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A Comparative Study on *In-vitro* Quality Control Parameters of Different Brands of Loratadine Tablets Commercially Available in Bangladesh

Rosy Fatema[1], Sumaiya Khan[1], A. S. M. Roknuzzaman[1], Ramisa Anjum[1] and Nishat Jahan[1*]

[1]Department of Pharmacy, University of Asia Pacific, 74/A Green Rd, Dhaka 1205, Dhaka, Bangladesh.

Authors' contributions

This work was carried out in collaboration among all authors. Author NJ designed the study and supervised the project. Authors RF and SK carried out the experiment. Author RF wrote the manuscript and managed the analyses of the study with support from authors NJ, SK, ASMR and. Author ASMR managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Loratadine, a second generation H1-receptor antagonist, works by blocking the action of histamine and is widely prescribed for itching, runny nose, watery eyes, and sneezing from "hay fever" and other allergic conditions. To ensure quality the main requirements for a medicinal product are safety, potency, efficacy and stability. This research work aimed to compare and assess the quality levels of different local brands of loratadine tablets available in the drug market of Bangladesh. Six different brands of loratadine 10 mg tablet manufactured by the local companies were used for the analysis. The evaluation was performed through the determination of weight variation, hardness, friability, percent potency, disintegration time, and dissolution profile in accordance with USP-NF specifications. All brands showed acceptable weight variation and % friability. The percent potency for tested samples by UV method ranges from 97.02%-108%, showing none of the brands contains less than 90% of the active principle as per the specification. The result of the physical

**Corresponding author: Email: nishatjahan@uap-bd.edu, jahan.nishat25@gmail.com;*

and chemical studies, such as *in-vitro* dissolution, disintegration, hardness, etc., has been found to differ but lie within the specified limit. After analyzing the data obtained from the tests, it can be claimed that loratadine 10 mg tablets manufactured and marketed by several local companies in Bangladesh meet the quality standard required to achieve the desired therapeutic outcomes.

Keywords: Loratadine; antihistamine; quality; efficacy; USP-NF; analysis; specification.

1. INTRODUCTION

Histamine plays a major role in triggering complex interaction between several inflammatory cells including, basophils, mast cells, neutrophils, dendritic cells, lymphocytes and eosinophils in response to various environmental/ allergic stimuli, resulting in allergic rhinitis, allergic asthma, pruritus, atopic dermatitis, etc [1]. Anti-histamines are capable of preventing or suppressing such pharmacological upshot of histamine [2]. A significant breakthrough in antihistamine production occurred in the 1980s with the advent of the second generation H1-antihistamine, which are minimally sedative or non-sedative due to their restricted penetration of the blood brain barrier. Furthermore, these medications are highly selective for the H1-receptor of histamine and have no anticholinergic effects [3].

Loratadine was approved by the FDA on December 21, 2001 [4]. It is a highly selective long acting H1-antihistamine which lacks central nervous system depressant effect often associated with some of the older antihistamines. Concomitant controlled clinical trials demonstrated that loratadine is a well-tolerated and credible antihistamine that can play a promising role to the patient with allergic rhinitis and urticaria [5]. Regarding the WHO's essential list of medicine it is one of the most important medicines used as antiallergics and in the management of anaphylaxis [6].

Loratadine is available in certain syrup and tablet forms [7,8]. The quality and effectiveness of pharmaceutical dosage forms usually depends on their formulation properties, and methods of manufacturing, thus, the efficacy of the dosage forms can vary from each other [9]. Pharmaceutical safety is a global issue; falsified medicine comprises a larger percentage of the drug market of the less developed countries [10]. Quality assessment of the drugs manufactured and sold is very important for understanding the actual status of medicines prescribed to the patients, for creating awareness among people, and to stop and take prompt action by the law enforcement authority against the offenders [11]. To ensure the desired quality the drug manufacturers are required to check their products during and after manufacture, and at different intervals during the product's shelf life [12].

Depending upon these facts, the present study was conducted to make an equivalent evaluation of different quality control parameters such as the weight variation, hardness, friability, disintegration, dissolution, percentage potency profile of commercially available six different pharmaceutical brands of loratadine in Dhaka, Bangladesh, and also to raise awareness among the medicine control authority and pharmaceutical manufacturers so that they become more conscious about maintaining the quality control standards provided by BP and USP guidelines.

