PREPARATION AND CYTOTOXIC EFFECT OF *PTEROCARPUS SANTALINUS* SELENIUM BASED MOUTHWASH

RUNNING TITLE: Cytotoxic effect of *Pterocarpus santalinus* selenium based mouthwash

Abstract

Introduction:A mouthwash or rinse cannot replace the regular oral hygiene routine of twice-daily tooth brushing and daily flossing.A mouthwash or rinse freshen breath, and control the bad breath.A mouthwash is a medicated liquid which is held in the mouth and swished by the action of perioral musculature to eliminate the oral pathogens.The medicinal plants have their application in pharmaceutical, cosmetic, agricultural and food industries.Medicinal plants act as a natural source for bioactive medicinal compounds.Selenium is a vita micronutrient that has excellent antimicrobial, anti cancerous, antidiabetic, and anti-inflammatory properties.The biological method of synthesis of Selenium nanoparticles has extensive application in the field of biomedicine due to low toxicity, targeted delivery of Nano drugs and stability.

Materials and method: Pterocarpus santalinus plant extract and mouthwash was prepared and cytotoxicity activity was performed.

Results: On day 1 all the 10 nauplii were alive in all the concentrations. On day 2 when the concentration was 5, 10, 20, 40,80 ,control the number of live nauplii was 10,8,8,8,7,10 respectively.Results were tabulated and graphically analyzed in SPSS software. Correlation analysis was done using SPSS software.

Conclusion: Increased concentration of selenium nanoparticles was not toxic to living nauplii as it did not cause the death of it.But the *Pterocarpus santalinus* extraction based selenium nanoparticles have less to no cytotoxicity.This study shows that mouth rinses from medicinal plants as a source of an excellent alternative with less common side-effects to chemical-based oral antimicrobial products.

Keywords: *Pterocarpus santalinus*, Cytotoxicity, mouthwash, selenium

UNDER PEER REVIEW

INTRODUCTION:

A mouthwash or rinse cannot replace the regular oral hygiene routine of twice-daily tooth brushing and daily flossing. The main function of most mouthwashes is to freshen breath, and control the bad breath (1).A mouthwash is a medicated liquid which is held in the mouth and swished by the action of perioral musculature to eliminate the oral pathogens (2). In ancient times the mouthwash was formulated with a mixture of decoct extracted from the olive tree leaves, milk, wine and oil, pomegranate peelings, nutgalls and vinegar. This paved way for mouthwash with traditional methods and herbs. Since then a variety of herbal remedies are available triphala, tulsi patra, jyeshtamadh, neem, clove oil, pudina, ajwain, white oak bark, horsetail herb, plantain leaf, aloe vera, organic echinacea angustifolia root, myrrh gum, organic lobelia herb and seed, organic peppermint leaf, wildcrafted goldenseal root, clove essential oil, peppermint essential oil, tea tree essential oil (3).

The medicinal plants have their application in pharmaceutical, cosmetic, agricultural and food industries. The use of the medicinal herbs for curing disease has been marked in the past Saga of all civilizations (4). Humans in the prehistoric era were not aware about the health hazards and their association with irrational therapy. With the commencement of research in medicine, it was concluded that plants contain active principles, which are responsible, for curative action of the disease (5). Before the synthetic era, man was completely dependent on medicinal herbs for prevention and treatment of diseases. With the introduction of scientific procedures, medical practitioners were able to understand about toxic principles present in the green flora. Medicinal plants act as a natural source for bioactive medicinal compounds (6). *Pterocarpus santalinus* (red sandalwood) is one of the medicinal plants used in traditional medicine, and is rich in flavonoids and phenols. Significant antidiabetic activity by reducing the elevated blood glucose levels and glycosylated hemoglobin, improving hyperlipidemia and restoring the insulin levels includes three new sesquiterpenes - namely isopterocarpolone, pterocarptriol and pterocarpdiolone (7).

Selenium is a vita micronutrient that has excellent antimicrobial, anti cancerous, antidiabetic, and anti-inflammatory properties (8) & (9), Nevertheless, it is in the traditional form, it has a low

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degree of absorption and high levels of toxicity (10). Nano-sized selenium has excellent biocompatibility with enhanced biological effects. The biological method of synthesis of Selenium nanoparticles has extensive application in the field of biomedicine due to low toxicity, targeted delivery of Nano drugs and stability (11). Seaweeds or marine algae are permanent sources of chemical compounds which consist of a plethora of biologically active secondary metabolites (12). They are considered as a potential source of antibiotic substances. Ulva lactuca is an edible green marine algae (Chlorophyta), which holds an antibacterial activity against oral pathogens. Ulvan is the sulfated polysaccharide of the algae Ulva Spp is declared to be responsible for its antibacterial activity and has no toxicity (13). Traditional oral antimicrobial agents in the form of mouth rinses or dental varnish are chemical-based (14) These chemicals based mouthwashes cause many side effects. This emphasized the need for non-toxic natural products based mouth rinses which is also effective in reducing the bacterial load (15).Our team has extensive knowledge and research experience that has translate into high quality (16) (17) (18) (19) (20) (21) (22) (23) (24) (25) (26) (27) (28) (29) .The Present Study is aimed at the preparation and cytotoxic effect of *Pterocarpus santa*linus selenium based mouthwash.

