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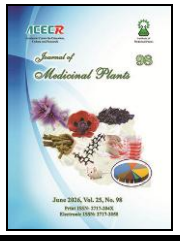

Research Article

Efficacy of ginger (*Zingiber officinale*) alone and in combination with yarrow (*Achillea millefolium*) mouthwash versus Nystatin in Type II denture stomatitis: a comparative clinical trial

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ABSTRACT

Background: Denture stomatitis is a common inflammatory condition in denture wearers primarily associated with *Candida* species. Conventional antifungal therapies are often limited by adverse side effects, high cost, and emerging drug resistance. **Objective:** To evaluate and compare the clinical efficacy of two herbal formulations - a ginger mouthwash and a combination ginger and yarrow mouthwash - against standard Nystatin suspension in patients with Type II denture stomatitis. **Methods:** In this double-blind, randomized clinical trial, 59 patients with Type II denture stomatitis were allocated to three intervention groups: ginger mouthwash, ginger–yarrow mouthwash, or Nystatin oral suspension. Palatal erythema was photographically evaluated on days 0, 7, 14, and 21. Surface area of erythema was quantified using ImageJ software. Inter- and intra-group differences were analyzed via one-way ANOVA and repeated-measures ANOVA, with statistical significance set at $P < 0.05$. **Results:** All three treatment regimens demonstrated a statistically significant reduction in palatal erythema over the 21-day period ($P < 0.001$). However, the Nystatin group achieved a significantly greater reduction in erythema area compared to both herbal mouthwash groups on days 7 and 14 ($P < 0.05$). By day 21, the difference between Nystatin and the herbal interventions was marginally significant ($P = 0.054$). **Conclusion:** While ginger and ginger–yarrow mouthwashes significantly reduce palatal inflammation, Nystatin suspension demonstrates superior speed and efficacy in the treatment of Type II denture stomatitis.

Abbreviations: ANOVA, analysis of variance; IRCT, Iranian Registry Of Clinical Trial; MIC, mean inhibitory concentration; *C. albicans*, *Candida albicans*; *C. glabrata*, *Candida glabrata*; *C. krusei*, *Candida krusei*.

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1. Introduction

Denture stomatitis is a common condition characterized by inflammation of the oral supporting tissues. It typically occurring in denture wearers and associated with *Candida* species. Clinical manifestations of denture stomatitis include erythematous lesions of variable severity and extent, often localized to the palatal mucosa [1].

The etiology is multifactorial. e, g :poor oral hygiene, long-term prosthethic usage, older age of the patient, xerostomia, systemic diseases such as diabetes, long-term use of corticosteroids or antibiotics. It is seen in medically compromised individuals with immune deficiency [1, 2]. Denture stomatitis has been reported in 20 – 67 % of individuals wearing complete dentures [3].

Various treatment approaches have been proposed at both local and systemic levels. These include the use of topical and systemic antifungal agents such as Nystatin, Miconazole and Fluconazole**,** ill-fitting denture adjustment, denture immersion in disinfectants and laser therapy for damaged mucosa, overnight denture removal, use of chlorhexidine or a combination of these approaches in some cases [1, 2].

Systematic review studies comparing diverse therapeutic strategies for denture stomatitis have failed to demonstrate significant differences between denture disinfection protocols and topical or systemic antifungal administration [2, 4]. Despite numerous proposed management strategies, a universally accepted gold standard treatment remains elusive [5]. Given the rising incidence of fungal infections and antifungal drug resistance, numerous studies have been conducted to explore the antifungal properties of different plants. Furthermore, the use of plants in traditional cultures of developing countries is extensive and diverse. The favorable safety profile and reduced side effects associated with many herbal extracts have positioned them as promising sources for novel therapeutic development.

