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COMPARATIVE STUDY OF PHYSICOCHEMICAL PROPERTIES OF LORATADINE TABLETS (10 MG) IN RETAIL OUTLETS IN KHARTOUM CITY, SUDAN

Amro Abdallah Hasanen Mohamed

Faculty of Pharmacy,
Graduate College,
University of Medical Sciences and Technology, Sudan

E-mail: amro198991@gmail.com

ABSTRACT

Purpose: The aim of this study is to evaluate the impact of poor monitoring system of Sudanese regulatory authorities on the quality of antihistamine tablet (Loratdine).

Methodology: This study includes three different brands of Loratadine tablets from a local private pharmacy, two of which are locally manufactured in Sudan and the third is manufactured in India. The tablets were evaluated against weight variation, friability, hardness, drug content, identification, disintegration time, diameter uniformity and along with *In-Vitro* dissolution test and then results were compared with international standards.

Findings: By the end of all tests, in the all three brands, friability is found to be less than 1%, hardness is within 4–12 kg, weight variation (there is no tablet deviates by more than twice that percentage), diameter uniformity (<5%), disintegration time (less than 15 min), identification (retention times of both standard and samples are 4 min), content percentage (90 to 110%) and dissolution was not less than 80%.

Originality/value: On the basis of the data submitted during the repeat use procedure, all brands demonstrated satisfactory results. Thus, no negative impact of the poor implemented systems can be considered in this paper.

***Keywords*:** quality; Sudan; Loratadine; evaluate; private pharmacy; HPLC; poor implemented systems; dissolution; identification.

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INTRODUCTION

Many questions are raised about the process of registration, quality monitoring and analysis of drugs in Sudan (Federal Board of Pharmacy and Poisons, 2005, Sudan). The performance of regulatory authorities in controlling many drugs, including local production drugs as well as drugs that are imported from outside the country, is getting worse (Federal Board of Pharmacy and Poisons, 2005, Sudan). For instance, Royal Honey® formulations, a formula produced by Etumax® (Malaysia) and used as a stimulant for those who suffer sexual impotence, has recently been withdrawn from the Sudanese market after many years, because Silindafil, a medication used to treat erectile dysfunction, was detected in the royal honey formula (Boolell et al., 1996). This active ingredient (Silindafil), which is contraindicated in many diseases including diabetes, hypertension and heart diseases (Cheitlin et al., 1999), is not labelled as an active ingredient on the package. This means that patients are at a higher risk after blind administering of such formulation. In addition, Yesepam®, produced by the General Medicine Company (GMC, Sudan), a medication containing benzodiazepine as an active ingredient, which is used as a sedative and hypnotic (Michel et al., 2002), is thought not to produce the required pharmacological actions according to many patients' claims. Thereby many late analytical tests are now conducted to ensure that any such claims are true or false.

As Sudan is banned from importing some important materials (Medhani, 2013) and because of the acute shortages in foreign exchange that are necessary for the drug production process (Federal Board of Pharmacy and Poisons, 2005, Sudan), this has led to the usage of low grade materials from other territories by company officials. In turn, this led to insignificant local drug production and, consequently, the quality of drugs and drugs regulation was markedly affected (Federal Board of Pharmacy and Poisons, 2005, Sudan).

Such claims about the poor quality of some Sudanese brands and some oversees brands in Sudan, and such late actions, can indicate a type of flagging from officials in the registration and monitoring of the quality of drugs, which in turn can threaten public health in Sudan.

Due to the above, it was necessary to conduct several analytical tests on some brands available in the Sudanese market. Two Sudanese brands and one Indian brand were selected. All these brands contain Loratadine only as an active ingredient.

Loratadine is an H_1 receptor antagonist used to treat Urticaria and allergies (Cox et al., 2008). Allergies are considered one of the big four major problems in public health in the world together with AIDS, tumours and cardiovascular diseases (Kostowski and Herman, 2010). In addition, Loratadine is considered to be an Over-The-Counter (OTC) medication, which means that patients can take it without the need for a prescription from medical doctors (Young, 2011). It is, therefore, a prevalent medication in Sudan.

