Preparation of Mouthwash Using Cranberry and Carrot Formulation and its Antimicrobial Activity and Cytotoxic Effect Comparison With Commercial Mouthwash

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**Abstract:** The aim of this study is to assess the antimicrobial activity and cytotoxic effect of cranberry and carrot formulated mouthwash and comparing with commercial mouthwashThe purpose of this study is to assess the antimicrobial activity and cytotoxic effect of cranberry and carrot formulated mouthwash and comparing with commercial mouthwashThe carrot and cranberry extract is collected from Synthetic Industries. Plant extract were prepared, Agar Well Diffusion Method was used to assess the antimicrobial efficacy.Cytotoxicity test was done using naupliis. After 24 hours, the ELISA plates were observed and noted for number of live nauplii’s present and calculated.Prepared carrot and cranberry mouth showed better antimicrobial activity against lactobacillus species than mutans. As the concentration of the extract increases the antimicrobial activity also increases. From the brine shrimp lethality test done it was noted that on the first day all that nauplii survived and on the second day only few survived at low concentration. Hence lower concentration can be used for biomedical applications.

**Keywords:** Mouth wash,Carrot, Cranberry, antimicrobial activity, herbal

# INTRODUCTION

Depending on the ingredients in the specific oral mouthwash, the most typical uses for oral rinses, sometimes called mouthwashes, are to control or minimise foul breath and to lessen the microbial burden in the oral cavity [(Pack, 1984)](https://paperpile.com/c/tOy1Fs/gi8Vv) . Prior to oral and periodontal procedures, such as tooth extraction or implant implantation, the antibacterial activity is employed for the control of supragingival plaque and gingivitis [(Aparna et al., 2021; Poornima et al., 2021; Verma & Muthuswamy Pandian, 2021)](https://paperpile.com/c/tOy1Fs/cPwZD+j6pvq+uYiqt). Allergic reactions to certain components are infrequently recorded2, notwithstanding the rarity of adverse effects caused by oral rinses. Because of these unusual occurrences, researchers have most likely conducted in vitro and preclinical studies on oral rinses to see whether they are cytotoxic and whether they have antimicrobial effects. [(Garvey et al., 2001)](https://paperpile.com/c/tOy1Fs/JFkMx).

As a result of the acidic environment and biofilm that bacteria produce when they proliferate in the mouth, dental caries can develop as a result of pathogenic infection [(Loesche, 1986)](https://paperpile.com/c/tOy1Fs/NunDv) . Tooth decay is caused by a variety of bacteria, the most common of which is Streptococcus mutans [(Merchant et al., 2022; Pandiyan et al., 2022)](https://paperpile.com/c/tOy1Fs/er0jQ+Zh3PZ),[(Ganapathy 2022; Pandiyan et al., 2022)](https://paperpile.com/c/tOy1Fs/er0jQ+Zh3PZ+fiaHV),[(Chokkattu et al., 2022; Ramamurthy et al., 2022)](https://paperpile.com/c/tOy1Fs/NN8MG+EycE0). Studies investigating the connection between S. mutans proliferation and dental caries have advanced consistently [(Zhou et al., 2013)](https://paperpile.com/c/tOy1Fs/4T7hO) .Glycosyltransferases (GtfB, GtfC, and GtfD) are three different enzymes that S. mutans generates [(Macphee, 1935)](https://paperpile.com/c/tOy1Fs/YG9M9). Dental plaque is formed in part by these Gtfs, which are involved in processes such as the adhesion of enamel and plaque to the tooth surface, the absorption of different oral microbes, and other similar processes [(Hamilton & Buckley, 1991)](https://paperpile.com/c/tOy1Fs/eMF4G) . S. mutans is commonly found on tooth surfaces before cavities form because of these characteristics. This led to the identification of S. mutans as a biofilm indication for dental caries[(Bowen & Koo, 2011)](https://paperpile.com/c/tOy1Fs/j48lJ).Since a person's oral health and way of life greatly influence the likelihood of developing dental caries, this infection is likely to persist for the duration of a person's life [(Monchois et al., 1999)](https://paperpile.com/c/tOy1Fs/BU4K5). Liquid mouthwashes have antibacterial, analgesic, and anti-inflammatory properties. Mouthwashes can be either chemical or herbal [(Chokkattu et al., 2022; Ramamurthy et al., 2022)](https://paperpile.com/c/tOy1Fs/NN8MG+EycE0),[(Marya et al., 2022)](https://paperpile.com/c/tOy1Fs/lippO),[(Jain & Verma, 2022; Marya et al., 2022)](https://paperpile.com/c/tOy1Fs/lippO+G3bfI). Chemical mouthwashes include chlorhexidine. Even after all these years, chlorhexidine is still the gold standard when it comes to dental plaque removal agents.   
Proper dental hygiene is essential, and many plant extracts have antimicrobial properties that make them ideal for this task[(Aspalli et al., 2014)](https://paperpile.com/c/tOy1Fs/Ouxns).