METHODS & MATERIALS:

Preparation of plant extract:

Commercially available dry powder of *Pterocarpus santalinus* was used for this experiment. This experiment was conducted in Saveetha Dental College,Chennai,Tamilnadu. This experiment was carried out by dissolving 1g of *Pterocarpus santalinus* in 100ml of water. This moisture was then boiled in a heating mantle st 70 degrees celsius for up to 10 minutes. The boiled mixture was then filtered using Whattman number 1 filter paper to obtain the plant extract. Then 40ml of plant extract was measured using a measuring cylinder and the mixture was added to 60ml of 1mM selenium dissolved in 60 ml distilled water.

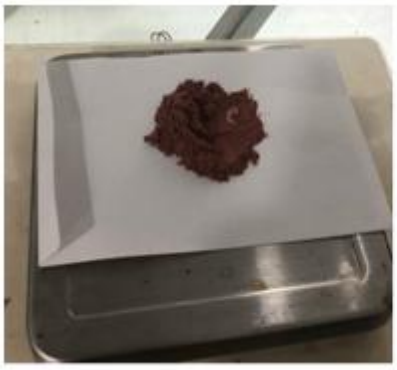

Figure 1:1g of *Pterocarpus santalinus* powder weighed and taken

Preparation of the mouthwash:

To a eppendorf tube, 10 ml of distilled water was taken then 0.3g of sucrose was measured using a electrical weighing scale and was added to the tube containing the water, the mixture was mixed well and then 0.01g of sodium lauryl sulphate and 0.001 g of sodium benzoate were added and mixed well. Then 12 drops of the plant pellet were added to the above mixture followed by adding 2 drops of peppermint oil and was mixed well.

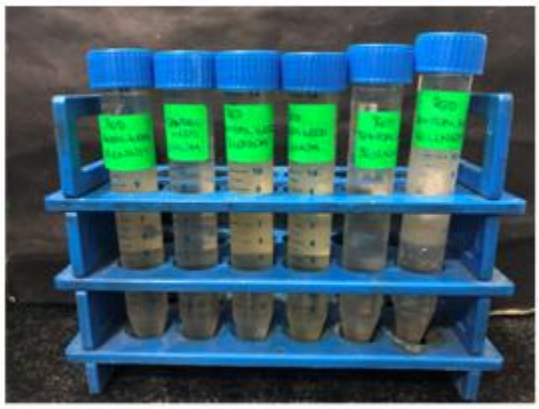

Figure 2: Prepared *Pterocarpus santalinus* selenium nanoparticles based mouthwash

Cytotoxicity activity -Brine shrimp lethality assay:

Salt water preparation:

Iodine free salt 2g was weighed and dissolved in 200 ml of distilled water. Then 6 wells of the ELISA plates were taken and 10-12 ml of saline water was filled respectively. To that 10 nauplii were slowly added to each well (20 , 40, 60, 80, 100).

Then the nanoparticles were added according to the concentration level. The plates were incubated for 24 hours. After 24 hours, the ELISA plates were observed and noted for the number of live nauplii present and calculated.

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RESULTS

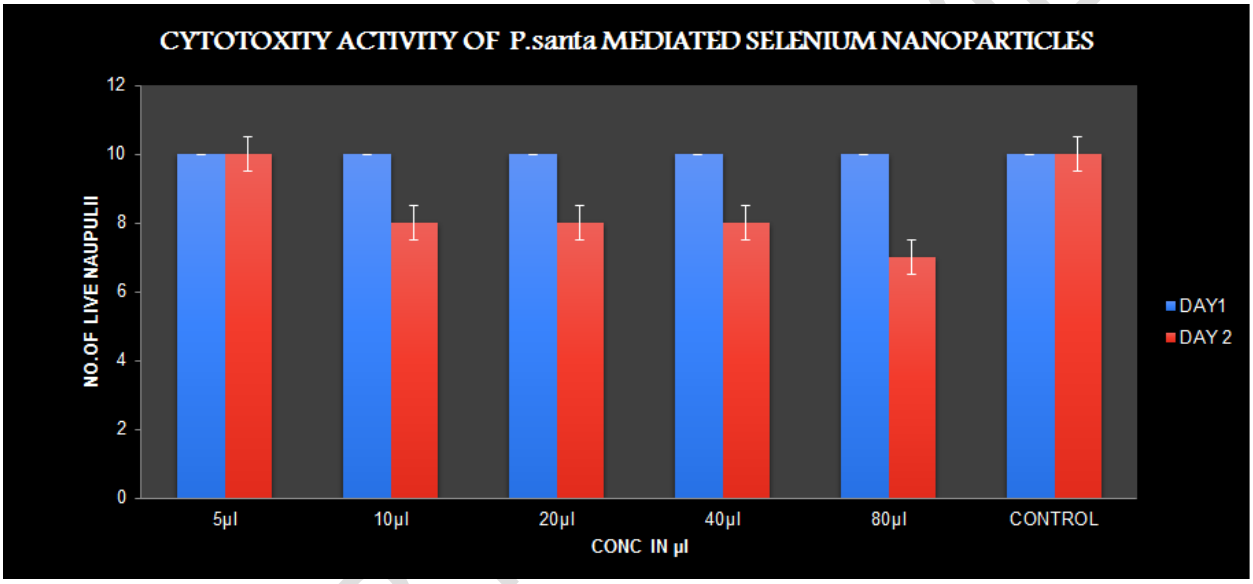

Figure 3: The bar graph represents the cytotoxic activity of the *Pterocarpus santalinus* selenium based mouthwash. X axis represents the concentration and Y axis represents the no. of live nauplii. The blue bar represents day 1 and the orange bar represents day 2.