2. MATERIALS AND METHODS

In this comparative analysis, the necessary test of quality control parameters of six different brands of loratadine 10 mg tablet was carried out in the Research Laboratory at University of Asia Pacific, Dhaka, Bangladesh. All the required tests were performed following the specified compendial methods.

2.1 Instruments and Equipment used in the Study

Laboratory equipment and instrument used in the study include: Test-tube, Beaker, Funnel, Pipette, Electronic Analytical Balance (Ohaus Pioneer, USA) Hardness Tester (Monsanto Hardness Tester, Shanghai, China), Friability Tester (Veego, India), UV-visible Spectrophotometer (Simadzu, Japan), Dissolution Test Apparatus (Electrolab, India), Disintegration Test Apparatus (Shimadzu, Japan).

2.2 Sample Collection

There are almost 30 brands of loratadine marketed by several pharmaceutical companies

of Bangladesh [13]. Among them 6 different brands were purchased from local medicine shop located in Farmgate and Panthapath, Dhaka. The brands were coded as A, B, C, D, E and F. The samples were properly checked for their physical appearance, name of manufacturer, batch number, manufacturing date, expiry date, manufacturing license number, D.A.R. Number and maximum retail price. The labelled active ingredient was 10 mg of loratadine and all were packaged in blisters.

The reference standard of loratadine (API) was collected from ACI Pharmaceuticals Ltd, Dhaka, Bangladesh.

2.3 Study Design

Comparative in-vitro quality control parameters of commercially available loratadine tablets of local pharmaceutical brands were studied through the evaluation of some pharmacopeial and non-pharmacopeial tests like; weight variation, hardness, percent friability, disintegration time, dissolution profile and percent potency following the United States Pharmacopoeia (USP) monograph [14].

2.4 In-Vitro Quality Control Tests

2.4.1 Weight variation test

Twelve tablets of each loratadine brand were weighed individually with the specified analytical balance and average weight and the percent deviation for each brand were calculated. The equation for calculation of percent weight variation is given below [15]:

$$Percentage\ weight\ variation = \frac{average\ weight - individual\ weight}{individual\ weight} \times 100$$

2.4.2 Hardness test

The Monsanto Hardness tester had a tablet mounted vertically on it. The load was then extended along the tablet's radial axis. The weight or load needed to break the tablet was noted down. The same procedure was repeated for 6 tablets of each brand.

2.4.3 Friability test

To perform the friability test, 10 tablets were weighed initially (initial weight, W_1) and then placed on a friabilator. The friabilator was rotated at 100 rpm for 4 minutes. After that, the tablets were taken out and reweighed (final weight, W_2). The percentage loss in tablet weight was calculated by using the following equation [16]:

$$Percent\ friability = \frac{initial\ weight - final\ weight}{initial\ \ weight} \times 100$$

2.4.4 Disintegration test

The in-vitro disintegration time of tablets was determined using disintegration test apparatus that consists of a basket-rack assembly. The basket-rack assembly contains six open-ended transparent tubes. For disintegration test, 3 tablets were taken randomly from each brand, and were placed inside 3 individual tubes. The basket rack was positioned in a 600 ml beaker of purified water at 37° C. A disc was added to each tube and the machine was started. The time, in seconds, taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus, was measured and recorded.

2.4.5 Preparation of standard curve

10 milligrams of standard loratadine powder was weighed with an electronic balance and placed in a 100 ml volumetric flask. Then 0.1N HCl solution [17] was added to the volumetric flask up to the 100 ml mark to prepare a solution with a final concentration of 100 µg/ml. After that 40 ml of this solution was taken into a 100 ml volumetric flask and was diluted up to 100 ml to make a solution of 40 µg/ml. 1 ml of that solution was taken in a test tube and 9 ml of 0.1N HCl solution was adjusted up to 10 ml to make a solution of 4 µg/ml. Similarly, a series of concentrations of loratadine solutions were prepared ranging from 4-40 µg/ml. Then absorbance was taken for the respective solutions by UV spectrophotometer at 276.2 nm against blank (0.1N HCl solution) and the absorbance was plotted against the respective concentrations to obtain the standard curve (Fig. 1) using Microsoft Excel 2007.

