https://doi.org/10.26682/sjuod.2022.25.2.41
Journal of University of Duhok., Vol. 25, No.2(Pure and Engineering Sciences), Pp 451-457, 2022

# PHARMACEUTICAL EVALUATION OF ACETAMINOPHEN TABLETS MARKETED IN DUHOK CITY-KURDISTAN

SUHAIL SABAH SHABA[*], DILVEEN MOSSA SULAIMAN[*], RABIE GABRIEL ABDULLAH[*], SINEM SINO SULAIMAN[**], SURDASH ISMAIL DAWOOD[**], HADI ISKENDER CHICHO[**] and BAREEN MUHAMMED HASSAN[**]

[*]College of Pharmacy, University of Duhok, Kurdistan Region-Iraq
[**]Graduated Pharmacist, College of Pharmacy, University of Duhok, Kurdistan Region-Iraq

***(Received: October 8, 2022; Accepted for Publication: November 28, 2022)***

## ABSTRACT

**Tablets are the most frequently administered oral solid dosage form. The presence of various brands at varying costs from different companies requires verification to see whether they pass control tests and to determine which one is more effective and economical.**

**Eight different brands were chosen, and their weight uniformity, hardness, friability, disintegration time, and drug content were tested. Then, prices were compared to quality to determine which brand was more effective and economical.**

**All brands selected pass the United States Pharmacopeia (USP) tests for weight variation, friability, and disintegration time. Maximum weight variation was expressed by brand C, whereas brand A expressed the minimum. Brand E has the highest friability, while brand D has the lowest. The maximum disintegration time expressed is by brands E and G, while the minimum is expressed by brands B, D, F, and H. All the selected brands have enough hardness to withstand handling and manufacturing processes, except brand A, C, and G shows hardness somewhat outside the acceptable range, but this did not affect their disintegration time. According to USP, only two brands (A and H) pass the drug content test, with brand H having the maximum drug content and brand E the minimum.**

**A and H were determined to be the most cost-effective brands based on a correlation between quality and prices.**

***KEYWORDS*:** Brand Evaluation, Paracetamol, Hardness, Friability, Disintegration time, Drug content test.

## INTRODUCTION

Most pharmaceuticals are administered to the body via the oral route; therefore, most drug dosage forms are formulated for oral ingestion, and tablets are the most frequently administered, primarily for ease of administration and safety (Aulton & Taylor, 2018). The increase in the number of drug products from numerous manufacturers has placed people involved in delivering health care in a position to select one from among several seemingly equivalent products. A large percentage of prescription drugs available were obtained from more than one source, and variable clinical responses to these dosage forms supplied by two or more drug manufacturers were documented. The reasons for such variation in responses may include formulation ingredients used, methods of handling, packaging, and storage, and even the rigors of in-process quality control (Covington, 1992). Thus, to ensure interchangeability, it is necessary to determine their pharmacological and therapeutic equivalence. (Odeniyi et al., 2003).

The quality of a pharmaceutical product can be assured by evaluating different physical characteristics of the product, such as weight variation, hardness, friability, disintegration, dissolution, and assay tests following standard methods given by different drug control authorities like USP and BP. Evaluation of the physical characteristics can ensure the drug's quality and impart optimum therapeutic activity and bioavailability (WHO, 2007).

An important physical property of tablets is their mechanical strength which is expressed in terms of hardness and friability (Allen & Ansel, 2014). The tablet must have adequate hardness to withstand chipping, abrasion, or breakage under storage, transportation, and handling



dilven.Sulaiman@uod.ac

conditions. The friability of tablets must be as limited as possible and within the accepted value mentioned in pharmacopeias (Troy, 2005). It is vital to ensure that the formulated tablet will withstand stresses like mechanical shocks and abrasion during the manufacturing, packing, and transportation processes without damage (British Pharmacopoeia, 2009).

To ensure the uniformity of dosage units, each unit in a given batch must contain the active ingredient within a narrow range around the label claim. Either the content uniformity or the weight of the tested units can be used to assess the uniformity of dosage units. (Pharmacopeia, 2009).

