International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 14, Issue 6, 2022

Original Article

A COMPARATIVE STUDY OF QUALITY CONTROL TESTING OF MEFENAMIC ACID TABLETS IN IRAQ

INAS F. ABDULRAZZAQ[1], YASMIEN A. SALAL[1], MAZIN THAMIR ABDUL-HASAN[1], HAYDER K. ABBAS[2], KARRAR MOHAMMED HASAN AL-GBURI[3]

[1]Department of Pharmaceutics, Faculty of Pharmacy, Kufa University, Al-Najaf, Iraq, [2]Department of Pharmaceutics, College of Pharmacy, University of Alkafeel, Al-Najaf, Iraq, [3]Department of Clinical Pharmacy, Faculty of Pharmacy, University of Kufa, Al-Najaf, Iraq
Email: enasf.abdulrazzaq@uokufa.edu.iq

Received: 01 Sep 2022, Revised and Accepted: 08 Oct 2022

ABSTRACT

Objective: This research was performed to assess the quality of different marketed tablets having mefenamic acid (500 mg). The selected tablets are produced by numerous companies and presented in the Iraqi pharmaceutical marketplace.

Methods: Different batches of mefenamic acid conventional tablets were exposed for several tests of quality control. These evaluation tests include hardness, weight variation, friability, disintegration time, drug content, and drug dissolution profile. The properties of these quality tests were made conferring to the specification of USP-pharmacopeia.

Results: The data of this study indicate that each tablet of mefenamic acid batches conformed to the requirement of USP pharmacopeia, the hardness was (6.87-8.06 Kg/cm^2), and the drug content results were (90.666-99.214%) within USP limitation. The data of disintegration time and weight uniformity were agreeable with pharmacopeia and the *in vitro* release assay showed that the release of each mefenamic acid marketed tablet was highest than (80 %) in 45 min, which reproducing compliance with the USP pharmacopeia's limitation.

Conclusion: From this study, it was proved that all of the marketed brands of mefenamic acid tablets meet the standard character in the USP pharmacopeia for *in vitro* quality control tests.

Keywords: Mefenamic acid, Quality test, Oral dosage form

DOI: https://dx.doi.org/10.22159/ijap.2022v14i6.46251. Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

Quality control tests of drug products are an essential process in the pharmaceutical industry that involves all methods assumed to confirm the purity, and uniformity and evaluate the level of quality of marketed drug products [1]. Oral conventional drug products such as tablets and capsules are important in pharmaceutical markets, due to their being widely distributed and used by the patient, so the quality level and therapeutic activity of these drug products are confirmed as the main process for each step of the manufacturing and the results data matched with standard limitation of the Pharmacopoeia [2]. Mefenamic acid has a white to off-white color in the form of microcrystalline powder. It is insoluble in water, highly soluble in dimethylformamide at 38.5 mg/ml but slightly soluble in ethanol at about (4.6 mg/ml) [3]. It is a lipophilic drug (logP = 5.12) and has weak acidic properties with a pKa equal to 4.2 [4]. Mefenamic acid is one type of non-steroidal medication and anti-inflammatory drug that is useful in decreasing mild and moderated pain such as headaches, toothache, dysmenorrhea, and rheumatoid arthritis [5]. It's available in the market as a caplet manufactured by different pharmaceutical companies in the world which vary in quality and accuracy from one company to another. So this study aimed to assess the quality parameter of mefenamic acid caplets that are produced by many companies with the pharmacopeia's specification and present in the marketplaces of Iraq. Majeed, *et al.* performed a study intended to evaluate quality control parameters of various brands of metronidazole tablets that are available in the Iraqi market, they approved that all brands follow the official limitation in the test of friability and the dissolution rate of different metronidazole tablets was within 40 min and the drug released amount between (84.6%-100%). So this study indicates that all brands of metronidazole tablets presented in Iraqi pharmacies conform to the USP standards [6].

MATERIALS AND METHODS

Materials

Mefenamic acid with a dosage strength of 500 mg from different brand batches was supplied by a private Iraqi pharmacy, as described in table 1. Pure mefenamic acid powder was provided from Hexia-chemical, China. The hydrochloric acid and $KHPO_4$ are provided by sd Fine-chem limited Mumbai. Na_2HPO_4 from Himedia Laboratories, India.

