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Comparison of chrysopogon zizanioides mouthwash with chlorhexidine mouthwash in chronic periodontitis patients: An clinical trial

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Abstract---Introduction: Chrysopogon zizanioides (Vetiver grass) is the source of a valuable essential oil, for which purpose it is often grown commercially. Amongst its many other uses, it provides material for thatch, has many medicinal applications and is cultivated to protect the soil from erosion. People take vetiver for nerve and circulation problems and for stomach pain. Vetiver is sometimes inhaled as aromatherapy for nervousness, insomnia, and joint and muscle pain. Vetiver oil has been used as anti-inflammatory, antiseptics, antioxidant and antibacterial activities. Materials and methods: Vetiver leaves have been extracted from and leaves are dried for 10 days then the extracted leaves are used for mouthwash preparation. The aqueous extract of prepared leaves was used for mouthwash preparation. Mouthwash preparation was done by the aqueous extract of chrysopogon zizanioides .20 patients with chronic periodontitis were selected for the study. In which 10 patients with the test group had Chrysopogon zizanioides mouthwash and 10 patients with the control group were given with chlorhexidine mouthwash. Each mouthwash was asked to use twice daily. Clinical parameters were assessed Probing depth, clinical attachment level and Bleeding index at baseline till 14 days. Results: Results of the study showed that chrysopogon zizanioides and chlorhexidine are equally effective in reducing plaque, gingival, and bleeding indices at 14-day intervals. However, no significant reductions in PD, CAL and BI in the 14-day interval in group 1 (Chrysopogon zizanioides) and group 2(Chlorhexidine mouthwash) when compared with chlorhexidine were evident. Conclusion: The results in the present study indicate that

chrysopogon zizanioides may prove to be as effective as chlorhexidine mouthwash in its ability in reducing all the three indices by reducing probing depth, clinical attachment level and bleeding index.

Keywords---Periodontitis, Chrysopogon zizanioides Chlorhexidine, Mouthwash.

1. Introduction

Chrysopogon zizanioides L. Nash, also called in the local language as Vetiver grass, is a lignocellulosic species that has been reported to be tolerant of various xenobiotics^{1,2}. Vetiver is non-invasive high biomass and an extensive root system^{3,4}. Chrysopogon Plant extract has medicinal value and also gives a successful outcome and also gives a stronger immune response against the bacteria. Nowadays research is based on plant extract because of its medicinal value^{3,4}. Chrysopogon zizanioides commonly known as vetiver is a perennial bunchgrass which is a native in India family of Poaceae, Genus of Chrysopogon and order polaes⁵. Chrysopogon zizanioides has been used as a cosmetic agent, sedatives and has anti-inflammatory activity. It is available as oil which has been used as an aromatic agent in India. The plant is well known for its oil that is used in medicine and perfumery⁵. Root is usually steam distilled to obtain the vetiver oil. Except for termiticidal and antimicrobial activity^{6,7}. Presence of natural antioxidants from various aromatic and medicinal plants is closely related to the reduction of chronic diseases such as DNA damage, mutagenesis, and carcinogenesis^{8,9}. Vetiver has been used in a research purpose for anti-tuberculosis and it also has an antioxidant potential. Chrysopogon zizanioides, also known as khas khas, khas or khus grass, is native to India. The leaves of Chrysopogon zizanioides is densely tufted grass, with long, thin and rigid leaves and can grow up to 1.5 meters high. The grass grows well in rich marshy soil that is found in plains and lower hills of India on the riverbanks. The plant is different from the other grass forms, in that instead of having mat-like root systems, it grows downwards and can grow up to 2-4 meters in depth. The plant is well known for its oil that is used in medicine and perfumery. Vetiver essential oil (VEO) is produced by steam distillation of the aromatic roots of the tropical grass *Vetiveria zizanioides*, which is native to the Indian subcontinent. VEO has a long history of use primarily due to its insect-repellent property and persistent green-woody note. Scientific studies have evaluated its insect-repellent, anti-inflammatory, antioxidant, and metabolic activities in several settings. Periodontitis is a chronic inflammatory disease during which microbes, host plays a crucial role within the progression of the disease. The disease which occurs as the inflammation reaches the periodontal ligament and alveolar bone which leads to tooth loss¹⁰. Periodontal pathogens generate by destruction of products and enzymes that dissolve the extracellular matrices as well as host cell membranes to generate nutrients for their growth and function¹¹. In which the treatment tend to concentrates in reducing the microbial load or killing the periodontal pathogens and allows the commensals to grow in the region. Dental plaque is considered as the primary etiologic factor for the causation of the disease. Plaque accumulation can be prevented by proper brushing and flossing. Certain pathogens hide inside the tissue and anatomical econiche and repopulate the