Therefore, ensuring that both Sudanese and non-Sudanese brands that contain Loratadine, which are marketed in local pharmacies in Sudan, adhere to international standards (US, British and Indian standards) is of great importance. Such tests are, in essence, to confirm the safe and effective use of such drugs.

MATERIALS AND METHODS

This study was conducted at the chemistry and pharmaceutical laboratories of the University of Medical Sciences and Technology. All chemicals and reagents used for this study were of analytical grade. The chemicals and materials used were as follows: Loratadine standard, Loratadine (Zylorat, Sudan; Noratin, Sudan; Lorhist, India), Acetonitrile HPLC grade, methanol (HPLC grade), mono and dibasic potassium phosphate, phosphoric acid solution 10%, distilled water (treated to be suitable for HPLC).

EXPERIMENTAL

Identification of Loratadine

Loratadine was identified using HPLC. The retention time of the major peak in the chromatogram of the three brands was then compared with the retention time of the standard (British Pharmacopoeia, 2012).

Drug content

The percentage content of the drug was determined using HPLC. The mobile phase was prepared by filtering and degassing a mixture of 0.01 M dibasic potassium phosphate, acetonitrile,

methanol, then adjusted to an apparent PH of 7.2 with phosphoric acid 10%. Similarly, diluents were prepared as follows: 400 ml of 0.05 N HCL and 80 ml of 0.6 M dibasic potassium phosphate were transferred to a 1000 ml volumetric flask, and then diluted with a mixture of methanol and acetoniztrile (1:1) to volume and mixed. An assay sample was prepared by accurately weighing 40 mg of Loratadine, transferring to a 100 ml volumetric flask, then dissolved and diluted to volume and finally mixed. The liquid chromatograph was equipped with a 240 nm detector and 4.6 mm × 15 cm column that contains 5 μm packing L7. The flow rate was 1 ml/min. The column temperature was maintained at 37°C. Finally, separately equal volumes of the standard preparation and the assay preparation were injected into the chromatograph, the chromatogram was recorded, and the areas of major peak were measured. The quantity of Loratadine was calculated (British Pharmacopoeia, 2012).

Physical characteristics of Loratadine tablets

Prepared tablets were evaluated for diameter using a Vernier Caliper (size 6 inch), friability using Friabilator (by: Copley-UK., Type: FR1000), hardness tester (by: Erweka, Type: TBH–210) and weight variation using Electronic Balance (by: Vayger Corporation) (British Pharmacopoeia, 2012; Indian Pharmacopoeia, 2011).

Disintegration test

One tablet was placed in each tube and a plastic disc was placed over the tablet (to prevent tablet floating during the test). The tubes were placed in a water bath and raised and lowered at a constant rate in the water. The time of disintegration then was measured (Lachman, 2014).

In-vitro dissolution test

Six tablets were placed in each tube of dissolution apparatus. The sample was withdrawn after one hour and assayed spectrophotometrically at 280 nm. The percentage concentration then was calculated (Lachman, 2014).

RESULTS

Identification of Loratadine

Chromatograms have been obtained for standard as well as samples enclosed with retention times for the purpose of identification shown in Figures 1–4.

Figure 1 illustrates the retention time of Loratadine, which is 4 min. This means all values of samples' retention time should be within this value so as to pass the test. The peak obtained in Figure 1 is symmetrical with no noise or baseline shift. Similarly, the retention time is 4 min.

