

Short communication

In vitro evaluation of the antimicrobial activity and cytotoxicity of a pomegranate peel extract–based toothpaste

Fatemeh Forouzanfar¹, Fatemeh Khalilzadeh^{2,7}, Ali Forouzanfar³, Omidreza Mohammadpour^{3,4}, Roshanak Salari⁵, Mostafa Boskabadi⁶, Aida Gholoobi^{7,*}

¹ Neuroscience Research Center, Basic Sciences Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran

² Metabolic Syndrome Research Center, Basic Sciences Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran

³ Department of Periodontics, Faculty of Dentistry, Mashhad University of Medical Sciences, Mashhad, Iran

⁴ Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran

⁵ Department of Pharmaceutical Sciences in Persian Medicine, School of Persian and Complementary Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

⁶ Faculty of Medicine, Mashhad University of Medical Sciences, Khorasan Razavi, Iran

⁷ Medical Genetics Research Center, Basic Sciences Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran

Article history:

Received: Nov 12, 2025

Received in revised form:

Jun 21, 2026

Accepted: Jul 25, 2026

Epub ahead of print

* Corresponding Author:

gholoubiad@mums.ac.ir

Keywords:

Punica granatum

Phytotherapy

Oral Microbiology

Streptococcus mutans

Lactobacillus plantarum

Candida albicans

Abstract

Objective: To evaluate the *in vitro* antimicrobial activity of a toothpaste containing pomegranate (*Punica granatum* L.) peel 70% hydroalcoholic extract (PPE) against oral microorganisms and to assess its cytotoxicity in mammalian cells.

Materials and methods: Cytotoxicity was evaluated using the MTT assay on L929 fibroblasts after 24 hr of exposure to PPE toothpaste at concentrations ranging from 62.5 to 2000 µg/mL. Antimicrobial activity was assessed using the agar well diffusion method against *Streptococcus mutans*, *Lactobacillus plantarum*, and *Candida albicans*. Two dilutions of PPE toothpaste (1:1 and 1:3 v/v) were compared with a commercial toothpaste. Chlorhexidine (CHX) was used as the positive control, and distilled water served as the negative control.

Results: PPE toothpaste showed no significant cytotoxicity at any tested concentration and produced inhibition zones against all tested microorganisms. Although the commercial comparator produced the largest inhibition zones overall, the 1:1 PPE dilution showed comparable effects, particularly against *C. albicans*, and its performance was similar to that of CHX. The differences compared with CHX were not statistically significant.

Conclusion: The PPE toothpaste showed no significant cytotoxic effect on L929 fibroblasts ($p > 0.05$) and exhibited *in vitro* antimicrobial activity against common oral pathogens, supporting further evaluation in biofilm models and clinical studies.

Please cite this paper as:

Forouzanfar F, Khalilzadeh F, Forouzanfar A, Mohammadpour O, Salari R, Boskabadi M, Gholoobi A. *In vitro* evaluation of the antimicrobial activity and cytotoxicity of a pomegranate peel extract–based toothpaste. Avicenna J Phytomed, 2026

Introduction

Pomegranate (*Punica granatum* L.), a member of the Punicaceae family that is well adapted to tropical and subtropical regions, has been cultivated for thousands of years. Its name is derived from the Latin term *Malum granatum*, meaning “granular apple” (Valero-Mendoza et al. 2023; Forouzanfar et al. 2022).

Pomegranate has been reported to possess several medicinal properties, including anticancer (Panth et al. 2017), antidiabetic (Mohammed et al. 2020), antioxidant (Saparbekova et al. 2023), anti-inflammatory (Pierdomenico et al. 2024), antimicrobial (Salim et al. 2023), antinociceptive (Guerrero-Solano et al. 2021), and hepatoprotective (Ali et al. 2021) activities. These biological effects are largely attributed to plant-derived bioactive compounds known as tannins (Valero-Mendoza et al. 2023). These tannins are naturally occurring compounds that protect plants against microbial invasion and herbivory. Their astringent properties enable them to bind to proteins and polysaccharides, thereby deterring potential threats to the plant (Valero-Mendoza et al. 2023). The peel accounts for approximately 50% of the total fruit weight, while the edible portion constitutes the remaining 50%. Within the edible portion, seeds represent about 22% (w/w) and juice about 78% (w/w) (Valero-Mendoza et al. 2023). Pomegranate peel contains a variety of structural tannins, which are largely hydrolyzable, along with water-soluble phenolic compounds. Based on their structural characteristics, these compounds can be classified into four major groups: complex tannins, condensed tannins, ellagitannins, and gallotannins (Mo et al. 2022).