A tablet that fails to disintegrate or disintegrates slowly may result in incomplete absorption or delay the drug's onset of action. The compaction force used in tablet manufacture can affect disintegration; the higher the force, the longer the disintegration time (Aulton & Taylor, 2018).

Acetaminophen (AAP), its recommended international nonproprietary name is paracetamol, is one of the most widely used over-the-counter medications. It has analgesic and antipyretic effects but low anti-inflammatory activity; it occupies a unique position among analgesic drugs (Bertolini et al., 2006).

This study aims to investigate and compare the physical equivalence and drug content of different brands of Acetaminophen 500 mg prepared by various pharmaceutical industries under different trade names. Also, to know the relation between the price and quality of various brands.

## MATERIALS AND METHODS

### Materials

The AAP tablets of eight brands supplied by Norseen medicine store were used to perform this study as listed in the table (1) in addition to DW (distilled water) supplied by the College of Pharmacy-Duhok University and AAP pure powder supplied by Awamedica medicine factory.

**Table (1):** The AAP tablets of various brands

**Table (1):** The AAP tablets of various brands

| Code | Price ID/10 tabs |
|---|---|
| E | 1000 |
| D | 2500 |
| H | 625 |
| G | 1250 |
| F | 625 |
| B | 600 |
| A | 625 |
| C | 250 |

### Instruments

The instruments used in this study are shown in table (2).

**Table (2):** The instruments and their manufacturers

| Instruments | Manufacturer |
|---|---|
| Analytical balance | Denver Instrument, Germany |
| Tablet hardness tester | HM-Pharmachine, China |
| Tablet disintegration tester | HM-Pharmachine, China |
| Tablet friability tester | HM-Pharmachine, China |
| *UV-Spectrophotometer* | JENWAY, Bibby Scientific UK |

**Methods**

**Preparation of AAP Standard Stock Solution**

The standard stock solution of AAP was made by dissolving 10 mg of AAP in a specific volume of DW, transferring 100 ml volumetric flask, then completing the volume to 100 ml with DW to make 0.1 mg/ml standard stock solution of AAP.

**Determination of λ max (maximum Lambda) for AAP Solution**

Different volumes (0.5, 1, 2, 2.5, 3 ml) of 0.1 mg/ml standard stock solution of AAP were accurately measured, transferred into a series of 10 ml volumetric flasks and complete the volume with DW to 10 ml to make solutions of various concentrations (0.005, 0.01, 0.02, 0.025, 0.03 mg/ml). Then all dilutions were scanned in UV-spectrophotometer at wavelengths between (200 – 400 nm) against blank (DW only). The wavelength at which maximum absorbance occurs will be the λ max.

**Preparation of Calibration Curve of AAP Solution**

The UV-absorbance of previously prepared dilutions was measured using UV-spectrophotometer at λ max wavelength. Then the UV-absorbance values of previously prepared dilutions were plotted against their concentrations to draw a calibration curve of the AAP solution.

**Data Analysis**

Data analysis was performed using Microsoft Excel 2016.

**Evaluation of Various Brands of AAP Tablets**

**1. Mass Uniformity**

The mass uniformity (not the content uniformity) is used to determine the uniformity of dosage forms because the selected brands were uncoated and contained more than 25 mg and more than 25% of AAP. According to USP, mass uniformity is enough to determine the uniformity of dosage forms. Mass uniformity is determined by weighing 20 tablets of each brand individually, then the average mass and standard deviations were calculated. The tablets met the requirements if no individual mass deviated from the average mass by ±5% w/w (weight by weight); if it deviated, it must be not more than two tablets and not more than ±10% w/w (Khreit et al., 2017). The percentage of weight variation can be measured using the following formula (Nasrin et al., 2011):

$$\text{Weight variation \%} = \frac{\text{average w} - \text{individual w}}{\text{average w}} \times 100$$

**2. Hardness Test**

The test was carried out using HM-Pharmachine hardness tester. The mean crushing strengths (average hardness values) were determined by dividing the total hardness by the number of tablets; three tablets were used for testing each brand (Pharmacopeia, 2009).