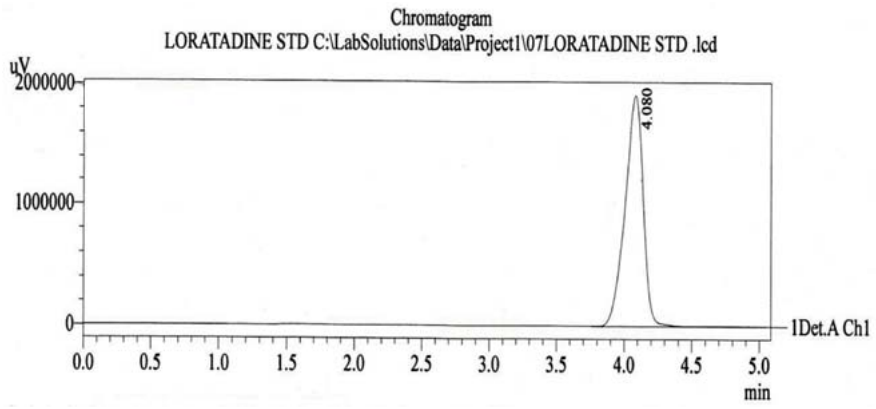

Figure 1 shows the chromatogram of Loratadine standard. System conditions:
Mobile phase: 0.01 M Dibasic potassium phosphate, acetonitrile, methanoal adjusted with phosphoric acid 10% to an apparent PH of 7.2. Stationary phase: C18. oven temperature: 37C. UV detection at 240 nm. Flow rate: 1ml/min.
Retention tim = 4:080min

Figure 1 The retention time of standard Loratadine

Figure 2 shows the retention time of Loratadine sample Noratine®, which was 4.010 min. This means the major peak emerged after 0.010 sec from the standard major peak.

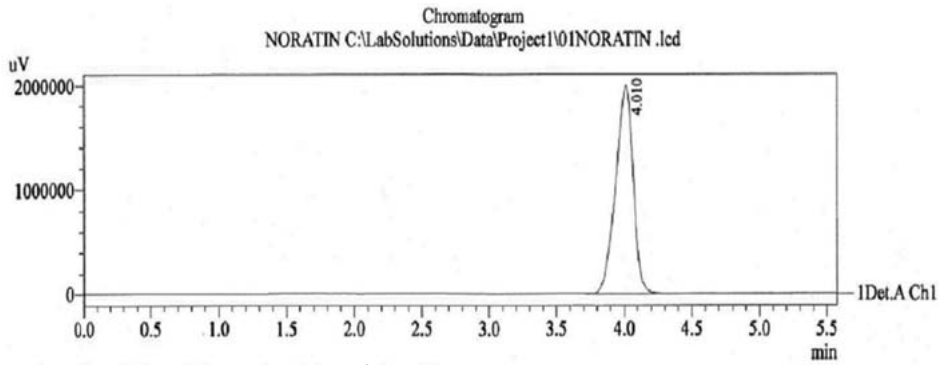

Figure 2 shows the chromatogram of loratadine (Noratine). System conditions:
Mobile phase: 0.01 M Dibasic potassium phosphate, acetonitrile, methanol (7:6:6) adjusted with phosphoric acid 10%. Stationary phase: C18. Oven temperature: 37C. UV detection at 240nm. Flow rate: 1ml/min.
Retention time = 4:010 min

Figure 2 The retention time of Loratadine sample Noratine®

Figure 3 illustrates the chromatogram of Lorhist®. The retention time was found to be 4.015 min.

This means the major peak of the prepared sample Lorhist® appeared after 0.015 sec of the standard peak.