Oral diseases are highly prevalent worldwide and include conditions such as dental caries, periodontal diseases, oral mucosal lesions, halitosis, endodontic infections, and oral cancers. Microbial activity has been identified as a primary etiological factor in many of these

conditions. Oral microorganisms metabolize carbohydrate-rich dietary substrates into acids, leading to the demineralization of tooth structures, progressive damage to enamel and gingival tissues, and increased susceptibility to opportunistic pathogens. Because oral health is closely linked with systemic conditions such as diabetes, hypertension, and cardiovascular diseases, maintaining proper oral hygiene is essential for overall health (Oluwasina et al. 2023).

Streptococcus mutans (*S. mutans*), a key contributor to dental caries, has also been implicated as a pathogenic organism responsible for the development of infective endocarditis (Kojima et al. 2012). A systematic review of microbiome studies has reported a significant association between the bacterial load of *S. mutans* and the incidence of dental caries (Mazurel et al. 2025). Oral candidiasis is another common opportunistic infection that may affect both healthy and immunocompromised individuals, most frequently caused by *Candida albicans* (*C. albicans*) (Yigit et al. 2008). *Lactobacillus plantarum* (*L. plantarum*) is a species of Gram-positive lactic acid bacteria known for its probiotic characteristics. This species shows considerable variation and has been shown to provide several health benefits, particularly in the gastrointestinal system, by supporting intestinal integrity, modulating the gut microbiota, and enhancing immune responses. In addition, probiotic *L. plantarum* has demonstrated potential in controlling dental caries, as evidenced by *in vitro* studies, animal experiments, and clinical trials (Huang X et al. 2024).

Our research aimed to formulate an herbal toothpaste based on pomegranate peel extract and evaluate its efficacy in protecting against the primary species associated with oral health, including *S. mutans*, *L. plantarum*, and *C. albicans*.

Materials and Methods

This *in vitro* experimental study was conducted to evaluate the cytotoxicity and antimicrobial activity of a pomegranate peel extract-based toothpaste against selected oral microorganisms.

Ethics approval

The experimental studies were approved by the local ethics committee (IR.MUMS.DENTISTRY.REC.1400.051).

Cell culture reagents and cell line

Dulbecco's Modified Eagle Medium (DMEM), fetal bovine serum (FBS), and penicillin–streptomycin was purchased from Gibco (Thermo Fisher Scientific, Grand Island, NY, USA). The L929 cell line was obtained from the Pasteur Institute Cell Bank (Tehran, Iran).

Microorganisms and media

Lactobacillus plantarum subsp. *plantarum* (ATCC 8014) and *mutans* (ATCC 35668) were obtained from the Iranian Research Organization for Science and Technology (IROST, Tehran, Iran). *Candida albicans* was a clinical isolate obtained from Ghaem University Hospital (Mashhad, Iran). The microorganisms were cultured in Sabouraud dextrose broth (SDB; Liofilchem, Roseto degli Abruzzi, Italy), De Man, Rogosa and Sharpe (MRS) broth (Ibresco Life Science, Tehran, Iran), and Brain Heart Infusion (BHI) broth (Quelab, Montreal, Canada), respectively. For solid media, 1.5% (w/v) agar (Liofilchem, Roseto degli Abruzzi, Italy) was added before sterilization. These strains were selected because *S. mutans* is a primary cariogenic bacterium (Mazurel et al. 2025), *C. albicans* is the principal etiologic agent of oral candidosis (Salim et al. 2023), and *L. plantarum* is a probiotic species that has been shown to contribute to the control of dental caries (Huang X et al. 2024).

