A randomized open-label trial of a novel anti-sensitivity dentifrice versus popular brand

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ABSTRACT

Objective: Dentinal sensitivity is a common complaint that dentists deal with in their practice. Despite agents already in use, the search for more effective agents continues. The purpose of this study was to compare the effectiveness in the relief of dentinal sensitivity, taste and tissue-friendliness of a novel anti-sensitivity dentifrice with a known popular brand.

Methods: A randomized mixed design with one between-subjects factor namely dentifrice group and one within-subjects factor namely, time. A two-point (four weeks apart) evaluation of dentinal sensitivity using a tactile stimulated response and subject-reported visual analogue scale scores. Data were analyzed using non-parametric alternatives due to violation of normality laws by post-treatment VAS data. Taste and adverse reactions were also compared.

Results: Both agents provided excellent relief from dentinal sensitivity except in two patients. Anti-sensitivity effectiveness judged by tactile stimulated, patient-reported VAS was similar between the two groups. There were no statistically-significant differences in effectiveness of relief from dentinal sensitivity. The taste of the popular brand was slightly better and there were no adverse effects. There were no adverse reactions recorded from either group.

Conclusion: The novel dentifrice was as effective as the popular brand in the relief of dentinal sensitivity.

Keywords: Dentine sensitivity, tooth sensitivity, dentine desensitizing agents

INTRODUCTION: Dental sensitivity is increasingly gaining prominence due to the changing diet[1] occupational acid exposure[2], gastric reflux[3] and aggressive toothbrushing[4]. It is also possible that increased emphasis on dental sensitivity might be unrelated to any of the aforementioned entities. It is in fact possible that an increased awareness of the possibility and availability of treatment might be the simple reason. One very likely reason, however, is the increasing prevalence because with dental sensitivity prevalence figures ranging from 53% to 70% among our Nigerians[5,6] there is an obvious need for safe and effective desensitization using agents that could be easily applied at home. Such agents reduce indirect costs to patients by reducing the need for frequent dental visits for the professional application of desensitizing agents-a goal readily met by the incorporation of such agents into daily-use dentifrices with different mechanisms of action There are various mechanisms of action and various agents tried over time in an attempt to offer relief to patients suffering from dentinal hypersensitivity[7,8,9]. The claims of manufacturers regarding the mechanism of action of their desensitizing dentifrices are varied. In 2015, West and colleagues[10] concluded through a review of the

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literature that stannous fluoride, arginine, calcium sodium phosphosilicate and strontium toothpaste appeared effective in the clinical relief dentin hypersensitivity. The studies included in their review were plagued heterogeneity between studies and the lack of direct comparison between agents which culminated in insufficient data to conduct a meta-analysis. Despite this, workers have attempted to classify the mechanism of action of desensitizing agents into occlusive agents which work by precipitation of proteins and neutral diffusion through the diffusion of potassium ions. To date, the hydrodynamic theory remains the most applicable theoretical plausibility though historically, it was believed that the direct diffusion of potassium ions blocks the nerve impulse conduction in the dentinal tubules through the alteration of their action potential[11,12]. In a recent systematic review, Wellington reiterated the current thinking that dentin desensitization has been achieved through non-invasive occlusion of dentinal tubules achieved with dentifrices with strontium salt with or without high fluoride concentration as well as iontophoresis[13]. As our understanding of the mechanisms behind dentinal sensitivity evolves, so will therapeutic alternatives. One of such alternatives presented by a new product in the Nigerian market necessitated this study. The objectives of this study were therefore to evaluate the desensitizing effectiveness of a novel anti-sensitivity Potassium nitrate dentifrice; determine the taste and friendliness of a novel anti-sensitivity dentifrice to tissues and compare the effectiveness and safety of novel anti-sensitivity dentifrice with a known popular brand.

METHODS

Two commercial dentifrices were used. A popular brand dentifrice is a known dentifrice used in the treatment of sensitivity with ingredients including Pentasodium Triphosphate, Sodium Saccharin, 0.454% Stannous Fluoride and 0.0721% w/w Sodium Fluoride amounting to 1450ppm Fluoride.