In recent years, phytotherapeutic preparations have been increasingly investigated for oral healthcare applications [6]. Ginger (*Zingiber officinale*) is a member of the Zingiberaceae family [7]. Among the notable pharmacological properties of ginger are its antibacterial and antifungal activities. Consequently, ginger-based mouthwash, owing to its palatable taste, user-friendliness, and widespread availability, demonstrates encouraging effects against diverse oral microorganisms, particularly *Candida* [8]. Yarrow (*Achillea millefolium*) has also been extensively investigated for its antifungal properties. This plant, from the Asteraceae family, holds a special place in traditional Persian medicine .it is used as an expectorant**;** and also has anticonvulsant, strengthening, and soothing effects.

Despite the studies conducted on the effects of medicinal plants on dental health and the pharmacological effects of ginger, few studies have investigated the effect of ginger or yarrow mouthwash on the treatment of denture stomatitis in vivo [8, 9].

Therefore, the aim of this double-blind clinical trial was to compare the therapeutic effect of two standardized commercial herbal mouthwashes - ginger-based (1-VO) and ginger-yarrow combination (2-IR) - with a reference Nystatin suspension (3-EM) in patients presenting with Type II denture stomatitis at the Faculty of Dentistry, Islamic Azad University, Tehran Medical Sciences, during 2023–2024.

2. Materials and methods

2.1. Study design and setting

This double-blind, randomized clinical trial was conducted at the Department of Oral Diseases, Faculty of Dentistry, Islamic Azad University, Tehran Medical Sciences, Iran, between 2023 and 2024.

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2.2. Sample size calculation

Sample size estimation was performed based on prior data [9] using the Advanced Repeated Measures ANOVA Power Analysis module in PASS 11 software. Assuming α = 0.05, an initial sample size of 18 participants per group yielded a statistical power ($1-\beta$) of 0.81 (β = 0.19) for evaluating between-group main effects with an effect size of 0.44, and a power of 0.999 (β = 0.001) for a repeated-measures variable with four time points (effect size = 1.84). To account for an anticipated dropout rate of 25 %, the minimum initial sample size was set at 22 participants per group (total N = 66).

2.3. Ethical approval and clinical trial registration

This study protocol was reviewed and approved by the Ethics Committee of the Islamic Azad University, Dental Branch (Ethics Code: IR.IAU.DENTAL.REC.1402.094). The clinical trial was prospectively registered in the Iranian Registry of Clinical Trials (IRCT ID: IRCT20231021059788N1). Written informed consent was obtained from all participants prior to enrollment in accordance with the Declaration of Helsinki.

2.4. Eligibility and diagnostic criteria

Adult male and female volunteers (≥ 18 years of age) with basic literacy who were diagnosed with Type II denture stomatitis and demonstrated the ability to comply with oral rinse protocols were screened for eligibility. Diagnosis and classification of denture stomatitis were established by a single, calibrated specialist in oral medicine following standardized guidelines [10] based on Newton's criteria:

- **Type I:** Localized erythematous patches or pinpoint hyperemic lesions caused by mechanical trauma from the denture.
- **Type II:** Generalized, diffuse erythema involving the palatal mucosa covered by the denture base.
- **Type III:** Diffuse erythema accompanied by a papillary or granular hyperplastic surface on the central palatal mucosa [10].

Exclusion Criteria: Patients were excluded if they met any of the following conditions:

- Hypersensitivity or allergy to ginger, yarrow, or nystatin.
- High habitual dietary intake of ginger.
- Systemic conditions altering mucosal immunity (e.g., uncontrolled diabetes mellitus or hypoparathyroidism).
- History of head and neck radiotherapy or systemic chemotherapy.
- Use of topical or systemic antibiotics, antifungals, or corticosteroids within the preceding 4 weeks.

2.5. Randomization, blinding, and interventions

Eligible participants were randomly assigned (1:1:1 allocation) into three intervention groups using computer-generated simple randomization (Microsoft Excel):

- **Group 1-VO:** Received a commercial ginger-based mouthwash.
- **Group 2-IR:** Received a commercial polyherbal mouthwash containing ginger and yarrow.
- **Group 3-EM:** Received standard Nystatin oral suspension at a dosage of 100,000 IU.

