*L*ibyan *M*edical *J*ournal
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Original article

Evaluation of Some Metformin Hydrochloride Film Coated Tablets Marketed in Tripoli Libya

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Citation. Elhedmi A, Atia A, Alshahrani M, Alfazaa D, Alborke S, Jemaa S. Evaluation of Some Metformin Hydrochloride Film Coated Tablets Marketed in Tripoli Libya. Libyan Med J. 2024;16(2):178-182.

Received: 11-08-2024
Accepted: 09-10-2024
Published: 18-10-2024

Funding*: This research received no external funding.*

Conflicts *of Interest: The authors declare no conflict of interest.*

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Abstract

Metformin hydrochloride is an anti-hyperglycemic agent; it lowers the blood glucose concentration without causing hypoglycemia. The aim of the present study was the evaluation and comparison of pharmaceutical equivalence of four different metformin hydrochloride 850 mg, which are commercially available in the private pharmacies in Tripoli city with different price ranges, produced by various pharmaceutical companies. The physicochemical quality control parameters of various brands of metformin hydrochloride tablets were evaluated using official Pharmacopoeia tests, including disintegration, uniformity of weight, and dissolving tests. All tested brands passed the official tests for uniformity of weight, disintegration, and dissolution. The IR spectrum test showed that all tested tablets have similar absorption bands to the IR spectrum of standard metformin. All brands of metformin tablets were inconsistent in their weight and showed different geometric dimensions. The deviation of the weight of the tablet from the average weight was within the permissible limit with a deviation of less than 5%. The present study confirmed that all four brands of metformin hydrochloride 850 mg tablets adhered to the quality control restrictions stated in the pharmacopeia.

Keywords: *Metformin Tablets, Evaluation, Bioequivalence.*

Introduction

Metformin hydrochloride, an antidiabetic drug, lowers both basal- and postprandial-elevated blood glucose in patients with non-insulin-dependent diabetes mellitus (NIDDM or type 2 diabetes) whose hyperglycemia cannot be satisfactorily managed by diet alone [1]. Some high incidence of concomitant Gastro-Intestinal (GI) symptoms, such as abdominal discomfort, nausea, and diarrhea, may occur during the treatment. Gastrointestinal absorption of metformin is incomplete with an absolute bioavailability of 40–60% (under fasting conditions) in combination with rapid elimination and 20–30% of an oral dose is recovered in faeces [2]. It decreases as the dose increases, suggesting some form of saturable absorption or permeability/transit time-limited absorption and the negligible hepatic metabolism of metformin happened in humans [3]. Side effects and the need for twice to three times a day administration when larger doses are required can also reduce patient compliance and hinder more successful therapy [4]. Administration of a sustained-release, once-a-day metformin dosage form could reduce the dosing frequency and improve patient compliance [5].

Multiple-unit sustained-release dosage forms, such as pellets, are believed to have many therapeutic advantages in comparison with the single-unit dosage forms. They can distribute in the GI tract homogeneously thus maximizing drug absorption and reducing peak plasma fluctuations, minimizing the risk of local GI tract irritation and dose dumping, decreasing dosing frequency and increasing patient compliance, improving the safety and efficacy of the active ingredient [6,7].

Metformin has been shown to be effective in treating NIDDM, as effective as sulfonylureas in diabetic patients who are nonobese or obese and whose diabetes cannot be controlled solely through diet [8]. Metformin may be useful as add on therapy in obese patients with diabetes uncontrolled by sulfonylureas and diet. Lipid profiles may be favorably influenced [9].

The availability of several brands of metformin tablets in Libyan pharmacies today places health practitioners and a pharmacist in a problem of drug substitution in case of a particular

brand is not available. The findings of the current study may help interested health authorities and professionals understand the good indicator for the evaluation of the idealness of commercial products and showed the importance of post marketing investigation for the drugs imported and distributed in Libya. Hence, the aim of this study was to evaluate and compare pharmaceutical quality control parameters of different metformin 850mg tablets marketed in the private pharmacy sector of Tripoli Libya.

Methods

Samples

Metformin tablets having label strength of 850 mg of four different brands were purchased from different private pharmacies in Tripoli Libya, during Feb 2023. The products were coded as A, B, C and D as illustrated in table 1, all drugs included in the study were within the validity date limit.

Table 1. Label information of 4 different brands of Metformin tablets under investigation

Product code	Batch No.	Manufacture Date	Expire Date	Price /tablet in LYD
A	4941	11/2022	11/2025	12
B	12053A	6/2021	06/2024	16
C	BUG090026	10/2021	10/2024	18
D	B0566	3/2021	03/2024	12

Materials

Distilled water, potassium dihydrogen orthophosphate, Na OH, KCL and Pure sample of metformin (Lot p500240 Sigma) was obtained from the National Center for Food and Drug Control.

