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Original Article

Quality Control and Testing Evaluation of Various Metoprolol Tartrate (50 mg) Tablets Available in Iraq Market

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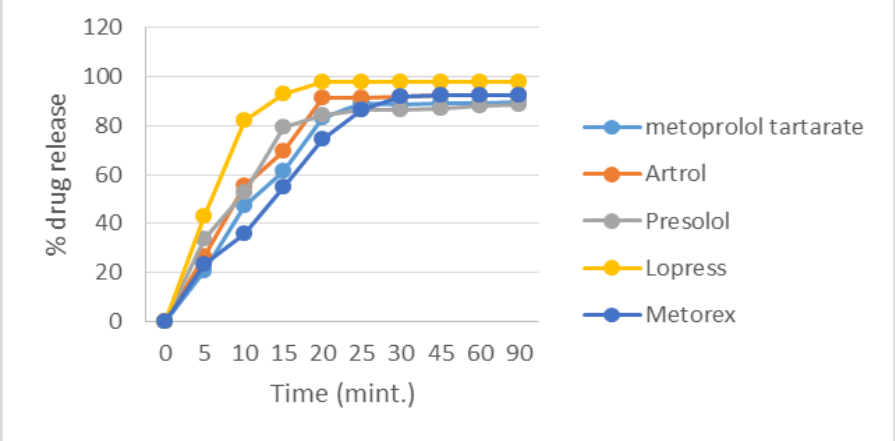
ABSTRACT

This study was done to assess the effectiveness of commercially available tablets of metoprolol tartrate (50 mg). The specified tablets were manufactured in different companies and existed in the Iraqi market. The quality control tests were performed on various batches of film-coated tablets containing metoprolol tartrate. Weight variations, friability, hardness, drug content, disintegration time, and drug dissolution assay were among the tests conducted. The results of these tests were compared with the specifications of the USP Pharmacopeia. The obtained data in this research showed that all tablets of metoprolol tartrate from different products followed the USP limitation, the hardness was (7.47-9.87 kg/cm^2), the drug content result was (93.4-99.4%) with in the USP limitation. The result of disintegration time and weight uniformity test were acceptable with pharmacopeia limitation, the *in vitro* release profile for all different batches was more than 85% in 30 minutes. This study clearly showed that all of the marketed batches of the metoprolol tartrate tablets were in a good agreement with the standards limitation of the USP pharmacopeia for the quality control tests.

GRAPHICAL ABSTRACT



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Introduction

The most used oral dosage forms is the tablet. Its benefits come from low manufacturing costs, accurate dosing, better chemical and physical stability, simplicity in preparation, and convenience of administration [1]. The regularity of drug dosage, the elegant and consistent tablet appearance, which includes the uniformity of tablet weight, size, and thickness to increase patient palatability, are just a few characteristics that indicate a high-quality product. In addition, the controlled and repeatable medication release that may be evaluated by dissolving tests is a key component of product quality. Therefore, the solid dosage form needs to be tough enough to withstand handling, transit, and use without breaking or eroding [2]. To ensure manufacturing and product consistency, all dosage forms should undergo *in vitro* dissolution testing as part of their quality control review. This involves analyzing the drug release profile for various batches of marketed products [3]. Metoprolol tartrate is β1-adrenergic blocking agent has a cardio selective effect used for treatment of heart failure, acute myocardial infarction, and mild to moderate hypertension. It is a white crystalline powder has a molecular weight 684.81. It is highly soluble in water and spontaneously soluble in ethanol (96%) [4]. Metoprolol tartrate is presented in Iraq market as the film coated tablets prepared by many companies. A quality control study was directed at testing the quality and effectiveness of five different brands of clopidogrel bisulfate tablets in Iraq's pharmaceutical market by using the quality control measures. The study demonstrates that all brands of clopidogrel tablets meet the USP guidelines. The tablets were subjected to numerous characteristics, including weight variation, friability, disintegration time, hardness, and *in vitro* release testing [5].