Table 1: Marketed conventional oral tablets of mefenamic acid

Name of batch	Manufactured company	Country
Mefenamic awa®	Awamedica	Iraq
Ponstidin®	SDI	Iraq
Meflam ®	Ajanta	India
Mefril®	Micro	India
Meflin®	Lincolin	India
Mefdol fort®	BAL Pharma	India
Ponamic®	MVC	India
Mefex®	Neopharma	United Arab Emirates

Methods

Melting point determination

The mefenamic acid powder melting point was evaluated by placing a small quantity of powdered drug in the glass capillary tube that was closed from one side only, then placing the capillary tube in a melting point apparatus and recording the melting temperature once complete melting happens [7].

Calibration curves for drug in (pH6.8)

The mefenamic acid calibration curve in (pH 6.8) phosphate buffer solution was made by making a series of dilutions from stock solutions containing 100 µg/ml of mefenamic acid. The measured absorbencies were considered against the corresponding concentrations to get a calibration curve.

Quality control tests

Weight variation assay

Weight variation assay was done for each choice batch by taking a weight of 20 tablets individually via a sensitive balance (GmbH.

Germany). The tablet´s average weight was calculated and a percentage of deviation for each tablet was measured [8].

Test of friability

This assay was done in the Erweka Friabilator tester. Twenty tablets were selected randomly and recorded their primary weight; after that the friabilator was run at 25 rpm speed and 100 revolutions for 4 min [9], the tablets weight were measured again and the friability was estimated by application of the following equation:

$$F = \frac{(\text{Initial weight} - \text{final weight})}{\text{Initial weight}} \times 100$$

The standard value for friability is 1%.

Hardness test

Hardness mean a force needed to completely break the tablets. This test can be done with aiding of a hardness tester (Erweka). A tester of 10 tablets was chosen from each brand and the force wanted to break down the tablets was documented as Kg/cm^2 [10].

Disintegration time assay

This test was done by using disintegration test apparatus (Erweka, Germany). Which contain a basket rack having 6 open-ended tubes, 1 tablet from each brand was employed in each tube and then immersed the rack in vessels containing 900 ml (pH6.8) phosphate buffer solution maintained at 37±2 °C, and the tablet´s floating was prevented by using of perforated plastic discs. To conform to the USP principles, all tablets must be disintegrating and the particles should be permitted over the 10 mesh screen [11].

Drug content assay

Mefenamic acid content was evaluated by weighing 10 tablets from each batch and crushing the tablets with mortar. A sample of mefenamic acid powder equal to 50 mg was taken and then transported into a volumetric flask filled with 100 ml of (pH 6.8) phosphate buffer solution [12]. The filled flask was shacked for 1 h. After that filtrated the solution via a (0.45µm) filter membrane. A sample of filtered solution equivalent to 1 ml was diluted to 100 ml with (pH6.8) phosphate buffer, and the absorbance was measured by a UV-visible spectrophotometer.

***In vitro* release assay**

The release profile of mefenamic acid (500 mg) oral tablets was determined via the USP-II dissolution apparatus (paddle method). A sample of one tablet from each batch of choices companies was immersed in 900 ml of phosphate buffer solution (pH 6.8). The machine operated at 50 rpm for 60 min with a heat temperature of about 37±0.5 °C. A sample of 5 ml was taken from the dissolution medium at time intervals (5, 10, 15, 20, 25, 30, 40, 50, and 60 min); after that 5 ml from the fresh medium of buffer solution must be replaced in each withdrawing to preserve sink condition. The drawing samples were filtered via (0.45 µm) filter syringe. The sample content was measured with aiding of a spectrophotometer; the assay was triplicated [13].

RESULTS AND DISCUSSION

Measurement of melting point

The mefenamic acid melting point was measured at 229 °C-231 °C, which is the same as that recorded in the official source and this indicates the purity of the drug [14].

Calibration curves in (pH6.8)

Calibration curves of mefenamic acid in a solution of phosphate buffer (pH 6.8) were made by setting the absorbencies in contrast to concentrations. A high regression (R^2) value and a straight line that was gotten indicate that the curve follows Beer Lambert's rule at λ max 285 nm, with a variety of concentrations used. Fig. 1 shows a calibration curve of the drug.