Toothpaste formulation

The main ingredients used in the pomegranate peel extract toothpaste (PPE

toothpaste) included pomegranate peel 70% hydroalcoholic extract, distilled water, sodium benzoate ($\geq 99\%$), sucralose ($\geq 98\%$), sodium dodecyl sulfate (SDS, $\geq 99\%$), tragacanth gum, and hydroxyapatite powder (all purchased from Sigma-Aldrich/Merck, St. Louis, MO, USA). The final paste (pH 7) was packaged in a tube and stored at 4°C for 24 hr to achieve the desired texture. Pomegranate peel extraction was performed using maceration, as previously described (Mohammadzadeh et al. 2019). The concentration of pomegranate peel extract in the toothpaste was selected based on previous reports demonstrating effective antimicrobial activity with acceptable biocompatibility at comparable levels (Salim et al. 2023; Pereira et al. 2006; El-Sherbini and Shoukry 2012).

L929 cell line culture

Cells were maintained in DMEM supplemented with 10% (v/v) FBS, 100 U/mL penicillin, and 100 µg/mL streptomycin at 37°C in a humidified incubator containing 5% CO₂.

Analysis of cell viability

Cell viability was assessed using the MTT assay, as previously described. (Prasanth 2011). Following exposure to PPE toothpaste at concentrations of 62–1000 µg/mL for 24 hr, 10 µL of MTT solution (5 mg/mL) was added per well and incubated for 4 hr. After removal of the MTT reagent, 100 µL of dimethyl sulfoxide (DMSO) was added to each well to dissolve the formazan crystals. Optical density was measured at 570 nm with a reference wavelength of 620 nm using a Stat Fax 303 microplate reader (Awareness Technology, Palm City, FL, USA).

Antimicrobial activity of PPE toothpaste

The antimicrobial activity of PPE toothpaste against *C. albicans*, *S. mutans*, and *L. plantarum* was evaluated using the agar well diffusion method as previously described. (Prasanth 2011) Chlorhexidine

2% (CHX) mouthwash (Vi-One; Rojin Cosmetic Laboratory, Tehran, Iran) was used as the positive control and double-distilled water (DDW) served as the negative control.

For each microorganism, a 0.5 McFarland standard suspension was prepared in sterile normal saline (optical density 0.08–0.12 at 620 nm; approximately 1.5×10^8 CFU/mL). A commercially available toothpaste (Nasim toothpaste; Paxan Co., Tehran, Iran; 1:1 dilution) and two dilutions of PPE toothpaste (1:1 and 1:3 v/v) were prepared in DDW. For the 1:1 dilution, 1 g of toothpaste was mixed with 1 mL of DDW and stirred for 15 min using a magnetic stirrer. The 1:3 dilution was prepared by further diluting the 1:1 mixture with DDW.

L. plantarum and *S. mutans* were cultured on MRS and BHI agar, respectively, and incubated for 48 hr in a candle-jar system at 37°C. *C. albicans* was cultured on Sabouraud dextrose agar (SDA) and incubated for 24 hr under standard conditions. Wells with a diameter of 8 mm were created in the agar plates using a sterile pipette tip and spaced approximately 2 cm apart. Two hundred microliters of each test or control preparation were added to the designated wells. Antimicrobial activity was determined by measuring the

diameter of the inhibition zones (mm). All experiments were performed in duplicate.

Due to limited availability of PPE toothpaste and contamination of some replicates, only a single data point was obtained for *S. mutans*. To evaluate the statistical significance of this result, Simul software was used to simulate statistical outcomes.

Statistical analysis

Data were analyzed using one-way analysis of variance (ANOVA), followed by Tukey's post hoc test for multiple comparisons. A p-value <0.05 was considered statistically significant. Statistical analyses were performed using GraphPad Prism (GraphPad Software, San Diego, CA, USA).

Results

Cytotoxicity on L929 cells

L929 fibroblasts were exposed to various concentrations of PPE toothpaste (62–1000 µg/mL) for 24 hr. The MTT assay showed no statistically significant reduction in cell viability at any tested concentration compared with the control group ($p>0.05$), indicating that PPE toothpaste did not exhibit cytotoxic effects on L929 cells (Figure 1).