The novel dentifrice is also a commercial dentifrice with its main active agents being 5 percent Potassium nitrate and 0.7 percent sodium monofluorophosphate amounting to 917ppm Fluoride.

Other active ingredients in the novel dentifrice include sodium saccharin and sodium benzoate. The slight similarity between the two dentifrices lies in their fluoride content but the novel dentifrice had higher fluoride content (1450 ppm) than the known popular brand (917ppm Fluoride). Despite this, there are significant differences in their other active ingredients; while the known popular brand contains Pentasodium Triphosphate, the novel dentifrice simply contains 5 percent Potassium nitrate as main active ingredient.

The study was conducted at the periodontics unit, department of preventive and community dentistry of Obafemi Awolowo University Teaching Hospital Complex (OAUTHC) in Ile-Ife, a sub-urban city in Osun State, south-western Nigeria. This was a randomized open-label trial approach was adopted to compare the effectiveness of a novel anti-sensitivity dentifrice with a known popular brand. Study participants were asked to brush twice daily with the given dentifrice. Taste was subjectively evaluated by study participants and described from an arbitrary, subjective range of good to unpleasant. The study participants consisted of consenting, consecutive participants aged 18years and over, attending the dental hospital of a sub-urban tertiary hospital in south-western Nigeria. Information sheet were explained and written informed consent obtained from all participants. Ethical approval was obtained from the college institutional review board.

Since an open-label approach was adopted, both patients and dentists were aware of the dentifrice administered. The approach was adopted because the authors considered the sterility concerns that might be associated with dispensing the dentifrices into generic containers. More so, scoring was based on patient-reported VAS scores upon stimulation by an examiner. To minimize possible bias possible from an open-label approach, the data analyst was blinded and was not involved with the study. He only became aware of the two groups upon completion of the study. Patients were also blinded to the use of an alternative dentifrice in the study. All adult patients (eighteen years and older) with dentinal

sensitivity who responded to the study advert were included in the study. Patients who presented with other types of dental pain arising from dental caries or its sequelae were excluded from the study. The sample size was determined by the formula for the comparison of means[14].

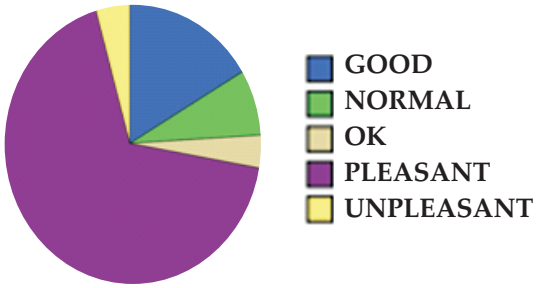
N = 4σ2 (zcrit+ zpwr) 2 /D2; Where ; N is the total sample size (the sum of the sizes of both comparison groups), σ is the assumed SD of each group; zcrit = 1.96 at 95% confidence level; zpwr -= 0.842 at 80% power (.80) and D is the minimum expected difference between the two means. This resulted in a calculated sample size of 31 but 50 participants were adopted (in order to make room for attrition) randomly assigned to the two groups picking of rolled papers containing an equal number of both groups hence each group consisted of 25 participants.