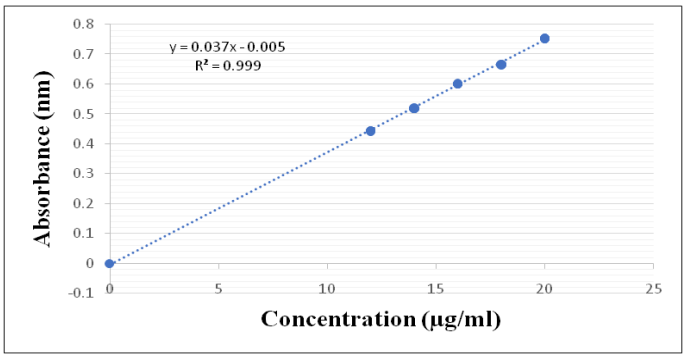

Fig. 1: Calibration curve of mefenamic acid in pH 6.8

Quality control tests

Weight variation assay

Based on USP-limitation, the weight variation percentage that is accepted for tablets (above 0.324 g) is (±5) [15]. As measured in all marketed products. So the weight variation test results for all companies in the accepted value as shown in table 2.

Friability test

The marketed batch would be accepted when the percent of drug loss is less than 1% (friability value) [16]. Table 3 shows the friability of marketed products which are ranged from (0.263 to 0.750 %) and this indicates that all products of mefenamic acid in accepted levels as mentioned in USP.

Table 2: Weight variation test

Name of batch	Weight(g) for 20 tablets*	Upper limit	Lower limit
Mefenamic awa®	0.697±0.004	0.732	0.662
Ponstidin®	0.606±0.019	0.636	0.576
Meflam®	0.838±0.008	0.88	0.797
Mefril®	0.849±0.009	0.891	0.806
Meflin®	0.691±0.002	0.726	0.657
Mefdol fort®	0.799±0.005	0.839	0.759
Ponamic®	0.91±0.011	0.955	0.864
Mefex®	0.735±0.007	0.772	0.698

*Data are represented as mean±SD, n=3

Table 3: Friability values of mefenamic acid marketed products

Batch name	Number of tablets	Weight before the test(g)*	Weight after the test(g)*	Mean friability (%loss)
Mefenamic awa®	20	0.697±0.0045	0.694±0.0041	0.480
Ponstidin®	20	0.606±0.019	0.604±0.021	0.365
Meflam®	20	0.838±0.008	0.832±0.010	0.750
Mefril®	20	0.849±0.0092	0.845±0.0099	0.423
Meflin®	20	0.691±0.002	0.690±0.002	0.263
Mefdol fort®	20	0.799±0.0055	0.796±0.0056	0.450
Ponamic®	20	0.910±0.011	0.906±0.012	0.417
Mefex®	20	0.735±0.00791	0.732±0.00792	0.387

*Data are represented as mean±SD, n = 3

Hardness test

This test evaluates the mechanical strength of the tablet, which saves it during the manufacturing process, packaging, and transportation. The stander value, according to USP-pharmacopeia, arranges between (4-8) kg for an uncoated tablet [17]. Hence the results of all different companies' tablets that were checked in this test appeared to be within acceptable limits as in table 4.

Disintegration time

The first step for drug absorption inside the body depends on the breakdown of the drug into smaller particles and converted to solution form, so disintegration is very important to facilitate the absorption and increase the bioavailability of the drug [18]. The accepted value of disintegration time in USP for uncoated tablets is less than 30 min [19]; therefore, the results (in pH1.2 and pH6.8) for all tablets tested in this study were within the standard level as revealed in table 4, and this result is agreed with the previously investigated by Abbas, *et al.* that study the quality parameter of mefenamic acid tablet available in Karachi, Pakistan [20].

Drug content

The drug content of eight brands of mefenamic acid was found in the range of (90.66-99.21%), and all of the batches obeyed the USP specification for the assessed test [21]. No tablet was found out of the limit of (85-115%); these results approved the uniformity of distributions with excellent amounts of drug content existing in all different companies' batches of mefenamic acid tablets. Table 4 explained the results of drug content.

