Original Article

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Comparison of the Physicochemical Properties and Release Profiles of Metformin Tablets of Eight Different Brands Available in the Northern Cyprus Pharmaceutical Market

Kuzey Kıbrıs İlaç Pazarında Mevcut Sekiz Farklı Markaya Ait Metformin Tabletlerin Fizikokimyasal Özelliklerinin ve Salım Profillerinin Karşılaştırılması

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ABSTRACT

Objective: In the study, it was aimed to compare the physicochemical and *in vitro* dissolution parameters of metformin hydrochloride (MET) tablet brands from Northern Cyprus to evaluate the pharmaceutical equivalence.

Methods: Seven brands of MET tablets which were bought from community pharmacies were compared and evaluated with the innovative product Glucophage®. The impurity of MET contained in the sample tablets was determined using Fourier transform infrared spectroscopy. Pharmacopoeia tests were used to evaluate the physicochemical equivalence of the tablets. *In vitro* dissolution test was performed and dissolution data were analyzed including dissolution difference (f_1) and similarity factors (f_2) were evaluated. In addition, the release kinetics of selected MET tablets were examined with a release kinetics software (KinetDS3).

Results: All the tablet brands complied with the official specifications for uniformity of weight hardness and disintegration. Brand MF failed the friability test (>1%); while brands MC, MF and MG failed the content uniformity (assay) test (<95%). Difference (f_1) and similarity factors (f_2) of all brands were calculated in pH 6.8 buffer medium and evaluated with reference to the innovative brand. The facts that MB's f_1 value (15.45) was greater than 15 and that the f_2 values of MB and MF (48.57, 47.13, respectively) were less than 50 indicated that the dissolution profiles of MB and MF formulations were different from the dissolution profile of the innovative brand.

ÖZ

Amaç: Çalışmada, Kuzey Kıbrıs'ta bulunan metformin hidroklorür (MET) içeren farklı markalardaki tabletlerin, fizikokimyasal ve *in vitro* çözünme parametrelerinin karşılaştırılması ve farmasötik eşdeğerliğinin değerlendirilmesi amaçlanmıştır.

Yöntemler: Eczaneden satın alınan farklı firmalara ait yedi MET, yenilikçi ürün Glucophage® ile karşılaştırılmış ve değerlendirilmiştir. Örnek tabletlerde bulunan MET'nin safsızlığı, Fourier transform kızılötesi spektroskopisi kullanılarak belirlenmiştir. Tabletlerin fizikokimyasal eşdeğerliğini değerlendirmek için farmakope testleri kullanılmıştır. *In vitro* çözünme testi yapılmış ve çözünme farkı (f_1) ve benzerlik faktörü (f_2) dahil olmak üzere analiz edilen çözünme verileri değerlendirilmiştir. Ek olarak, seçilen MET tabletlerinin salım kinetikleri, KinetDS3 yazılımı ile incelenmiştir.

Bulgular: Tüm tablet markalarının ağırlık sapması, sertlik ve dağılma özelliklerinin resmi spesifikasyonlara uyduğu saptanmıştır. MF markası friabilite testinde (>%1) başarısızken; MC, MF ve MG markalarının içerik tekdüzeliği (etkin madde miktar tayini) testinde (<%95) başarısız olduğu tespit edilmiştir. pH 6,8 tampon ortamında tüm markaların fark (f_1) ve benzerlik faktörü (f_2) hesaplanmış ve yenilikçi marka referans alınarak değerlendirilmiştir. Buna göre MB'nin f_1 değeri (15,45) 15'ten büyük; MB ve MF'nin f_2 değerlerinin (sırasıyla 48,57, 47,13) 50'den küçük olması MB ve MF formülasyonlarının çözünme profillerinin yenilikçi markanın çözünme profilinden farklı olduğunu belirlemiştir.

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Conclusion: Five of the eight tablet brands passed all the official tests and could be regarded as pharmaceutically equivalent but f_2 analysis showed only five brands were similar to the reference brand. The study has shown that all the MET tablet brands sampled in Northern Cyprus are not pharmaceutically equivalent.

