: Distribution of percentage friability across 10 individual tablet samples.

Table 5: Statistical summary of weight variation for left-half and right-half tablets, including mean difference, standard deviation, and relative standard deviation.

	Left half tablets	Right half tablets
Mean difference	0.348%	0.270%
Standard deviation	1.348%	1.212%
Relative Standard Deviation	66.58%	72.32%

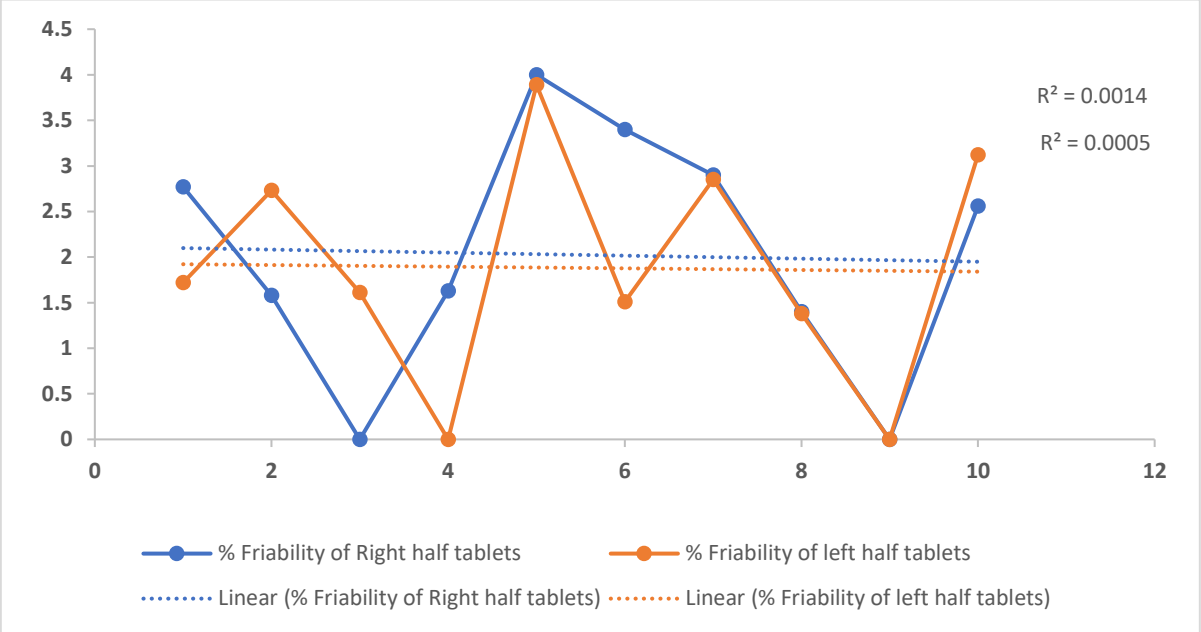

Figure 4: Comparative analysis of percentage friability for right-half and left-half tablet segments across 10 samples with linear trendlines.

5. DISCUSSION

The evaluation of 0.5 mg alprazolam tablets reveals that while intact tablets consistently meet USP standards for weight and disintegration, the process of subdivision introduces significant dosing inaccuracies. The observed weight variation, with differences exceeding 7% between halves, and an alarmingly high friability of 8.94%—well beyond the 1% pharmacopeial limit—suggest that the mechanical integrity of this specific formulation is insufficient for splitting. The drastic reduction in disintegration time from 92 to 32 seconds for split halves further suggests that subdivision may alter the pharmacokinetics of the drug by increasing the surface area exposed to gastric fluids. These findings align with previous research indicating that manual or mechanical splitting of unscored, high-potency medications often fails to achieve the uniformity required for safe therapeutic outcomes, particularly for drugs with a narrow therapeutic index like alprazolam.

6. CONCLUSION

This study concludes that splitting 0.5 mg alprazolam tablets significantly compromises dose uniformity and structural integrity, directly contradicting the goal of maintaining accurate medication delivery. The data supports the new hypothesis that high baseline friability is the primary mechanism behind the excessive fragmentation and mass loss observed during subdivision. Given the high relative standard deviation (RSD) in split halves and the potential for fluctuating plasma levels, we conclude that tablet splitting is not a reliable method for dose adjustment for this formulation. These results emphasize the need for clinicians to exercise caution when recommending split doses and highlight the necessity for manufacturers to improve scoring designs and tablet hardness to ensure patient safety.