All formulations were commercially registered and available in Iranian pharmacies for dental prescription. Both herbal formulations (1-VO and 2-IR) were phytochemically standardized by the manufacturer based on total

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active marker constituents, specifically gingerol and shogaol content.

To maintain double-blinding, a third-party investigator not involved in clinical evaluation or data analysis placed all mouthwashes into identical, opaque bottles bearing unique alphanumeric codes. Both the clinical investigators and the patients remained blinded to treatment assignments throughout the trial. Mouthwashes were stored at controlled room temperature (20-25 °C).

2.6. Baseline assessment and treatment protocol

Demographic data and clinical history (including age, sex, duration of denture use, nocturnal denture wear, prosthetic cleaning protocols, and frequency of daily rinses) were documented at baseline. Prior to treatment initiation, all participants received standardized oral and prosthetic hygiene instruction delivered via printed educational pamphlets and practical demonstrations.

All participants received written step-by-step instructions and the primary investigator's contact number. Patients were instructed to use 5 mL of their assigned coded mouthwash four times daily, swishing for 2 minutes before expectorating, and to refrain from eating or drinking for 30 minutes post-rinsing [9].

2.7. Image acquisition and digital photogrammetry

Clinical evaluations were performed at baseline (Day 0) and follow-up visits on Days 7, 14, and 21. For each examination, patients rested for 1 minute in a quiet, well-ventilated room before being seated in a semi-upright position in a dental chair. A standardized mouth retractor was positioned to ensure complete palatal exposure. Adhering to strict infection control measures, clinical photographs of the palatal mucosa were captured under uniform lighting and distance parameters using a digital camera integrated into a smartphone (Xiaomi Poco M3; primary sensor specifications: 48 MP, f/1.8 aperture [wide], 1/2.0" sensor size, 0.8 µm pixel size, phase detection autofocus [PDAF]).

2.8. Digital image processing and surface area quantification

The surface area of palatal erythema (mm^2) was measured by a single blinded evaluator using ImageJ software (v1.x, National Institutes of Health, Bethesda, MD, USA) [11]. ImageJ is a Java-based public domain image processing system that enables spatial calibration, region-of-interest (ROI) boundary tracing, and pixel-area calculation across 8-bit, 16-bit, or 32-bit digital images. Brightness, contrast manipulation, and digital zooming (up to 32:1) were applied uniformly to optimize delineation of erythematous mucosal margins against healthy tissue.

2.9. Statistical analysis

Statistical analyses were performed using SPSS software (v26.0; IBM Corp., Armonk, NY, USA). Continuous quantitative variables were presented as mean ± standard deviation (SD). One-way Analysis of Variance (ANOVA) was used to compare differences in the surface area of erythema between the three treatment groups at each individual time point (Days 0, 7, 14, and 21). Repeated-measures ANOVA was conducted to evaluate intra-group changes in erythema area over time as well as time-by-treatment group interactions, considering mouthwash type as the between-subject factor. A two-tailed P-value of < 0.05 was considered statistically significant.

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3. Results

3.1. Demographic data

A total of 60 patients were evaluated in this study; only 1 was excluded from the study after randomization. There were 28 (40 %) male and 31 (60 %) female participants. The mean age of the study participants was 63 years, and the mean prosthesis age was 12 years. In terms of the distribution of individuals in the experimental groups, there was no significant difference in gender (P = 0.72), age (P = 0.88), or prosthesis age (P = 0.29) between the groups. The data are shown in Table 1.

