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Original article

Comparative *in-vitro* Evaluation of Some Desloratadine Tablets Marketed in Tripoli Libya

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ABSTRACT

Background and aims*. Desloratadine is a tricyclic, potent, rapidly effective, long acting, non-sedative antihistamine, which has a selective and peripheral H1 receptor antagonist action, used to treat the allergies. The availability of several brands of Desloratadine 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 aim of the present study was the evaluation and comparison of pharmaceutical equivalence of five different Desloratadine tablets 5 mg, which are commercially available in the private pharmacies in Tripoli city with different price ranges, produced by various pharmaceutical companies.* ***Methods****. The pharmaceutical evaluation of five brands of Desloratadine tablets were done using official and unofficial quality control tests prescribed in different Pharmacopoeia including uniformity of weight, thickness, hardness, disintegration time, drug content as well as dissolution rate and identification test. Acceptable external features as well as uniformity in diameter and thickness were revealed for all the tablets.* ***Results****. The entire selected brands complied with the official specifications for uniformity of weight, hardness and disintegration, more than 80% of their drug dissolved in the medium within 60 minutes.* ***Conclusion****. It can be concluded that all the brands could be regarded as bioequivalent and therefore can be interchanged in the clinical practice; this sort of study is 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.*

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INTRODUCTION

The oral route is most frequently used for introducing drugs into the body, and in fact the vast majority of drug dosages forms are designed for orally ingestion [1]. Tablets are the most frequently administered oral solid dosage form because of the low cost of therapy and this type of route of administration lead to high levels of patient compliance. The increases in the number of generic drug products from multiple sources has placed people involved in the delivery of health care in a position of having to select one from among several apparently equivalent products [2].

Generic substitution is the prescribing different brand or an unbranded drug which contains the same active pharmaceutical ingredient at similar strength and dosage form [3]. Branded drug products of top pharmaceutical companies are better in terms of efficacy but as a consequence of its high cost patients from low income countries cannot afford it [4].

The prevalence of allergic rhinitis ranges from 10-25% worldwide, and is increasing. Histamine H_1 receptor antagonists have been widely used in the management of allergic disorders, such as rhinitis and chronic idiopathic urticarial for more than half a century [5].

Desloratadine is a second generation, tricyclic anti histamine, which has a selective and peripheral H1-antagonist action. It is used in the treatment of allergies.

Desloratadine structure as shown in Figure (1) has the molecular formula C19H19ClN2, with molecular weight 310.8 g/ mol. The chemical name is 8-chloro-11-piperidin-4 ylidene-6,11-dihydro-5Hbenzo [5,6] cyclohepta [1,2-b] pyridine.

Desloratadine is the orally active metabolite of the non-sedating antihistamine Loratadine [6]. It is a potent and selective histamine H_1 receptor antagonist with a half-life of 21-24 hours [7]. It's *in vivo* features include long duration of action with minimal sedation.