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Author contributions: Vijay Pujar served as the corresponding author, designing the study and performing core experimental work on weight variation, content uniformity, and mechanical properties. Prashanth K U executed the laboratory experiments and assisted in data collection for dissolution and disintegration profiles. Nirmal T H conceptualized the

split tablet framework and provided the theoretical foundation for the implications of subdivision in pharmaceutical care. Pradeep H K and Yashwanth A M conducted the overall critical review of the article, verified scientific accuracy, and performed the technical and grammatical editing of the final manuscript.

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Ethical Approval: Not applicable. This study involved *in vitro* laboratory testing of commercially available pharmaceutical products and did not involve human subjects or animal experiments.

REFERENCES

[1] Greenblatt DJ, Wright CE. Clinical pharmacokinetics of alprazolam: therapeutic implications. Clinical pharmacokinetics. 1993 Jun;24(6):453-71.

[2] Alprazolam (Xanax): Uses & Side Effects n.d. https://my.clevelandclinic.org/health/drugs/19498-alprazolam-tablets (accessed March 5, 2025).

[3] Kimaro E, Tibalinda P, Shedafa R, Temu M, Kaale E. Formulation development of chewable albendazole tablets with improved dissolution rate. Heliyon. 2019 Dec 1;5(12).

[4] Rahman M, Akter K, Rahman M, Shorna J, Lahiry A. Comparative Analysis of In vitro Quality Parameters of Different Brands of Marketed Ciprofloxacin Tablets Available in Bangladesh. AcademiaEdu n.d.

[5] Teshome Y, Kassahun H, Said Y, Wondesen A. In vitro Comparative Quality Assessment of Different Brands of Hydrochlorothiazide Tablets Marketed in Northeast Ethiopia 2023.

[6] Freeman M, … WW-TCP, 2012 undefined. Tablet splitting: A review of weight and content uniformity part 1 of a 2-part series. Next month: Table splitting—A review of the clinical and economic outcomes and. IngentaconnectCom n.d.

[7] Quinzler R, Gasse C, Schneider A, Kaufmann-Kolle P, Szecsenyi J, Haefeli WE. The frequency of inappropriate tablet splitting in primary care. Eur J Clin Pharmacol 2006;62:1065–73. https://doi.org/10.1007/S00228-006-0202-3.

[8] Habib WA, Alanizi AS, Abdelhamid MM, Alanizi FK. Accuracy of tablet splitting: Comparison study between hand splitting and tablet cutter. Saudi Pharmaceutical Journal : SPJ 2013;22:454. https://doi.org/10.1016/J.JSPS.2013.12.014.

[9] Tahaineh LM, Gharaibeh SF. Tablet splitting and weight uniformity of half-tablets of 4 medications in pharmacy practice. J Pharm Pract 2012;25:471–6. https://doi.org/10.1177/0897190012442716.

[10] Olgac S, Yilmaz Usta D, Incecayir T. Comparison of tablet splitting techniques for dosing accuracy of nebivolol tablets: Hand splitting versus tablet cutter and knife. Saudi Pharm J 2021;29:1486–91. https://doi.org/10.1016/J.JSPS.2021.11.005.

[11] Introduction to Tablet Splitting n.d. https://chatgpt.com/c/683a8a4e-a07c-8013-87f8-5bb1fe2c09c6 (accessed May 31, 2025).

[12] Okamoto N, Higashino M, Yamamoto H, Sugano K. Dissolution Profiles of Immediate Release Products of Various Drugs in Biorelevant Bicarbonate Buffer: Comparison with Compendial Phosphate Buffer. Pharmaceutical Research 2024;41:959–66. https://doi.org/10.1007/S11095-024-03701-6.

[13] Machado JC, Lange AD, Todeschini V, Volpato NM. Development and Validation of a Discriminative Dissolution Method for Atorvastatin Calcium Tablets using in vivo Data by LC and UV Methods. AAPS PharmSciTech 2013;15:189. https://doi.org/10.1208/S12249-013-0053-Z.

[14] Vranić E, Uzunović A. INFLUENCE OF TABLET SPLITTING ON CONTENT UNIFORMITY OF LISINOPRIL/ HYDROCHLORTHIAZIDE TABLETS. Bosn J Basic Med Sci 2007; 7:328. https://doi.org/10.17305/BJBMS.2007.3022.

[15] Rosenberg JM, Nathan JP, Plakogiannis F. Weight Variability of Pharmacist-Dispensed Split Tablets. Journal of the American Pharmaceutical Association (1996) 2002; 42:200–5. https://doi.org/10.1331/108658002763508498.

[16] Chaity NI, Archie SR, Ahmed N. Preparation and In vitro Evaluation of Orally Disintegrating Tablets (ODTs) of Alprazolam. Dhaka University Journal of Pharmaceutical Sciences 2019; 18:129–33. https://doi.org/10.3329/dujps.v18i1.41430.