Keywords: Metformin tablets, comparison, dissolution, pharmaceutical equivalency, physicochemical properties

Sonuç: Sekiz tablet markasından beşinin tüm farmakope testlerini geçtiği ve farmasötik açıdan eşdeğer olarak kabul edilebilir olduğu saptanmıştır. Ancak f_2 analizi, yalnızca beş markanın referansa benzer olduğunu göstermiştir. Çalışma, KKTC'de örneklenen tüm MET tablet markalarının farmasötik açıdan eşdeğer olmadığını ortaya koymuştur.

Anahtar Sözcükler: Metformin tabletleri, karşılaştırma, çözünme, farmasötik eşdeğerlik, fizikokimyasal özellikler

Introduction

Diabetes mellitus (DM) is a disease of fat and carbohydrate metabolism characterized by chronic hyperglycemia as a result of inadequate insulin secretion and activity (1). In the first diabetes screening conducted in the Cyprus in 1996; 7.3% of the population had previously known DM. In addition, 4% of the participants were found to have previously unrecognized DM. The same study was repeated in 2008, and DM was found in 11.5% of the population aged 20-80 years (2).

Metformin hydrochloride (MET) (1,1-dimethyl biguanide hydrochloride) works as an antihyperglycemic medication by inhibiting gluconeogenesis and improving insulin action in skeletal muscles. Thus, it can be said that MET is a commonly prefered drug in the treatment of type II DM (3,4).

In Northern Cyprus and in many other countries, numerous brands of generic metformin tablets are available in the pharmaceutical markets. Generic drug products are often more widely available and less expensive than innovator ones. Since many generic products are available on the pharmaceutical market, the question of whether the products are bioequivalent becomes important. Especially, considering that the product is a drug, choosing products that have formulated the same active ingredient in the same dosage form but have different trade names should not cause health problems (5,6). In addition, there has been an increasing number of drug counterfeiting incidents in recent years. When adequate safe precautions are not taken, many pharmaceutical products imitated in primitive conditions can be found in the drug market (7). Therefore, drug products are expected to have comparable quality properties before they become clinically modifiable (8).

As a result, in order to be acceptable alternatives, generics must have pharmacological and therapeutic qualities comparable to innovator drugs. The determination of whether a product is chemically and biopharmaceutically identical is a key step in determining therapeutic equivalence.

Physicochemical properties of metformin tablets, which were available on the Northern Cyprus pharmaceutical market, were determined in this study. Additionaly, in order to provide information on the differences and similarities in their dissolving patterns, f_1 and f_2 factors of these tablets were calculated.

Methods

MET was gifted by Abdi İbrahim İlaç, Turkey. On the other hand, eight brands (generic and innovator brands) of commercial uncoated MET tablets having 500 mg of MET were purchased from community pharmacies in Northern Cyprus. The general characteristics of the tablets are shown in Table 1. In addition, all chemicals were purchased from Sigma-Aldrich.

Isolation of Metformin Hydrochloride from Tablets

A powdered tablet containing 50 mg of MET was mixed with 50 mL of ethyl alcohol and filtered. The filtrate was dried, and the residue was dried for 1.5 hours at 100 °C. The method was repeated for other brands of tablets, and the residues were used for infrared examination (9).

Recognition of Isolated Metformin Hydrochloride Using FTIR

A sufficient amount of powder mass was taken and placed in the device and the IR spectrum was determined in the range of 500-4,000 cm^{-1}. The process was repeated for the mass of powder from each brand and compared with the reference metformin spectrum.

Weight Variation Test

Twenty tablets of each brand were randomly selected and weighed with Shimadzu balance and standard deviation values were calculated. The process was repeated for all brands (10).

Friability Test

Ten tablets were chosen at random from the each brand, weighed together, then placed in a friabilator for 100 rpm. They were weighed again, and the % weight reduction was measured (10,11).

Hardness Test

Ten randomly chosen tablets from each brand were tested with an Erweka tester, determining the hardness of the tablets in Newton. For each brand, the standard deviation value of hardness was computed (9).