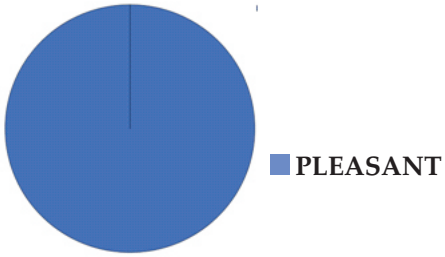
Significance of the study : This study provides baseline data regarding the safety and effectiveness of a novel desensitizing dentifrice in Nigeria. It will help to shape the opinion of the Nigerian Dental Association and its members regarding this novel dentifrice. The patients were partly blinded in the study because each patient was not aware that any other dentifrice was being tested. Examiners were however not blinded to the study since an open-label approach was adopted. More so, the reported findings depended on subjective, patient-reported responses to the sensitivity test conducted by the examiners. Randomization was done using computer software to assign study participants into two groups namely; novel anti-sensitivity dentifrice group (A) and gold standard group (B). Participants were asked to describe the taste of the toothpaste in their own words and to state if there were any undesirable effects associated with the use of each toothpaste. Subjective response to assessment of sensitivity was obtained from participants using a 10-point evenly -divided Visual Analogue Scale (VAS) from no sensitivity to severe sensitivity. Two time- point measurements were performed at baseline and after 4 weeks of toothpaste home use. There is much controversy on the appropriate test for such measures but it is generally agreed that a between-subjects factor and a within-subjects factor should exist as independent variables when using a mixed-ANOVA. We could have chosen the mixed ANOVA for the analysis because, a mixed ANOVA though similar to a two-way repeated measures ANOVA since both tests involve two factors, yet in a mixed ANOVA, the subjects that undergo each condition are different, in contradistinction to the latter in which the subjects in both groups undergo both conditions 15. However, there were outliers in the data and removing outliers would have negatively affected our interpretation considering the limited sample size. Again, though the pre and post - intervention VAS scores for the two dentifrices were normally distributed as assessed by visual inspection of Normal Q-Q Plots, unfortunately, despite the seeming normality from the above scores, the data failed the Shappiro Wilk test for normality affecting mainly the post-intervention test values. This was not surprising considering the effectiveness of both dentifrices in reducing VAS scores. This same normality failure precluded the use of ANCOVA despite "robust" claim of ANOVA to deviations from normality[15]. All efforts at data transformation using standard data transformation techniques failed to produce normality. For this reason we had to use a non-parametric rank analysis of covariance. In order to conduct the non-parametric rank analysis of covariance, we first ran ranked the dependent variable (post-test VAS scores) and the covariate (pre-test VAS scores), for all cases, ignoring the grouping variable using the default settings in the SPSS RANK procedure[16]. Next, we ran a linear regression of the ranks of the dependent variable on the ranks of the covariate, saving the (Unstandardized) residuals, again ignoring the grouping factor. Finally, we ran a one-way analysis of variance (ANOVA), using the residuals from the regression in the previous step as the dependent variable with the grouping variable serving as the factor. The F test resulting from this ANOVA represents the F statistic as used by Quade[17].

RESULTS

Fifty participants eventually completed the study out of the initial 58 with eight dropouts who simply did not return to complete the study. Only data from these fifty patients were included in the analysis. Data are medians

Tables and figures





unless otherwise stated. The age of the study participants ranged from 23 to 75 years, with a mean age of 47.02. There were 22 males (12 novel dentifrice group, 10 popular brand group) and 28 females (13 and 15 in each group respectively) in the sample population with a male to female ratio of 1:1.27. The mean ages (SD) of the novel and popular brand groups were 51.0 (15.1) years and 47.0 (15.8) years respectively with no statistically significant difference (F=0.118, p=0.733). No adverse reactions were reported from either group. The novel dentifrice group taste description ranged from good to pleasant while the popular brand all described the dentifrice as pleasant. (Figures 1a and 1b) Differences in pre- and post- intervention VAS scores between the two groups were almost an exact replica with a mean difference (SD) of the novel and popular brand groups being 4.44 (2.10) and 4.40 (1.85) for the novel and popular brand groups respectively. The minor differences in the modal, median and range of VAS score reductions are median values are as presented in Table 1. The distributions of post-intervention reduction in VAS scores were also similar between the two groups as presented below for the novel and popular brand group respectively. (Figures 2a and 2b) Forty-eight of the fifty participants reported reduced sensitivity whereas two participants (one per group) saw no improvement. Because the post-test scores were not normally distributed, a Wilcoxon signed-rank test determined that there was a statistically significant median decrease post-intervention visual analogue scale ratings (z= -4.299, p < .0001; z= -4.305, p < .0001 with dentifrice A and B respectively. Median differences were of between 4 and 5 points for novel dentifrice and the known popular brand respectively. Overall, there was a significant improvement between pre- and post-intervention VAS scores of the participants in the two groups. (z = -6.052, p < .0001)