The present study observed that in figure 3, on day 1 all the 10 nauplii were alive in all the concentrations. On day 2 when the concentration was 5, 10, 20, 40,80 ,control the number of live nauplii was 10, 8, 8, 8, 7, 10 respectively.

DISCUSSION:

It is eminent that the oral ailments are a global health apprehension with a substantial impact on the general public. Additionally the amplified intake of sugars in the diet, consumption of tobacco, inadequate exposure to fluorides, and lack of approach to dental care, are the expected incidence of dental caries and periodontal disease which will continue to rise (30). S. mutans is the foremost etiological agent of dental caries (31). *E. faecalis* is an opportunistic pathogen, *S. aureus* and *C. albicans* are secluded from persistent apical periodontal lesions. Oral microflora is considered as a Vital factor in both caries and periodontal disease, and causes the ailment pathogenesis by producing the biofilms (32). Therefore, the use of various types of mouth rinses are given a proper importance to proceed against the harmful microorganisms associated with oral diseases or infections (33). Conversely, apprehensions regarding the development of antibiotic-resistant strains and hostile effects of contemporary mouth rinses have directed the attention in the use of non conventional or alternative medicines and plant extracts. Many previous reports have recommended the possible use of plant extracts in oral care for effective and efficient inhibition of microflora by natural antimicrobials (31,34)(10). Nevertheless, the potential benefits of chemotherapeutic formulations in mouth rinses provide thrust for research in verdict effective mouth rinses for oral care (35) & (36).

The previous study done by Mohanakumari (37), any antimicrobial agents are expected to have minimal cytotoxic effect on host cells. This previous study results demonstrated the cytotoxic effect of both CP and LS on cultured HGF (38). Nevertheless, no significant differences were observed in the reduction of HGF cells by irradiated and non irradiated mouth rinses. Importantly, an earlier report on the effect of E-beam on sodium dodecyl sulfate demonstrated the reduction in toxicity of the surfactant (39).The previous study demonstrated the similar result concluded as in the present study.

Microculture tetrazolium assays are sensitive, quantitative, and reliable methods to assess the cellular metabolic activity, where methyl thiazolyl tetrazolium obtains a dark purple colored formazan through cellular mitochondrial dehydrogenase enzyme. A study done by Geethashri Anand (40), the percentage survival rate of HGF cells and V79 cells dealt with cashew and mango established a significant PI-based mouth rinses than the CHX-based. This indicates less toxicity and long time usage of active components of these plants as an alternative to commercial mouth rinses which is in accordance with the present study .

In a recent study, 1-h exposure to as low as 0.1% Persica solution produced irreversible cytotoxic effects on the cells engaged in the wound healing process (41). While the presence of FCS (10%) offered a protection from drug toxicity, the diminution in the cytotoxic effect of Persica in the

presence of FCS is due to the binding of potent toxic compounds of the mouthwash to serum proteins(42). Our team has extensive knowledge and research experience that has translate into high quality publications (43–47),(48),(49),(50),(51),(52),(53),((45,54,55),(56–60) (61),(62) . It is pragmatic that the toxic compounds of Persica solution put forth their effects through irreversible binding to cellular proteins, thereby reassuring their function. The aim of the Present study is set out with the same result (63).

CONCLUSION:

Increased concentration of selenium nanoparticles was not toxic to living nauplii as it did not cause the death of it.But the *Pterocarpus santalinus* extraction based selenium nanoparticles have less to no cytotoxicity(64-73).A Previous study done by Ryeo-Woon Kim(74) discussed that the cytotoxicity assay conducted in this study demonstrated that the Dendropanax morbifera Léveille extracts retained high cell viability (> 60%) at all concentrations. The cytotoxicity test performed using Human keratinocyte cells in a previous study revealed that the *Dendropanax morbifera Léveille* leaf extracts exhibited no cytotoxicity at concentrations lower than 50 µm/mL. This result was in concurrence to the result obtained in the present study. This study shows that mouth rinses from medicinal plants as a source of an excellent alternative with less common side-effects to chemical-based oral antimicrobial products.

NOTE:

The study highlights the efficacy of "traditional medicine" which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable.