**3. Friability Test**

The test was performed using HM-Pharmachine friabilator. Since the average weight of a tablet from the selected brands is 650 mg, 6.5 g of tablets (about ten tablets) from each brand were weighed, dusted, and placed in a friability tester. The tester was set to rotate at a speed of 25 rpm for 4 minutes (mean 100 rounds). After minutes the sample was removed from the tester, carefully dusted, and weighed (Pharmacopeia, 2009). The percentage of weight loss is calculated using this formula (Vv et al., 2013):

$$Friability\ \% = \frac{w\ initial - w\ final}{w\ initial} \times 100$$

**4. Disintegration Time Test**

The test was performed using HM-Pharmachine disintegrator. The beaker of the tester is filled with 900 ml of DW, and the temperature inside the beaker is controlled to 37±0.5˚C. From each brand, six tablets were applied to the tester, then directly started to run. The tester was run for about 30 cycles/minute.

**5. Content Assay**

Twenty tablets were selected from each brand, weighed and finely powdered, transferred an accurately weighed portion of powder equivalent to 250 mg of AAP to a 500 ml volumetric flask, dissolved with enough DW, then completed the volume to 500 ml. 1 ml of that solution is filtered with a 0.45 µm syringe filter and transferred to a 100 ml volumetric flask, and complete the volume to 100 ml. The absorbance of the final solution was measured at λ max (previously determined) using UV-spectrophotometer. The calibration curve was used to figure out the concentration and the percentage of the content. The tablets must have between 90% and 110% of the labeled amount of AAP (British Pharmacopoeia, 2009 and Pharmacopeia, 2009).



dilven.Sulaiman@uod.ac

## Results

### Determination of λ max for AAP solution

Two bands were demonstrated, showing maximum absorbance at wavelength 244 nm, regarded as λ max.

### Calibration Curve for AAP Solution

Figure (1) shows the calibration curve of AAP in DW at λ max (244 nm) wavelength and 37°C temperature.

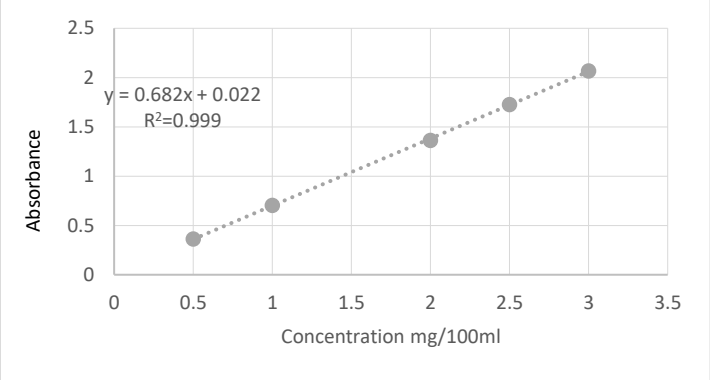


**Fig. (1):** Calibration curve of AAP in DW at λ max (244 nm) wavelength and 37°C temperature

### Evaluation of Different Brands of AAP Tablets

#### 1. Mass Uniformity

Table (3) shows the average weight of different brands of AAP, ranging from 0.555 g (brand B) to 0.686 g (brand E); also, the maximum weight variation was shown by brand C, while the minimum weight variation was shown by brand A.

**Table (3)** The average weight of various brands of AAP.

| Brands | Average weight (g) ± SD |
|---|---|
| A | 0.642 ± 0.0023 |
| B | 0.555 ± 0.0063 |
| C | 0.608 ± 0.0128 |
| D | 0.677 ± 0.0077 |
| E | 0.686 ± 0.0099 |
| F | 0.561 ± 0.0066 |
| G | 0.591 ± 0.0065 |
| H | 0.649 ± 0.0064 |

### Hardness

Figure (2) shows the average hardness of each brand; brand C shows maximum hardness, while brand D shows minimum hardness.