Materials and Methods

Metoprolol tartrate with strength of 50 mg film coated tablets of 5 different brands was obtained from in Baghdad private pharmacy, Iraq and is presented in Table 1. Metoprolol powder was gained from Hexia-chemical, China. Hydrochloric acid and $KHPO_4$ were obtained from sd Fine-chem limited, Mumbai. Na_2HPO_4 was supplied by Himedia laboratories, India.

Table 1: Metoprolol tartrate with strength of 50 mg film coated tablets of 5 different brands

Batch name	Factory-made company	Country
Lopress®	Asia	Syria
Metorex®	FBI	Iraq
Artrol®	DarAl Dawa	Jordan
Presolol®	Hemofarm	Serbia
Metoprolol tartrate®	Bristol	United Kingdom

Melting point measurement

The metoprolol tartrate melting point was determined by placing a little amount of the medication's powder in a capillary tube, inserting it into a melting point instrument, and recording the temperature at that point [6].

Calibration curve of drug

The calibration curve of metoprolol tartare was made by preparing stock solution containing 10 mg from drug in 100 mL of phosphate buffer of pH 6.8. Different dilutions from stock solution were prepared and the absorbance determined by using spectrophotometer at 200-400 nm.

Quality control test assessment
Weight variation test

An evaluation of the weight variation for the batches was made through weighing of 20 tablets randomly, and then weighing individually by a digital balance (GmbH. Germany). The twenty tablets average weights were calculated. Next, the deviation percentage was documented [7].

Friability test

The test of friability was done by using a friabilator to evaluate the tablet tendencies to break or crumble during handling or compression. Firstly, the weight of tablets was determined, and then they were putted in the instrument and the friabilatore operated at 100 rpm. Thereafter, the tablets were weighted again after the specified revolution numbers and the loss in weight was measured [8]. If the percentage of the loosed weight lies between 0-1% of tablet weight, the tablets are acceptable. The following equation can be used to calculate the friability percentage.

$$F = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Hardness test

The hardness reflects the forces required to break the tablet which measured by the hardness tester (Erweka, GmbH. Germany). A sample of 10 tablets for each brand was taken and recorded the forces needed to break these tablets as kg/cm^2 [9].

Disintegration test

The disintegration test machine (Erweka, Germany) was used to determine the disintegration time for 10 tablets sample of each brands of metoprolol tartrate. The tester had a basket rack holding 6 open-ended tubing, one tablet was placed in each tube, and then the rack was dipped in a (1000 mL) vessel having 900 mL of (pH 1.2, 6.8 pH) phosphate buffer preserved at 37±2 °C. The required period to completely dissolve each tablet was noted as the disintegration time [10].

Drug content assay

The metoprolol tartrate content in a specific batch was firm by weighted of ten tablets and grinding the tablets into the fine powder in a mortar, and then dissolve sample of 50 mg from the powder in a 100 mL volumetric flask containing of pH 6.8 phosphate buffer. After that, the flask was shaken for an hour. The solution was then filtered by using a 0.45 m filter syringe, and a sample of one ml of the filtered solution was obtained and diluted with 100 mL of phosphate buffer. A spectrophotometer was used to measure the absorbance. If the percentage of the drug presented in each tablet fell within the range of 85–115% of the labeled content of the drug, and the batch should be approved [11].

Dissolution test

In this test, the USP dissolution apparatus type II (paddle method) was used. To assay the dissolution, one tablet for each metoprolol tartrate companies batch was putted in a vessel filled by 900 mL of pH 6.8, and phosphate buffer solution was preserved at 37±0.5 °C. The rotating speed for the machine was held at 100 rpm. At pre-determined intervals (5, 10, 15, 20, 25, 30, 40, 50, and 60 min). A 5 mL sample of the dissolving medium was obtained, and this was immediately replaced by an equal volume of new test media. The samples were filtered through a 0.45 m filter membrane, and the drug content was determined by using the UV-visible spectrophotometer at 221 nm [12].

Results and Discussion

Melting point

Metoprolol tartrate's tested melting point ranged from 120 °C to 123 °C. This reading matches that in the official source and shows the purity of the medication powder utilized in the study [13].