There are several reasons to use a mouthwash. One is to keep your teeth and gums clean. Another is to prevent cavities and gum disease [(Wadhwani et al., 2022)](https://paperpile.com/c/tOy1Fs/Xz4RT),[(Sreevarun et al., 2023)](https://paperpile.com/c/tOy1Fs/6BRLo),[(Adel et al., 2023)](https://paperpile.com/c/tOy1Fs/r30kb). Lastly, after brushing your teeth, you should rinse your mouth with a mouthwash to reach areas that were hard to reach before. It eliminates bad breath-causing bacteria and freshens the breath, two things that toothpaste can't do. Tooth plaque is still the root cause of oral health issues for the vast majority of the world's population. Dental caries is the most prevalent and avoidable infectious disease affecting the mouth. Dental caries is an infection of the tooth's hard tissues that, if untreated, can go all the way to the tooth's periapical zone and even damage the pulp tissue[(Bostanci & Belibasakis, 2017; Fejerskov et al., 2015; Nagaratnam et al., 2016)](https://paperpile.com/c/tOy1Fs/lzsGF+0yoh0+nWbZc) One example of a herb that fits this description is the cranberry, or Vaccinium macrocarpon, a shrub that grows abundantly in the cold peat bogs of North America's Northeast. Along with blueberries (Vaccinium spp.) and Concord grapes (Vitus labrusca, often called the fox grape) [(Bonifait & Grenier, 2010)](https://paperpile.com/c/tOy1Fs/DN9tm), it is one of the three native fruits of North America. The most common forms of cranberry distribution include fresh fruit, dried fruit, juice, and powders in capsules. Among the many polyphenols included in cranberry extracts are flavonoids, which may have beneficial pharmacological effects on human health[(Cranberry Fruit: Vaccinium Macrocarpon Aiton : Standards of Analysis, Quality Control, and Therapeutics, 2002; van Belle & Kerr, 2012)](https://paperpile.com/c/tOy1Fs/OJTpY+3CEjg) .Cranberries have been used medicinally since the 17th century, when they were mostly utilised to treat scurvy, liver and stomach problems. There is mounting evidence that cranberry juice can prevent female urinary tract infections due to its high-molecular-weight polyphenols (tannins), which inhibit the adhesion of the bacterium Escherichia coli to the urinary tract mucosa[(Burger et al., 2000, 2002; Miklós, 2014)](https://paperpile.com/c/tOy1Fs/ajl1B+EaEsM+gKu6q). The same chemicals can also inhibit Helicobacter pylori from adhering to the stomach mucosa, which is a crucial step in the development of gastric ulcers in humans. Additionally, the seasonal influenza virus's adhesion and dissemination can be inhibited by several cranberry formulations. Almost all bacterial pair coaggregate can be reversed by the high molecular weight nondialyzable material (NDM) found in cranberry juice. NDM is highly soluble in water and has tannin-like properties [(Khairnar et al., 2015)](https://paperpile.com/c/tOy1Fs/mvzfF). Bacteria precoated with NDM had their biofilm-building abilities reduced. Cranberries' proanthocyanidins and flavonols are what really make them effective against S. mutans. According to a survey of recent research, no studies have looked at the effects of cranberry mouthwash on actual people in India [(Prasain et al., 2008; Sethi & Govila, 2011)](https://paperpile.com/c/tOy1Fs/eblNU+NzEnU)It is this species that produces carotene, a naturally occurring food colourant. Essential to human survival are members of the Umbelliferae family, which includes carrots and a large number of other herbaceous plants. Carrots are a substantial root vegetable that has several health benefits due to their abundance of bioactive components, such as dietary fibre and carotenoids, among many others [(Merrill et al., 1956)](https://paperpile.com/c/tOy1Fs/tPWDT) . Carrots are a good source of vitamin C, folic acid, thiamin, riboflavin, and caffeic acid, the most common phenolic acid in carrots. Reducing swelling and speeding up the development of granulation tissue and epithelialisation, caffeine acid also had a good impact on the recovery of oral surgical wounds. Before this, researchers looked at the effects of carrot extracts on yeast and food-borne bacteria[(Babic et al., 1994)](https://paperpile.com/c/tOy1Fs/wfsMZ).Previous study was done on carrot extracts on food-borne bacteria and yeast [(Babic et al., 1994)](https://paperpile.com/c/tOy1Fs/wfsMZ) , Dental students' streptococcal colonisation and cranberry and chlorhexidine mouthwash[(Khairnar et al., 2015)](https://paperpile.com/c/tOy1Fs/mvzfF) ,Clinical uropathogenic Escherichia coli is molecularly inhibited by cranberry juice cocktail when consumed orally [(Tao et al., 2011)](https://paperpile.com/c/tOy1Fs/zmym3) .​​It was decided to undertake this study because none had previously been done to evaluate the cytotoxic and antibacterial effects of carrot and cranberry. The study's goal was to evaluate the mouthwash made with cranberries and carrots and compare its cytotoxic effects to those of conventional mouthwash as well as its antibacterial activities.