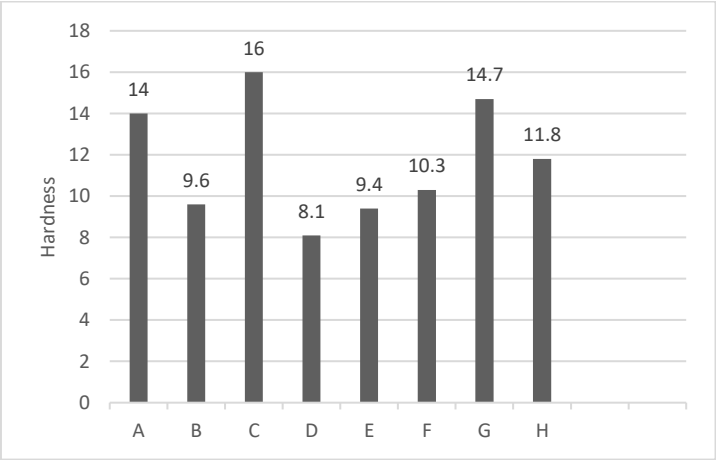


**Fig. (2):** The average hardness

**Friability**

It has been found that brand D had higher durability than other brands, while brand E had lower, as shown in figure (3); brand D showed minimum weight loss, while brand E showed maximum weight loss.

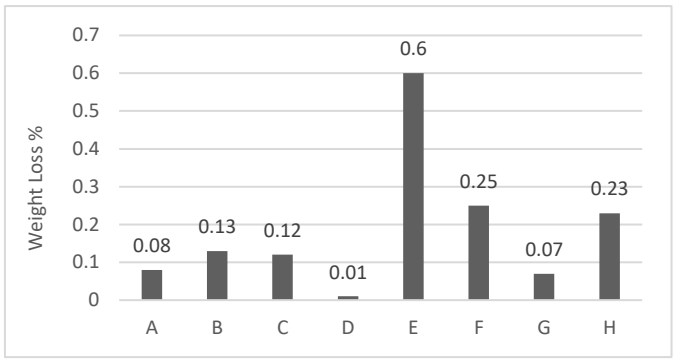


**Fig. (3):** The percentage of weight loss

**Disintegration Time**

Figure (4) shows that tablets of all tested brands showed an average disintegration time between (0.8 – 4) minutes the average disintegration times of brands E and G were the longest (4 min), and brands B, D, F, and H showed a minimum average disintegration time (0.8 min). As opposed to that, brands A and C showed relatively medium average disintegration time (2.5) and (2) minutes, respectively.

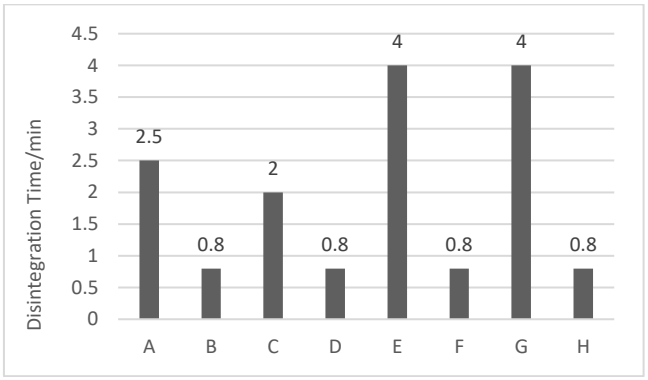


**Fig. (4):** Average disintegration time

**Drug Content**

Figure (5) shows that the percentages of drug content were between 63% (brand E) and 95% (brand H).