Table 4: Hardness value with disintegration time and drug content of marketed products

Batch name	Hardness (kg/cm2)	Disintegration time (min)		Content of drug (%)
		pH (1.2)	pH (6.8)	
Mefenamic awa®	7.88±0.583	9.5±0.5	13.666±0.577	97.623
Ponstidin®	7.67±0.871	15±1	17±0.782	98.684
Meflam®	8.06±0.015	10±0.5	8.5±0.5	99.214
Mefril®	6.89±0.063	9±0.5	9.5±0.521	96.032
Meflin®	7.15±0.380	3.333±0.763	3.5±0.5	93.379
Mefdol fort®	6.87±1.034	4.333±0.288	4.5±0.511	90.666
Ponamic®	7.02±0.720	4.5±0.5	4.5±0.5	91.726
Mefex®	7.45±1.085	7.5±0.5	10±1.02	97.305

Value of hardness with disintegration time are given IN mean±SD, n= 3

Drug release assay

The bioavailability of the oral dosage form would be influenced by the dissolution rate. Hence, it is very essential to assess the dissolution percent and match the release outlines for all marketed products. Conferring to USP specification, the percent of drug release for oral uncoated tablets should not be less than 80% within 60 min. In this research, the patterns of *in vitro* release indicate that the marketed products of mefenamic acid of different companies are agreeable with USP specifications; fig. 2 shows that Meflam®products release a higher amount of mefenamic acid 99.4 % while Ponamic® products released the lowest quantity among different products 90.7%. Zafar *et al.* showed the valuation of (250 - mg) mefenamic acid tablets available in Pakistan; the study showed drug release percentages that ranged from 87.65% to 91.22% and these results were meeting the USP official limits [22].

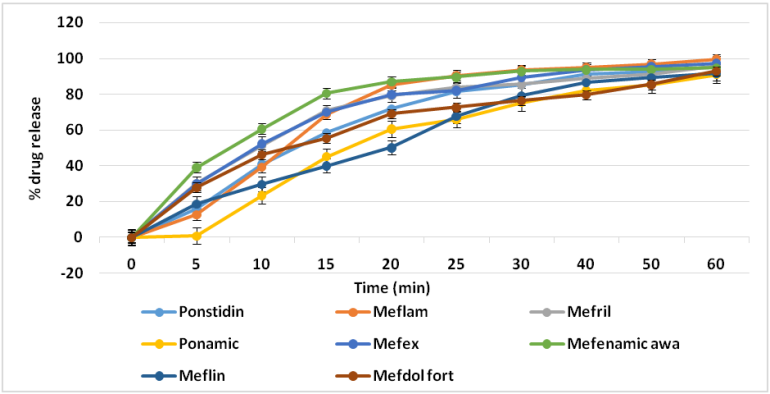

Fig. 2: *In vitro* dissolution profile of mefenamic acid marketed tablets in (pH 6.8) solution. Error bars indicate the standard deviation of replicates (n=3)

CONCLUSION

This study has established that the features of mefenamic acid oral tablets for all batches were in accepted value according to the limitation of the USP-Pharmacopeia. Tested features were including hardness, disintegration time, friability, weight variation, and drug release profile. The percent of product content ranged from 90.666 to 99.214 % as well as the percentage of medication´s release was greater than (80%) in 45 min. The examination of the chosen tablets exposed that all product batches were synthetic in an appropriate way for the purposes to which is suggested.