# MATERIALS AND METHODS

## Study Design

In vitro study.

## Collection and Preparation

The carrot and cranberry extract is collected from Synthetic Industries, with a product code: 4010000370. Cranberry , scientifically known as *Vaccinium macrocarpon* , belongs to the family Ericaceae and carrot , scientifically known as Daucus , belongs to the family Apiaceae

## Preparation of Plant Extract

100 ml of distilled water and 2.5 grams of fresh powdered extract made from carrot and cranberry were combined in the beaker and heated for 10 to 20 minutes on the heating mantle. Filter paper was used to remove impurities from the boiling extract (Fig. 1).Before being heated for 10 to 20 minutes, 100 milliliters of distilled water and 2.5 grams of freshly powdered cranberry and carrot extract were combined in a 1:1 ratio in the beaker. The boiling extract was purified with filter paper.

## Antimicrobial Activity

Agar Well Diffusion Method was used to assess the antimicrobial efficacy

## Media Preparation

A 100 mL sterile Mueller Hinton agar, which is effective against Candida albicans, Staphylococcus aureus, and Streptococcus mutans, was produced and then added to the Petri plates. After that, the plates were left to harden.

## Swabbing

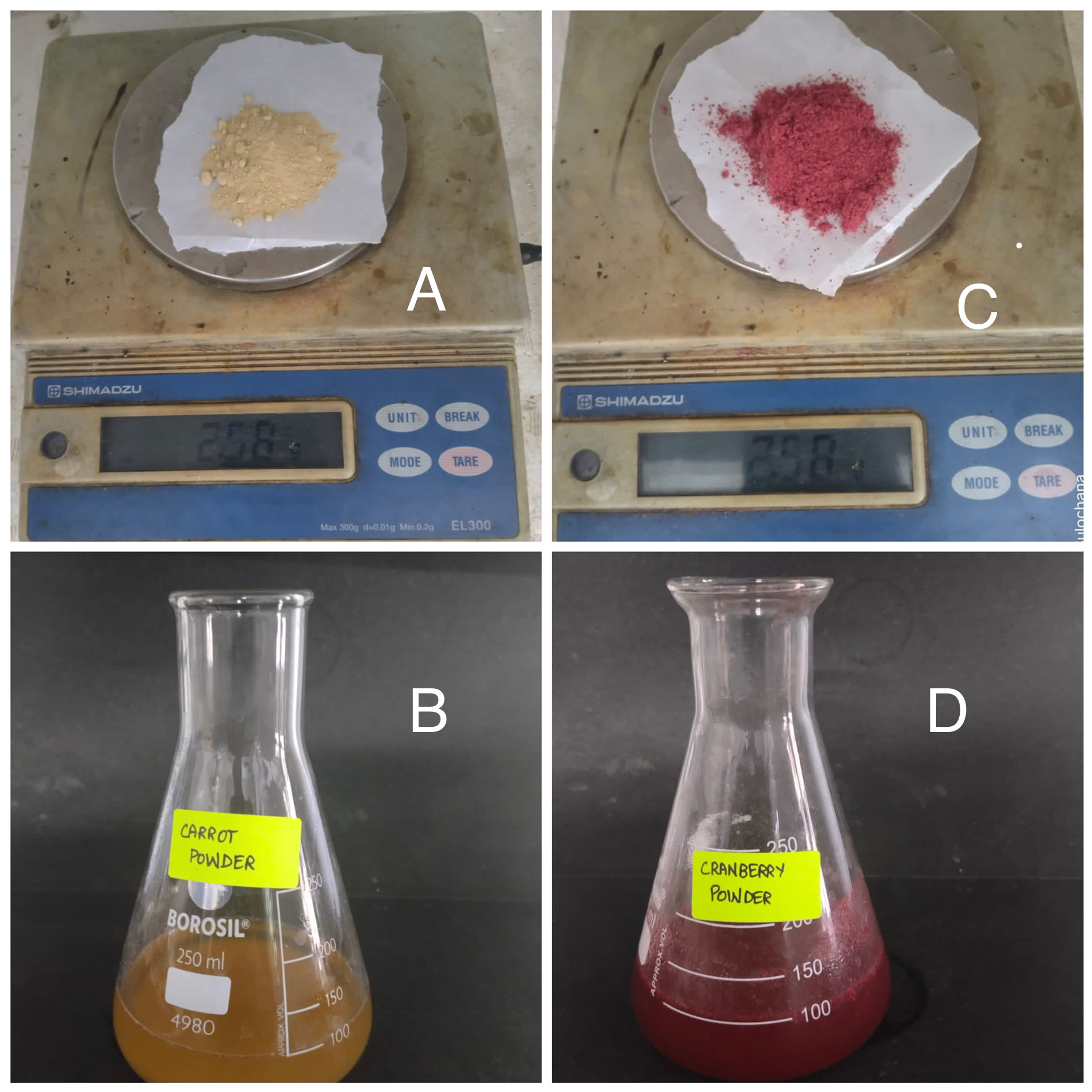
The oral pathogens, Streptococcus mutans and Lactobacillus sp., were swabbed onto the corresponding plates once they had solidified .

## Well Formation

Using a gel puncher, four wells were created on each plate following swabbing. The four wells were filled with a mixture of 25 µL, 50 µL, and 100 µL of carrot and cranberry solution, as well as the control group. After placing the plates in an incubator set at 37°C for 24 hours, we measured and estimated the zone of inhibition .

## Cytotoxic Activity

## Salt water preparation



**Fig. 1.** Represents 2.5gms of carrot that has been measured in a weighing machine B) addition of distilled water into the extract of carrot , C) Represents 2.5 gms of cranberry that has been measured in a weighing machine , D ) addition of distilled water into the extract of cranberry

2g of iodine free salt was weighed and dissolved in 200ml of distilled water. 6 well ELISA plates were taken and 10-12 ml of saline water was filled. To that 10 nauplii were slowly added to each well (5µL,10 µL,20 µL,40 µL,80 µL and control). 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 number of live nauplii’s present and calculated by using following formula, number of dead nauplii**/**number of dead nauplii+number of live nauplii×100