Calibration figure of drug in phosphate buffer (pH 6.8)

The calibration curves of drug in phosphate buffer solution (pH 6.8) were organized by putting the absorbencies in front of concentrations. A high value of the regression coefficient with a straight line was gained [14]; this indicates the curve agreement with Beer Lambert law at the maximum wavelength equal to 221 nm with utilized concentrations. Figure 1 displays the calibration curve of the drug.

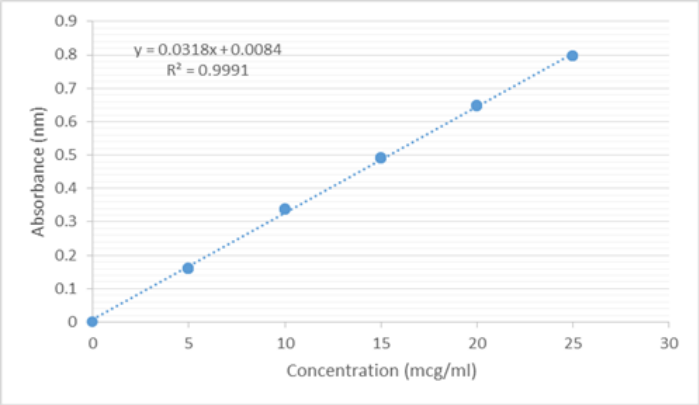

Figure 1: Calibration curve of metoprolol tartrate in pH 6.8

Quality control tests

Weight variation test

Depending on the USP specification, the accepted percentages of weight variation for tablets which have a weight over 0.130 g is (±7.5) as noted in (Metorex®, Artrol®, Presolol®, and Metoprolol Tartrate®) and for tablet over 0.324 gm is (±5), as showed in product (Lopress®) [15]. Therefore, the value of all the marketed products of metoprolol tartrate was with in agreeable limitation, as presented in Table 2.

Friability test

The accepted value for percentage of drug loss (friability test) should be less than 1% [16]. Table 3 described the friability results which were ranged from 0.117 to 0.85 and this supply an indication that all batches of different companies of metoprolol tartrate tablets were consistent with the US pharmacopeia limitation.

The tablets harnesses were measured to determine the tablets capability to resist the mechanical shocks of handling during manufacture process, transportation, and storage. Depending on USP, the tablets would be acceptable when the hardness value about (4-10 kg) for coated tablet [17] and this give an indication that all batches of drug product acceptable range, as presented in Table 4.

Table 2: Weight variation test (mean± SD; n= 3)

Batch's name	Average weight (g) of 20 tablets	Upper limit	Lower limit
Lopress®	0.359±0.003	0.377	0.341
Metorex®	0.181±0.004	0.195	0.167
Artrol®	0.158±0.0019	0.170	0.146
Presolol®	0.170±0.0010	0.183	0.157
Metoprolol® tartrate	0.153±0.0013	0.164	0.141

Table 3: Friability data of metoprolol tartrate marketed batches

Batch name	Number of tablets	weight before test (g)	weight after test (g)	Friability (%loss)
Lopress®	20	0.35985	0.35905	0.222
Metorex®	20	0.1814	0.18115	0.137
Artrol®	20	0.1588	0.1574	0.85
Presolol®	20	0.17055	0.17035	0.117
Metoprolol tartrate®	20	0.15319	0.15215	0.678

Table 4: The hardness, time of disintegration, and drug content of different marketed products

Batches names	Hardness (kg/cm²)	Time of disintegration (min)		Content of drug (%)
		pH 1.2	pH 6.8	
Lopress®	9.71 ± 0.307	4.1±0.2	4.8±0.2	93.4
Metorex®	7.47 ± 0.522	7.8±0.2	8.3±0.2	95.5
Artrol®	9.87 ± 0.267	10±1	10.5±0.5	99.4
Presolol®	8.65 ± 0.201	10.5±0.5	10.5±0.5	96.7
Metoprolol tartrate®	9.38 ± 0.461	12.5±0.5	12.5±7	97.5

Hardness test

Disintegration time

The disintegration time is a very important parameter in the quality test because the disintegration is an initial step in drug absorption [18]. Depending on USP, the disintegration time for coated tablet is 30 min [19]. Therefore, all the tablets of different companies of metoprolol tartrate were in an accepted value. Table 4 listed the disintegration time in artificial (gastric and intestinal) fluid.