REFERENCES:

1. Barma MD, Kannan SD, Indiran MA, Rajeshkumar S, Pradeep Kumar R. Antibacterial Activity of Mouthwash Incorporated with Silica Nanoparticles against S. aureus, S. mutans, E. faecalis: An in-vitro Study [Internet]. Journal of Pharmaceutical Research International. 2020. p. 25–33. Available from: http://dx.doi.org/10.9734/jpri/2020/v32i1630646

2. Matthews RW. Hot saltwater mouth baths [Internet]. Vol. 194, British Dental Journal. 2003. p. 584–584. Available from: http://dx.doi.org/10.1038/sj.bdj.4810228

3. Manipal S. The Mouthwash War - Chlorhexidine vs. Herbal Mouth Rinses: A Meta-Analysis [Internet]. JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH. 2016. Available from: http://dx.doi.org/10.7860/jcdr/2016/16578.7815

4. Herbal Sources Used by The Public Against Infections [Internet]. Vol. 12, International Journal of Pharmaceutical Research. 2020. Available from: http://dx.doi.org/10.31838/ijpr/2020.sp1.015

5. Shi-Lin Chen,Hua Yu,corresponding , Hong-Mei Luo,Qiong Wu,Chun-Fang Li, André Steinmetz. Conservation and sustainable use of medicinal plants: problems, progress, and prospects. Chin Med [Internet]. 2016;11(6). Available from: http://dx.doi.org/ 10.1186/s13020-016-0108-7

6. Niveditha AS, Sankari Niveditha A, Geetha RV, Arivarasu L. Will Alternative Medicine Help Us to Fight Against COVID-19 [Internet]. International Journal of Current Research and Review. 2020. p. 112–6. Available from: http://dx.doi.org/10.31782/ijcrr.2020.sp47

7. M. Eshrat Halim AM. The effects of the aqueous extract of Pterocarpus santalinus heartwood and vitamin E supplementation in streptozotocin-induced diabetic rats. Journal of Medicinal Plants [Internet]. 2011;5(3):398–409. Available from: https://academicjournals.org/journal/JMPR/article-full-text-pdf/736711624896

8. Shree MK, Kavya Shree M, Arivarasu L, Rajeshkumar S. Cytotoxicity and Antimicrobial Activity of Chromium Picolinate Mediated Zinc Oxide Nanoparticle [Internet]. Journal of

Pharmaceutical Research International. 2020. p. 28–32. Available from: http://dx.doi.org/10.9734/jpri/2020/v32i2030726

9. Jaisankar AI, Arivarasu L. Free Radical Scavenging and Anti-Inflammatory Activity of Chlorogenic Acid Mediated Silver Nanoparticle [Internet]. Journal of Pharmaceutical Research International. 2020. p. 106–12. Available from: http://dx.doi.org/10.9734/jpri/2020/v32i1930715

10. Hosnedlova B, Kepinska M, Skalickova S, Fernandez C, Ruttkay-Nedecky B, Peng Q, et al. Nano-selenium and its nanomedicine applications: a critical review. Int J Nanomedicine [Internet]. 2018 Apr 10;13:2107–28. Available from: http://dx.doi.org/10.2147/IJN.S157541

11. Karthik V, Arivarasu L, Rajeshkumar S. Hyaluronic Acid Mediated Zinc Nanoparticles against Oral Pathogens and Its Cytotoxic Potential [Internet]. Journal of Pharmaceutical Research International. 2020. p. 113–7. Available from: http://dx.doi.org/10.9734/jpri/2020/v32i1930716

12. Vikneshan M, Saravanakumar R, Mangaiyarkarasi R, Rajeshkumar S, Samuel SR, Suganya M, et al. Algal biomass as a source for novel oral nano-antimicrobial agent [Internet]. Vol. 27, Saudi Journal of Biological Sciences. 2020. p. 3753–8. Available from: http://dx.doi.org/10.1016/j.sjbs.2020.08.022

13. Shankar SB, Barani Shankar S, Arivarasu L, Rajeshkumar S. Biosynthesis of Hydroxy Citric Acid Mediated Zinc Nanoparticles and Its Antioxidant and Cytotoxic Activity [Internet]. Journal of Pharmaceutical Research International. 2020. p. 108–12. Available from: http://dx.doi.org/10.9734/jpri/2020/v32i2630845

14. G S, Saurabh G, Komal S. Comparative Characterization for Antimicrobial Activity and Bioactive Compounds Present in Leaf Extract of Ocimum sanctum [Internet]. Vol. 03, Journal of Food & Industrial Microbiology. 2018. Available from: http://dx.doi.org/10.4172/2572-4134.1000121

15. Marsh PD. Dental plaque as a biofilm and a microbial community – implications for health and disease [Internet]. Vol. 6, BMC Oral Health. 2006. Available from: http://dx.doi.org/10.1186/1472-6831-6-s1-s14

16. Pushpaanjali G, Geetha RV, Lakshmi T. Knowledge and Awareness about Antibiotic Usage and Emerging Drug Resistance Bacteria among Dental Students. Journal of Pharmaceutical Research International [Internet]. 2020 Aug 24 [cited 2021 Aug 31];34–42. Available from: https://www.journaljpri.com/index.php/JPRI/article/view/30647

17. Aathira CM, Geetha RV, Lakshmi T. Knowledge and Awareness about the Mode of Transmission of Vector Borne Diseases among General Public. Journal of Pharmaceutical Research International [Internet]. 2020 Aug 24 [cited 2021 Aug 31];87–96. Available from: https://www.journaljpri.com/index.php/JPRI/article/view/30652