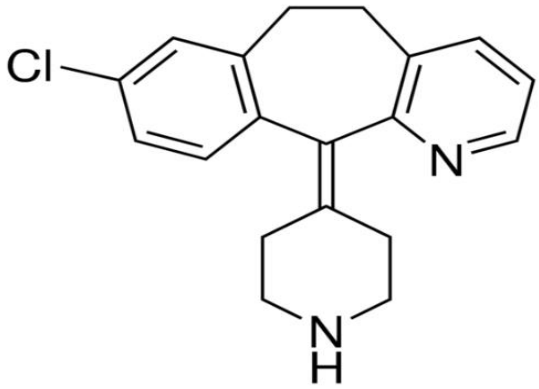

Figure 1. Chemical Structure of Desloratadine

Drug products that are chemically and bio-pharmaceutically equivalent must be identical in strength, quality, purity, active ingredient release profile and should be in the same dosage form, for the same route of administration [8].
In Libya, there are many different brands of Desloratadine tablets available from different multinational companies. Each brand has its own formulation which affects the release and delivery of drug and produce variable clinical responses. Evaluation of *in-vitro* release and the physicochemical properties of these brands are very important as it can be used to evaluate the bioavailability and pharmaceutical equivalence [9]. Various brands available in the market are considered pharmaceutically equivalent if they contain the same amount of active ingredients in the identical dosage form and meet the same compendia standards in strength, quality, purity and identity but may differ in shape, packaging, excipients, expiration time and labeling requirements [10]. According to World Health Organization (WHO) the prevalence of fake medicines was higher in developing countries with weak regulations, enforcement, and scarcity of supply of essential medicines, unregulated market, and unaffordable prices [11]. For these reasons, the safety, quality , and efficacy of drug products especially in developing countries cannot be granted, therefore post market qualitative studies are important, few drug quality control studies have been conducted so far in Tripoli Libya, these studies encouraged to examine the medicine quality for continuous monitoring and to control drug products in the market that might prevent the prevalence of counterfeits and sub-standard medicines and ensure the use of medicines of standard quality and different brands available are pharmaceutically equivalent [12-15] .
Quality control is a procedure or set of procedures intended to ensure that a manufactured product is complied with specifications. Quality control has an important role in pharmaceutical field, it's an investigation applied to drug and drug products, including all those factors which contribute directly or indirectly to safety, effectiveness and reliability of product. Patient safety is the most important value in all drug factories; the basic goal is to provide efficient, safe and compatible products for the prevention and treatment of illness [16].
The aim of this study was to evaluate and compare pharmaceutical quality control parameters of different Desloratadine 5mg tablets marketed in the private pharmacy sector of Tripoli Libya. The parameters include evaluation of weight uniformity, diameter, thickness, hardness, dissolution, disintegration, identification, and price of tablets, to ascertain that all the brands under investigation are pharmaceutically equivalent.

MATERIALS AND METHODS

Desloratadine tablets having label strength of 5 mg of five different brands were purchased from different private pharmacies in Tripoli Libya. The products were coded as A, B, C, D and E as illustrated in Table 1 all drugs included in the study was within the validity date limit.
Distilled water, 0.1N hydrochloric acid, KCL and Pure sample of Desloratadine (DEL.TA.PHARMA) lot No.AL4005003 was obtained from the National Center for Food and Drug Control.

Table 1. Label information of five different brands of Desloratadine tablets under investigation

Product code	Batch No.	Manufacture Date	Expire Date	Price /tablet in LYD
A	0016	6/2020	6/2022	0.80
B	20T0145	5/2020	04/2023	1
C	190337	12/2019	12/2022	1
D	ID820001	8/2020	07/2022	1.05
E	R002	Not present	01/2022	1

Visual Inspection

Samples of Twenty 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 [17].

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/cm^2. Tablet thickness and diameter should be controlled within a ±5% of a standard value [18, 19].

Disintegration Test

Samples of six tablets were selected from each brand. Tablets were placed in six tubes of the basket-rack assembly of the disintegration time tester PTZ Auto 1EZ (Pharma test, Germany) and perforated cylindrical plastic discs were put on top surface of each tablet. The assembly was allowed to move up and down in a beaker containing 1 liter of 0.1N HCl at 37±0.5^{0}C, as per condition described by USP. The time taken to break each tablet into small particles and pass out through the mesh at the bottom of the tube was recorded. Mean disintegration time was calculated for each one of the brands [20].

Preparation of the standard curve

A stock solution of pure Desloratadine powder was prepared by dissolving 50 mg of pure Desloratadine in 50 ml of 0.1 N HCl to produce a 1mg/ml solution. 10 ml of stock solution was transferred to a measuring flask and the volume was made to 100 ml with 0.1 N HCl. Different concentrations of pure Desloratadine were prepared from stock solution. The absorbance of the different concentrations including blank which was taken at 280nm using UV- spectrophotometer and plotted against Desloratadine concentration.