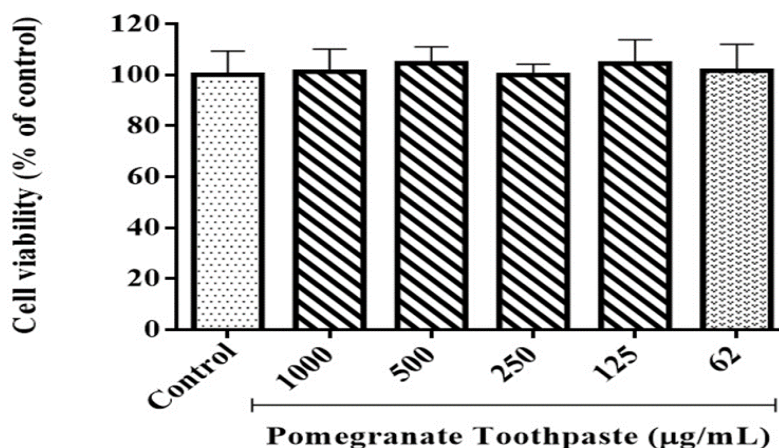


Figure 1. Effect of PPE toothpaste on L929 cell viability. Data are presented as the mean $\pm$ SD (n = 9).

PPE-based toothpaste: antimicrobial and cytotoxicity

Antimicrobial activity

The antimicrobial activity of PPE toothpaste was evaluated against *S. mutans*, *L. plantarum*, and *C. albicans* using the agar well diffusion method. The diameters of inhibition zones were compared among PPE toothpaste (1:1 and 1:3 v/v), a

commercial toothpaste (Nasim), chlorhexidine (CHX 2%), and a negative control (double-distilled water, DDW). An overview of the main findings is presented in Table 1, with visual presentations shown in Figures 2 and 3.

Table 1. Antimicrobial activity of PPE toothpaste by agar well diffusion (mean $\pm$ SD, mm)

Group	<i>L. plantarum</i> (Mean $\pm$ SD)	<i>C. albicans</i> (Mean $\pm$ SD)	<i>S. mutans</i> (Mean $\pm$ SD)
Pomegranate 1:1	21 $\pm$ 4.24	24 $\pm$ 2.83	28.5 $\pm$ 2.83
Pomegranate 1:3	15 $\pm$ 4.24	21.5 $\pm$ 2.12	28 $\pm$ 1.41
Nasim [‡]	20.5 $\pm$ 2.12	26.5 $\pm$ 2.12	36 $\pm$ 2.83
CHX (2%) [†]	25 $\pm$ 4.24	16 $\pm$ 0	30 $\pm$ 2.83
P*	0.218	0.027*	0.101

* p values from one-way ANOVA; p<0.05 considered statistically significant. [†] Positive control: chlorhexidine (CHX), 2%. [‡] Commercial toothpaste: Nasim.

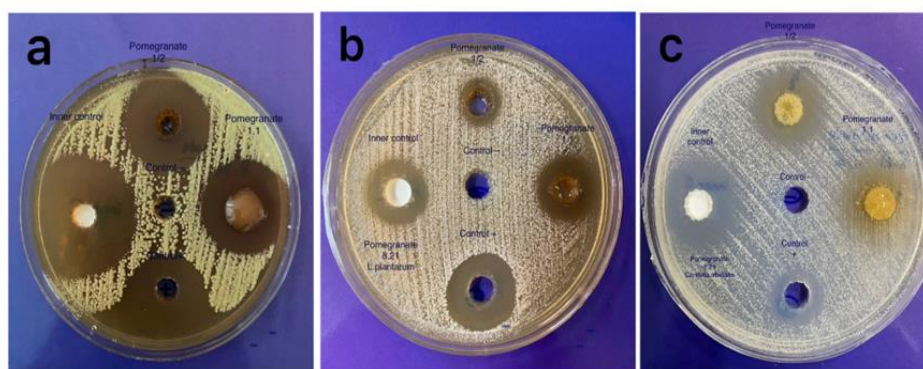


Figure 2. Antimicrobial effects of PPE toothpaste depicted as inhibition zones against (a) *S. mutans*, (b) *L. plantarum*, and (c) *C. albicans*, relative to positive and negative controls.