Table 1. Frequency table of VAS score.
Multiple modes exist. The smallest value is shown

	Novel dentifrice	Popular brand dentifrice
Mean	4.44	4.40
Median	4.00	.37
Mode	3.00[a]	.4.00a
Std. Deviation	2.10	1.85
Variance	4.42	3.42
Range	9.00	7.00
Minimum	.00	.00
Mode	3.00[a]	7.00
Std. Deviation	2.10	4.40
Variance	4.42	.37
Range	9.00	.4.00a
Minimum	.00	1.85
Maximum	9.00	3.42
Sum	111.00	110.00

Figure 1a (Novel group)
Figure 1b (Popular brand group)

DISCUSSION

This study gave us the opportunity to evaluate the effectiveness claims of a new dentifrice in offering relief for dentinal sensitivity against a known popular brand. The procedure is standard for the research and scientific committee of the Nigerian Dental Association which works very closely with dental products committee of the same association. These evaluations are only conducted after the products have been certified safe for human consumption by regulatory authorities enabled by law to do so. The job of the committee complements that of the regulatory authority by verifying effectiveness claims of oral health

Figure 2: Distribution of differences between post- and pre-intervention VAS scores.

Figure 2a (Novel group)

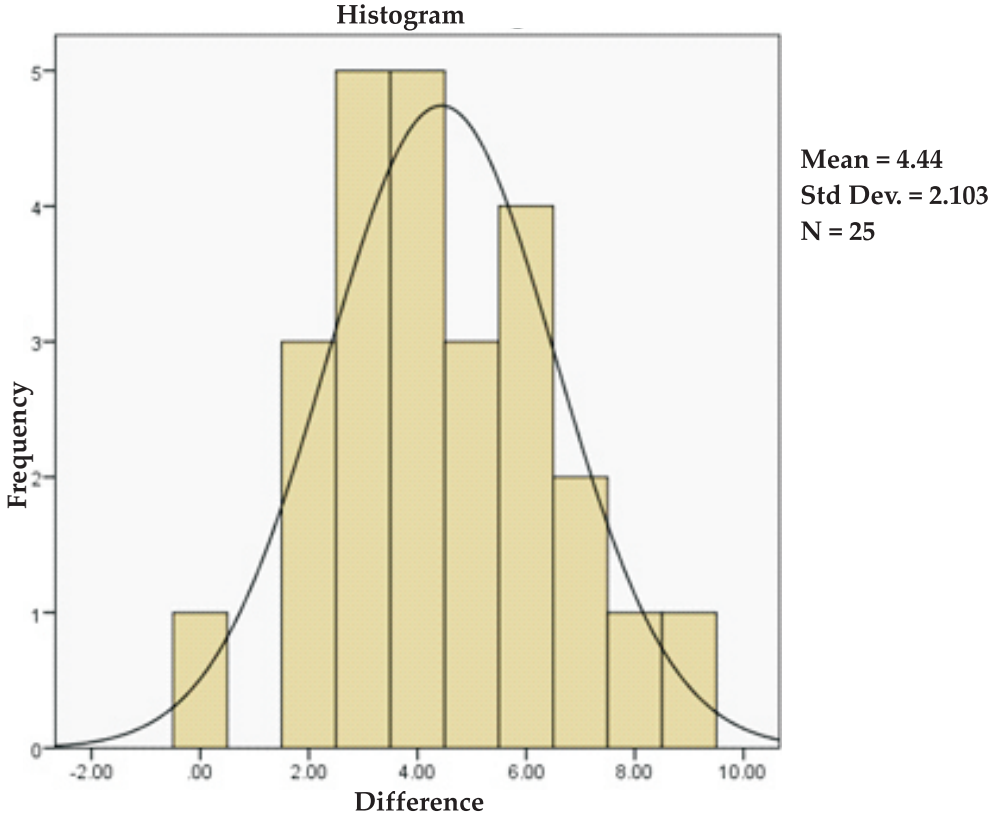
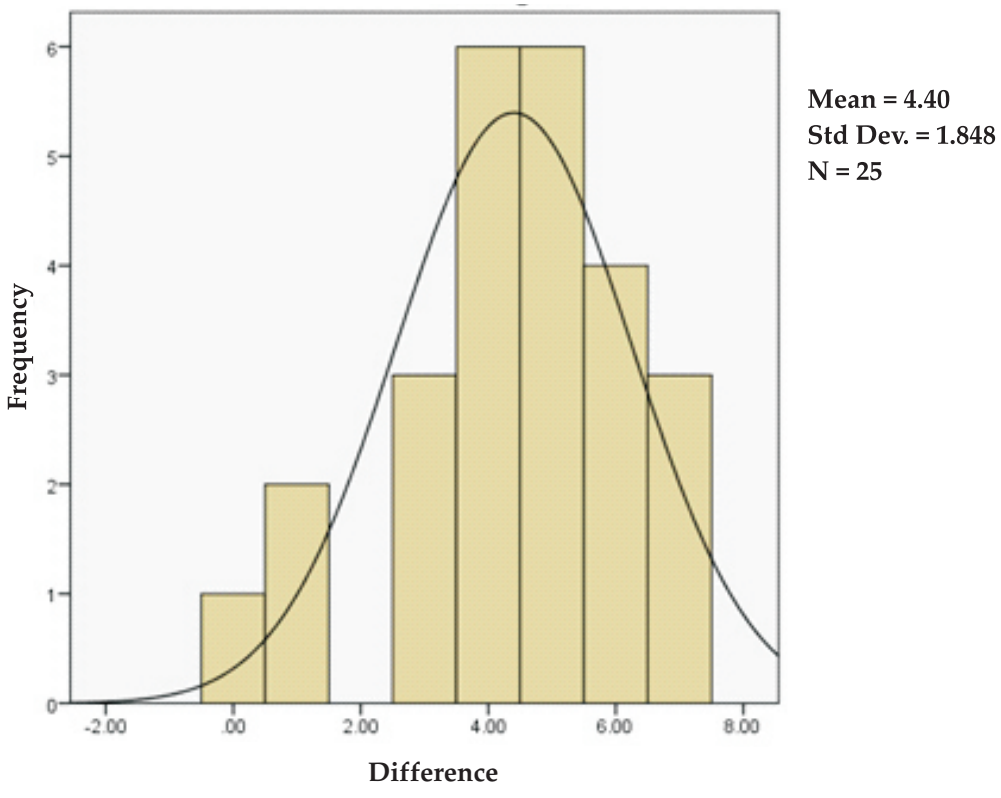


Figure 2b (Popular brand group)