2.4.6 Percent potency

Two tablets from each brand were selected and crushed separately in mortar and pestle. Then the crushed powder equivalent to 10 mg loratadine was taken and dissolved and made up to 100 ml with media (0.1 N HCl) in a 100 ml volumetric flask. After that, 4 ml solution was

taken and diluted up to 10 ml with media in a test-tube. Then the prepared sample was analyzed by using UV spectrophotometer at 276.2nm. The potency of the tablets was calculated using the following formulas:

$$\%\ Potency = \frac{drug\ present\ in\ a\ single\ tablet}{strength} \times 100$$

Where,

$$Drug\ present\ in\ a\ single\ tablet = \frac{Conc\ \left(\frac{mg}{ml}\right) \times dilution\ factor\ \times total\ volume\ (ml) \times average\ weight}{Sample\ taken\ (mg)}$$

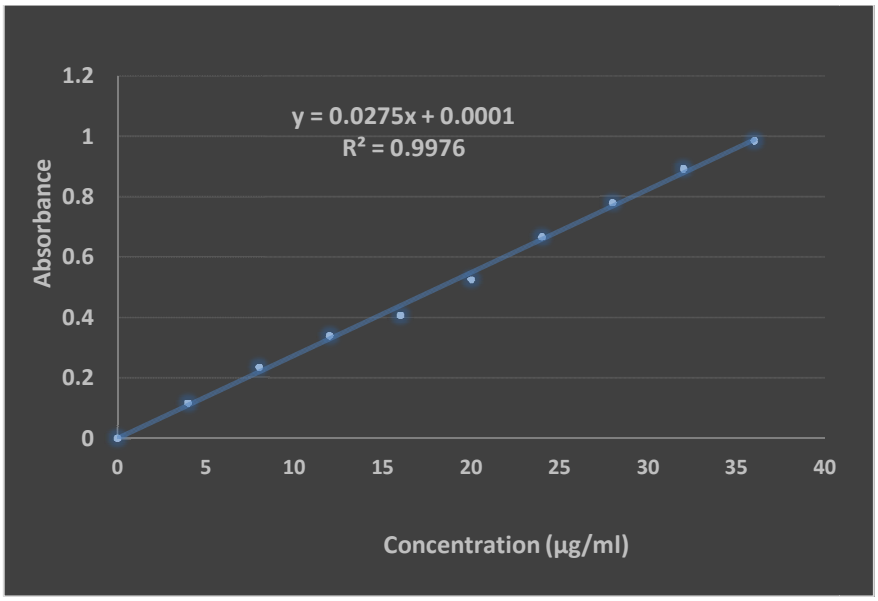

Fig. 1. Standard curve of Loratadine. A series of different concentrations of loratadine (4, 8, 12, 16, 20, 24, 28 32, 36 µg/ml) were taken to measure absorbance at 276.2 nm against a blank by UV spectrophotometer. The measured absorbance was plotted against the respective concentrations of loratadine solutions to obtain a straight line with R^2 value of 0.9976

2.4.7 Dissolution test

Dissolution test of the tablets was performed using USP dissolution apparatus II (paddle) in 900 ml 0.1N HCl as dissolution media [17], at 50 rpm and 37±0.5°C temperature. Test sample (10 ml) was withdrawn at 5, 15, 30, 45, 60 minutes and replaced with 0.1N HCl solution of same volume and maintained at the same temperature. Collected samples were filtered and analyzed after suitable dilution by UV- Spectrophotometer at 276.2 nm against 0.1N HCl media as blank. Release rate was calculated as percent release by the following equation:

$$\%\ Drug\ release = \frac{amount\ of\ drug\ released\ (mg)}{strength} \times 100$$

3. RESULTS AND DISCUSSION

In this study, 6 different brands of loratadine tablets of 10 mg were coded randomly as A, B, C, D, E, and F. For comparative studies, weight variation test, hardness, friability, disintegration time, potency, *in-vitro* dissolution profile of the loratadine 10 mg tablets of these 6 different brands were performed. All the brands of the loratadine 10 mg tablet were within the shelf-life and no irregularity was observed in the physical appearance in any of the sample used throughout the analysis.