18. Baskar K, Lakshmi T. Knowledge, Attitude and Practices Regarding HPV Vaccination

among Undergraduate and Postgraduate Dental Students in Chennai. Journal of Pharmaceutical Research International [Internet]. 2020 Aug 25 [cited 2021 Aug 31];95–100. Available from: https://www.journaljpri.com/index.php/JPRI/article/view/30672

19. Manya Suresh LT. Wound Healing Properties of Aloe Barbadensis Miller-In Vitro Assay. Journal of Complementary Medicine Research [Internet]. 2020 [cited 2021 Aug 31];11(5):30–4. Available from: http://www.ejmanager.com/fulltextpdf.php?mno=63687

20. First Report on Marine Actinobacterial Diversity around Madras Atomic Power Station (MAPS), India [Internet]. [cited 2021 Aug 31]. Available from: http://alinteridergisi.com/article/first-report-on-marine-actinobacterial-diversity-around-madras-atomic-power-station-maps-india/

21. Physicochemical Profile of Acacia Catechu Bark Extract – An in Vitro Stud - International Journal of Pharmaceutical and Phytopharmacological Research [Internet]. [cited 2021 Aug 31]. Available from: https://eijppr.com/article/physicochemical-profile-of-acacia-catechu-bark-extract-an-in-vitro-stud

22. Lakshmi T. Antifungal Activity of Ficus racemosa Ethanolic Extract against Dermatophytes-An in vitro Study. Journal of Research in Medical and Dental Science [Internet]. 2021 [cited 2021 Aug 31];9(2):191–3. Available from: https://www.jrmds.in/abstract/antifungal-activity-of-ficus-racemosa-ethanolic-extract-against-dermatophytesan-in-vitro-study-63386.html

23. Awareness of Drug Abuse among Teenagers - International Journal of Pharmaceutical and Phytopharmacological Research [Internet]. [cited 2021 Aug 31]. Available from: https://eijppr.com/article/awareness-of-drug-abuse-among-teenagers

24. Mangal CSK, Anitha R, Lakshmi T. Inhibition of Nitric oxide Production and Nitric oxide Synthase Gene Expression in LPS Activated RAW 264 .7 Macrophages by Thyme oleoresin from Thymus vulgaris. J Young Pharm [Internet]. 2018 [cited 2021 Aug 31];10(4):481. Available from: http://dx.doi.org/10.5530/jyp.2018.10.104

25. COX2 Inhibitory Activity of Abutilon Indicum - Pharmaceutical Research and Allied Sciences [Internet]. [cited 2021 Aug 31]. Available from: https://ijpras.com/article/cox2-inhibitory-activity-of-abutilon-indicum

26. Jibu RM, Geetha RV, Lakshmi T. Isolation, Detection and Molecular Characterization of Staphylococcus aureus from Postoperative Infections. Journal of Pharmaceutical Research International [Internet]. 2020 Aug 24 [cited 2021 Aug 31];63–7. Available from: https://www.journaljpri.com/index.php/JPRI/article/view/30626

27. Sindhu PK, Thangavelu L, Geetha RV, Rajeshkumar S, Raghunandhakumar S, Roy A. Anorectic drugs: an experimental and clinical perspective ❖A Review. Journal of Complementary Medicine Research [Internet]. 2020 [cited 2021 Aug 31];11(5):106–12. Available from: http://www.ejmanager.com/fulltextpdf.php?mno=63714

28. Nivethitha R, Thangavelu L, Geetha RV, Anitha R, RajeshKumar S, Raghunandhakumar S.

In Vitro Anticancer Effect of Sesamum Indicum Extract -. Journal of Complementary Medicine Research [Internet]. 2020 [cited 2021 Aug 31];11(5):99–105. Available from: https://www.bibliomed.org/?mno=63711

29. Mariona P, Roy A, Lakshmi T. Survey on lifestyle and food habits of patients with PCOS and obesity. Journal of Complementary Medicine Research [Internet]. 2020 [cited 2021 Aug 31];11(5):93–8. Available from: http://www.ejmanager.com/fulltextpdf.php?mno=63710

30. Goyal A, Student PG, Department of Public Health Dentistry, Jaipur Dental College, Jaipur, Rajasthan, et al. Analysis Of pH, Titratable Acidity and Total Soluble Solid Content of Mouthrinses with Different Active Ingredients and Concentration Commercially Available in India: An in Vitro Study [Internet]. Vol. 2, International Journal of Scientific Research. 2012. p. 447–51. Available from: http://dx.doi.org/10.15373/22778179/may2013/151

31. Filoche S, Wong L, Sissons CH. Oral Biofilms: Emerging Concepts in Microbial Ecology [Internet]. Vol. 89, Journal of Dental Research. 2010. p. 8–18. Available from: http://dx.doi.org/10.1177/0022034509351812

32. S SK, Satheesha KS. In-Vitro Antibacterial Activity of Black Tea (Camellia sinensis) Mediated Zinc Oxide Nanoparticles Against Oral Pathogens [Internet]. Vol. 13, Bioscience Biotechnology Research Communications. 2020. p. 2077–80. Available from: http://dx.doi.org/10.21786/bbrc/13.4/66