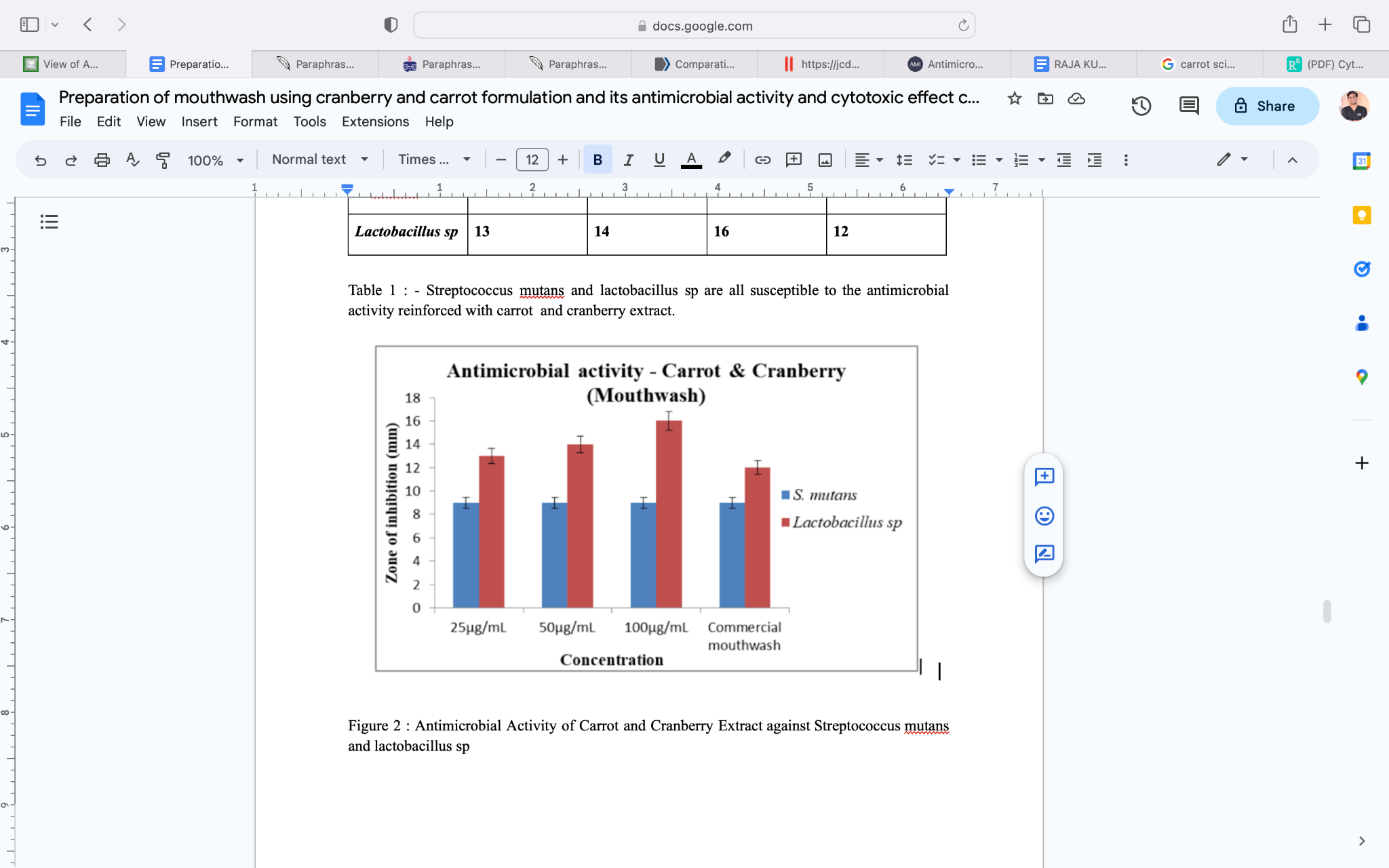
# RESULT

Figure 1 depicts the antimicrobial activity of with carrot and cranberry extract against Lactobacillus sp. Zone of inhibition was found to be highest at concentration of 100 μL (16 mm) and it also found that at 50 μL ( 14 mm ) so it is good outcome . The antimicrobial activity of with carrot and cranberry extract against extract against Staphylococcus aureus it was found that concentration of Zone of inhibition was found to be highest at concentration of 100 μL (9 mm) and at 50 μL ( 9 mm ) . Lactobacillus sp shows higher zone of inhibition which shows sensitivity to carrot and cranberry . Cytotoxic activity in herbal mouthwash, four different concentrations have been taken in the study (5μl, 10μl, 20μl, 80μl, control). At each concentration, 10 nauplii (live nauplii)have been dropped. Artemianauplii is a stage of copepod life cycle of larvae is inexpensive, easy available, and can be used for short term study. On day 1, all the 10 nauplii were alive in all the concentration levels (Figure 4). On day 2, the significant increase in the concentration, decreased the nauplii count in the extract . This clearly showed the influence of the cytotoxic effect in the solution. The count of nauplii remains alive on the first day of study in all five concentration levels. At 5μl concentration, the live nauplii count decreased from ten to nine in number. At 10μl concentration, the live nauplii count reduced to eight in number. At 20μl concentration, the live nauplii count was seven in number. In 40μl concentration, the live nauplii count remained as seven and finally, at 80μl concentration, none of the nauplii were alive. This massive variation in the nauplii count in various concentration levels proved the presence of cytotoxicity . Spearman correlation analysis reveals a negative correlation with the rise in concentration and decrease in the number of live nauplii (r=-1) which reveal the effective cytotoxic activity of carrot and cranberry based mouth wash .