Dissolution Rate Determination

Dissolution test was carried out by a dissolution apparatus operating at 100 rpm for 60 min, using 0.1N Hydrochloric acid (900 ml) prepared as a dissolution medium, at 37C˚ ±2C˚. Six tablets from each brand were placed in a small wire mesh basket fastened to the bottom of the shaft connected to a variable speed motor. Samples were withdrawn at intervals of 5, 10, 20,30,40,50, and 60 min, on each time, samples were diluted at first by withdrawing 5ml and replacing it with 5ml fresh medium in a 25ml capacity flask, then withdrawing from it 1ml and diluting it again by fresh medium in a 25ml capacity flask. Samples were filtered and absorbance measured at 280nm using pure medium as a blank. The percentage of average drug release for each brand was plotted against time.

Content uniformity test

Twenty tablets selected randomly and powdered then the average weight was calculated. The average weight of the tablet powdered was dissolved in 100 ml of 0.1N Hydrochloric acid with pH1.2, followed by stirring for 20 minutes at room temperature. The solution was filtered through membrane filter and filtrate collected. One ml of the filtrate is diluted to 100ml with 0.1N Hcl. The absorbance of resultant solution was measured at 242nm using 0.1 N Hcl as blank and content of Desloratadine is estimated [21].

Identification

The test was done simply by grinding 10 tablets and from the grinded powder about 3mg was taken, added to 300 mg of KCl powder (FTIR background window) then mixed together till homogenous mixture was obtained. The prepared sample pellet (disc) was achieved or obtained by compression all the mixture and finely measured for spectrum [22]. In case of differences seen in the spectra of solid state, the substance and the reference substance has to be dissolved separately in methyl isobutyl ketone R, then evaporate to dryness and a new spectrum is recorded using the residues.

RESULTS AND DISCUSSION

Five commercial Desloratadine 5 mg tablets (Table 1) 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 blue colors. Only brand A 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.

Table 2. Appearance features of the different brands of Desloratadine 5mg tablets

Parameter	Brand A	Brand B	Brand C	Brand D	Brand E
Shape and color	Rounded blue	Rounded blue	Rounded blue	Rounded blue	Rounded blue
Surface texture and Convexity	Smooth and biconvex	Smooth and biconvex	Smooth and biconvex	Smooth and biconvex	Smooth and biconvex
Monograms and score lines	YES	NO	NO	NO	NO
Defect in the tablet coat	NO	NO	NO	NO	NO

All brands of Desloratadine tablets were consistent in their weight and exhibited uniform geometrical dimension parameters (Table 3). The deviation of the tablets weight from the average were in the permitted limit with a deviation less than ± 7.5 %. Brand B and C exhibited quite similar average weight and all the investigated brands demonstrated similar diameters except brand D that showed to be the largest in average weight, as well as the most expensive one among the selected brands. The thickness of all brands range from 2.9 mm to 3.4 mm. The hardness test results (Table 3), showed that brand A exhibited greater capability in resisting chipping, while brand B demonstrated the lowest and weakest solidity in comparison to the other brands.

All brands passed the disintegration time test according to the official limit. Tablets were broken up and disaggregated into their original granules and particles within 15 minutes. Brand D demonstrated very rapid disintegration time compared to the other brands (Table 3), while brand E showed a more prolonged disintegration time with average (0:1:15min). It was found that all brands were in compliance with the standard limit for dissolution test Figure (3). The drug release values were more than 75% in one hour, all the assessed brands exhibited similar patterns of drug dissolution excluding brand E which had the fastest drug release with more than 90% in 10 min.

Figures (4) to (9) show the IR spectrum of different commercial brands of Desloratadine and the standard. It was observed that all spectra obtained for different samples of Desloratadine have similar absorption bands to the IR spectrum of standard Desloratadine. The similarity between the spectra is strongly indicative of the identity of Desloratadine in all of

the samples analyzed using IR technique. Our resulted spectrum is completely matched with Desloratadine reference standard in range of 98 to 99 % for all samples from A to E.