33. Devaraj E, Roy A, Veeraragavan GR, Magesh A, Sleeba AV, Arivarasu L, et al. β-Sitosterol attenuates carbon tetrachloride–induced oxidative stress and chronic liver injury in rats [Internet]. Vol. 393, Naunyn-Schmiedeberg's Archives of Pharmacology. 2020. p. 1067–75. Available from: http://dx.doi.org/10.1007/s00210-020-01810-8

34. Aspalli S, Shetty VS, Devarathnamma MV, Nagappa G, Archana D, Parab P. Evaluation of antiplaque and antigingivitis effect of herbal mouthwash in treatment of plaque induced gingivitis: A randomized, clinical trial. J Indian Soc Periodontol [Internet]. 2014 Jan;18(1):48–52. Available from: http://dx.doi.org/10.4103/0972-124X.128208

35. Nasim I, Kamath K, Rajeshkumar S. Evaluation of the re-mineralization capacity of a gold nanoparticle-based dental varnish: An in vitro study [Internet]. Vol. 23, Journal of Conservative Dentistry. 2020. p. 390. Available from: http://dx.doi.org/10.4103/jcd.jcd_315_20

36. Barma MD. Synthesis of Triphala Incorporated Zinc Oxide Nanoparticles and Assessment of its Antimicrobial Activity Against Oral Pathogens : An In-Vitro Study [Internet]. Vol. 13, Bioscience Biotechnology Research Communications. 2020. p. 74–8. Available from: http://dx.doi.org/10.21786/bbrc/13.7/14

37. Shetty A, Geethashri A, Kumar B, Palaksha KJ, Sridhar KR, Sanjeev G. Effect of electron-beam irradiation on antimicrobial, antibiofilm activity, and cytotoxicity of mouth rinses [Internet]. Vol. 27, Indian Journal of Dental Research. 2016. p. 145. Available from: http://dx.doi.org/10.4103/0970-9290.183116

38. Rajeshkumar S, Sherif MH, Malarkodi C, Ponnanikajamideen M, Arasu MV, Al-Dhabi NA, et al. Cytotoxicity behaviour of response surface model optimized gold nanoparticles by utilizing fucoidan extracted from padina tetrastromatica [Internet]. Vol. 1228, Journal of Molecular Structure. 2021. p. 129440. Available from: http://dx.doi.org/10.1016/j.molstruc.2020.129440

39. Romanelli MF, Moraes MCF, A L C, Borrely SI. Evaluation of toxicity reduction of sodium dodecyl sulfate submitted to electron beam radiation [Internet]. Vol. 71, Radiation Physics and Chemistry. 2004. p. 411–3. Available from: http://dx.doi.org/10.1016/j.radphyschem.2004.03.038

40. Shetty A, Anand G, Ravinanthan M, Basaviah R. In vitro antimicrobial and cytotoxic effects of Anacardium occidentale and Mangifera indica in oral care [Internet]. Vol. 7, Journal of Pharmacy and Bioallied Sciences. 2015. p. 69. Available from: http://dx.doi.org/10.4103/0975-7406.148780

41. Rajeshkumar S, Malarkodi C, Al Farraj DA, Elshikh MS, Roopan SM. Employing sulphated polysaccharide (fucoidan) as medium for gold nanoparticles preparation and its anticancer study against HepG2 cell lines [Internet]. Vol. 26, Materials Today Communications. 2021. p. 101975. Available from: http://dx.doi.org/10.1016/j.mtcomm.2020.101975

42. Shunmugam R, Balusamy SR, Kumar V, Menon S, Lakshmi T, Perumalsamy H. Biosynthesis of gold nanoparticles using marine microbe (Vibrio alginolyticus) and its anticancer and antioxidant analysis [Internet]. Vol. 33, Journal of King Saud University - Science. 2021. p. 101260. Available from: http://dx.doi.org/10.1016/j.jksus.2020.101260

43. Rajeshkumar S, Kumar SV, Ramaiah A, Agarwal H, Lakshmi T, Roopan SM. Biosynthesis of zinc oxide nanoparticles usingMangifera indica leaves and evaluation of their antioxidant and cytotoxic properties in lung cancer (A549) cells. Enzyme Microb Technol [Internet]. 2018 Oct;117:91–5. Available from: http://dx.doi.org/10.1016/j.enzmictec.2018.06.009

44. Nandhini NT, Rajeshkumar S, Mythili S. The possible mechanism of eco-friendly synthesized nanoparticles on hazardous dyes degradation. Biocatal Agric Biotechnol [Internet]. 2019 May 1;19:101138. Available from: https://www.sciencedirect.com/science/article/pii/S1878818118308235

45. Vairavel M, Devaraj E, Shanmugam R. An eco-friendly synthesis of Enterococcus sp.–mediated gold nanoparticle induces cytotoxicity in human colorectal cancer cells. Environ Sci Pollut Res [Internet]. 2020 Mar 1;27(8):8166–75. Available from: https://doi.org/10.1007/s11356-019-07511-x