products for the purposes of endorsement which is in accordance with global best practices[18]. Both dentifrices were free from adverse effects as reported by the limited sample population who participated in the study. Taste is another important parameter mostly to patients who suffer from dentinal sensitivity. This parameter was no major consequence in the current study as just one of the fifty participants described the taste of the dentifrice as unpleasant. Nonetheless, manufacturers are conscious of this dilemma imposed by the taste of the active constituents in anti-sensitivity compositions. For-instance, potassium and strontium salts which are among the popular currently-used active agents tend to confer some unpleasantness in taste which presents a dilemma of enduring the taste of living with sensitivity! It is noteworthy that some manufacturers resorting to making agents like baking soda to overcome the dilemma[19]. The absence of adverse reactions/effects in this study is heartwarming since investigators would have needed to secure the safety of the public and discontinue the study if there were any serious adverse effects[19]. Bain clearly stated conditions that would warrant such discontinuation as (i) diminished benefit (ii) increased risk like adverse effects/ drug interactions, and unsafe use which includes high-risk medicaments in older adults[20]. This would also be in strict compliance with the NAFDAC pharmacovigilance guidelines[21,22] of particular interest are the near mirror-image results emanating from this study. One immediate explanation might be that the active agents in the two dentifrices are similar. It turns out that this is not the case because the popular brand's advertized active ingredients include several sodium salts like Pentasodium Triphosphate, Sodium Saccharin, 0.454% Stannous Fluoride and 0.0721% w/w Sodium Fluoride amounting to 1450ppm Fluoride. The novel dentifrice also boasts of several sodium salts like sodium saccharin, sodium benzoate but states its main active agents as 5 percent Potassium nitrate and 0.7 percent sodium monofluorophosphate amounting to 917ppm Fluoride. It is therefore safe to propose that the ingredients are equally effective in offering quick relief from dentinal sensitivity. Previous Nigerian studies had evaluated the prevalence of dentine sensitivity. Savage and colleagues[23] had identified the frequency and characteristics of toothbrushing as the major determinants of dentine sensitivity in Nigeria. These factors were outside the scope of our study but would definitely be of interest from a management point of view. Unfortunately, despite the high prevalence (33.8%)[24] of this entity among Nigerians there seems to be a paucity of data on studies comparing the effectiveness of dentifrices in the Nigerian population. Despite this, it is noteworthy that just as seen from our study, there are several techniques available for the treatment of dentinal sensitivity. As Bamise and Esan [25] rightly observed however, a lot of doubt still exists as to the superiority of any one method of treatment over another, leading to a multiplication of treatment modalities. Unfortunately, we must agree with them that there is "no conclusive evidence of reliable, successful treatment regimens." It is only prudent to mention that a major limitation of 10-point likert scales which is the absence of a numerical zero point. A 0-10 scale will amount to an eleven-point likert scale while a 1-10 maintains a 10-point scale. The obvious problem here, however, is the absence of zero meaning that those who report complete relief of absence of pain must still be scored as 1. This study adopted a randomized open-label approach appears to be disadvantageous. However, some of the reasons for blinding including examiner bias and reporting bias are not strongly applicable to this study. The fact that examiners needed to depend on patient-reported VAS scores already introduces some inevitable subjectivity into the study which might not completely removed even with blinding. To minimize this effect, the same examiner examined the patients before and after the use of the dentifrices. Th open-label randomized approach in this instance could therefore be considered an alternative rather than an inferior approach. The almost mirror-image replica of the findings appears too strong to have been significantly influenced by adopting an open-label approach. In the words of Beyer-Westendorf and Buller " open-label trials are less complex and can be conducted at lower costs, which could be used to recruit more patients and to improve the value of trial results. Thus, in some respects, the

two trial designs offer complementary strengths and weaknesses" Despite this, it would be interesting to replicate this study using a double-blind approach to see if this influences the findings.

CONCLUSION

We found a novel dentifrice that squarely measured-up to a known popular brand anti-sensitivity dentifrice in its effectiveness in offering relief from dentinal sensitivity. The taste parameter appears to slightly favor the gold dentifrice even though we considered making any statistical inferences on this quite un-necessary. This is because the differences were so small (only one person reported a difference) to warrant any significant statistical analyses or inferences. We do hope that our results will provide guidance for Dental professionals and patients in making informed decisions in their future choice of anti-sensitivity dentifrice.

Conflict of interest: This study was sponsored by a grant from the manufacturers of the novel dentifrice.