area. Hence chemical plaque control agents function as an adjunct to mechanical plaque control in maintaining the oral hygiene of the patient. Chlorhexidine (CHX), a cationic bisbiguanide is a gold standard among all mouthwashes particularly because of its substantivity and broad spectrum antibacterial activity^{12,13}. However, CHX has been reported to have a number of side effects like brown discoloration of teeth, salt taste perturbation, oral mucosal erosions, and enhanced supragingival calculus formation, which limit its long-term use¹⁴. Chlorhexidine (CHX) has been commonly used in dental practice as an antiseptic agent as it has long-lasting antibacterial activity with a broad-spectrum of action¹⁵. Many clinical trials have shown effective results of CHX for the clinical management of dental plaque and gingival inflammation and bleeding^{16,17}. In vitro study has been reporting positive results of CHX in reducing the proliferation of bacterial species associated with periodontal disease, such as Enterobacteria, Porphyromonas gingivalis, Fusobacterium nucleatum and different species of Actinomyces and Streptococcus, including Streptococcus mutans, which is considered the main etiological agent of dental caries¹⁸. Studies reported that the use of CHX was effective in the treatment of halitosis, especially in reducing the levels of halitosis-related bacteria colonizing the dorsal surface of the tongue¹⁹. Hence the aim of the current study is to compare the chlorhexidine mouthwash vs chlorhexidine mouthwash to detect whether Chrysopogon zizanioides has an effective role against chlorhexidine mouthwash.

2. Materials and Methods

The study was done to 20 patients with chronic periodontitis in the Department of Periodontics visiting Saveetha Dental College and Hospitals

Inclusion criteria

1. Patient with chronic periodontitis
2. Patients who have not undergone periodontal treatment in the past 6 months.

Exclusion criteria

1. Patients with a history of systemic diseases
2. Pregnancy and lactating women
3. Patients on antibiotic therapy from the past 3 months
4. Patients with adverse habits

The patients enrolled in the study were divided into two groups

1. Group 1 (Test group)-Patient receiving Chlorhexidine Mouthwash 10 ml twice daily (10 Patients)
2. Group 2 (Control group)-Patient receiving Chrysopogon Zizanioides 10 ml twice daily (10 Patients)

In all the participants, oral hygiene status assessment was carried out by probing depth (PD) Clinical attachment level (CAL) and Bleeding index (BI) and the scores were recorded at baseline. Thorough professional scaling was carried out and participants were instructed to rinse with 10 ml of respective mouthwashes for 1 min, twice daily. All indices were repeated and recorded on the 7th day and 14th day, respectively.

2.1 Preparation of leaf Extract Aqueous extract is prepared by following procedure

Chrysopogon zizanioides leaves are dried for 1 week under room temperature and the leaves are washed and cut into pieces. Then the dried leaves are kept in a beaker along with distilled water and heated at 100 Celsius for 2 hours and kept at room temperature to cool. After cooling the prepared aqueous plant then filtered with filtered paper.

2.2 Preparation of Chrysopogon zizanioides Mouthwash Preparation:

After preparation of leaf aqueous extract of chrysopogon zizanioides mouthwash preparation was done

Sucrose-15g

Sodium Benzoate-0.05g

Sodium Lauryl sulphate-0.5g

100ml Peppermint oil-5ml

Water-500ml

Chrysopogon Zizanioides-50 ml

3. Statistical analysis

All the data were analyzed using the SPSS version 20. Mean difference between probing depth, clinical attachment level and Bleeding on probing were assessed.