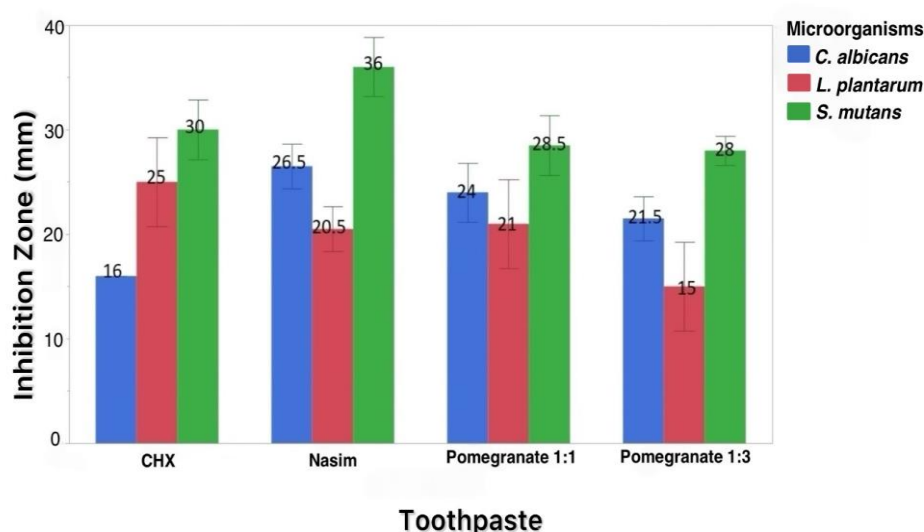


Figure 3. Comparison of the mean zone of inhibition (mm) of different toothpaste formulations against the tested microbial strains (*C. albicans*, *L. plantarum*, and *S. mutans*).

Results for *S. mutans*

All toothpaste groups showed antimicrobial activity against *S. mutans*, with Nasim toothpaste producing the largest inhibition zone (36 ± 2.83 mm). PPE toothpaste also showed inhibitory activity, with the 1:1 dilution producing an inhibition zone of 28.5 ± 2.83 mm. Due to contamination, replicate data were limited; therefore, the results for *S. mutans* are presented descriptively and no inferential statistical analysis was performed.

Results for *C. albicans*

For *C. albicans*, the 1:1 dilution of PPE toothpaste (24 ± 2.83 mm) demonstrated stronger inhibition zone than CHX (16 ± 0 mm). One-way ANOVA revealed statistically significant differences among groups ($p=0.027$). Tukey's post hoc analysis showed that CHX had significantly lower activity compared with the Nasim toothpaste ($p=0.024$). Comparisons

between PPE toothpaste and the control groups were not statistically significant.

Results for *L. plantarum*

For *L. plantarum*, no statistically significant differences were observed among the treatment groups ($p= 0.218$). The 1:1 dilution of PPE toothpaste showed inhibition zone comparable to those of the Nasim toothpaste (21 ± 4.24 mm vs 20.5 ± 2.12 mm), while CHX showed the highest mean inhibition zone (25 ± 4.24 mm).

Statistical evaluation

Overall, although, a statistically significant difference among groups was observed for *C. albicans* (with CHX showing lower activity than Nasim toothpaste), the antimicrobial activity of PPE toothpaste was generally comparable to that of the commercial toothpaste and CHX, especially at the 1:1 dilution (see Table 1 and 2, and Figures 2 and 3).

Table 2. Tukey's post hoc pairwise comparisons (*C. albicans*)

Multiple comparison	Mean difference	95% CI	p
Pomegranate 1:1 vs Pomegranate 1:3	2.500	-5.89 to 10.89	0.652
Pomegranate 1:1 vs Nasim	2.500	-5.89 to 10.89	0.652
Pomegranate 1:1 vs CHX	8.000	-0.39 to 16.39	0.058
Pomegranate 1:3 vs Nasim	5.000	-3.39 to 13.39	0.214
Pomegranate 1:3 vs CHX	5.500	-2.89 to 13.89	0.169
CHX vs Nasim	10.500	2.11 to 18.89	0.024*

* Statistically significant difference ($p<0.05$). † One-way ANOVA followed by Tukey's post hoc multiple comparisons.

