

30 **INTRODUCTION:**

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

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

55 Selenium is a vita micronutrient that has excellent antimicrobial, anti-cancerous, antidiabetic,
56 and anti-inflammatory properties (8) & (9), Nevertheless, **it is in the traditional form**, it has a low
57 degree of absorption and high levels of toxicity (10). Nano-sized selenium has excellent
58 biocompatibility with enhanced biological effects. The biological method of synthesis of
59 Selenium nanoparticles has extensive application in the field of biomedicine due to low toxicity,
60 targeted delivery of Nano drugs and stability (11). Seaweeds or marine algae are permanent
61 sources of chemical compounds which consist of a plethora of biologically active secondary
62 metabolites (12). They are considered as a potential source of antibiotic substances. *Ulva lactuca*

Comment [vv3]: In its traditional form

63 is an edible green marine algae (Chlorophyta), which holds an antibacterial activity against oral
64 pathogens. Ulvan is the sulfated polysaccharide of the algae. Ulva Spp is declared to be
65 responsible for its antibacterial activity and has no toxicity (13). Traditional oral antimicrobial
66 agents in the form of mouth rinses or dental varnish are chemical-based (14) These chemicals
67 based mouthwashes cause many side effects. This emphasized the need for non-toxic natural
68 products based mouth rinses which is also effective in reducing the bacterial load (15).Our team
69 has extensive knowledge and research experience that has translate into high quality (16) (17)
70 (18) (19) (20) (21) (22) (23) (24) (25) (26) (27) (28) (29) .The Present Study is aimed at
71 the preparation and cytotoxic effect of *Pterocarpus santalinus* selenium based mouthwash.

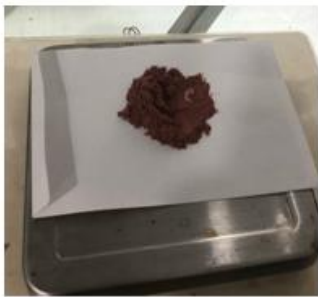
72 **METHODS & MATERIALS:**

73 **Preparation of plant extract:**

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

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

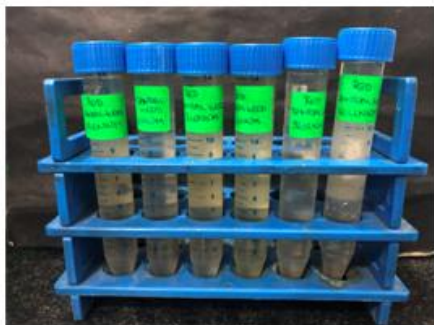
83 **Preparation of the mouthwash:**

84 To a Eppendorf tube, 10 ml of distilled water was taken, ~~then~~ 0.3g of sucrose was measured
85 using a electrical weighing scale and was added to the tube containing the water, the mixture was
86 mixed well and then 0.01g of sodium lauryl sulphate and 0.001 g of sodium benzoate were added

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87 and mixed well. Then 12 drops of the plant pellet were added to the above mixture followed by
88 adding 2 drops of peppermint oil and was mixed well.



89

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

91

92 **Cytotoxicity activity -Brine shrimp lethality assay:**

93 **Salt water preparation:**

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

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

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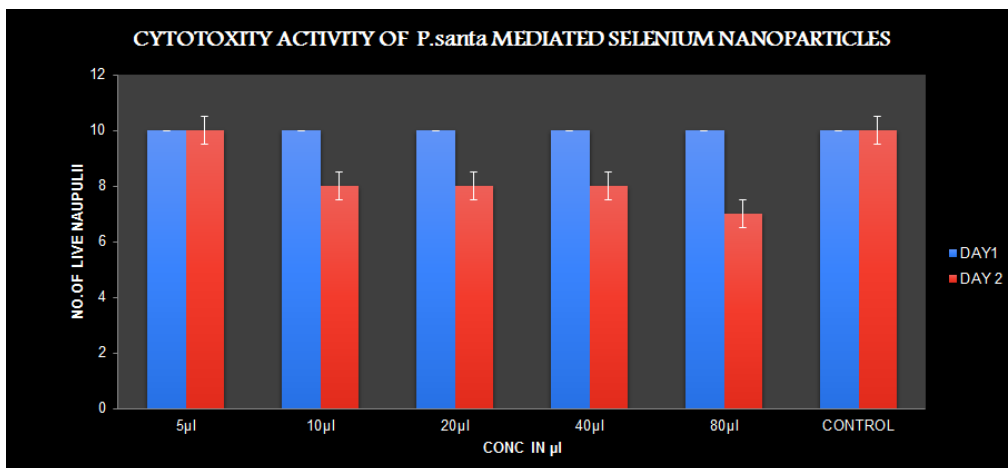
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107 **RESULTS**