4. Results

Patient with chronic periodontitis were reported to after 14 days assessment of both test group and control group

Test group (Chrysopogon zizanioides)-Shows minimal amount of reduction in BOP, Probing depth and Clinical attachment level.

In which the control group shows reduction bleeding index, Probing depth and Clinical attachment level. In which (figure 1) shows the mean differences in probing depth between test and control group (figure 2) shows the mean differences in Clinical attachment level between test and control group (figure 3) shows the mean differences in Bleeding on probing between test and control group

Table 1
Baseline Patients with Chronic Periodontitis

Pre operative Probing depth	Pre operative clinical attachment level	Pre operative Bleeding on probing
6	8	2
6	8	2

6	8	2
7	9	2
6	8	2
7	9	2
6	8	2
7	9	2
6	8	2

Table 2
Post operative after chlorhexidine mouthwash (After 14 days)

Post operative Probing depth	Post operative clinical attachment level	Post operative Bleeding on probing
3	3	0
3	3	0
3	3	0
3	3	0
4	3	0
3	3	0
3	3	0
4	3	0
3	3	0

Table 3
Post operative with Chrysopogon zizanioides (After 14 days)

Post operative Probing depth	Post operative clinical attachment level	Pre operative Bleeding on probing
5	5	0
5	5	2

4	5	0
4	6	2
4	4	2
5	4	0
4	4	2
5	4	0
5	5	0

Statistical analysis

Table 1-†shows mean and standard deviation of probing depth pre chrysopogon zizanioides probing depth (Preczpd) pre chlorhexidine mouthwash probing depth (pre chx pd) post chrysopogon zizanioides probing depth (post cz pd) post chlorhexidine mouthwash probing depth (post chx pd)

	Preczpd	postczpd	pre chx pd	post chx pd
Mean	7.160	6.350	6.970	4.920
N	10	10	10	10
Std. Deviation	.7961	.8489	.8629	.9449

Table 2-†shows mean and standard deviation of Clinical attachment level pre chrysopogon zizanioides probing depth (Preczcal) pre chlorhexidine mouthwash Clinical attachment level (pre chx cal) post chrysopogon zizanioides Clinical attachment level (post cz cal) post chlorhexidine mouthwash Clinical attachment level(post chx cal)

	precalcz	postcalcz	prechx	precalchx
Mean	5.1500	4.5400	4.9100	3.7400
N	10	10	10	10
Std. Deviation	.52122	.48120	.61001	.34705

Table 3-†shows mean and standard deviation of bleeding index pre chrysopogon zizanioides probing depth (Pre cz bl) pre chlorhexidine mouthwash bleeding index (pre chx bl) post chrysopogon zizanioides bleeding index (post cz bl) post chlorhexidine mouthwash bleeding index(post chx bl)

	preopblcz	preopblchx	postopblchx	postopblcz
Mean	3.500	2.870	.520	3.230
N	10	10	10	10
Std. Deviation	.8260	.5187	.1549	.7761

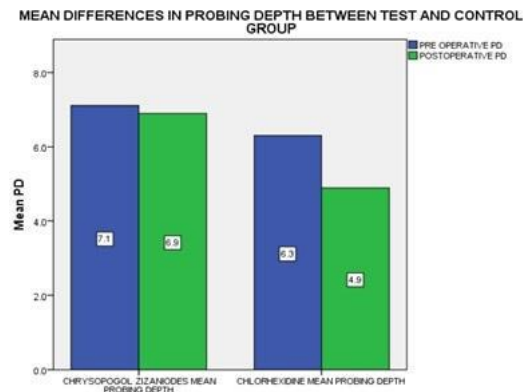


Figure 2-*shows the mean differences in probing depth between test group (Chrysopogon zizanioides) and Control group (Chlorhexidine mouthwash). In which X axis shows the probing depth of chrysopogon zizanioides and chlorhexidine mouthwash and Y axis shows mean probing depth. In which baseline denotes (Blue colour) and (green colour) denotes reduction from baseline.