3.1 Weight Variation Test

Weight variation test is a very important quality control parameter as it is a valid indication of the corresponding variation in the drug content. Thus, the weight variation test is performed to get proper tablet hardness and friability by controlling weights with a tight range provided by the pharmacopoeia and to check the content uniformity of the tablet [18].

The USP provides criteria for tablet weight variation test which states that, if the average weight is less than 130 mg, the percentage difference should be ±10, if it is between 130-324 mg, percentage differences should be ±7.5 and if it is above 324 mg, the percentage difference should be ±5 [15]. According to the experimental result, the average weight of brand A, B, D, E, and F were found to be within 130-324 mg, and the percent differences complied with the limit ±7.5%; the average weight of brand C was less than 130 mg and complied with the specified limit ±10%. Therefore, it can be concluded that all the tablets conformed to the USP specifications. The results of the weight variation study is graphically represented in Fig. 2.

3.2 Hardness Test

Tablet hardness is an important parameter in the pharmaceutical industry, as pharmaceutical tablets must have the capacity to withstand the handling forces during packaging and shipping. When hardness exceeds a certain limit, it increases the time for disintegration, which eventually affects the bioavailability [18]. As hardness is not an official indicator, there is no such compendial limit for hardness but a crushing strength of between 4-6 kgf (kilogram of force), that is, approximately between 40-60 N is considered to be the minimum requirement for a satisfactory tablet [19]. The average hardness of all the tested tablets was within the limits as shown in Table 1.

3.3 Friability Test

Shock and frictional forces can cause damage or breakage to the tablets. With this test, the capacity of the tablet to withstand abrasion in packing, storage, and shipping, expressed as a percentage, can be measured [20]. According to the USP, the allowed limit of friability is not more than 1.0% [21].

The friability values for loratadine tablet brands ranged from 0% to 0.74% (Table 1). For all brands, the percent (%) friability was less than 1% which ensures that all the tablets of each brand were mechanically stable.

3.4 Disintegration Test

In the context of tablet technology, disintegration involves the penetration of the tablet by an aqueous liquid, the disruption of internal bonds and the subsequent breakdown of the tablet. The longer the time of disintegration required the lower the dissolution rate and poor absorption followed. Thus, disintegration is a crucial part for therapeutic action of a drug [22].

According to BP/USP specification, film coated tablets should disintegrate within 1800 seconds [23]. All of the samples (A, B, C, D, E and F) were film coated and the average disintegration time was found to be 65.33 seconds, 1021 seconds, 61.66 seconds, 716 seconds, 74 seconds and 866 seconds (Table 1). So, all the samples met the requirement and thus complied with the USP specification.

3.5 Percent Potency

Potency is one of the quality parameters of a drug and it is an expression of the activity of a drug in terms of the concentration or amount of the drug required to produce a defined effect. Potency test is important for determining the toxic and therapeutic effect of the drug. The potency of the tablet should comply with the specification because a very highly potent drug may give toxic effect and very less potent drug may give sub-therapeutic effect [22].

According to the USP, potency of loratadine 10 mg tablet should be within the range of 90-110% [17]. In normal condition, potency found for sample A is (103.02%) followed by sample B (101.66%), C (108.0%), sample D (105.6%), sample E (97.06%) and F (107.2). The graphical representation of percent potency is shown in Fig. 3. According to the analysis, the highest potency was exhibited by sample C (108.0%) and the lowest potency was exhibited by sample E (97.06%) and the rest of the samples exhibited % potency within this range.

3.6 Dissolution Time

Dissolution is an official test. Under standardized condition, it is defined as the rate of mass transfer from a drug substance to the dissolution medium or solvent. It is a complex property that

changes over time and describes the process of obtaining a homogeneous mixture of a solid or a liquid in a solvent [24]. It is used to measure the rate of drug release from solid dosage forms. It also gives the knowledge of bioavailability of drugs by correlating the drug dissolving pattern in the gastrointestinal tract before reaching the systemic circulation [25].

The dissolution study of loratadine tablet was carried out in acidic (0.1N HCl) media. Results found in dissolution study of 6 different brands of Loratadine tablet are presented in Table 2. According to USP, the percent release of drug from the tablet should not be less than 80% in 60 minutes [17]. From Table 2, it can be seen that all the brands meet this specification. Following the table, a line chart is given in Fig. 4 describing the upward trend of average cumulative drug release of different brands over time.