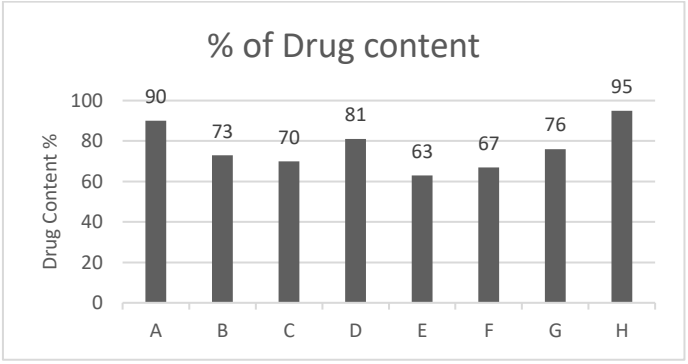


**Fig. (5):** The percentage of drug content

**Prices**

As is shown in figure (6), the price range from 250 ID/10 tablets for brand C to 2500 ID/10 tablets for brand D.



dilven.Sulaiman@uod.ac

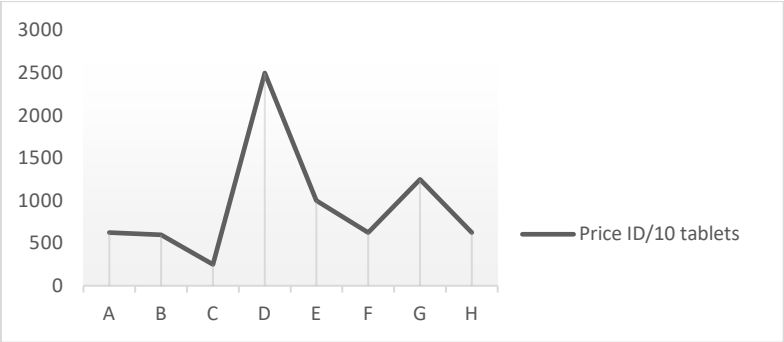


**Fig. (6):** The price of various brands of AAP

## DISCUSSION

The results of mass uniformity indicate an accepted preparation method and good manufacturing practices; because all the brands meet the requirement of USP for mass uniformity, no individual mass deviates from average weight by more than ±5% w/w (Troy, 2005).

The resistance of the tablet to chipping, abrasion, or breakage under storage, transportation, and handling conditions before usage depends on its hardness, and according to USP, the ordinary tablet hardness should range between 2.5 to 10 kg/cm$^2$, the hardness of all brands we tested is enough to resist these conditions, and at the same time it is within the acceptable range provide satisfactory disintegration and dissolution results; except brand A, C, and G shows hardness outside the acceptable range and this may affect tablet disintegration time because if the tablet is too hard, it may not disintegrate in the required time to meet dissolution specifications (Pharmacopeia, 2009 and Nasrin et al., 2011)

The friability results indicate that all brands resist the stress of mechanical shocks and abrasion during the manufacturing, packing, and transportation processes. The tablets met the USP requirements if no tablet was cracked, cleaved, or broken after tumbling in the tester and if the maximum mean weight loss was not greater than 1% (Pharmacopeia, 2009).

The disintegration results indicate an excellent disintegration time for all brands; this could be due to enough amount and a suitable type of disintegrant used because the disintegration time of the tablet is a function of the composition and manufacturing conditions and may thus depend on several factors; therefore the choice of disintegrant is of obvious importance but other excipients, such as the type of filler and lubricant, can also be of significant importance for tablet disintegration (Aulton & Taylor, 2018). According to USP, the immediate-release tablets must disintegrate within half hour to release their drug efficiently (Pharmacopeia, 2009).

The results of drug content indicate that only the tablets of two brands (A, H) met USP's content assay requirements (90 – 110%); every tablet unit should contain the amount of drug substance equivalent to its label amount (Pharmacopeia, 2009) but still, the tablets of brand D and G are close to the USP requirements of drug content because in general, an industrial product is of good quality if there is a slight fluctuation in its active content in drug products and its average value is close to the nominal value (Bánfai et al., 2007).

The result of brands that shows minimum drug content could suggest that these brands did not comply with the label claims and the actual active drug content with USP/BP (British Pharmacopeia) specification; this may result in diminished medication efficacy (Khreit et al., 2017).

The fluctuation of prices of different brands indicates that different types and amounts of ingredients of different qualities were used. Also, the cost of production as the cost of workers, transportation from different origins, cost of packaging, and the percentage of profit, play a role in the fluctuation of prices, the price is vital to know the most economically available brand may be used, as the pharmaceutical outcomes are promising too (Bano et al., 2011).