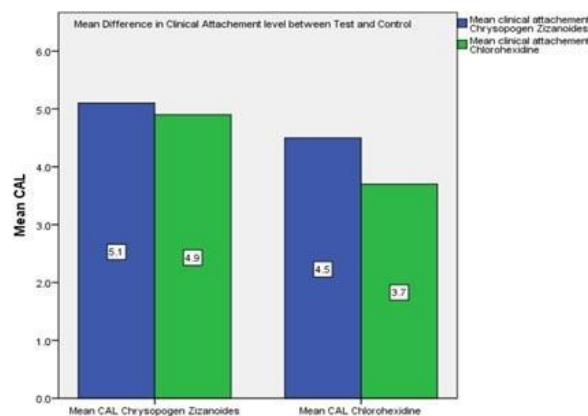


Figure 3-*shows the mean differences in Clinical attachment loss test group (Chrysopogon zizanioides) and Control group (Chlorhexidine mouthwash). In which X axis shows mean value of clinical attachment level of Chrysopogon zizanioides and mean clinical attachment level of chlorhexidine mouthwash and Y

axis shows mean clinical attachment level. In which baseline denotes (Blue colour) and (green colour) denotes reduction from baseline.

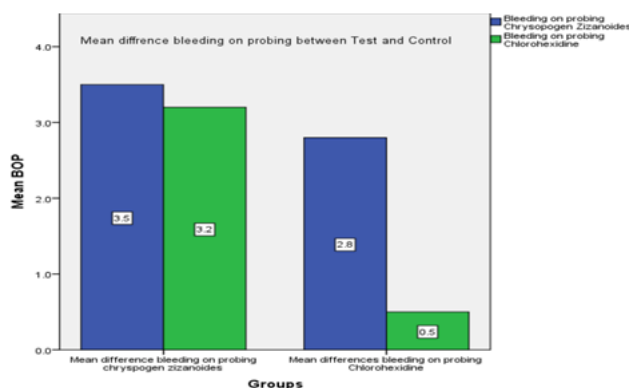


Figure 4-*shows the mean differences in Bleeding on Probing test group (Chrysopogon zizanioides) and Control group (Chlorhexidine mouthwash). In which X axis shows mean differences bleeding on probing chrysopogon zizanioides and Y axis shows the mean differences bleeding on probing in chlorhexidine mouthwash and Y axis shows the mean differences in bleeding on probing. In which baseline denotes (Blue colour) and (green colour) denotes reduction from baseline

Statistical analysis

Table 1-†shows mean and standard deviation of probing depth pre chrysopogon zizanioides probing depth (Preczpd) pre chlorhexidine mouthwash probing depth (pre chx pd) post chrysopogon zizanioides probing depth (post cz pd) post chlorhexidine mouthwash probing depth (post chx pd)

	Preczpd	postczpd	pre chx pd	post chx pd
Mean	7.160	6.350	6.970	4.920
N	10	10	10	10
Std. Deviation	.7961	.8489	.8629	.9449

Table 2-†shows mean and standard deviation of Clinical attachment level pre chrysopogon zizanioides probing depth (Preczcal) pre chlorhexidine mouthwash Clinical attachment level (pre chx cal) post chrysopogon zizanioides Clinical attachment level (post cz cal) post chlorhexidine mouthwash Clinical attachment level(post chx cal)

	precalcz	postcalcz	prechx	precalchx
Mean	5.1500	4.5400	4.9100	3.7400
N	10	10	10	10
Std. Deviation	.52122	.48120	.61001	.34705

	preopblcz	preopblch x	postopblchx	postopblcz
Mean	3.500	2.870	.520	3.230
N	10	10	10	10
Std. Deviation	.8260	.5187	.1549	.7761