108 **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.

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

Comment [vv8]: not necessary just ass FIG 3 in brackets at the end.

117 **DISCUSSION:**

118 It is eminent that the oral ailments are a global health apprehension with a substantial impact on
119 the general public. Additionally the amplified intake of sugars in the diet, consumption of
120 tobacco, inadequate exposure to fluorides, and lack of approach to dental care, are the expected
121 incidence of dental caries and periodontal disease which will continue to rise (30). *S. mutans* is
122 the foremost etiological agent of dental caries (31). *E. faecalis* is an opportunistic pathogen, *S.*
123 *aureus* and *C. albicans* are secluded from persistent apical periodontal lesions. Oral microflora is
124 considered as a Vital factor in both caries and periodontal disease, and causes the ailment
125 pathogenesis by producing the biofilms (32). Therefore, the use of various types of mouth rinses
126 are given a proper importance to proceed against the harmful microorganisms associated with
127 oral diseases or infections (33). Conversely, apprehensions regarding the development of

128 antibiotic-resistant strains and hostile effects of contemporary mouth rinses have directed the
129 attention in the use of non conventional or alternative medicines and plant extracts. Many
130 previous reports have recommended the possible use of plant extracts in oral care for effective
131 and efficient inhibition of microflora by natural antimicrobials (31,34)(10). Nevertheless, the
132 potential benefits of chemotherapeutic formulations in mouth rinses provide thrust for research in
133 verdict effective mouth rinses for oral care (35) & (36).

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

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

148 In a recent study, 1-h exposure to as low as 0.1% Persica solution produced irreversible cytotoxic
149 effects on the cells engaged in the wound healing process (41). While the presence of FCS (10%)
150 offered a protection from drug toxicity, the diminution in the cytotoxic effect of Persica in the
151 presence of FCS is due to the binding of potent toxic compounds of the mouthwash to serum
152 proteins(42). Our team has extensive knowledge and research experience that has translate into
153 high quality publications (43–47),(48),(49),(50),(51),(52),(53),(45,54,55),(56–60) (61),(62) . It
154 is pragmatic that the toxic compounds of Persica solution put forth their effects through
155 irreversible binding to cellular proteins, thereby reassuring their function. The aim of the Present
156 study is set out with the same result (63).

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158

159 **CONCLUSION:**

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Comment [vv10]: Reference no. at the end of next sentence.

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160 Increased concentration of selenium nanoparticles was not toxic to living nauplii as it did not
161 cause the death of it. But the *Pterocarpus santalinus* extraction based selenium nanoparticles
162 have less to no cytotoxicity(64-73). A Previous study done by Ryeo-Woon Kim(74) discussed
163 that the cytotoxicity assay conducted in this study demonstrated that the *Dendropanax morbifera*
164 *Léveille* extracts retained high cell viability (> 60%) at all concentrations. The cytotoxicity test
165 performed using Human keratinocyte cells in a previous study revealed that the *Dendropanax*
166 *morbifera Léveille* leaf extracts exhibited no cytotoxicity at concentrations lower than 50
167 $\mu\text{m}/\text{mL}$. This result was in concurrence to the result obtained in the present study. This study
168 shows that mouth rinses from medicinal plants as a source of an excellent alternative with less
169 common side-effects to chemical-based oral antimicrobial products.

Comment [vv12]: Add this in discussion

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171 NOTE:


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

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