According to the results of weight variation, hardness, friability, disintegration, drug content, and price of the tested brands, it was found that it is more effective and economical to consume or use brands A and H because they meet most of the USP requirements for the mentioned tests. Their price is relatively medium if it is compared with the price of other brands.

## CONCLUSION

All the tested AAP brands met most requirements of USP for mass uniformity, hardness, and disintegration except for drug content; only two brands (A and H) and brands (D and G) are close to the normal range. Brand C shows the minimum price but does not meet the USP requirements for drug content; therefore, it may be more effective and economical to consume or use brands A and H because they met all the USP requirements for the mentioned tests, and their price is relatively medium compared with the price of other brands; a high price is not necessarily a reliable indicator of good quality, sometimes the high prices are due to high production costs, high packaging costs, high-profit percentage, and high shipping costs. Our next steps will be directed towards studying the dissolution for the selected brands to study the release profile and the absolute bioavailability study; to know the percentage of drugs that reach the systemic circulation from each brand.

## REFERENCES


Allen, L. V., & Ansel, H. C. (Eds.). (2014). Ansel's pharmaceutical dosage forms and drug delivery systems (10th ed.). Lippincott Williams & Wilkins.

Aulton, M. E., & Taylor, K. M. (Eds.). (2018). Aulton's Pharmaceutics: The Design and Manufacture of Medicines (5th-Editio ed., Vol. 5, Issue 1). Elsevier Ltd.

Bánfai, B., Ganzler, K., & Kemény, S. (2007). Content uniformity and assay requirements in current regulations. Journal of Chromatography A, 1156(1-2 SPEC. ISS.), 206–212.

Bano, R., Gauhar, S., Naqvi, S. B. S., & Mahmood, S. (2011). Pharmaceutical evaluation of different brands of levofloxacin tablets (250 mg) available in local market of Karachi (Pakistan). International Journal of Current Pharmaceutical Research, 3(1), 15–22.

Bertolini, A., Ferrari, A., Ottani, A., Guerzoni, S., Tacchi, R., & Leone, S. (2006). Paracetamol: New vistas of an old drug. In CNS Drug Reviews (Vol. 12, Issues 3–4, pp. 250–275).

British Pharmacopoeia (Ed.). (2009). The British pharmacopoeia (Vol. 2, Issue 1238). MHRA.

Covington, T. R. (1992). Generic drug utilization: Overview and guidelines for prudent use. Clinical Research and Regulatory Affairs, 9(2), 103–126.

Khreit, O. I., Alkailani, H. A., & Alqathafi, W. S. (2017). A Comparative Study of Physical and Chemical Parameters of Selected Paracetamol Tablets Available in the Pharma Market of Libya. 9(2), 1–6.

Nasrin, N., Asaduzzaman, M., Mowla, R., Rizwan, F., & Alam, A. (2011). A comparative study of physical parameters of selected ketorolac tromethamine tablets available in the pharma market of Bangladesh. Journal of Applied Pharmaceutical Science, 1(8), 101–103.

Odeniyi, M. A., Adegoke, O. A., Adereti, R. B., Odeku, O. A., & Itiola, O. A. (2003). Comparative analysis of eight brands of sulfadoxine-pyrimethamine tablets. Tropical Journal of Pharmaceutical Research, 2(1), 161–167.

Pharmacopeia. (2009). USP 32 NF 27 (United States Pharmacopeia/National Formulary) (1st ed.). United States Pharmacopeial.

Troy, D. B. (Ed.). (2005). Remington: The Science and Practice of Pharmacy (21st ed). Lippincott Williams and Wilkins.

Vv, P., Sarkar, S., Tribedi, S., Mathappan, R., & Mathew, S. T. (2013). Research and Reviews : Journal of Pharmacy and Pharmaceutical Sciences Formulation and Evaluation of Orodispersible Tablets of Salbutamol Sulphate. RRJPPS, 2(3), 26–36.

WHO. (2007). Quality assurance of pharmaceuticals: A compendium of guidelines and related materials. In WHO Press (2nd edition). WHO Press.