## Carrot & Cranberry (mouthwash)

**Table 1:** Streptococcus mutans and lactobacillus sp are all susceptible to the antimicrobial activity reinforced with carrot andcranberry extract.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Organism | 25μg/mL | 50μg/mL | 100μg/mL | Commercial mouthwash |
| *S. mutans* | 9 | 9 | 9 | 9 |
| *Lactobacillus sp* | 13 | 14 | 16 | 12 |



**Figure 2:** Antimicrobial Activity of Carrot and Cranberry Extract against Streptococcus mutans and lactobacillus sp

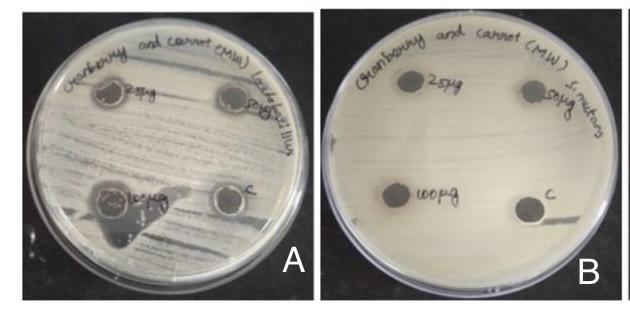
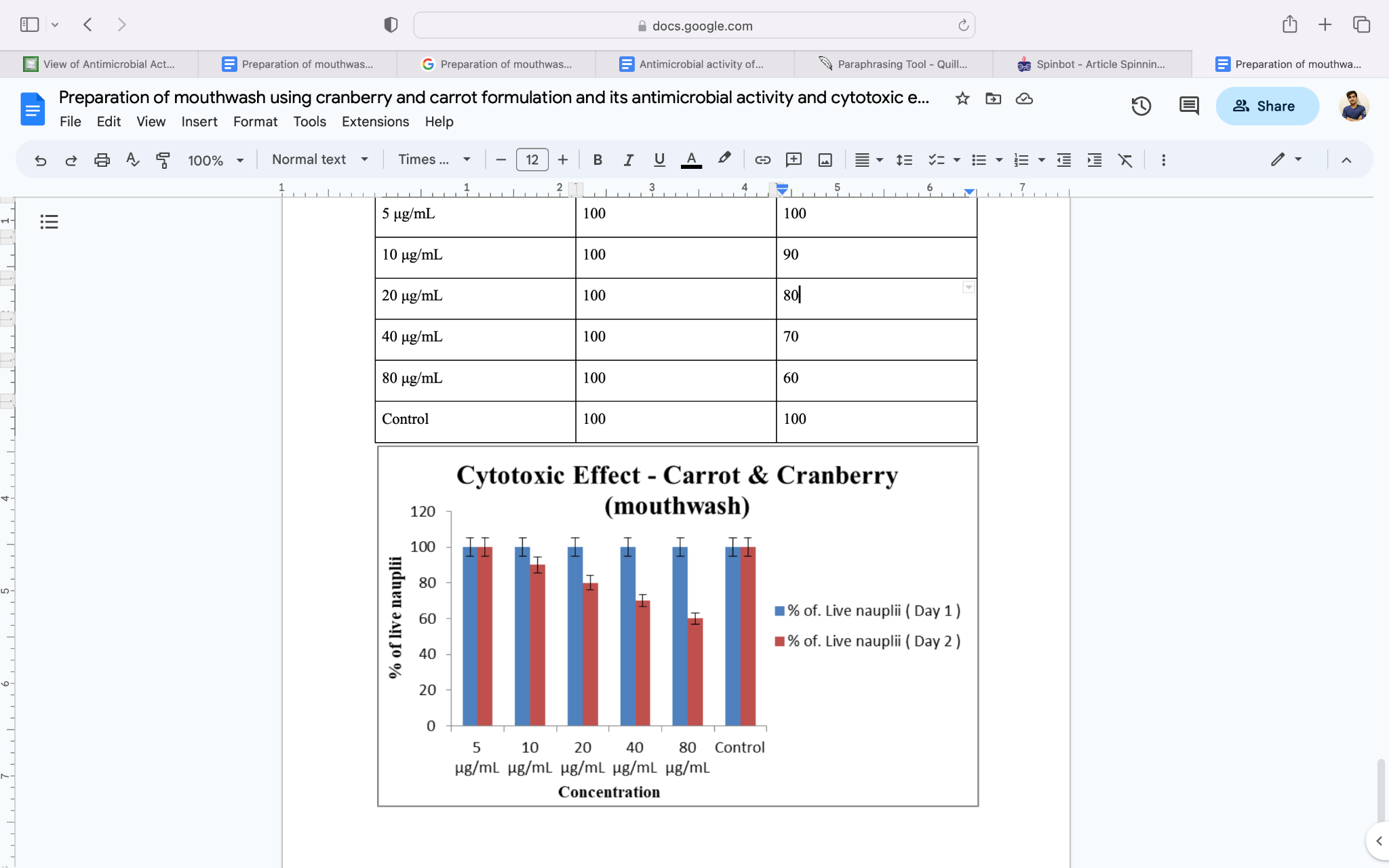