46. Gomathi M, Prakasam A, Rajkumar PV, Rajeshkumar S, Chandrasekaran R, Anbarasan PM. Green synthesis of silver nanoparticles using Gymnema sylvestre leaf extract and evaluation of its antibacterial activity [Internet]. Vol. 32, South African Journal of Chemical Engineering. 2020. p. 1–4. Available from: http://dx.doi.org/10.1016/j.sajce.2019.11.005

47. Rajasekaran S, Damodharan D, Gopal K, Rajesh Kumar B, De Poures MV. Collective

influence of 1-decanol addition, injection pressure and EGR on diesel engine characteristics fueled with diesel/LDPE oil blends. Fuel [Internet]. 2020 Oct 1;277:118166. Available from: https://www.sciencedirect.com/science/article/pii/S0016236120311625

48. Santhoshkumar J, Sowmya B, Venkat Kumar S, Rajeshkumar S. Toxicology evaluation and antidermatophytic activity of silver nanoparticles synthesized using leaf extract of Passiflora caerulea. S Afr J Chem Eng [Internet]. 2019 Jul;29:17–23. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1026918519300253

49. Raj R K, D E, S R. β-Sitosterol-assisted silver nanoparticles activates Nrf2 and triggers mitochondrial apoptosis via oxidative stress in human hepatocellular cancer cell line. J Biomed Mater Res A [Internet]. 2020 Sep;108(9):1899–908. Available from: http://dx.doi.org/10.1002/jbm.a.36953

50. Saravanan M, Arokiyaraj S, Lakshmi T, Pugazhendhi A. Synthesis of silver nanoparticles from Phenerochaete chrysosporium (MTCC-787) and their antibacterial activity against human pathogenic bacteria. Microb Pathog [Internet]. 2018 Apr;117:68–72. Available from: http://dx.doi.org/10.1016/j.micpath.2018.02.008

51. Gheena S, Ezhilarasan D. Syringic acid triggers reactive oxygen species–mediated cytotoxicity in HepG2 cells. Hum Exp Toxicol [Internet]. 2019 Jun 1;38(6):694–702. Available from: https://doi.org/10.1177/0960327119839173

52. Ezhilarasan D, Sokal E, Najimi M. Hepatic fibrosis: It is time to go with hepatic stellate cell-specific therapeutic targets. Hepatobiliary Pancreat Dis Int [Internet]. 2018 Jun;17(3):192–7. Available from: http://dx.doi.org/10.1016/j.hbpd.2018.04.003

53. Ezhilarasan D. Oxidative stress is bane in chronic liver diseases: Clinical and experimental perspective. Arab J Gastroenterol [Internet]. 2018 Jun;19(2):56–64. Available from: http://dx.doi.org/10.1016/j.ajg.2018.03.002

54. Gomathi AC, Xavier Rajarathinam SR, Mohammed Sadiq A, Rajeshkumar S. Anticancer activity of silver nanoparticles synthesized using aqueous fruit shell extract of Tamarindus indica on MCF-7 human breast cancer cell line. J Drug Deliv Sci Technol [Internet]. 2020 Feb 1;55:101376. Available from: https://www.sciencedirect.com/science/article/pii/S1773224719313693

55. Dua K, Wadhwa R, Singhvi G, Rapalli V, Shukla SD, Shastri MD, et al. The potential of siRNA based drug delivery in respiratory disorders: Recent advances and progress. Drug Dev Res [Internet]. 2019 Sep;80(6):714–30. Available from: http://dx.doi.org/10.1002/ddr.21571

56. Ramesh A, Varghese S, Jayakumar ND, Malaiappan S. Comparative estimation of sulfiredoxin levels between chronic periodontitis and healthy patients - A case-control study. J Periodontol [Internet]. 2018 Oct;89(10):1241–8. Available from: http://dx.doi.org/10.1002/JPER.17-0445

57. Arumugam P, George R, Jayaseelan VP. Aberrations of m6A regulators are associated with

tumorigenesis and metastasis in head and neck squamous cell carcinoma. Arch Oral Biol [Internet]. 2021 Feb;122:105030. Available from: http://dx.doi.org/10.1016/j.archoralbio.2020.105030

58. Joseph B, Prasanth CS. Is photodynamic therapy a viable antiviral weapon against COVID-19 in dentistry? Oral Surg Oral Med Oral Pathol Oral Radiol [Internet]. 2021 Jul;132(1):118–9. Available from: http://dx.doi.org/10.1016/j.oooo.2021.01.025

59. Ezhilarasan D, Apoorva VS, Ashok Vardhan N. Syzygium cumini extract induced reactive oxygen species-mediated apoptosis in human oral squamous carcinoma cells. J Oral Pathol Med [Internet]. 2019 Feb;48(2):115–21. Available from: http://dx.doi.org/10.1111/jop.12806

60. Duraisamy R, Krishnan CS, Ramasubramanian H, Sampathkumar J, Mariappan S, Navarasampatti Sivaprakasam A. Compatibility of Nonoriginal Abutments With Implants: Evaluation of Microgap at the Implant-Abutment Interface, With Original and Nonoriginal Abutments. Implant Dent [Internet]. 2019 Jun;28(3):289–95. Available from: http://dx.doi.org/10.1097/ID.0000000000000885