Visual inspection

Samples of ten tablets from each batch were selected randomly and inspected for their external characteristics such as color, surface texture and shape, presence of grooves (monograms and coat). The tablets were described based on the visual observation.

Weight uniformity

Twenty tablets of each product code were weighed using an electronic digital balance, each tablet was weighed individually then the average weight was calculated for each brand. Tablets were examined for their uniformity of weight and the percentage deviation allowed by USP generally ±10% for tablets weighing 130 mg or less, ±7,5% for tablets weighing more than 130 mg to 324 mg and ±5% for tablets weighing more than 324mg.

Hardness and tablet dimensions

Hardness, thickness, and diameter of samples of 20 tablets were determined using tablet combination tester (Erweka TBH 320 WTD Multi-Check tester, Germany). In the hardness test, pressure was applied on the tablet and the force causing the tablet to break up was recorded. The optimum hardness regarded for coated tablets is 10-20 kg/cm2. Tablet thickness and diameter should be controlled within a ±5% of a standard value [10].

Dissolution rate determination

Dissolution testing was used to evaluate the performance of pharmaceutical products. This study compared the dissolution profiles of four metformin HCl 850-mg formulations, in simulated intestinal fluid (SIF) at pH 6.8 buffer without enzymes. The basket apparatus was used at 100 rev./min at 37 ± 0.5 °C. Samples of 10 ml were removed at 10, 20, 30, 40, and 45 min with replacement of media.

Results and discussion

Four commercial metformin 850 mg tablets were assessed for their pharmaceutical quality according to the described requirements that are stated in the official compendia. The evaluation tests were performed on the samples while in their intended shelf life. The apparent physical characteristics of the samples based on visual inspection were described in (Table 2). All tablets were found to have an attractive appearance with smooth surface texture,

biconvex and round in shape, with uniform white colors. Brand A, B, and C have monograms or score lines which were marked on the surface with symbols indicating the drug name or strength and the company name or logo for further product identification, there were no defects in the tablets coat integrity. These results were in line with previous study conducted in Libya [11].

Table 2. Appearance features of the different brands of Metformin 850mg tablets

Parameters	Brand A	Brand B	Brand C	Brand D
Shape and color	White	White	White	Yellow
Surface texture and Convexity	Smooth and biconvex	Smooth and biconvex	Smooth and circular	Smooth and biconvex
Monograms and score lines and numbers	Yes	Yes	Yes	No
Defect in the tablet coat	No	No	No	No

Since dissolution test releases the medication from its dosage form and allows for gastrointestinal absorption, it is crucial to evaluate the product's quality when it comes to pharmaceutical solid dosage forms [12]. Table 3 shows the standard limit for dissolution test. The drug release values were more than 75% in 30 minutes, the assessed brands C and D exhibited similar patterns of drug dissolution Avg %Q - value = 85.42 excluding brand A which had fastest Avg %Q - value = 101.59, then brand B which had the drug release Avg %Q - value = 97.76. The results obtained from the evaluation of active ingredients content were within the limits (95-105) results. This rate of dissolution eliminates the chance that drug dissolution could cause issues with bioavailability. Similar to this study, previous local studies had found that all tested brands of metformin tablets met the dissolution requirement [11,13].

Table 3. The dissolution and assay test for Metformin 850 mg tablets

Brand	A	B	C	D
Assay %	97.01	99.68	99.26	102.21
Dissolution %	101.59	97.76	85.42	85.42

The IR spectrum is the fundamental representation of the sample's IR color pattern characteristics. Each component contributes a distinct absorption pattern to the overall spectrum, which is determined by the distinct set of molecular vibration characteristics of each individual molecular specimen. This is the foundation for quantification. In the current study, it was observed that all spectra obtained for different samples of metformin 850mg have similar absorption bands to the IR spectrum of standard metformin. The similarity between the spectra is strongly indicative of the identity of metformin 850mg in all of the samples analyzed using IR technique. Our resulted spectrum is completely matched with metformin reference standard in range of 93.4 to 94 % for all samples from A to D (Figure 1). The obtained result was in line with previous study conducted in Ghana [14].

All brands of metformin tablets were inconsistent in their weight and showed different geometric dimensions (Table 4). The deviation of the weight of the tablet from the average weight was within the permissible limit with a deviation of less than 5%, which was similar to metformin tablets tested in a study conducted in Ethiopia [15]. Brands A, B and C in the current study showed a very different average weight. All brands examined showed different diameters and thicknesses, Brand B the largest by diameter, and brand A the largest by thickness. Similarly, Akasha et al., showed that all tested metformin hydrochloride tablets gave values that compiled with USP specification and deviated less than 5 % from the mean value [11].