Drug content

The measured amount of metoprolol tartrate was complied with USP restrictions. The percentage of drugs presented in all batches was (93.4-99.4%). No tablet was over the limit (85-115%). These findings indicate that tablets from all different companies had excellent dispersion and acceptable components [20], as shown in Table 4.

In vitro release study

The effectiveness of tablet products and variations in bioavailability between formulations are both closely related to the dissolution rate of the drug [21]. The percentages of drug release at 45 minutes should not be less than 75% to meet the USP-NF standards. Plans for *in vitro* release in this study revealed that all metoprolol tartrate products made by various companies were accepted with USP restrictions. Figure 2 indicates that through the comparison between batches, the Lopress® batch released a higher percentage of the medicine (97.8%), while the Presolol® batch released a lower percentage (88.6%).

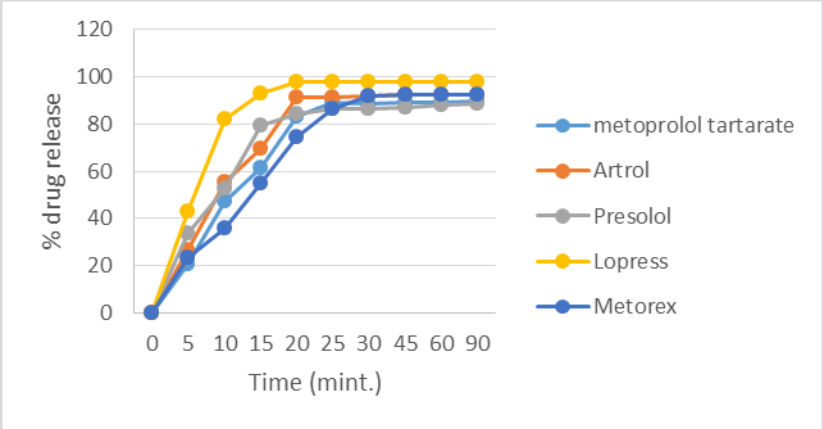

Figure 2: In vitro release pattern of marketed tablets of metoprolol tartrate in pH 6.8 solution

Conclusion

This study made it abundantly evident that all batches of metoprolol tartrate film coated tablets complied with the USP pharmacopeia standards. Friability test, hardness test, weight variation, disintegration time, and *in vitro* drug release were the attributes that were put to the test. The medication's content ranged from 93.4 to 99.4 % and the drug release ranged from 88.6 to 97.8 % in 30 minutes. The investigation of the tablets used in this study revealed that they were all made in a way that was appropriate for the specified goals.

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Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

The author declared that they have no conflict of interest.

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References

[1]. Arshad M.S., Zafar S., Yousef B., Alyassin Y., Ali R., AlAsiri A., Chang M.W., Ahmad Z., Elkordy A.A., Faheem A., Pitt K., A review of emerging technologies enabling improved solid oral dosage form manufacturing and processing, *Advanced drug delivery reviews*, 2021, **178**:113840 [Crossref], [Google Scholar], [Publisher]

[2]. Hammoodi S.H., Ismael S.S., Mustafa Y.F., Mutual prodrugs for colon targeting: A review, *Eurasian Chemical Communications*, 2022, **4**:121251 [Crossref], [Google Scholar], [Publisher]

[3]. Tavakoli F., Shafiei H., Ghasemikhah R., Kinetic and thermodynamics analysis: effect of eudragit polymer as drug release controller in electrospun nanofibers, *Journal of Applied Organometallic Chemistry*, 2022, **2**:235 [Crossref], [Google Scholar], [Publisher]

[4]. European pharmacopoeia 5.0, 01/2005:1028, monograph of Metoprolol Tartrate. 2033-2034. [Publisher]