61. Gnanavel V, Roopan SM, Rajeshkumar S. Aquaculture: An overview of chemical ecology of seaweeds (food species) in natural products. Aquaculture [Internet]. 2019 May 30;507:1–6. Available from: https://www.sciencedirect.com/science/article/pii/S0044848618328072

62. Markov A, Thangavelu L, Aravindhan S, Zekiy AO, Jarahian M, Chartrand MS, et al. Mesenchymal stem/stromal cells as a valuable source for the treatment of immune-mediated disorders. Stem Cell Res Ther [Internet]. 2021 Mar 18;12(1):192. Available from: http://dx.doi.org/10.1186/s13287-021-02265-1

63. Mohammadi M, Mozaffari B, Rajabalian S. Cytotoxicity evaluation of Persica mouthwash on cultured human and mouse cell lines in the presence and absence of fetal calf serum [Internet]. Vol. 20, Indian Journal of Dental Research. 2009. p. 169. Available from: http://dx.doi.org/10.4103/0970-9290.52894

64. Rajendran R, Kunjusankaran RN, Sandhya R, Anilkumar A, Santhosh R, Patil SR. Comparative Evaluation of Remineralizing Potential of a Paste Containing Bioactive Glass and a Topical Cream Containing Casein Phosphopeptide-Amorphous Calcium Phosphate: An in Vitro Study. Pesqui Bras Odontopediatria Clin Integr [Internet]. 2019 Mar 12 [cited 2021 Sep 15];19(0):4668. Available from: http://revista.uepb.edu.br/index.php/pboci/article/view/4668

65. Ashok BS, Ajith TA, Sivanesan S. Hypoxia-inducible factors as neuroprotective agent in Alzheimer's disease. Clin Exp Pharmacol Physiol [Internet]. 2017 Mar [cited 2021 Sep 15];44(3). Available from: https://pubmed.ncbi.nlm.nih.gov/28004401/

66. Malli SN, Selvarasu K, Jk V, Nandakumar M, Selvam D. Concentrated Growth Factors as an Ingenious Biomaterial in Regeneration of Bony Defects after Periapical Surgery: A Report of Two Cases. Case Rep Dent [Internet]. 2019 Jan 22 [cited 2021 Sep 15];2019. Available from: https://pubmed.ncbi.nlm.nih.gov/30805222/

67. Mohan M, Jagannathan N. Oral field cancerization: an update on current concepts. Oncol Rev [Internet]. 2014 Jun 30 [cited 2021 Sep 15];8(1). Available from: https://pubmed.ncbi.nlm.nih.gov/25992232/

68. Menon S, Ks SD, R S, S R, Vk S. Selenium nanoparticles: A potent chemotherapeutic agent and an elucidation of its mechanism. Colloids Surf B Biointerfaces [Internet]. 2018 Oct 1 [cited 2021 Sep 15];170. Available from: https://pubmed.ncbi.nlm.nih.gov/29936381/

69. Samuel SR, Acharya S, Rao JC. School Interventions-based Prevention of Early-Childhood Caries among 3-5-year-old children from very low socioeconomic status: Two-year randomized trial. J Public Health Dent [Internet]. 2020 Jan [cited 2021 Sep 15];80(1). Available from: https://pubmed.ncbi.nlm.nih.gov/31710096/

70. Praveen K, Narayanan V, Muthusekhar MR, Baig MF. Hypotensive anaesthesia and blood loss in orthognathic surgery: a clinical study. Br J Oral Maxillofac Surg [Internet]. 2001 Apr [cited 2021 Sep 15];39(2). Available from: https://pubmed.ncbi.nlm.nih.gov/11286449/

71. Neelakantan P, Subbarao C, Subbarao CV, De-Deus G, Zehnder M. The impact of root dentine conditioning on sealing ability and push-out bond strength of an epoxy resin root canal sealer. Int Endod J [Internet]. 2011 Jun [cited 2021 Sep 15];44(6). Available from: https://pubmed.ncbi.nlm.nih.gov/21255047/

72. Oligonucleotide therapy: An emerging focus area for drug delivery in chronic inflammatory respiratory diseases. Chem Biol Interact [Internet]. 2019 Aug 1 [cited 2021 Sep 15];308:206–15. Available from: http://dx.doi.org/10.1016/j.cbi.2019.05.028

73. Kumar MS, Vamsi G, Sripriya R, Sehgal PK. Expression of matrix metalloproteinases (MMP-8 and -9) in chronic periodontitis patients with and without diabetes mellitus. J Periodontol [Internet]. 2006 Nov;77(11):1803–8. Available from: http://dx.doi.org/10.1902/jop.2006.050293

74. Kim R-W, Lee S-Y, Kim S-G, Heo Y-R, Son M-K. Antimicrobial, Antioxidant and Cytotoxic Activities of Dendropanax morbifera Léveille extract for mouthwash and denture cleaning solution [Internet]. Vol. 8, The Journal of Advanced Prosthodontics. 2016. p. 172. Available from: http://dx.doi.org/10.4047/jap.2016.8.3.172

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