ACKNOWLEDGEMENT

The authors would like to thank the department of pharmaceutics, the faculty of pharmacy, and the University of Kufa for everything they have done for the completion of this research.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Xhafaj D, Malaj L, Mileti M. A comparative quality control study of cetirizine hydrochloride 10 mg tablets on the Albanian pharmaceutical market. Int J Pharm Pharm Sci. 2015;7(1):504-7.
2. Hasan A, Dewan SA, Ahamed SK, Kai MM. Quality control studies on cetirizine hydrochloride tablets available in Bangladesh drug market. Int J Pharm Biol Sci. 2013;3(1):349-54.
3. Remington HS. The Sci Pract Pharm, volume I and volume II. 22nd ed. J Med Libr Assoc. 2014 Jul;102(3):220-1.
4. PubChem. Bethesda: National Library of Medicine; 2004-. PubChem Compound Summary for CID 4044, Mefenamic acid. National Center for Biotechnology Information. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Mefenamic-acid. [Last accessed on 20 Aug 2022]
5. Daraji NK, Patel VP, Ramani VD. Formulation optimization and characterization of aqueous injection containing poorly soluble drug using mixed hydrotropic solubilization. Int J Curr Pharm Sci. 2021;13(5):100-7. doi: 10.22159/ijcpr.2021v13i5.1908.
6. Majeed SM, Al-Shaheen K, Al-Zidan RN. Quality control study on Conventional metronidazole tablets available in the Iraqi market. Res J Pharm Technol. 2021;14(2):803-8. doi: 10.5958/0974-360X.2021.00141.4.
7. Moffat AC, Osselton MD, Widdop B. Clark's analysis of drugs and poisons. 4th ed. London: Pharmaceutical Press; 2011. p. 1617.
8. Gupta MM, Gupta M. Comparative pharmaceutical quality control testing of different brands of paracetamol tablets available in Trinidad and Tobago, West Indies. Int J Pharm Sci Res. 2016;7(7):2830-6.
9. Ramakrishna S, Mihira V, Raja Vyshnavi K, Ranjith V. Design and evaluation of drug release kinetics of meloxicam sustained release matrix tablets. Int J Curr Pharm Res. 2012;4:90-9.
10. Uddin MS, Mamun AA, Tasnu T, Asaduzzaman M. In-process and finished products quality control tests for pharmaceutical tablets according to pharmacopoeias. J Chem Pharm Res. 2015;7(9):180-5.
11. Shah MR, Nasiri MI, Anwer S, Ali T, Zaheer K, Ahmed K. Pharmaceutical quality assessment of different brands of moxifloxacin 400 mg tablets available in Pakistan. RADS. J Pharm Pharm Sci. 2019;7(1):2-8.
12. Raza A. Spectrophotometric determination of mefenamic acid in pharmaceutical preparations. J Anal Chem. 2008;63(3):244-7. doi: 10.1134/S106193480803009X.
13. Kumar S, Parkash C, Kumar P, Singh SK. Application of some novel techniques for solubility enhancement of mefenamic acid, A poorly water-soluble drug. Int J Pharm Sci Drug Res. 2009;1(3):164-71.
14. Seetha Lekshmi S, Guru Row TN. Conformational polymorphism in a non-steroidal anti-inflammatory drug, mefenamic acid. Cryst Growth Des. 2012;12(8):4283-9. doi: 10.1021/cg300812v.
15. The United States Pharmacopeia. USP30-NF25. Convention Inc Rockville MD General tests and assays CD; 2007.
16. Neamah AJ, Hasan A-GKM, Talib Khudhair AHK. Design and characterization of candesartan cilexetil oral nanoemulsion containing garlic oil. Int J Appl Pharm. 2019;6:116-24.
17. Parrot EL, Saski W. Solid pharmaceuticals. In: Experimental pharmaceutical technology. 3rd ed. Minneapolis: Burgess Publishing Co; 1971. p. 58-106.
18. Aulton ME, Taylor K. Aulton's pharmaceutics the design and manufacture of medicines. 4th ed. New York: Churchill livingstone Elsevier; 2013.
19. Lachman L, Lieberman HA, Kanig JL. Theory and practice of industrial pharmacy. New Delhi: CBS Publishers and Distributors Pvt, Ltd; 2009. p. 229-345.
20. Abbas SS, Hassan F, Naveed S, Qamar F, Hameed A. Pharmaceutical equivalent study of mefenamic acid formulation available in Karachi, Pakistan. RADS-JPPS. 2015;3(2):113-6.
21. Satish NP, Satish KN. Design and optimization of fast-dissolving tablets containing metoprolol by sublimation method. Int Res J Pharm. 2010;1(1):346-57.
22. Zafar F, Ali H, Shah NS, Naveed S, Siddiqui S. Quality assessment and dissolution profile comparison studies on 250 mg mefenamic acid tablets available in the local market of Karachi. J Chin Pharm Sci. 2015;24(10):673-7.