Diameter and Thickness Test

Ten metformin tablets were chosen at random from each brand to be tested with an Erweka tester and diameter and thickness of the tablets were measured. For all groups of tablet, the standard deviation values of diameter and thickness were computed (9,10).

Disintegration Test

Disintegration is the operate of breaking the tablet into granules and is the first step in dissolution, therefore it is part of the *in*

vitro and *in vivo* correlation, and the disintegration test indicates the time required to break the tablet. The disintegration period of the tablets in purified water at 37±0.5 °C was calculated (9).

Content Uniformity Test (Assay Test)

The UV spectrophotometric method was used to determine the amount of metformin in solution. For this purpose, first of all, the standard metformin solution was prepared by using 100 mg MET in 1,000 mL of 6.8 buffer solution in a volumetric flask with vigorous shaking. This solution was further diluted to get a set of solutions containing MET in vary concentrations. Absorbance values of the solutions at 235 nm were determined UV spectrophotometrically. Analytical parameters were determined by ANOVA.

The amount of MET in a tablet was determined by using UV spectrophotometric method. A standard MET solution was prepared into 6.8 phosphate buffer solution and sample solutions were prepared dissolving MET tablets from each batch in the same medium. The MET amount in each solution was determined spectrophotometrically (10).

***In vitro* Dissolution Test**

The dissolution studies on metformin tablets were performed according to USP paddle method at 100 rpm. The dissolution medium was selected as 1,000 mL of 6.8 buffer at 37±0.5 °C. The samples were taken at definite time and assayed spectrophotometrically at 235 nm. The % released of MET from the tablets were determined (12,13).

Comparison of the Dissolution Data

According to the dissolution data obtained, the f_1 and f_2 of the other brands were calculated by comparing them to the reference drug (Glucophage®).

The difference factor ranges from 0 to 15. If f_1 ≤15, the two dissolution profiles are identical or similar, and the two products can be changed. If f_1 >15, it indicates that the dissolution profiles are different and so the products can not be interchanged.

The similarity factor ranges from 0 to 100. If f_2 ≥50, the two dissolution profiles are identical or similar, and the two brands can be changed. If f_2 <50, it indicates that the dissolution profiles are different and so the brands can not be interchanged (9,12).

Results

Each of the eight brands of metformin tablets bought had at least three months of expire dates left, and all analytical measurements were performed prior to the expire dates. While one brand was produced in Northern Cyprus, seven brands were imported. All metformin tablets were uncoated tablets. Details of the selected tablets are shown in Table 1.

The FTIR spectrum obtained from metformin isolated from each metformin brand represented absorption bands at 1,520, 1,630 and 3,458 cm^{-1} similar to FTIR spectrum of pure MET (10). FTIR spectrums are shown in Figure 1.

The amount of metformin HCl in the tablets was determined by UV spectrophotometric method (14). Method validation details are shown in Table 2.

The metformin tablet brands generally had acceptable characteristics. The tablet's weight uniformity and friability test results were suitable except brand MF (1.05%). All eight uncoated tablet brands disintegrated in the medium <15 minutes. The MET amount rate of the tablet brands was in the range of 90.08-99.15%. Five metformin tablet brands passed the content uniformity test (Assay test), but three (MC, MF, MG) had lower doses. The dissolved drug amount in 30 min, in all the tablet brands was higher than 80% (15).

Figure 2 depicts the dissolution profiles of MET tablets in pH 6.8 buffer. The tablets represented counterpart dissolution profiles and achieved higher than 80% release in 30 minutes in the dissolution medium. f_1 and f_2 of the MET tablet brands are shown in Table 4. All metformin tablets exhibited high dissolution properties (>90%) in pH 6.8 phosphate buffer. For all metformin brands in buffer pH 6.8, f_2 values were not higher than 50. While the f_2 value of the MB coded metformin tablet was 48.57, the f_2 value of the MF coded tablet was 47.13.