Table 3. Evaluated physicochemical parameters of the five brands of Desloratadine tablets

Brands	Average weight (g)	Dissolution (%)	Hardness (kP)	Disintegration (min)	Diameter (mm)	Thickness (mm)	Content Uniformity (%)
A	0.1251	94.01	11.9290	0:00:18	6.00	3.4685	98.5
B	0.1048	91.8	5.0645	0:00:23	6.053	2.9055	99.2
C	0.1047	91.8	7.4860	0:00:33	6.06	3.0535	101.2
D	0.1726	95.4	8.8440	0:00:15	7.97	3.0645	96.7
E	0.1154	93.6	6.3425	0:01:51	6.029	3.4355	98.7

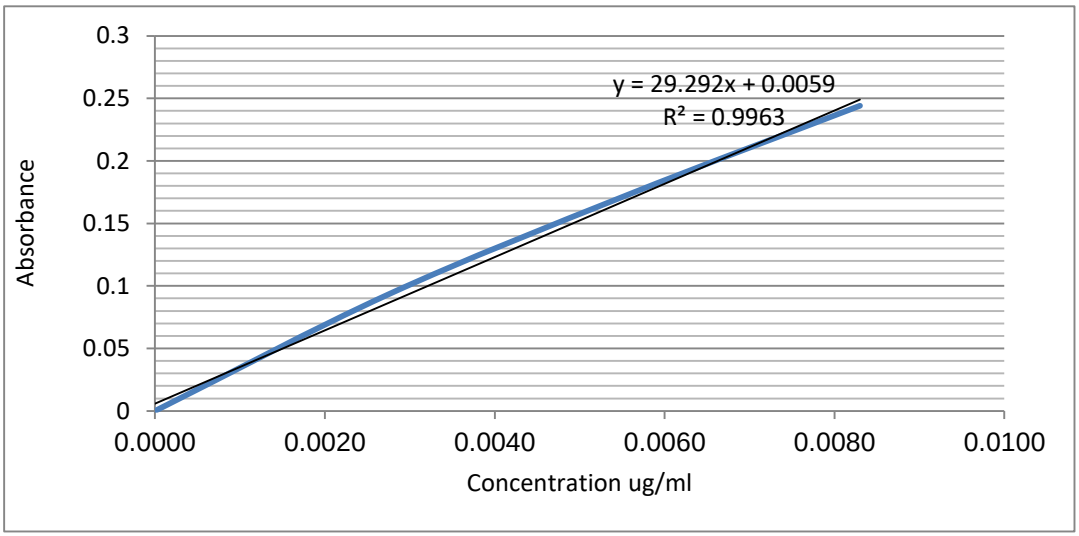