Figure 3:(a)(b) Antimicrobial activity observed in agar plates containing different microorganisms, A) Zone of inhibition of S.mutans , B) Zone of inhibition of Lactobacillus sp

Table 2: Concentration

|  |  |  |
| --- | --- | --- |
| **Concentration** | **% of. Live nauplii ( Day 1 )** | **% of. Live nauplii ( Day 2 )** |
| 5 μg/mL | 100 | 100 |
| 10 μg/mL | 100 | 90 |
| 20 μg/mL | 100 | 80 |
| 40 μg/mL | 100 | 70 |
| 80 μg/mL | 100 | 60 |
| Control | 100 | 100 |



**Figure 4 -** Graph showing Cytotoxic activity of carrot and cranberry using brine shrimp lethality test. X- Axis shows concentration the carrot and cranberry (µL) and Y-Axis shows number of live nauplii

# DISCUSSION

Some salivary micro floras like S. mutans play an important role in initiation and progression of dental caries [(Mehta et al., 2013)](https://paperpile.com/c/tOy1Fs/dDS0b). Chlorhexidine is an excellent option for effective plaque control in dental clinics and has antimicrobial properties. However, it has a number of side effects, including alteration of taste, desquamation of oral mucosa, and restricted usage in paediatric patients(Rafi et al., 2024). It should not be used for long periods of time due to these concerns. Using it with tea and coffee also results in extrinsic stains. Chlorhexidine and herbal mouthwash have been compared in a plethora of studies. In comparison to chlorhexidine mouthwash, several herbal mouthwashes improve oral hygiene due to their anti-inflammatory, antimicrobial, and anti-oxidant characteristics.