Table 1. Some details of studied metformin hydrochloride tablets

MET tablet code date	Origin	Lot number	Expiry
MA	Northern Cyprus	112	08/2021
MB	Turkey	064	01/2022
MC	United Kingdom	082	09/2021
MD	Turkey	099	09/2021
ME	Turkey	108	01/2022
MF	United Kingdom	096	06/2021
MG	United Kingdom	820	07/2021
MH	France	306	04/2021

Table 2. Analytical method validation parameters for the assay of MET by UV spectrophotometric method

Parameter	Result
Linearity range (µg/mL)	1-12
Slope (m)	0.0738
RSD of m (%)	0.21
SE of m	0.022
Intercept (n)	0.1839
RSD of n (%)	3.5
SE of n	0.004
Determination coefficient (r^2)	0.9978
LOD (µg/mL)	0.0198
LOQ (µg/mL)	0.06
RSD for precision (%)	2.03
RSD for accuracy	0.38

RSD: Relative standard deviation, SE: Standard error

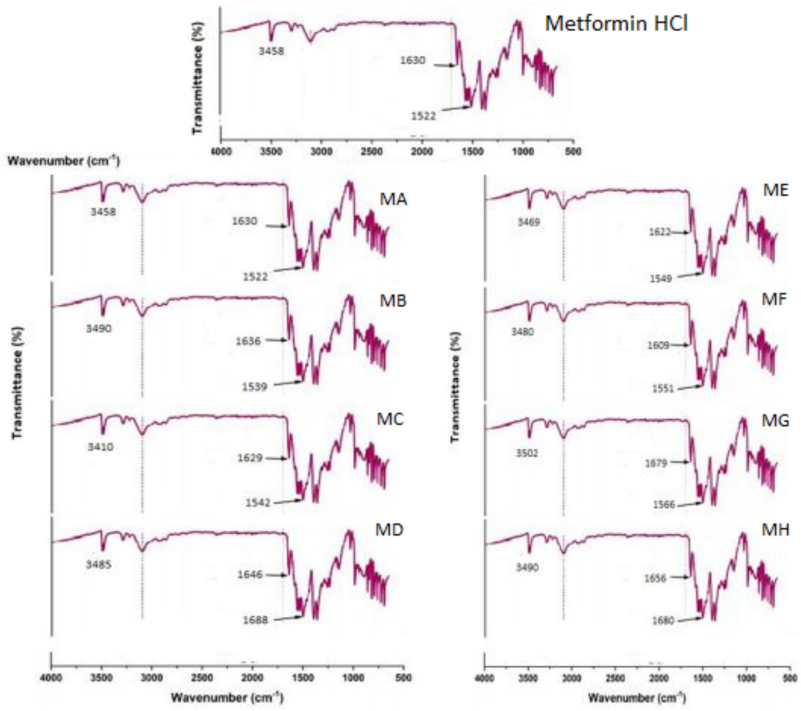

Figure 1. FTIR spectrums of pure metformin HCl and metformin tablets

Table 3. Results of physicochemical tests of metformin hydrochloride tablet brands

MET tablet	Weight (mg) (Xmean ± SD)	Diameter (mm) (Xmean ± SD)	Thickness (mm) (Xmean ± SD)	Hardness (N) (Xmean ± SD)	Friability (%) (Xmean ± SD)	Disintegration time (min.sec) (Xmean ± SD)	Content uniformity
MA	535.37±2.84	11.06±0.02	5.93±0.03	445.7±1.09	0.01±0.001	8.42±0.001	99.01±0.32
MB	589.37±4.21	11.10±0.02	5.57±0.02	423.6±1.23	0.05±0.001	8.34±0.006	95.67±0.55
MC	544.43±3.92	11.05±0.01	5.68±0.02	408.4±1.09	0.04±0.018	7.59±0.002	90.12±0.48
MD	550.41±1.92	11.12±0.01	5.55±0.04	474.7±1.55	0.05±0.002	8.42±0.001	97.11±0.22
ME	541.32±2.52	10.92±0.02	5.47±0.02	445.7±1.01	0.11±0.003	6.18±0.002	96.14±0.37
MF	560.87±1.23	11.02±0.02	5.71±0.05	446.1±0.88	1.05±0.009	5.70±0.001	90.08±0.62
MG	552.88±2.12	11.32±0.03	5.48±0.01	445.7±0.92	0.02±0.001	8.01±0.001	92.77±0.44
MH	538.44±1.55	11.05±0.01	5.38±0.01	408.5±0.71	0.01±0.001	5.45±0.003	99.15±0.19