5. Discussion

Dental plaque is a biofilm that forms naturally on the surfaces of exposed teeth and other areas of the mouth and is the main etiological factor for many of the oral diseases. Plaque control, which is an efficient method within the elimination of plaque biofilm, could also be mechanical and chemical¹⁶. While mechanical plaque control with the usage of brushes and interdental aids plays an important role in maintaining the oral hygiene of a private, it requires the patient's motivation. On the opposite hand, chemical plaque control also facilitates good oral hygiene with the usage of adjuvants. Among the various agents advocated for chemical plaque control, mouth rinse plays an essential role. Among them chlorhexidine is one essential mouth rinse which is taken into account to be the gold standard. Apart from its various advantages, it also has drawbacks such as alteration in taste sensation and staining of teeth¹⁶. To overcome such side effects, herbal medications have also been introduced for attaining total plaque-free mouth. Previously numerous studies have been done on *Chrysopogon zizanioides*, one study used *Chrysopogon* in the treatment of diabetes where Streptozotocin-induced diabetes is characterized by severe loss in body weight due to the degradation of structural proteins, which are responsible for the changes in body weight. However, treatment with *Chrysopogon zizanioides* methanolic extract showed beneficial effects and the weight suggested its recovery activity against diabetes. The exact treatment in STZ rats led to marked increase in body weight due to increased adipose tissue mass, an observation also seen in humans treated⁵. In the present study, the clinical parameters, namely PI, GI and BI were evaluated at baseline, 14 days. *Chrysopogon zizanioides* possesses strong anti-inflammatory activity¹⁸. In *Chrysopogon zizanioides* its constituents like β -vetinone, β -vetinene and α -vetinone are responsible for its antioxidant properties and high content of flavonoids found in *Chrysopogon zizanioides* have been attributed to its antioxidant effect²⁰. The antioxidant and anti-inflammatory properties of *Chrysopogon Zizanioides* are responsible for its antidepressant effect²¹. *Chrysopogon zizanioides* is also used as an antituberculosis agent but also indicates prospect for isolation and identification of antituberculosis compounds from bioactive hexane fraction of plant²². *Chrysopogon zizanioides* are effective against drug-resistant bacteria from both Gram-positive and Gram-negative groups²³. Vetivers have been reported to treat inflammatory bowel disease²², urinary tract infection²³) and have been reported in making insect repellent²⁴. The extract root of vetiver which has been used for headache and toothache, the leaf paste is used for lumbago, sprain, and rheumatism, the stem decoction for urinary tract infection, the leaf juice of *chrysopogon zizanioides* acts as an anthelmintic, the vapors for malarial fever, and the root ash is given for acidity relief. An in vitro study based on cytotoxic activity test was done in aqueous

extract of chrysopogon zizanioides to detect the mortality rate of Chrysopogon zizanioides in which mortality rate of biologic organism were tested in nauplii with different concentration of 10 µl, 20 µl, 30 µl, 40 µl and 50 µl which in the mortality rate was seen in each concentration 10 µl has 40%, 20 µl has 30%, 30 µl has 30%, 40 µl has 20% and 50µl has 20%.²⁵.Chrysopogon would be useful for the treatment of periodontitis. Since it has antibacterial property against gram negative microbes it would be interesting to study the effects on periodontal pathogens. The extract has antioxidant and anti-inflammatory properties which adds more value towards periodontal treatment. The antimicrobial action of vetiver and chamomile oils against *E. faecalis*. The effectiveness and clinical efficacy of chamomile have been reported selectively in removing smear layer, oral mucositis, plaque, scurvy, gingivitis, and patients undergoing orthodontic treatment. Chlorhexidine is a positively charged particle that reacts with negatively charged molecules present on the bacterial cell wall and destroyed cell homeostasis has been known for its activity against *E. faecalis*^{26,27}. Studies show a good effectiveness of chamomile oils in root canal infection of *E. faecalis* at different time intervals compared to chlorhexidine and calcium hydroxide. Vetiver oil did not sustain their activity for a longer duration²⁸.

5. Conclusion

Within the limitation of the study, however, chlorhexidine mouthwash is gold standard which reduces probing depth, clinical attachment level and bleeding index. In which chrysopogon zizanioides shows a little effect in reducing the periodontal disease compared with chlorhexidine mouthwash. Further studies have to be done before using this novel product as mouthwash in periodontal disease.