Research contrasts chlorhexidine with natural mouthwash. With a herbal mouthwash that contains 20% babool chaal, 10% darim leaves, 10% chameli leaves (an anti-microbial agent), 5% mulethi (an astringent), 2% neem, and other ingredients like alum, suhaga, kapoor, laung, and methanol, nearly 0.2% CHXG causes brown staining of teeth, desquamation of oral mucosa, and irritation in the mouth. Compared to 0.2% CHXG, this mouthwash was superior. Herbal mouthwash and chlorhexidine have comparable antigingivitis and plaque-inhibiting capabilities.Extract from German chamomile reduced gingival index scores by 0.31 when compared to chlorhexidine in another investigation. In a comparison with chlorhexidine, around half of the T. chebula, an antiplaque agent, and half of the cinnamon extract, an antibacterial and antifungal agent, were used [(Rinaudo & Goycoolea, 2019)](https://paperpile.com/c/tOy1Fs/pVOwk). There was a decrease in plaque. The following pathogens are inhibited by T. chebula extract: Helicobacter pylori, Xanthomonas campestris pr.citri, Salmonella typhoid, HIV-1, and herpes simplex virus Type 1. It changes the oral flora and has the same effect on plaque management. Myrrh, chamomile, and Echinacea, when combined, suppress the growth of Actinomyces viscosus and S. mutans. For gum swelling and bleeding, try A. vera mouthwash. It has vitamin C, hyaluronic acid, and dermatan sulphate, all of which aid in collagen synthesis (Tuluwengjiang et al., 2024). It works against plaque in a manner analogous to chlorhexidine [(Chauhan et al., 2020)](https://paperpile.com/c/tOy1Fs/6rFMV) . Recently, researchers found that an oral rinse including extracts from a variety of plants—including Staphysagria, Chamomilla, Echinacea, plantago, Ocimum, and cistus—was more effective than chlorhexidine at lowering the number of mutant streptococci in saliva [(Vyas et al., 2008)](https://paperpile.com/c/tOy1Fs/r5mut)[(Subramanian & Harikrishnan, 2023)](https://paperpile.com/c/tOy1Fs/gyhOT),[(Solanki et al., 2023)](https://paperpile.com/c/tOy1Fs/SKThS),[(Ganapathy 2021)](https://paperpile.com/c/tOy1Fs/EsSAb)[(Vyas et al., 2008)](https://paperpile.com/c/tOy1Fs/r5mut). Certain herbal extracts, like chamomile, can inhibit the production of biofilms and reduce inflammation in the gums. Ocimum, on the other hand, has antimicrobial effects on S. mutans and echinacea, which is an agent that stimulates the immune system, kills microbes, and reduces inflammation [(Chokkattu et al., 2023)](https://paperpile.com/c/tOy1Fs/oc8qX),[(Laghari et al., 2023; Ramakrishnan et al., 2023)](https://paperpile.com/c/tOy1Fs/X2pdU+Fw4Lu),[(Muthuswamy Pandian et al., 2022)](https://paperpile.com/c/tOy1Fs/aBR97). Plaque buildup and the aerobic oral bacterial load can both be mitigated with a green tea rinse. The container is both safe and non-toxic, and it comes over bad breath caused by bacterial infection [(R. C. Gupta et al., 2021)](https://paperpile.com/c/tOy1Fs/CzxqN).

The advantages of herbal mouthwash compared to chlorhexidine mouthwash have been the subject of numerous comparative research. When tested against several strains of lactobacillus, the prepared carrot and cranberry mouth proved to be more effective than mutans. The antibacterial activity grows in direct proportion to the extract concentration . The brine shrimp lethality test was used to evaluate the cytotoxic activity of the herbal oral formulation [(Muthuswamy Pandian et al., 2022; Ramakrishnan et al., 2023)](https://paperpile.com/c/tOy1Fs/aBR97+X2pdU). All brine prawns in the wells treated with the extract survived the first day, indicating that the mouthwash formulation did not have cytotoxic effects. The results of the brine shrimp lethality test showed that the nauplii survived in full force on the first day, but at low concentrations, only a small percentage survived on the second. Therefore, biomedical applications of lower concentrations are feasible [(R. K. Gupta et al., 2014)](https://paperpile.com/c/tOy1Fs/V4XyB). Many comparative studies have been conducted in benefits of herbal mouthwash with chlorhexidine mouthwash.Prepared carrot and cranberry mouth showed better antimicrobial activity against lactobacillus species than mutans. As the concentration of the extract increases the antimicrobial activity also increases.The cytotoxic activity of herbal mouth was formulation was assesses by using brine shrimp lethality test. The mouthwash formulation did not showed cytotoxic activity on brine shrimp as all the shrimps in all the wells in which the extract were added survived on the first day. From the brine shrimp lethality test done it was noted that on the first day all that nauplii survived and on the second day only few survived at low concentration. Hence lower concentration can be used for biomedical applications.

# CONCLUSION

The therapeutic uses of carrots and cranberries are extensive. Our research shows that a mouthwash composition including two extracts works well. The antibacterial activity grows in direct proportion to the extract concentration. At low concentrations, the cytotoxic activity was observed to be more effective. As a result, the herbal mouthwash recipe can be used for regular dental hygiene at lower dosages.

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