Discussion

Despite the growing interest in herbal oral care products, the safety and antimicrobial efficacy of many such formulations particularly those containing pomegranate peel remain insufficiently established. The present study evaluated a novel toothpaste formulated with PPE in terms of cytotoxicity and its activity against three common oral microorganisms, namely *S. mutans*, *C. albicans*, and *L. plantarum*.

The MTT assay demonstrated that PPE toothpaste did not significantly reduce the

viability of L929 fibroblasts at any tested concentration. This finding suggests favorable biocompatibility, which is an essential characteristic for oral hygiene products intended for routine use. Many conventional antimicrobial agents used in oral care, such as CHX, are associated with adverse effects including mucosal irritation, taste disturbances, and tooth staining. Therefore, the absence of detectable cytotoxicity in PPE toothpaste supports its potential as a safer, plant-based alternative (Patel R et al. 2022; Chen et al. 2020). Recent investigations have also reported favorable biocompatibility profiles for

plant-derived oral formulations containing polyphenolic compounds, supporting their potential application in oral hygiene products. These findings are in agreement with the present results which demonstrated no significant reduction in fibroblast viability following exposure to PPE toothpaste.

The antimicrobial assay revealed inhibitory activity of PPE toothpaste against all three microorganisms. Although the commercial toothpaste (Nasim) exhibited the strongest overall effect especially against *S. mutans* the 1:1 dilution of PPE toothpaste demonstrated comparable inhibition activity. Notably, PPE toothpaste produced a larger inhibition zone against *C. albicans* than the positive control (CHX), although the difference was not statistically significant. These findings highlight the antifungal potential of bioactive compounds present in pomegranate peel, particularly punicalagin and ellagitannins. These compounds are believed to exert antimicrobial effects by disrupting microbial cell membranes and interfering with microbial adhesion to host tissues (Salim et al. 2023; Endo et al. 2010). This mechanism is consistent with other polyphenol-rich extracts which have been shown to inhibit key virulence factors such as glycosyltransferase activity in *S. mutans* and hyphal formation in *C. albicans* (Huang Y et al. 2024; Patel R et al. 2022). Several studies have similarly reported antimicrobial effects of pomegranate peel extracts against oral pathogens, particularly *S. mutans* and *C. albicans* (Pereira et al. 2006; Yigit et al. 2008; Salim et al. 2023). The inhibitory activity observed in the present study is therefore consistent with previously reported antibacterial and antifungal effects of pomegranate-derived polyphenols.

Regarding *L. plantarum*, PPE toothpaste also exhibited antimicrobial activity, although CHX showed greater inhibition. Considering the beneficial role of *L. plantarum* in maintaining oral microbial balance, moderate antimicrobial

activity may be advantageous as it could prevent excessive suppression of beneficial oral microbiota (Huang X et al. 2024). The reduced antimicrobial activity observed at the 1:3 dilution further supports a concentration-dependent effect of the active compounds, which is consistent with previous reports describing concentration-dependent antimicrobial activity of pomegranate peel extract (Pereira et al. 2006; El-Sherbini and Shoukry 2012).

Recent investigations have provided additional support for the antimicrobial potential of pomegranate peel-derived bioactive compounds in the context of oral health. In particular, polyphenol-rich extracts obtained from *Punica granatum* have been shown to exert inhibitory activity against several clinically relevant oral microorganisms, notably *S. mutans* and *C. albicans*. The proposed mechanisms underlying these effects include disruption of microbial cell membrane integrity and interference with biofilm formation (Patel R et al. 2022; Huang Y et al. 2024). These observations are largely in agreement with the findings of the present study, in which the PPE-toothpaste exhibited demonstrable antimicrobial activity against the tested microbial strains. Nevertheless, discrepancies in the magnitude of antimicrobial efficacy reported across studies are to be expected and may be primarily ascribed to variations in extraction methodologies, differences in the concentration and bioavailability of active constituents, and the diversity of *in vitro* models employed for antimicrobial evaluation. Such heterogeneity likely contributes, at least in part, to the observed differences in inhibition zone diameters between the PPE toothpaste and the commercial comparator in the current investigation.