REFERENCES

1. O'Sullivan EA, Curzon ME. A comparison of acidic dietary factors in children with and without dental erosion. ASDC J Dent Child 2000; 67(3):186-92, 160.
2. Chikte UM, Naidoo S, Kolze TJ, Grobler SR. Patterns of tooth surface loss among winemakers. SADJ 2005; 60(9):370-374.
3. Bartlett DW, Evans DF, Anggiansah A, Smith BG. A study of the association between gastro-oesophageal reflux and palatal dental erosion.Br Dent J 1996; 181(4):125-131.
4. Khocht A, Simon G, Person P, Denepitiya JL Gingival recession in relation to history of hard toothbrush use. J Periodontol 1993 ; 64(9):900-905.
5. Azodo CC, Amayo AC. Dentinal sensitivity among a selected group of young adults in Nigeria. Niger Med J 2011;52(3):189-192.
6. Bamise CT, Kolawole KA, Oloyede EO, Esan TA.Tooth sensitivity experience among residential university students. Int J Dent Hyg 2010; 8(2):95-100.
7. Irvine JH. Root surface sensitivity: A review of aetiology and management. J N Z Soc Periodontol. 1988;66:15-18.
8. Rapp R, Avery JK, Strachan DS. Possible role of the acetylcholinesterase in neural conduction within the dental pulp. In: Finn SB, editor. Biology of the dental pulp organ. Vol. 31. Birmingham: University of Alabama press; 1968. pp. 309-331.
9. Brännström M, Åström A. A study on the mechanism of pain elicited from the dentin. J Dent Res 1964;43(4):619-25.
11. West NX. Dentin hypersensitivity: preventive and therapeutic approaches to treatment Periodontology 2000 2000; 48(1): 31-41.
12. Peacock JM, Orchardson R. Effects of potassium ions on action potential conduction in A- and Cfibers of rat spinal nerves. J Dent Res 1995; 74(2): 634-641.
13. Markowitz K, Bilotto G, Kim S. Decreasing intradental nerve activity in the cat with potassium and divalent cations Arch Oral Biol 1991;36(1): 1-7.
14. de Oliveira da Rosa WL, Lund RG, Piva E, da Silva AF. The effectiveness of current dentin desensitizing agents used to treat dental hypersensitivity: A systematic review. Quintessence Int 2013;44(7):535-546.
15. Rosner B. *Fundamentals of biostatistics* 5th ed. Pacific Grove, Calif: Duxbury, 2000; 308.
16. Laerd Statistics (2015). Two-way mixed ANOVA using SPSS Statistics. Statistical tutorials and software guides. Retrieved from https://statistics.laerd.com/11/08/2020.
17. Quade D. Rank analysis of covariance. J Am Stat Asso 1967; 62(320): 1187-1200.
18. Unilever. Pepsodent, key facts. Retrieved https://www.hul.co.in/brands/personal-care/pepsodent.html. 11/08/2020.
19. Alfano MC, Synodis JD, Smetana AJ, Leight RS, Yeh KC, inventors; Block Drug Co Inc, assignee. Taste masked desensitizing compositions. United States patent US 5,939,048. 1999 Aug 17.
20. Bain KT, Holmes HM, Beers MH, Maio Vet al. Discontinuing medications: A novel approach for revising the prescribing stage of the medication-use process. J Am Ger Soc 2008 Oct;56(10):1946-1952.

21. Olowofela A, Fourrier-Réglat A, Isah AO. Pharmacovigilance in Nigeria: an overview. Pharm Med 2016;30(2):87-94.
22. NAFDAC Good Pharmacovigilance Practice Guidelines 2016 V13_New.Cd Retrieved from http://apps.who.int/medic inedocs/documents/s23028en/s23028en. pdf. 11/08/2020.
23. Savage KO, Oderinu OH, Oginni AO, Uti OG, Adegbulugbe IC, Dosumu OO. Dentine hypersensitivity and associated factors: a Nigerian cross-sectional study. Pan Afr Med J 2019 Jul 30;33:272.
24. Oderinu OH, Savage KO, Uti OG, Adegbulugbe IC. Prevalence of self-reporte hypersensitive teeth among a group of Nigerian undergraduate students. Niger Postgrad Med J 2011;18(3):205-9.
25. Bamise CT, Esan TA. Mechanisms and treatment approaches of dentine hypersensitivity: a literature review. Oral Health Prev Dent 2011;9(4):353-67.