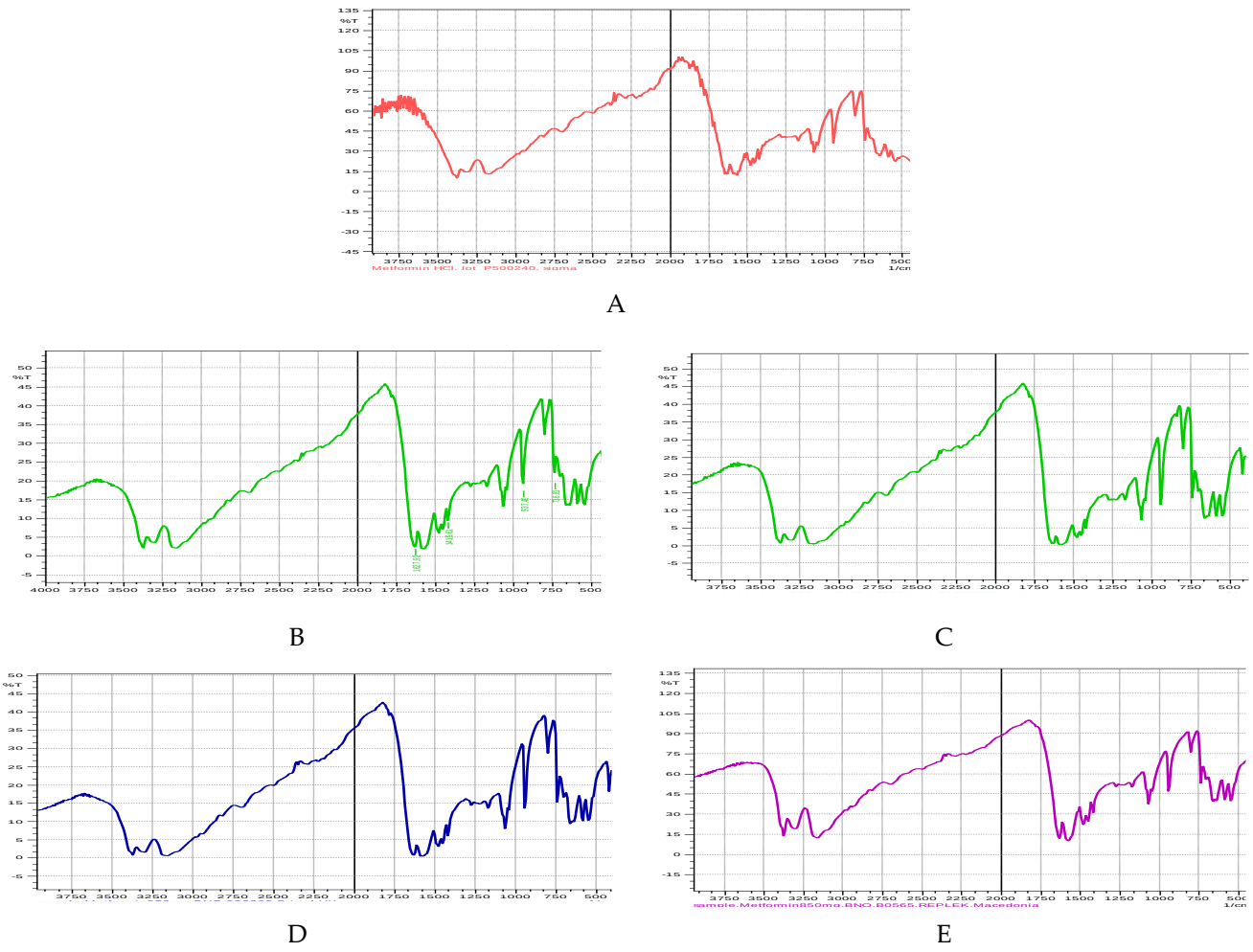

Figure 1. Spectroscopy results for the samples. a) spectroscopy results for standard metformin; b) spectroscopy of brand A metformin; c) IR spectroscopy of brand B metformin; e) IR spectroscopy of brand C metformin; e) IR spectroscopy of brand D metformin

The results of the hardness test showed that brand A exhibited the greatest ability to resist chipping, while brand B showed the lowest and weakest hardness compared to other brands. These variation between the different test brands were also reported in a recent study done in Libya [16].

Table 4. Physical results of the samples A, B and C of Metformin 850mg

Brand	Average weight g	Hardness (N)	Diameter (mm)	Thickness (mm)
A	898.76	41.22	17.96	7.18
B	941.23	26.47	21.96	6.15
C	1009.10	30.56	13.57	6.66

Conclusion

Several quality-control tests were done on four generic brands of metformin hydrochloride tablets circulating in Tripoli City, including weight variation, hardness, and disintegration time. All tested tables had equally effectiveness and complied with the British Pharmacopeia (BP) and the United States Pharmacopeia (USP). The post-market surveillance program for drugs needs to be strengthened, and manufacturers should definitely consider doing the same.