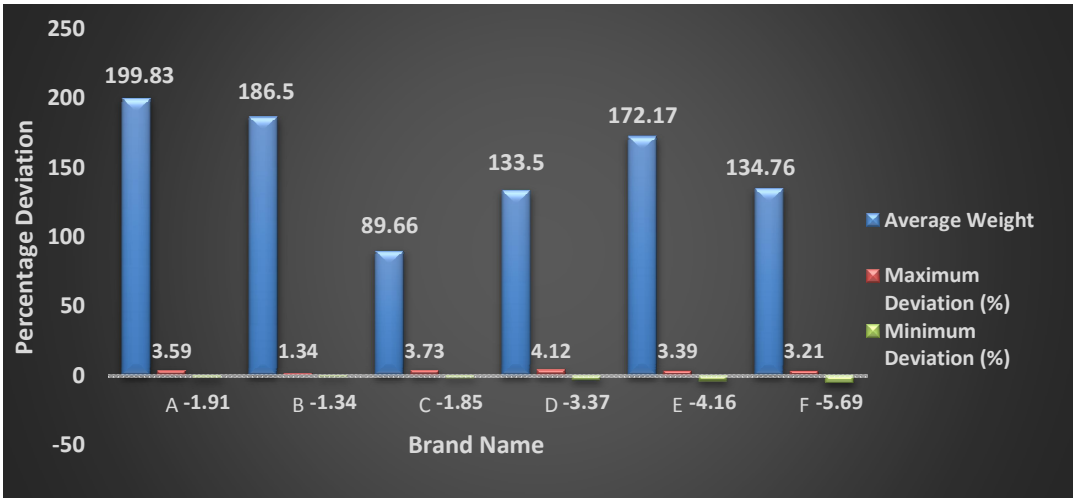

Fig. 2. According to the data, maximum average weight deviation occurred in case of brand D and minimum deviation occurred in case of brand F

Table 1. The average output of hardness, friability and disintegration time of the tablets from six different brands

Sample Code	Average Hardness (Newton)	Average % Friability	Average Disintegration Time (Second)
A	11.76	0.16	65.33
B	13.39	0.08	1021
C	11.43	0.18	61.66
D	11.27	0.74	716
E	11.76	0.38	74
F	12.02	0.61	866

Table 2. Dissolution profile of loratadine tablet

Time (min)	Average % Release of Brand A	Average % Release of Brand B	Average % Release of Brand C	Average % Release of Brand D	Average % Release of Brand E	Average % Release of Brand F
0	0	0	0	0	0	0
5	41.203	56.258	42.348	38.65	35.90	39.80
15	60.970	66.701	60.164	56.44	53.63	57.45
30	75.551	83.635	73.737	66.16	64.94	73.70
45	89.142	93.222	88.155	85.57	78.84	82.95
60	93.220	98.978	97.294	97.37	91.76	96.05