SD: Standard deviation, min: Minimum

Table 4. Difference (ƒ1) and similarity (ƒ2) factors for reference (MH) versus test brands

	MA	MB	MC	MD	ME	MF	MG
ƒ1 values	7.81	15.45	6.17	5.59	8.11	9.14	10.05
ƒ2 values	81.14	48.57	78.26	85.45	79.33	47.13	88.21

When the release kinetics of the tablets were examined, it was determined that the highest r^2 values were observed in the first order kinetic and Hixson-Crowell release models. Table 5 shows the release kinetic details for each tablet.

Discussion

To determine the identity of the active pharmaceutical ingredient, 8 MET tablets were exposed to FTIR analysis. Identification testsensured that all brands of metformin tablets contained MET as active ingredient and were not imitation products. MET tablets were tested for quality and pharmaceutical equivalency using pharmacopoeia and other methods. Weight variation, friability, thickness, disintegration time, hardness, dissolution and drug content were evaluated. During production, these criteria are used to measure the uniformity of quality across multiple batches of tablets (16). The quality factors are interconnected and have a significant impact on bioavailability (17). The majority of the

Table 5. Kinetic parameter results of dissolution data for metformin tablets

		MA	MB	MC	MD	ME	MF	MG	MH
First order kinetic	RMS	1.921	1.690	2.614	1.815	1.922	1.754	1.669	1.915
	k	0.013	0.006	0.021	0.014	0.016	0.039	0.022	0.028
	r^2	0.984	0.996	0.985	0.982	0.979	0.991	0.975	0.999
Hixson-crowell	RMS	4.659	3.226	4.202	4.442	4.521	3.996	4.205	4.336
	k	0.190	0.002	0.159	0.080	0.140	0.208	0.184	0.121
	r^2	0.929	0.903	0.955	0.901	0.916	0.892	0.902	0.896

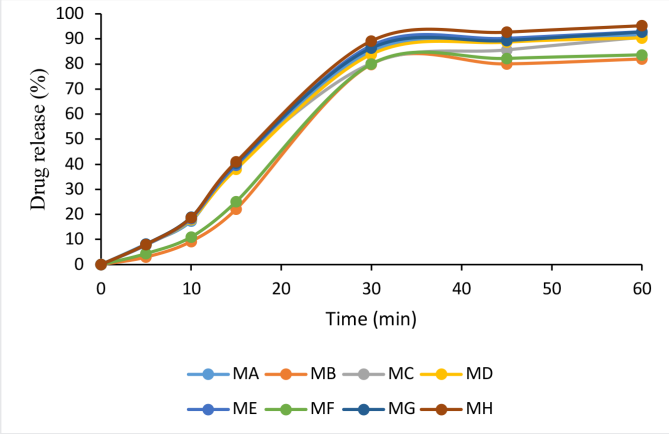

Figure 2. Dissolution profiles of metformin tablets

quality evaluation tests performed on the tablet brands under consideration were passed. Because of differences in granulation density and compression force applied to the tablets, the thickness of a tablet may fluctuate while the weight remains constant.

The weight uniformity test is used to ensure consistent dosing among tablets within a batch, preventing overdosage or underdosage. The change in drug content of a tablet is directly affected by its weight variation. Because all MET tablets weigh higher than 500 mg, no more than two individual tablet weights should differ from the average weight by higher than 5%, and no tablet should differ by more than twice the permissible percentage deviation (14). All MET tablets evaluated met this requirement and hence passed the weight uniformity test.

The friability test is performed to determine a tablet's ability to tolerate abrasion during packaging and transportation. The nature and amount of binder used in tablets influence this feature (18). For pharmaceutical items, friability should be lower than 1% of the tablets (14,15). All of the brands passed the friability test, with the exception of MF, which had a 1.05 friability. The failure of MF could be attributed to the use of inadequate binder or the use of not enough amount of compaction force.