Conflict of interest

The authors report no conflicts of interest in this work.

References

1. Alarbi A, Abired A, Atia A. Prescribing pattern of anti-diabetic drugs in Libyan diabetics patients. A cross sectional survey. Pharm Pharmac Rep. 2018;1(2):24-30
2. Nabrdalik K, Skonieczna-Żydecka K, Irlik K, Hendel M, Kwiendacz H, Łoniewski I, Januszkiewicz K, Gumprecht J, Lip GYH. Gastrointestinal adverse events of metformin treatment in patients with type 2 diabetes mellitus: A systematic review, meta-analysis and meta-regression of randomized controlled trials. Front Endocrinol (Lausanne). 2022 Sep 14;13:975912. doi: 10.3389/fendo.2022.975912.
3. He L. Metformin and Systemic Metabolism. Trends Pharmacol Sci. 2020 Nov;41(11):868-881. doi: 10.1016/j.tips.2020.09.001.
4. Kanto K, Ito H, Noso S, Babaya N, Hiromine Y, Taketomo Y, Toma J, Niwano F, Yasutake S, Kawabata Y, Ikegami H. Effects of dosage and dosing frequency on the efficacy and safety of high-dose metformin in Japanese patients with type 2 diabetes mellitus. J Diabetes Investig. 2017 Sep 30;9(3):587–93. doi: 10.1111/jdi.12755.
5. Kenechukwu FC, Nnamani DO, Duhu JC, Nmesirionye BU, Momoh MA, Akpa PA, Attama AA. Potential enhancement of metformin hydrochloride in solidified reverse micellar solution-based PEGylated lipid nanoparticles targeting therapeutic efficacy in diabetes treatment. Heliyon. 2022 Mar 13;8(3):e09099. doi: 10.1016/j.heliyon.2022.e09099.
6. Wadher KJ, Kakde RB, Umekar MJ. Study on sustained-release metformin hydrochloride from matrix tablet: Influence of hydrophilic polymers and in vitro evaluation. Int J Pharm Investig. 2011 Jul;1(3):157-63. doi: 10.4103/2230-973X.85966.
7. Tarry-Adkins JL, Grant ID, Ozanne SE, Reynolds RM, Aiken CE. Efficacy and Side Effect Profile of Different Formulations of Metformin: A Systematic Review and Meta-Analysis. Diabetes Ther. 2021 Jul;12(7):1901-1914. doi: 10.1007/s13300-021-01058-2.
8. Inzucchi SE. Oral antihyperglycemic therapy for type 2 diabetes: scientific review. JAMA. 2002 Jan 16;287(3):360-72. doi: 10.1001/jama.287.3.360.
9. Klepser TB, Kelly MW. Metformin hydrochloride: an antihyperglycemic agent. Am J Health Syst Pharm. 1997 Apr 15;54(8):893-903. doi: 10.1093/ajhp/54.8.893. Erratum in: Am J Health Syst Pharm 1997 Jun 1;54(11):1335.
10. British Pharmacopoeia (BP). 2002 Appendix: XII, pp. H A2-53.
11. Akasha A, Ahdeya E, Bsebsu Z. Comparative study between five brands of metformin hydrochloride available in Libyan drug market. Mintage J Pharm Med Sci. 2019;8(3):37-41.
12. Long M, Chen Y. Dissolution testing of solid products. Developing Solid Oral Dosage Forms Elsevier. 2009;319–340.
13. Elghnimi T, Bzezi W, Siaan M, Elgreew W, Benmansour H. Comparative in-vitro Evaluation of Some Commercial Brands of Metformin Tablets Marketed in Tripoli-Libya. Eur J Bio Pharm Sci. 2019;6(6):138–143.
14. Sougi A, Ofori-Kwakye K, Kuntworbe N, Kipo S, Boakye-Gyasi M. Evaluation of the Physicochemical and in vitro Dissolution Properties of Metformin Hydrochloride Tablet Brands Marketed in Five Cities in Ghana. J Pharm Res Inter. 2015;9(1):1–14. doi: 10.9734/BJPR/2016/21862.
15. Abatea K, Temesgen A, Nigatu M. Comparative In Vitro Evaluation Of Different Brands Of Metformin Hydrochloride Film Coated Tablets Marketed In Addis Ababa, Ethiopia. Asian J Pharm Res Dev [Internet]. 2020 Jun. 15 [cited 2024 Apr. 10];8(3):44-50.
16. Abozaid D, SalehW. Evaluation of some metformin hydrochloride brands available in the Libyan market. Mediterr J Pharm Pharm Sci. 2022;2(4):6-12. doi: 10.5281/zenodo.7479690.