Overall, the present findings are consistent with previous studies demonstrating the antibacterial and antifungal properties of pomegranate peel

extract (Salim et al. 2023; Yigit et al. 2008). Earlier research has reported antimicrobial activity against several oral pathogens, including *S. mutans*, *S. mitis*, *L. casei*, and *C. albicans*, with some studies indicating superior anti-adherence effects compared with CHX (Pereira et al. 2006). The results of the current study further support the potential of pomegranate peel-based formulations as effective and biocompatible alternatives for oral health management.

While this study provides preliminary evidence of the biocompatibility and antimicrobial potential of PPE toothpaste, certain limitations should be acknowledged. The antimicrobial data for *S. mutans* were limited in replicates due to contamination-related sample loss, which may reduce statistical confidence. Nevertheless, the observed inhibitory trend was consistent with the results for other microorganisms and supported by findings from previous studies. Additionally, the agar well-diffusion method used here although widely accepted for antimicrobial screening does not fully capture the complexity of *in vivo* oral environments. Future investigations should employ biofilm models, simulated salivary conditions, and clinical trials to validate these results. Finally, aspects such as formulation stability, long-term safety, and user acceptability remain important topics for future work.

Acknowledgment

The authors gratefully acknowledge the support received from Mashhad University of Medical Sciences, Iran.

Conflicts of interest

The authors declare that they have no conflict of interest.

Funding

This research was supported by a grant (992261) from the Vice-Chancellor for Research and Technology, Mashhad University of Medical Sciences (MUMS),

Mashhad, Iran, based on the DDS thesis of Mr. Omidreza Mohammadpour.

Ethical Considerations

The MUMS Ethics Committee approved the experimental studies.

Code of Ethics

IR.MUMS.DENTISTRY.REC.1400.051

Authors' Contributions

FF, AF, and AG conceptualized and designed the study. FK, OM, and RS performed experimental procedures and data collection. MB conducted statistical analysis and advised on quantitative interpretation. FF, FK, OM, and AG analyzed data and drafted the manuscript. AF, FF, RS, and AG critically revised the manuscript for intellectual content. Supervision: FF and AF. All authors approved the final manuscript.

Abbreviations

PPE: Pomegranate peel extract
 DDW: Double-distilled water
 CHX: Chlorhexidine
 DMEM: Dulbecco's Modified Eagle Medium
 FBS: Fetal bovine serum
 SDS: Sodium dodecyl sulfate
 DMSO: Dimethyl sulfoxide
 SDB: Sabouraud dextrose broth
 MRS: De Man, Rogosa and Sharpe (broth)
 BHI: Brain Heart Infusion
 ATCC: American Type Culture Collection
 MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
 ANOVA: Analysis of variance

References

- Ali H, Jahan A, Samrana S, Ali A, Ali S, Kabir N, et al. (2021) Hepatoprotective potential of pomegranate in curbing the incidence of acute liver injury by alleviating oxidative stress and inflammatory response. *Front Pharmacol* 12:694607
- Chen J, Liao C, Ouyang X, Kahramanoğlu I, Gan Y, Li M. (2020) Antimicrobial activity of pomegranate peel and its applications on food preservation. *J Food Qual* 2020:8850339