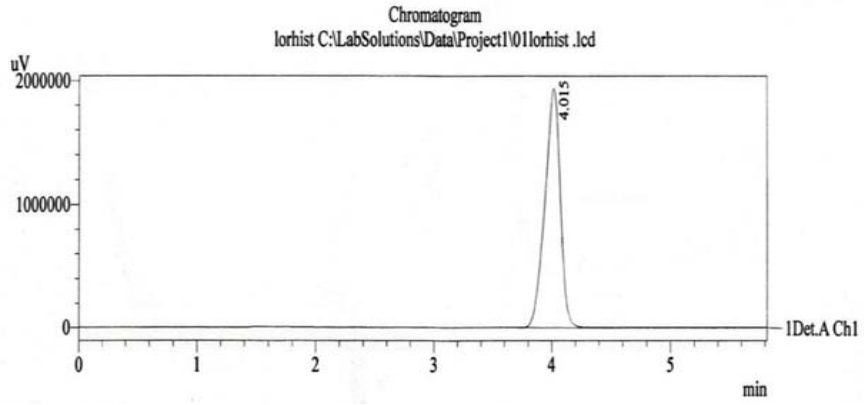

Figure 3 shows the chromatogram of loratadine (Lorhist), system conditions:
Mobile phase: 0.01M Dibasic potassium phosphate, acetonitrile, methanol (7:6:6) adjusted with phosphoric acid 10% to an apparent PHof 7.2, stationary phase : C18, oven temperature 37C, UV detection at 240 nm. Flow rate: 1ml/min
Retention time = 4:015min

Figure 3 The retention time of Loratadine sample Lorhist®

Figure 4 shows the chromatogram of Loratadine sample Zylorat®; the retention time of Zylorat was found to be 4.014 min.

This similarly means that there is 0.014 sec needed to the major peak of the sample Zylorat to emerge after the standard time which is 4 min.

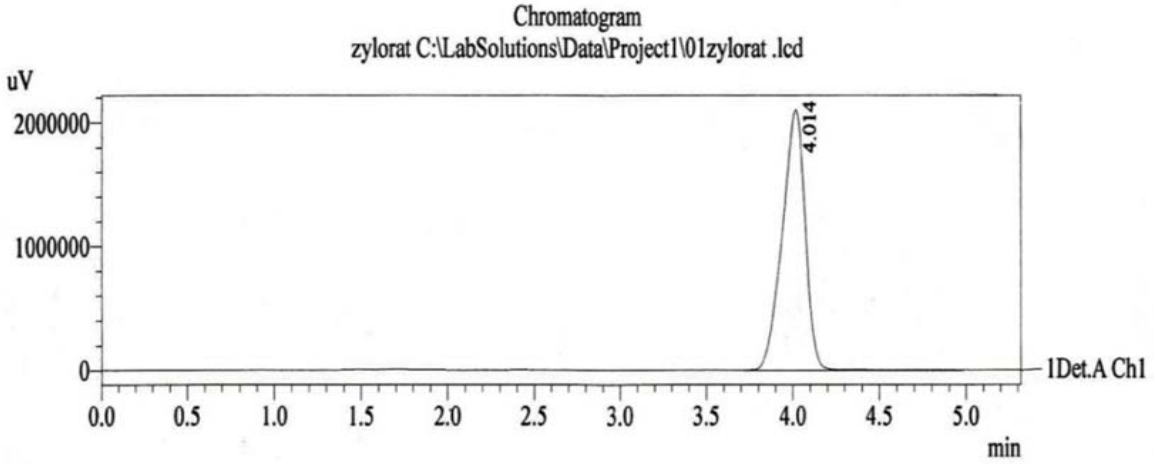

Figure 4 shows the chromatogram of loratadine(zylorat), System conditions:
Mobile phase: 0.01 M Dibasic potassium phosphate, acetonitrile, methanol adjusted with phosphoric acid 10% to an apparent PH of 7.2. stationary phase: C18. oven temperature :37C. UV detection at 240nm. Flow rate: 1ml/min
Retention time = 4:014 min