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7. Conflict Of Interest

The authors declare no potential conflict of interest

References

1. Afennich F, Slot DE, Hossainian N, Van der Weijden GA. The effect of hexetidine mouthwash on the prevention of plaque and gingival inflammation: a systematic review. *Int J Dent Hyg*. 2011;9(3):182-190.
2. Afkhami F, Akbari S, Chiniforush N. *Enterococcus faecalis* Elimination in Root Canals Using Silver Nanoparticles, Photodynamic Therapy, Diode Laser, or Laser-activated Nanoparticles: An In Vitro Study. *J Endod*. 2017;43(2):279-282.
3. Antiochia R, Campanella L, Ghezzi P, Movassaghi K. The use of vetiver for remediation of heavy metal soil contamination. *Analytical and Bioanalytical Chemistry*. 2007;388(4):947-956. doi:10.1007/s00216-007-1268-1

4. Chen Y, Shen Z, Li X. The use of vetiver grass (*Vetiveria zizanioides*) in the phytoremediation of soils contaminated with heavy metals. *Applied Geochemistry*. 2004;19(10):1553-1565. doi:10.1016/j.apgeochem.2004.02.003
5. Craig WJ. Health-promoting properties of common herbs. *The American Journal of Clinical Nutrition*. 1999;70(3):491s - 499s. doi:10.1093/ajcn/70.3.491s
6. Egamberdieva D, Shrivastava S, Varma A. *Plant-Growth-Promoting Rhizobacteria (PGPR) and Medicinal Plants*. Springer; 2015.
7. Eick S, Goltz S, Nietzsche S, Jentsch H, Pfister W. Efficacy of chlorhexidine digluconate-containing formulations and other mouthrinses against periodontopathogenic microorganisms. *Quintessence Int*. 2011;42(8):687-700.
8. Evaluation of Cytotoxic Activity of Chrysopogon Zizanioides Mouthwash - An In Vitro Study. *International Journal of Pharmaceutical Research*. 2020;12(sp1). doi:10.31838/ijpr/2020.sp1.431
9. Fedorowicz Z, Aljufairi H, Nasser M, Outhouse TL, Pedrazzi V. Mouthrinses for the treatment of halitosis. *Cochrane Database Syst Rev*. 2008;(4):CD006701.
10. Flötra L, Gjermo P, Rölla G, Waerhaug J. Side effects of chlorhexidine mouth washes. *European Journal of Oral Sciences*. 1971;79(2):119-125. doi:10.1111/j.1600-0722.1971.tb02001.x
11. Gupta R, Sharma KK, Afzal M, et al. Anticonvulsant activity of ethanol extracts of *Vetiveria zizanioides* roots in experimental mice. *Pharmaceutical Biology*. 2013;51(12):1521-1524. doi:10.3109/13880209.2013.799710
12. James P, Worthington HV, Parnell C, et al. Chlorhexidine mouthrinse as an adjunctive treatment for gingival health. *Cochrane Database Syst Rev*. 2017;3:CD008676.
13. Joshua MT, Department of Medical Laboratory Science, Rivers State University Port Harcourt. Evaluation of the effects of Aqueous and Ethanolic Extracts of *Morus mesozygia* Linn. Stapf., Leaves on Lipid Profile and Renal Indices of Streptozotocin- Induced Diabetic Rats. *Journal of Medical Science And clinical Research*. 2019;7(9). doi:10.18535/jmscr/v7i9.77
14. Lang NP, Lindhe J. *Clinical Periodontology and Implant Dentistry, 2 Volume Set*. John Wiley & Sons; 2015.
15. Loe H, Rindom Schiott C. The effect of mouthrinses and topical application of chlorhexidine on the development of dental plaque and gingivitis in man. *Journal of Periodontal Research*. 1970;5(2):79-83. doi:10.1111/j.1600-0765.1970.tb00696.x
16. Luqman S, Srivastava S, Darokar MP, Khanuja SPS. Detection of Antibacterial Activity in Spent Roots of Two Genotypes of Aromatic Grass *Vetiveria zizanioides*. *Pharmaceutical Biology*. 2005;43(8):732-736. doi:10.1080/13880200500387471
17. Maistrello L, Henderson G, Laine RA. Efficacy of Vetiver Oil and Nootkatone as Soil Barriers Against Formosan Subterranean Termite (Isoptera: Rhinotermitidae). *Journal of Economic Entomology*. 2001;94(6):1532-1537. doi:10.1603/0022-0493-94.6.1532
18. Nix KE, Henderson G, Zhu BCR, Laine RA. Evaluation of Vetiver Grass Root Growth, Oil Distribution, and Repellency Against Formosan Subterranean Termites. *HortScience*. 2006;41(1):167-171. doi:10.21273/hortsci.41.1.167