[5]. Abdul-Hasan M.T., Al-Shaibani A.J.N., Wannas A.N., Al-Gburi K.M.H., Quality Control Testing Of ConventionalClopidogrel Bisulfate Tablets Marketed In Iraq, *International Journal of Applied Pharmaceutics*, 2022, **14**:221 [Crossref], [Google Scholar], [Publisher]

[6]. Baghernejad B., Hojjati Taromsari S.M., Aqueous media preparation of 2-amino-4H-benzopyran derivatives using cerium oxide nanoparticles as a recyclable catalyst, *Asian Journal of Green Chemistry*, 2022, 194-202 [Crossref], [Publisher]

[7]. Gupta M.M., Gupta M., Comparative pharmaceutical quality control testing of different brands of paracetamol tablets available in the Trinidad and Tobago, West Indies, *International Journal of Pharmaceutical SCIENCES and Research*, 2016, **7**:2830 [Crossref], [Google Scholar], [Publisher]

[8]. US Pharmacopoeia. United States Pharmacopoeial Convention, Thirty Seventh Edition 2014:342 [Publisher]

[9]. Uddin M.S., Mamun A.A., Tasnu T., Asaduzzaman M., In process and finished products quality control tests for pharmaceutical tablets according to pharmacopoeias, *J. Chem. Pharm. Res.*, 2015, **7**:180 [Crossref], [Google Scholar], [Publisher]

[10].Quodbach J., Kleinebudde P., A critical review on tablet disintegration, *Pharmaceutical Development and Technology*, 2016, **21**:763 [Crossref], [Google Scholar], [Publisher]

[11].Shailaja T., Latha K., Alkabab A.M., Formulation and evaluation of orodispersible tablets of metoprolol tartrate with natural and synthetic superdisintegrants, *Int. J. Pharm. Pharm. Sci.*, 2012, **4**:148 [Publisher]

[12].Satpute M.M., Tour N.S., Formulation and in vitro evaluation of fast dissolving tablets of metoprolol tartrate, *Brazilian Journal of Pharmaceutical Sciences*, 2013, **49**:783 [Crossref], [Google Scholar], [Publisher]

[13].Mohan A., Hendre L., Pm S.S., Formulation and evaluation of immediate and sustained release bilayer tablets of metoprolol tartrate, *J. Crit. Rev.*, 2020, **7**:4395 [Google Scholar]
[14].Zakaria S.A., Al-Saffar R.S., Othman N.S., A Simple Spectrophotometric Method for the Determination of Famotidine via Reaction with Alizarin Red S, *Chemical Methodologies*, 2022, **6**:228 [Crossref], [Google Scholar], [Publisher]
[15].The United State Pharmacopeia. USP30-NF25. Convention Inc.Rockville MD. General tests and assays CD; 2007 [Publisher]
[16].US Pharmacopoeia. United States Pharmacopoeial Convention,Thirty-Seventh Edition, 2019, **11**:116 [Crossref], [Google Scholar], [Publisher]
[17].Lalitha L.J., Chenthilnathan A., Vidyasagar V., Process validation of clopidogrel bisulphate 75-mg tablets, *Der Pharmacia Lettre,* 2014, **6**:72 [Google Scholar], [Publisher]
[18].Aulton M.E., Taylor K., *Aulton's pharmaceutics: the design and manufacture of medicines*. Elsevier Health Sciences, 2013 [Google Scholar], [Publisher]
[19].Banker G.S., Anderson, N.R.. Tablets. In Lachman, L. and Lieberman, H.A, The theory and practice of industrial pharmacy. CBS Publishers and Distributors Pvt. Ltd., India, Special Indian ed., 2009, 229 [Publisher]
[20].Nushrat S.A., Nasreen W., Deepa K.N., In vitro comparative study of quality control parameter of some brand of ketorolac tablets available in Bangladesh. *World journal of pharmacy and pharmaceutical science*, 2017, **6**:146 [Crossref], [Google Scholar], [Publisher]
[21].Hosseini S.M.H., Naimi-Jamal M.R., Hassani M., Preparation and Characterization of Mebeverine Hydrochloride Niosomes as Controlled Release Drug Delivery System, *Chemical Methodologies*, 2022, **6**:591 [Crossref], [Google Scholar], [Publisher]

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