Figure 2. Calibration Curve of Desloratadine in 0.1N HCl

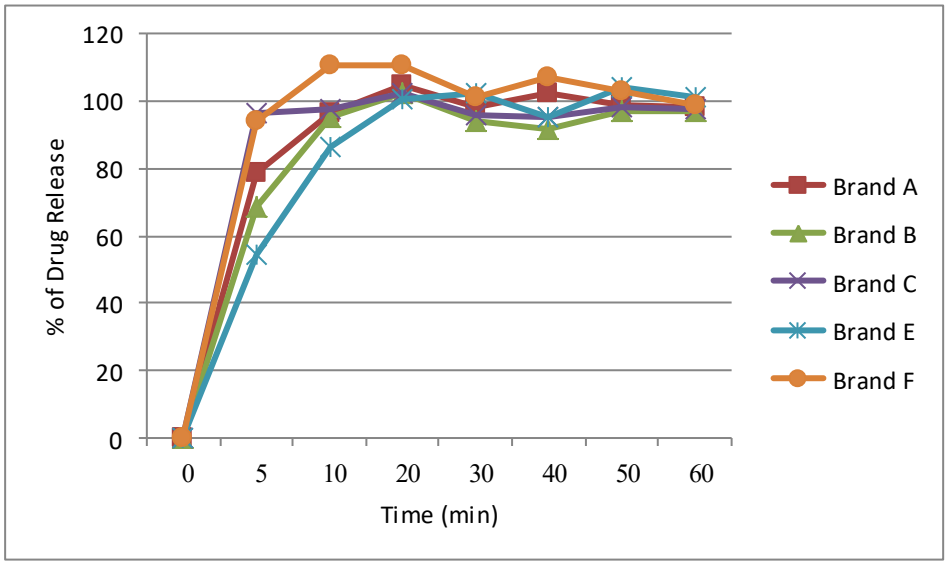

Figure 3. Dissolution curve of different brands of Desloratadine tablet

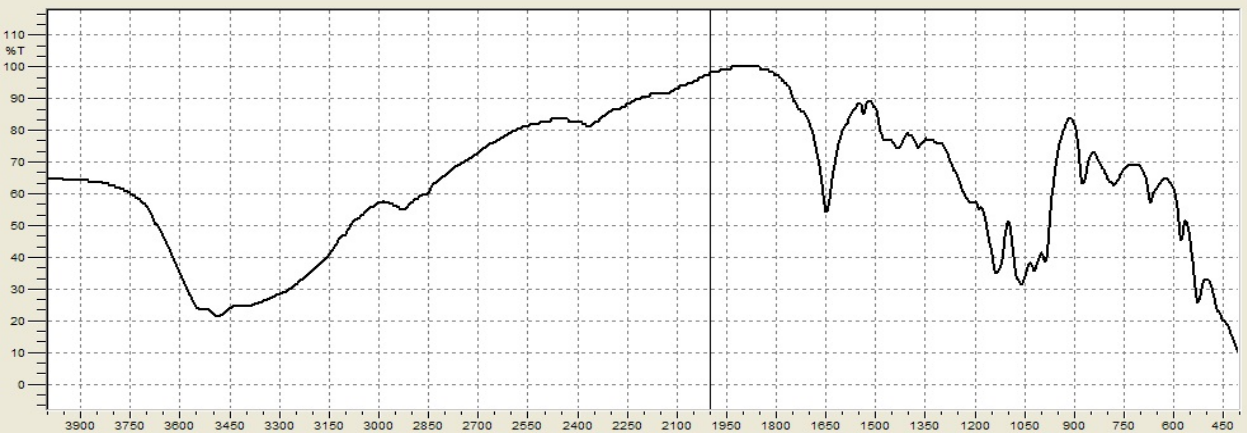

Figure 4. IR spectroscopy results for standard Desloratadine

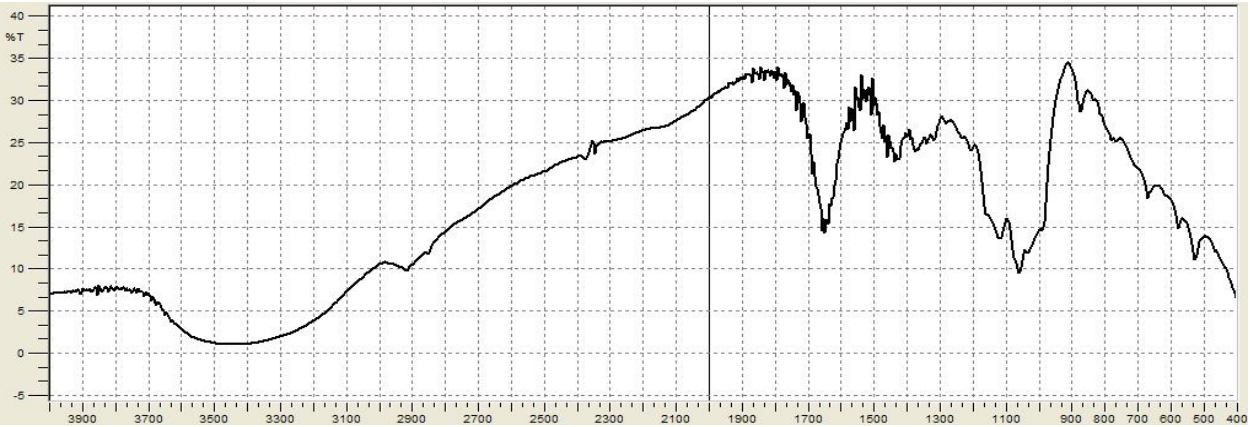

Figure 5. IR spectrum of brand A Desloratadine

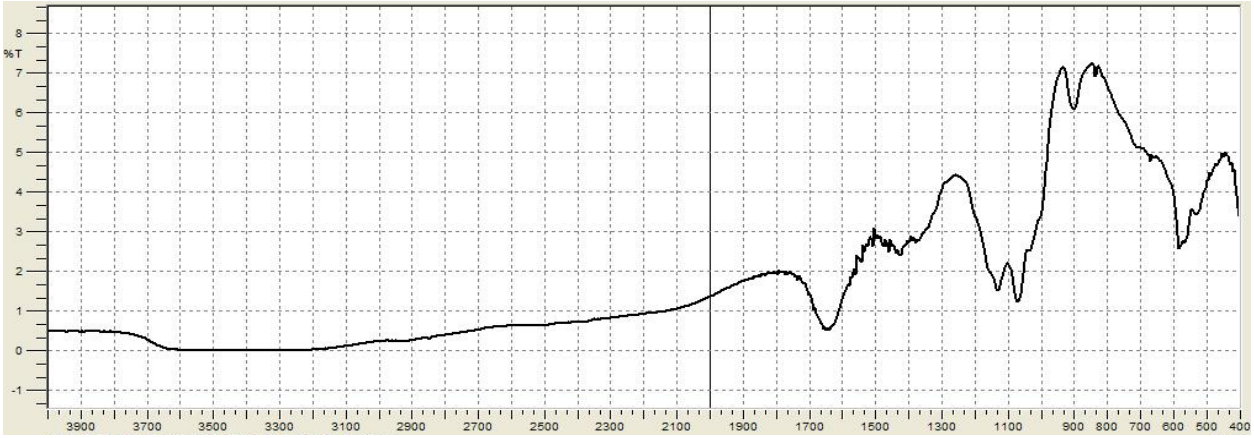

Figure 6. IR spectrum of brand B Desloratadine

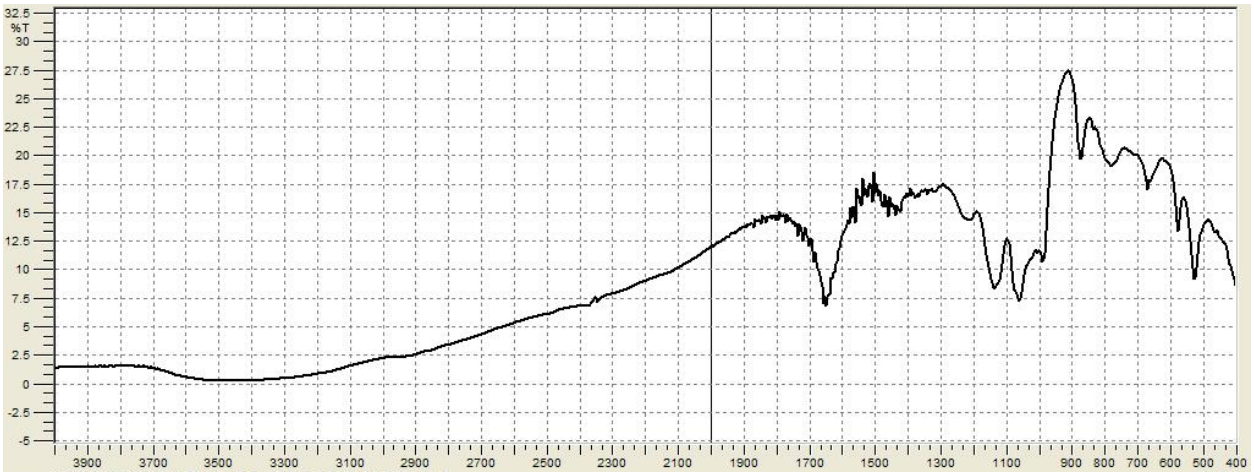

Figure 7. IR spectrum of brand C Desloratadine