Table 1. Distribution of patients by prosthetic age, age, and gender

Type of study mouthwash	Average prosthesis age (years)	Average age (years)	Male (%)	Female (%)
Ginger (1-VO)	12.70	63.85	50	50
Ginger and Yarrow (2-IR)	10.80	62.95	40	60
Nystatin (3-EM)	12.53	61.84	52.6	47.4
Total	12	62.90	47.5	52.5
P value	0.29	0.88	0.72	

3.2. Distribution of patients by side effects and mouthwash flavor satisfaction

Out of all the participants, only 5 people reported dry mouth symptoms. In terms of the type of prosthesis used by the patients, only 4 people used partial dentures, and all but one used complete dentures. In terms of personal hygiene and cleanliness, 45.8 % of the participants cleaned their dentures only with water, 37.3 % with a toothbrush, and only 16.9 % with denture cleaners. In total, 59.3 % did not remove their dentures from their mouths at night. In terms of the frequency of denture cleaning, 10.2 % stated that they did not do it regularly and only rinsed them with water. A total of 25.4 % had a minimum requirement of washing their dentures once a week. Furthermore, 16.9 % cleaned their dentures twice per week, 27.1 % three times, and 20.3 % more than three times.

Systemic diseases were absent in 69.5 % of participants; the remainder presented with conditions including hypercholesterolemia, hypertension, or were receiving anti-anxiety and antidepressant medications. In terms of education, 30.5 % were illiterate, 25.4 % had less than a high school diploma, 27.1 % had a high school diploma, and 16.9 % had a bachelor's degree, and none had a degree higher than a bachelor's. Regarding the side effects of the prescribed medications, only 3 people in the nystatin group reported feeling slightly nauseous after taking it. However, the nystatin group overall expressed the most dissatisfaction with the taste of the prescribed medication. The data are shown in Table 2.

Table 2. Distribution of patients by mouthwash flavor satisfaction

Type of study mouthwash	Satisfaction with mouthwash taste: No	Satisfaction with mouthwash taste: Yes
Ginger (1-VO)	80 %	20 %
Ginger and Yarrow (2-IR)	90 %	10 %
Nystatin (3-EM)	47.4 %	52.6 %
Total	72.9 %	27.1 %

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3.3. Changes in Erythema area on days 0, 7, 14, and 21 (mm²) and between groups

At the beginning of the study, the area of erythema was similar in the three groups (P = 0.582). On day 7, the mean change in erythema area in the Nystatin was 292.3 mm², in the Ginger and Yarrow mouthwash group it was 146.7 mm², and in the Ginger group it was 215.4 mm². These values indicate a 99.9 % superiority of nystatin over Ginger and Yarrow mouthwash and a 35.7 % superiority over Ginger mouthwash (P = 0.0004). The data are shown in Table 3.

Measurements on day 14 showed that the mean change in erythema area in the Nystatin group compared to day 0 was 546.9 mm², which was 59.6 % more than Ginger and Yarrow mouthwash group (204.2 mm²) and 26.9 % more than the Ginger group (116.1 mm²) (P = 0.0165). The data are shown in Table 3.

Finally, measurements on day 21 showed that the mean change in erythema area in the Nystatin compared to day 0 was 784.2 mm², which was 51.2 % more than Ginger and Yarrow group (265.7 mm²) and 17.3 % more than the Ginger group (115.4 mm²) (P = 0.0542). The data are shown in Table 3.

Erythema on days 0, 7, 14, and 21 after receiving Ginger and Yarrow is indicated in Table 4. Erythema on days 0, 7, 14, and 21 after receiving Nystatin mouthwash is shown, and erythema on days 0, 7, 14, and 21 after receiving Ginger is presented in Table 4.

Statistical analysis using repeated measures ANOVA showed that the changes in erythematous area were significant between the groups (P < 0.0001). The results for Ginger and Yarrow mouthwash, Nystatin and Ginger mouthwash all indicate significant changes (P < 0.0001) over the measurements in consecutive weeks. The data are shown in Chart 1.