Tablet hardness measurements are used to detect whether or not tablet machines require pressure adjustments. A highly hard tablet can not disintegrate in the requisite time in an aqueous solution, whereas a very soft tablet can not resist handling activity (9). The minimum crushing force for a good tablet is 400 N (14). All MET tablet brands performed well in terms of fracture resistance, exceeding the minimum of 400 N.

Disintegration is a critical process before medication release from immediate release dosage formulations. Uncoated tablet disintegration time should not exceed 15 minutes (14). According to the findings, all tablets disintegrated at suitable time. MET tablets should contain 95-105 % of the drug's label claim upon assay, according to the British and American pharmacopoeias (14,15). The spectrophotometric measurements (Table 3) revealed that all brands, with the exception of MC, MF, and MG, met this pharmacopoeia standard. Brands MC, MF, and MG had drug content percentages lower than the minimal level of 95% and could be deemed of inferior quality. The failure of the MC, MF, and MG assay tests could be attributable to inaccuracies in API weighing and inadequate mixing during the tableting process.

Oral solid dose forms can be absorbed after they have been disintegrated and dissolved. Therefore, the dissolution test is used to predict product behavior *in vivo*. The dissolution test can be considered an *in vitro* bioequivalence test to examine whether solid dosage forms are equivalent (19). In 30 minutes, immediate release formulations should release 80% of the specified dosage (14). The study's findings demonstrated that all of the MET tablets had good dissolving profiles as instant release tablets.

Study Limitations

According to FDA, f_1 (difference factor) value, which is one of the parameters used to express that the dissolution profiles are not different, should be 0-15. In our study, when we compared the dissolution profiles of the metformin containing tablets of different manufacturers with the innovative company's product, it was determined that the f_1 value (15.45) of only the MB formulation was more than 15. On the other hand, the two brands (MB and MF) did not have f_2 values in the dissolution media within the range specified by the FDA (50-100) (20). Therefore, it should be considered that these brands do not have the same drug release bioequivalence as the MH (reference brand) in pH 6.8 phosphate buffer medium. Two oral dosage forms are accepted as bioequivalent if they release drugs at the same rate. *In vivo* bioequivalence studies are typically used to determine a product's bioequivalence. These *in vivo* bioequivalence studies, on the other hand, are typically costly and involve the use of intrusive methods. The most significant benefits of *in vitro* dissolution studies include lower costs and a more accurate assessment of product performance. Because the drug is soluble in physiological settings, generic metformin tablets with varying dissolving characteristics may nonetheless provide equal therapeutic efficacy *in vivo*.

Conclusion

Eight MET tablets were determined to comply with pharmacopoeia specification for disintegration, weight variation, dissolution test and hardness for uncoated tablets. One brand failed the friability test, while three failed the assay test. Two of the sampled MET tablet brands showed that dissolution profiles were not similar to the reference brand (MH) in pH 6.8 buffer medium in terms of similarity factors. Based on the results of the study, it can be said that in order to ensure the quality and therapeutic efficacy of metformin tablets on the market, the drug regulatory authorities in Northern Cyprus should intensify post-market inspection and surveillance.

Ethics

Ethics Committee Approval: Ethics committee approval was not required.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: E.D.Ö., T.Ç., Design: E.D.Ö., T.Ç., Data Collection or Processing: E.D.Ö., T.Ç., Analysis or Interpretation: E.D.Ö., T.Ç., Literature Search: E.D.Ö., T.Ç.,Writing: E.D.Ö., T.Ç.