- El-Sherbini GT, Shoukry NM. (2012) In vitro effect of pomegranate peel extract on *Trichomonas tenax*. *Life Sci J* 9:791–797
- Endo EH, Cortez DAG, Ueda-Nakamura T, Nakamura CV, Dias Filho BP. (2010) Potent antifungal activity of extracts and pure compound isolated from pomegranate peels and synergism with fluconazole against *Candida albicans*. *Res Microbiol* 161:534–540
- Forouzanfar F, Ahmadpoor M, Farahi MM, Hadianfar A, Sahebkar A, Esmaily H, et al. (2022) The effect of pomegranate juice and sumac consumption in the treatment of outpatients with COVID-19. *Mediators Inflamm* 2022:6850342
- Guerrero-Solano JA, Bautista M, Velázquez-González C, De la O-Arciniega M, González-Olivares LG, Fernández-Moya M, et al. (2021) Antinociceptive synergism of pomegranate peel extract and acetylsalicylic acid in an animal pain model. *Molecules* 26:5434
- Huang X, Bao J, Yang M, Li Y, Liu Y, Zhai Y. (2024) The role of *Lactobacillus plantarum* in oral health: a review of current studies. *J Oral Microbiol* 16:2411815
- Huang Y, Li X, Chen J, Wang Y, Zhao L, Zhang Q, et al. (2024) Antifungal and antibiofilm activity of plant-derived polyphenols against *Candida albicans* in oral microbial environments. *Oral Microbiol Immunol* 39:112–120.
- Kojima A, Nakano K, Wada K, Takahashi H, Katayama K, Yoneda M, et al. (2012) Infection of specific strains of *Streptococcus mutans*, oral bacteria, confers a risk of ulcerative colitis. *Sci Rep* 2:332
- Mazurel D, Brandt B, Boomsma M, Crielaard W, Lagerweij M, Exterkate R, et al. (2025) *Streptococcus mutans* and caries: a systematic review and meta-analysis. *J Dent Res* :00220345241303880
- Mo Y, Ma J, Gao W, Zhang L, Li J, Li J, et al. (2022) Pomegranate peel as a source of bioactive compounds: a mini review on their physiological functions. *Front Nutr* 9:887113
- Mohammadzadeh F, Babazadeh R, Salari R, Afiat M, Heidarian Miri H. (2019) The effect of pomegranate peel gel on orgasm and sexual satisfaction of women in reproductive age: a triple-blind, randomized, controlled clinical trial. *Iran J Obstet Gynecol Infertil* 22:66–76
- Mohammed C, Mohamed A, Ahmed A, Mariod A. (2020) Antioxidant and anti-diabetic activity of pomegranate (*Punica granatum* L.) leaves extracts. *Foods Raw Mater* 8:329–336
- Oluwasina OO, Idris SO, Ogidi CO, Igbe FO. (2023) Production of herbal toothpaste: physical, organoleptic, phyto-compound, and antimicrobial properties. *Heliyon* 9:e13892
- Panth N, Manandhar B, Paudel KR. (2017) Anticancer activity of *Punica granatum* (pomegranate): a review. *Phytother Res* 31:568–578
- Patel M. (2022) Oral cavity and *Candida albicans*: colonisation to the development of infection. *Pathogens* 11:335
- Patel R, Shah M, Desai K, Mehta P, Trivedi H, Kumar V, et al. (2022) Antimicrobial activity of polyphenol-rich *Punica granatum* peel extract against common oral pathogens including *Streptococcus mutans*. *J Herbal Med* 32:100523.
- Pereira JV, Pereira MSV, Sampaio FC, Sampaio MCC, Alves PM, Araújo CR, et al. (2006) In vitro antibacterial and antiadherence effect of the extract of the *Punica granatum* Linn. upon dental biofilm microorganisms. *Rev Bras Farmacogn* 16:88–93
- Pierdomenico M, Riccioni C, Benassi B. (2024) Anti-inflammatory effect of a pomegranate extract on LPS-stimulated HepG2 cells. *Nat Prod Res* 38:727–734
- Prasanth M. (2011) Antimicrobial efficacy of different toothpastes and mouthrinses: an in vitro study. *Dent Res J (Isfahan)* 8:85
- Salim A, Deiana P, Fancello F, Molinu MG, Santana M, Zara S. (2023) Antimicrobial and antibiofilm activities of pomegranate peel phenolic compounds: varietal screening through a multivariate approach. *J Bioresour Bioprod* 8:146–161
- Saparbekova A, Kantureyeva G, Kudasova D, Konarbayeva Z, Latif A. (2023) Potential of phenolic compounds from pomegranate (*Punica granatum* L.) by-product with significant antioxidant and therapeutic effects: a narrative review. *Saudi J Biol Sci* 30:103553
- Valero-Mendoza A, Meléndez-Rentería N, Chávez-González M, Flores-Gallegos A, Wong-Paz J, Govea-Salas M, et al. (2023) The whole pomegranate (*Punica granatum* L.), biological properties and important findings: a review. *Food Chem Adv* 2:100153
- Yigit N, Aktas E, Ayyildiz A. (2008) Antifungal activity of toothpastes against oral *Candida* isolates. *J Mycol Med* 18:141–146