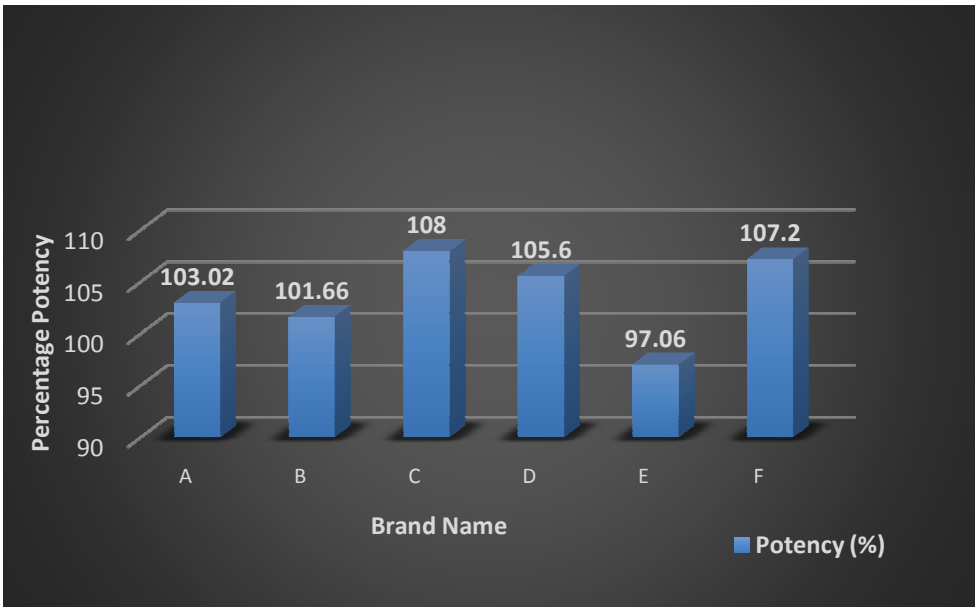

Fig. 3. Graphical representation of percent potency of loratadine tablet showing maximum and minimum potency exhibited by brand C and brand E, respectively

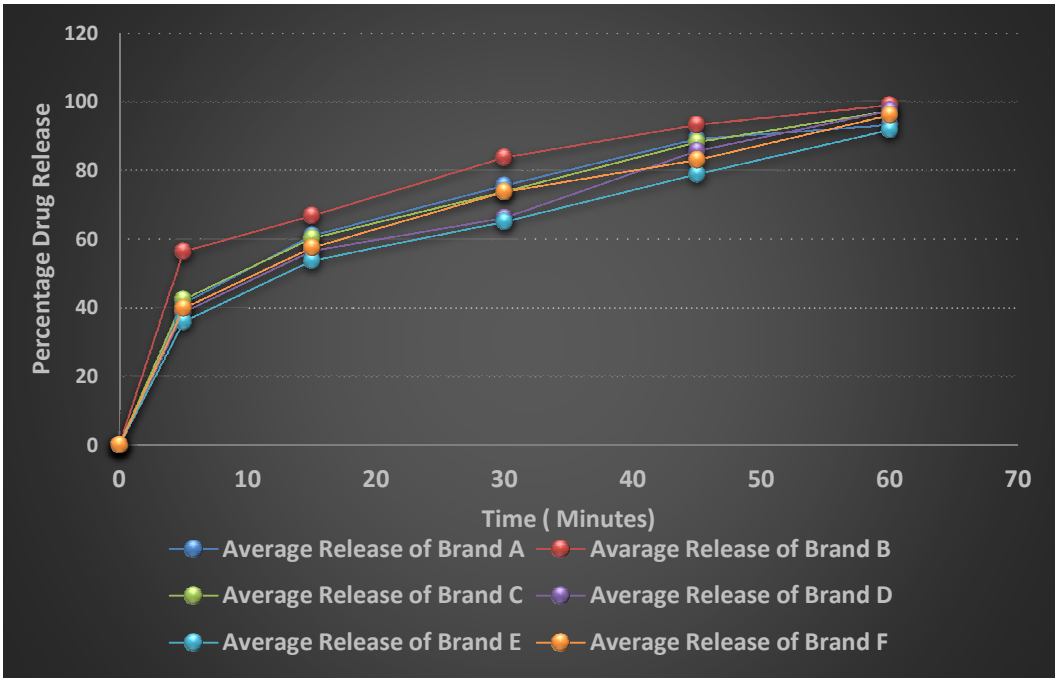

Fig. 4. The average cumulative drug release of 6 brands of loratadine tablets

4. CONCLUSION

Since quality control parameters are related to one another from the early step to the pharmacological action of the medication, a high-quality tablet should meet all standard quality parameters to produce the desired therapeutic response. The physical and chemical in-vitro evaluation of selected commercial products of loratadine available in Dhaka, Bangladesh illustrated the efficacy and reliability of the brands in accordance with USP specifications. There is

often quantitative variation among drugs of different brands which may be due to the use of different types of excipients and the processes followed. In our study, it was seen that despite the slight variation in the test results, all the results were within the official limit provided by the pharmacopoeia. It indicates that these formulations would certainly generate the required antihistamine effects in patients.

Although this comparative study involving a few companies does not illustrate the entire scenario of the quality of loratadine tablets in Bangladesh, still it will help the drug control authority and the pharmaceutical companies with a reflection of the quality status of the antihistamine, loratadine 10 mg tablets available in Bangladesh.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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