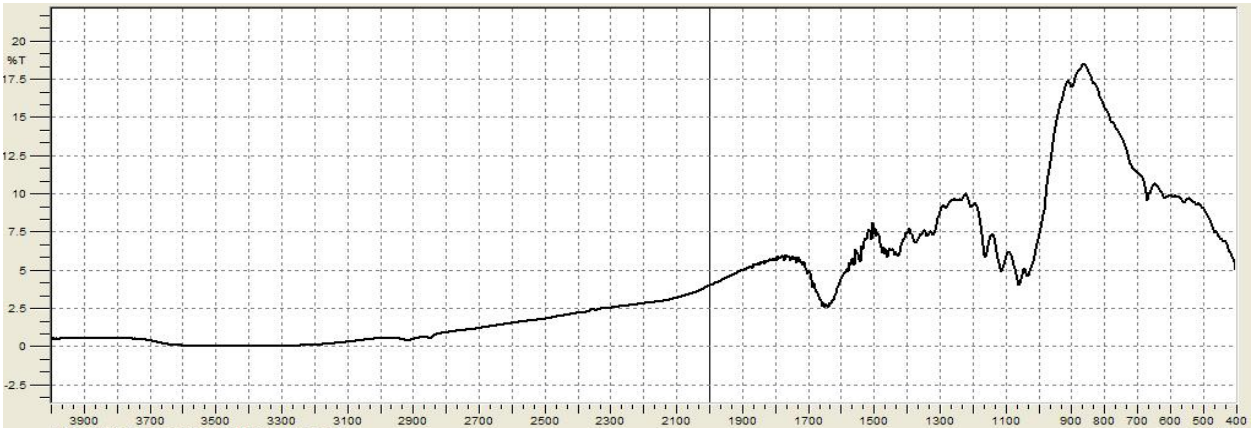

Figure 8. IR spectrum of brand D Desloratadine

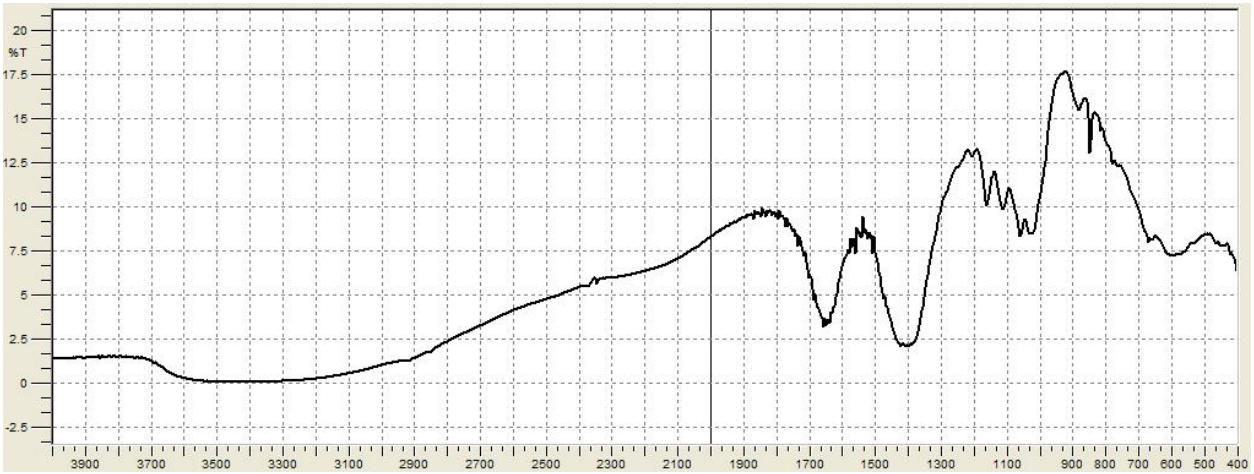

Figure 9. IR spectrum of brand E Desloratadine

CONCLUSION

This study has shown that all brands of 5mg Desloratadine tablets available in the local market of Tripoli Libya complied with USP and BP standards, and can be interchangeable with no significant variation in the quality of the tested drugs leading to the conclusion that the brands tested of Desloratadine tablets are pharmaceutically equivalent. This study has also highlighted the need for focusing on the post-marketing evaluation of pharmaceutical products from different manufacturers circulating in the developing countries markets.

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Disclaimer

The article has not been previously presented or published, and is not part of a thesis project.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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