Figure 4 The retention time of Loratadine sample Zylorat®

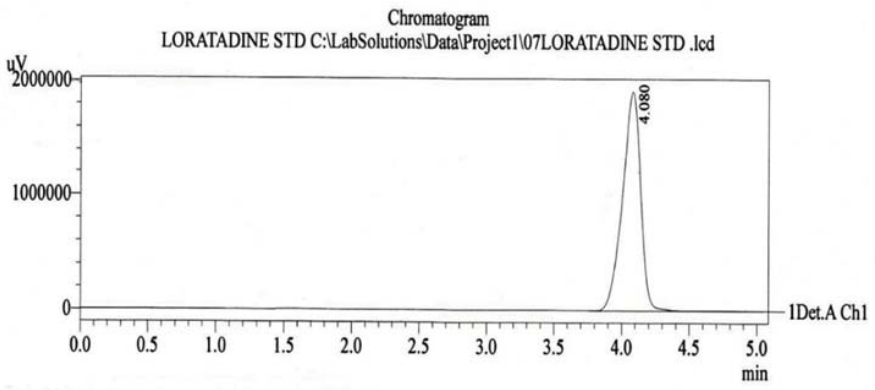

Figure 5 shows the chromatogram of Loratadine standard. System conditions:
Mobile phase: 0.01 M Dibasic potassium phosphate, acetonitrile, methanol adjusted with phosphoric acid 10% to an apparent PH of 7.2. Stationary phase: C18. oven temperature: 37C. UV detection at 240nm.Flow rate: 1ml/min.
Peak area of loratadine standard = 17814890

Figure 5 Loratadine standard chromatogram shows peak area

The results of the identification test illustrates that the values of samples obtained are almost identical to the standard value.

Thus, it is clear that these retention times correspond to that of Loratadine standard, which means, the three samples contain Loratadine as an active pharmaceutical ingredient.

Percentage content

The standard range for the content percentage was 90–110%. The peak area for Loratadine standard was found 17,814,890, as shown in Figure 5.

Similarly, the peak area of samples was found to be 17,915,884, 17,576,874, 19,349,022 for Noratin®, Zylorat®, Lorhist®, respectively, as shown in Figures 6–8.

The content percentage for all samples is shown in Table 1.

It is clear that all samples were within the range 90–110%, therefore all tablets contain the proper amount of the active ingredient. Hence, the drug will produce the desired effect.

Table 1 Samples with content percentage

Sample	*Content Percentage*
Noratine	17,915,884 ÷ 17,814,890 × 100% = 100.5%
Lorhist	17,576,874 ÷ 17,814,890 × 100% = 98.6%
Zylorat	19,349,022 ÷ 17,814,890 × 100% = 108.6%

Physical characteristics of Loratadine tablets

The results from the three Loratadine brands are listed in Table 2. Results indicate acceptable physical characteristics. Results concerning physical characteristics are shown as follows.

Diameter of uniformity

The diameter of all three brands was within 65% variation of the standard value. Thus, tablets show a uniform diameter.

Weight variation

No tablet deviated by twice the accepted percentage, and the percentage weight variation was within limits (5% for Noratine and Lorhist, and 7.5% for Zylorat). So, all tablets passed the test.

Hardness

The three brands showed a mechanical strength of between 4 and 12 Kg. This indicates adequate mechanical strength.

Friability

The minimum friability among the three formulations was found in Noratin®, while the two remaining formulations had a comparable friability. However, the percentage friability was less than one for all brands, ensuring the tablets were mechanically stable.

Disintegration test

The times required for the disintegration of six tablets for the three brands are listed in Table 3, placed in each tube of disintegration apparatus was less than 15 min at 37 ± 2°C. However, Noratin® had the shortest disintegration time, while Lorhist® had the longest. This means all tablets were not highly compressed during the manufacturing process and subsequently they will be broken up *in-vivo*: this is the first step toward a successful dissolution process.

In-vivo dissolution study

The percentage drug release of all three brands of Loratadine tablets are listed in Table 4. However, Noratine® showed the best drug release and the percentage drug release of Lorhist® and Zylorat® were comparable (Table 4).