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References

1. Rohani B. Oral manifestations in patients with diabetes mellitus. World J Diabetes 2019;10:485-9.
2. Votsi C, Toufexis C, Michailidou K, Antoniades A, Skordis N, Karaolis M, et al. Type 2 Diabetes Susceptibility in the Greek-Cypriot Population: Replication of Associations with TCF7L2, FTO, HHEX, SLC30A8 and IGF2BP2 Polymorphisms. Genes (Basel) 2017;8:16.
3. Garba, MA, Dauda NJ, Mohammed M, Bello SS. Comparative quality control studies on three brands of metformin hydrochloride tablets marketed in Kaduna, Nigeria. Journal of Pharmaceutical and Allied Sciences 2019;16:3086-93.
4. Migdadi EM, Courtenay AJ, Tekko IA, McCrudden MTC, Kearney MC, McAlister E, et al. RF Hydrogel-forming microneedles enhance transdermal delivery of metformin hydrochloride. J Control Release 2018;285:142-51.
5. Simionato LD, Petrone L, Baldut M, Bonafede SL, Segall AI. Comparison between the dissolution profiles of nine meloxicam tablet brands commercially available in Buenos Aires, Argentina. Saudi Pharm J 2018;26:578-84.
6. Adegbolagun OA, Olalade OA, Osumah SE. Comparative evaluation of the biopharmaceutical and chemical equivalence of some commercially available brands of ciprofloxacin hydrochloride tablets. Tropical Journal of Pharmaceutical Research 2007;6:737-45.
7. Uddin M. Blockchain Medledger: Hyperledger fabric enabled drug traceability system for counterfeit drugs in pharmaceutical industry. International Journal of Pharmaceutics 2021;597:120235.
8. Blackstone EA, Fuhr JP Jr, Pociask S. The health and economic effects of counterfeit drugs. Am Health Drug Benefits 2014;7:216-24.
9. Çomoğlu T, Gönül, N. Quality control studies on conventional Carbamazepine tablets available on the Turkish drug market. Turkish Journal of Med Sci 2005;35:217-21.
10. Sougi A, Ofori-Kwakye K, Kuntworbe N, Kipo SL, El Boakye-Gyasi M. Evaluation of the physicochemical and in vitro dissolution properties of metformin hydrochloride tablet brands marketed in five cities in Ghana. Br J Pharm Res 2016; 9:1-14.
11. Munde MK, Kulkarni NS, Khiste RH, Sen DB. Development and Validation of Novel Analytical Method for Empagliflozin and Metformin Hydrochloride in Bulk and Pharmaceutical Dosage Form by Four Different Simultaneous Estimation Approaches using UV Spectroscopy. Research Journal of Pharmacy and Technology 2020;13:1236-42.
12. Sahle SB, Ayane AT, Wabe NT. Comparative quality evaluation of paracetamol tablet marketed in Somali region of Ethiopia. International Journal of Pharmaceutical Sciences and Research 2012;3:545.
13. Gündoğan M, Çomoğlu T, Gönül N. Comparison of the quality and in vitro dissolution profiles of commercial losartan potassium film tablets. Turk J Pharm Sci 2008;5:75-88.
14. XXXII, U. (2009). USP 32: United States Pharmacopeia. In Rocville: United States Pharmacopeial Convention (pp. 2905-2906).
15. British Pharmacopoeia. Her Majesty's Stationery Office, London. 2013;2.
16. Chavan H, Chhabra G, Gujarathi N, Jadhav A. Comparative study of In-process and finished products quality control test for tablet and capsules according to pharmacopoeias. Asian Journal of Pharmaceutical Research and Development 2018;6:60-8.
17. Liu Y, Wang A, Wen L, Yang Z, Yang X, Zhang X, Yan D. A Chinese medicine formula (Jinqi Jiangtang Tablet): a review on its chemical constituents, quality control, pharmacokinetics studies, pharmacological properties and clinical applications. Journal of Ethnopharmacology 2019;236:1-8.
18. JI O, Onyemelukwe J I. Comparative assessment of ginger and cassava starch as a binder on ibuprofen tablet formulation. Int J Life Sci Scienti Res 2018;2455:1716.
19. Zhang Y, Yang F, Zhang J, Sun G, Wang C, Guo Y, et al. Quantitative fingerprint and quality control analysis of Compound Liquorice Tablet combined with antioxidant activities and chemometrics methods. Phytomedicine 2019;59:152790.
20. Davit BM, Stier E, Jiang X, Anand, O. Expectations of the US-FDA regarding dissolution data in generic drug regulatory submissions. Biopharma Asia 2013;2:14-21.