19. Orstavik D. *Essential Endodontology: Prevention and Treatment of Apical Periodontitis*. John Wiley & Sons; 2020.
20. Phytoremediation of Soils Contaminated by Heavy Metals, Metalloids, and Radioactive Materials Using Vetiver Grass, *Chrysopogon zizanioides*. *Phytotechnologies*. Published online 2012:280-307. doi:10.1201/b12954-17
21. Rølla G, Løe H, Rindom Schiøtt C. Retention of chlorhexidine in the human oral cavity. *Archives of Oral Biology*. 1971;16(9):1109-IN33. doi:10.1016/0003-9969(71)90215-9
22. Saikia D, Parveen S, Gupta VK, Luqman S. Anti-tuberculosis activity of Indian grass KHUS (*Vetiveria zizanioides* L. Nash). *Complementary Therapies in Medicine*. 2012;20(6):434-436. doi:10.1016/j.ctim.2012.07.010
23. Sinha S, Jothiramajayam M, Ghosh M, Jana A, Chatterji U, Mukherjee A. Vetiver oil (Java) attenuates cisplatin-induced oxidative stress, nephrotoxicity and myelosuppression in Swiss albino mice. *Food and Chemical Toxicology*. 2015;81:120-128. doi:10.1016/j.fct.2015.04.018
24. Sofiani E, Wahyunigrum H. Differential effectiveness of calcium hydroxide with 2% chlorhexidine digluconate and 25% propolis as a root canal medicament against *Enterococcus faecalis* (In vitro). *Scientific Dental Journal*. 2021;5(1):37. doi:10.4103/sdj.sdj_45_20
25. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2022). Post-pandemic health and its sustainability: Educational situation. *International Journal of Health Sciences*, 6(1), i-v. <https://doi.org/10.53730/ijhs.v6n1.5949>
26. Thaib, P. K. P., & Rahaju, A. S. (2022). Clinicopathological profile of clear cell renal cell carcinoma. *International Journal of Health & Medical Sciences*, 5(1), 91-100. <https://doi.org/10.21744/ijhms.v5n1.1846>
27. Van Leeuwen MPC, Slot DE, Van der Weijden GA. Essential Oils Compared to Chlorhexidine With Respect to Plaque and Parameters of Gingival Inflammation: A Systematic Review. *Journal of Periodontology*. 2011;82(2):174-194. doi:10.1902/jop.2010.100266
28. Vyas SP, Sihorkar V, Mishra V. Controlled and targeted drug delivery strategies towards intraperiodontal pocket diseases. *Journal of Clinical Pharmacy and Therapeutics*. 2000;25(1):21-42. doi:10.1046/j.1365-2710.2000.00261.x
29. Website. Antiochia R, Campanella L, Ghezzi P, Movassaghi K. The use of vetiver for remediation of heavy metal soil contamination [Internet]. Vol. 388, Analytical and Bioanalytical Chemistry. 2007. p. 947–56. Available from: <http://dx.doi.org/10.1007/s00216-007-1268-1>
30. Zakariya U, Umar U, Dambazau S, Sulaiman A. Comparative Hepatotoxic Effects of Aqueous and Phenolic Extracts of Avocado (*Persea americana*) Seed in Wistar Albino Rats. *International Journal of Biochemistry Research & Review*. 2016;10(4):1-6. doi:10.9734/ijbcrr/2016/23196