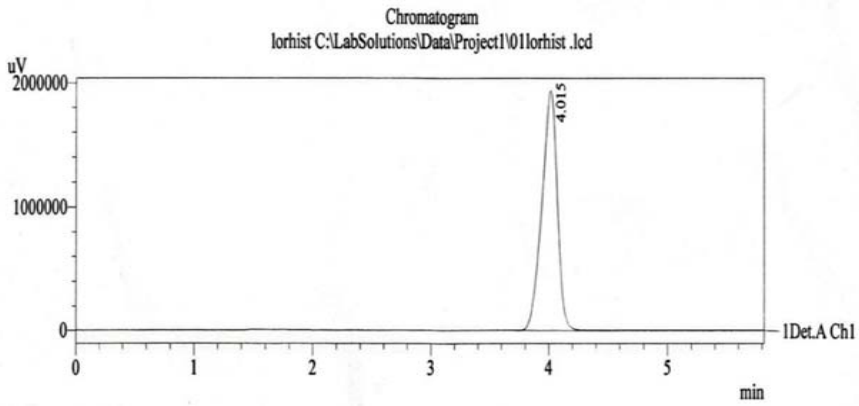

Figure 6 shows the chromatogram of loratadine (Lorhist), system conditions:
Mobile phase: 0.01M Dibasic potassium phosphate, acetonitrile, methanol(7:6:6) adjusted with phosphric acid 10% to an apparent PH of 7.2, stationary phase: C18, oven temperature 37C, UV detection at 240nm. Flow rate: 1ml/min
Peak area of Loratadine (Lorhist) = 17576874

Figure 6 The chromatogram of Lorhist® with its peak area obtained

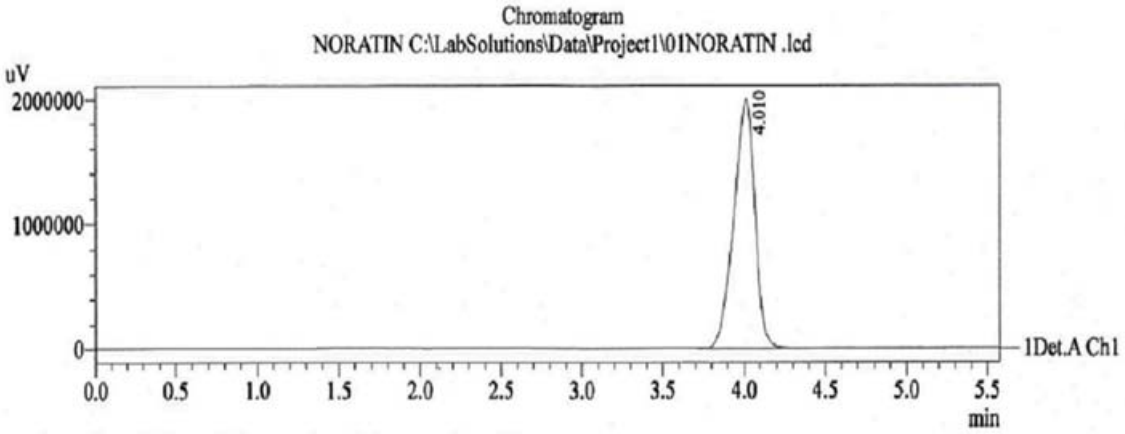

Figure 7 shows the chromatogram of loratadine (Noratine). System conditions:
Mobile phase: 0.01M Dibasic potassium phosphate, acetonitrile, methanol (7:6:6) adjusted with phosphoric acid 10%. Stationary phase: C18. Oven temperature: 37C. UV detection at 240nm. Flow rate: 1ml/min.
Peak area of loratadine(Noratine) = 17915884

Figure 7 The chromatogram of Noratine® with its peak area obtained

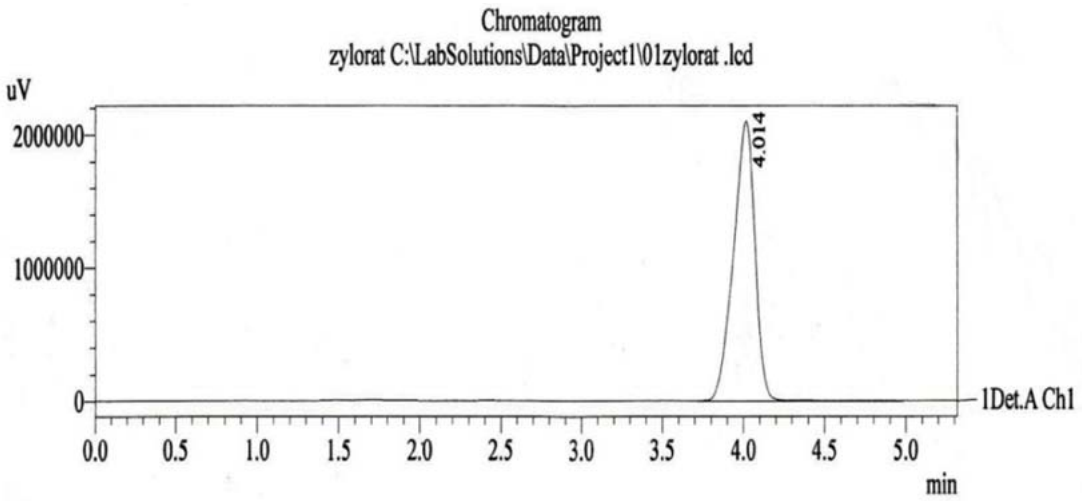

Figure 8 shows the chromatogram of loratadine (zylorat), System conditions:
Mobile phase: 0.01M Dibasic potassium phosphate, acetonitrile, methanol adjusted with phosphoric acid 10% to an apparent PH of 7.2. stationary phase: C18. oven temperature: 37C. UV detection at 240nm. Flow rate: 1ml/min
Peak area = 19349022

Figure 8 The chromatogram of Zylorat with its peak area obtained

Table 2 Physical characteristics of Loratadine brands

Zylorat®	*Lorhist®*	*Noratine®*	*Brand*
1.37	0	0	Diameter Uniformity (RSD%)
4.24	1.68	1.04	Weight variation (RSD%)
5.12	9.81	10.25	Hardness (Average force Kg)
0.21	0.23	0.02	Friability %

Table 3 Disintegration times for Loratadine brands

Disintegration time	*Brand*
42 sec	Noratine®
4:36 min	Lorhist®
1:36 min	Zylorat®

Table 4 Percentage drug release of all three brands of Loratadine tablets

Percentage drug release	*Brand*
101.8	Noratine®
87.2	Lorhist®
85.4	Zylorat®

DISCUSSION

The results obtained in this paper showed acceptable results for all physicochemical tests. The results comply with those obtained by Sateesh et al. (2013), in that excipients of the brands analysed during the identification test did not interfere in the analysis. However, the retention times were different from those obtained in our results. The results also comply with those of Ruperez et al. (2002) when RP-HPLC was used to determine the content percentage of Loratadine. Similarly, the results concerning diameter uniformity, weight variation, friability and hardness tests comply to those of Patel et al. (2010).

However, the *in-vitro* dissolution test carried out by Patel et al. (2010), showed a comparison of the *in-vitro* release profile of marketed products in which sampling was performed at different times and consequently a figure was obtained. However, in this paper, although all tablets showed acceptable results for the dissolution test (not less than 80%), according to the USP monograph, samples were taken at a single time specified after 60 min, which makes a comparison of *in-vitro* comparison of the release profile harder to obtain.

To sum up, the scientific conclusion reached by the researcher during the evaluation process cannot give a final and complete conclusion to the impact of a poor system of drugs analysis and registration in Sudan. Thus, many more analytical and statistical analysis methods are needed in the future, say, stability studies, manufacturing process monitoring, clinical and non-clinical aspects, ANOVA as well as *T*-test. Additionally, more brands of Loratadine tablets are needed.

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BIOGRAPHICAL NOTES

Amro Abdallah Hasanen Mohamed hold a master degree in Pharmaceutical Analysis and Quality Control from University of Medical Sciences and Technology (UMST), Sudan. He is currently applying to complete his PhD on enhancing the Bio-availability of an Oral Anticancer Drug through Liposomal Drug Delivery System.