Table 3. Changes in erythema area (mm²) between groups

Type of study mouthwash	Day 0	Day 7	Day 14	Day 21
Ginger (1-VO)	836.62 ± 374.13	215.4 ± 91.1	430.8 ± 234.1	668.8 ± 289.3
Ginger and Yarrow (2-IR)	728.52 ± 373.49	146.7 ± 64.0	342.7 ± 15.7	518.5 ± 248.2
Nystatin (3-EM)	851.41 ± 460.3	292.3 ± 143.2	546.9 ± 291.5	784.2 ± 423.7
P value	0.582	0.0004	0.0165	0.0542

Table 4. Erythema area (mm²) on days 0, 7, 14, and 21 after receiving mouuthwashes

Type of Study mouthwash	Day 0	Day 7	Day 14	Day 21
Ginger (1-VO)	836.62 ± 374.13	621.19 ± 309.62	405.8 ± 234.1	167.8 ± 110.96
P value	--	P < 0.001	P < 0.001	P < 0.001
Ginger And Yarrow (2-IR)	728.52 ± 373.49	581.84 ± 316.81	385.85 ± 224.92	210.01 ± 122.23
P value	--	P < 0.0001	P < 0.0001	P < 0.0001
Nystatin (3-EM)	851.41 ± 460.3	559.11 ± 318.53	304.49 ± 186.17	67.25 ± 58.12
P value	--	P < 0.0001	P < 0.0001	P < 0.0001

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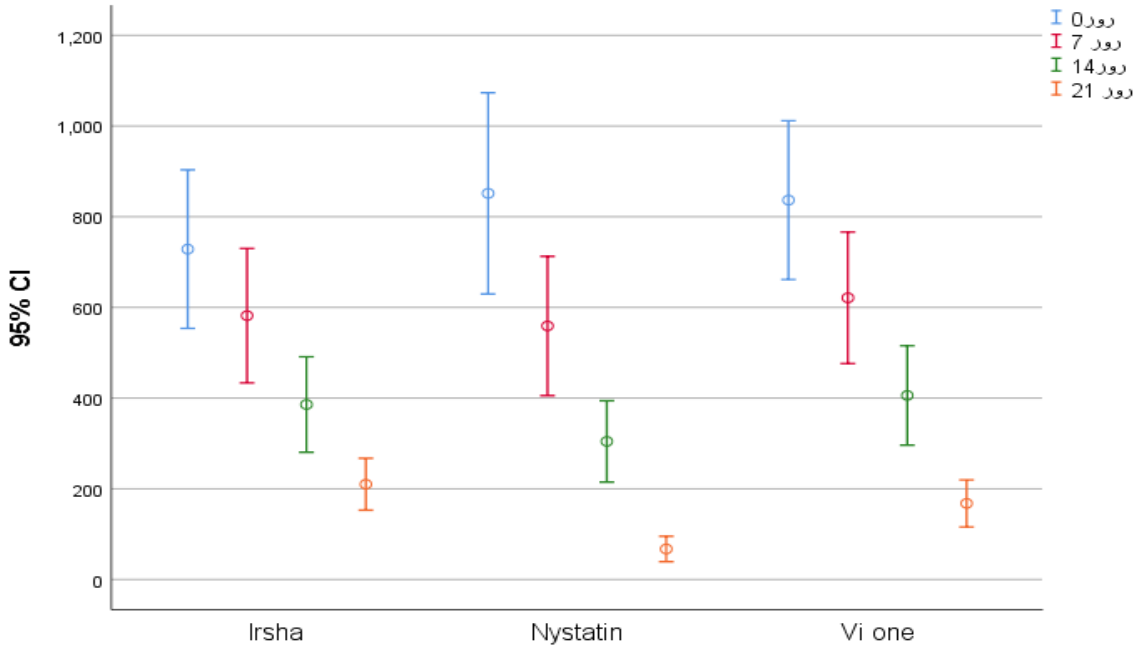

Chart 1. Erythema area before and after treatment according to drug type and measurement day

4. Discussion

The main findings of study were that all mouthwashes improved erythema in type II denture stomatitis, and the overall effect was greater for the Nystatin (3-EM) group. The results on days 7 and 14 showed a significant difference between the three experimental groups ($P < 0.05$), but this difference was weakly significant in the third week ($P < 0.1$).

Alirezaei, et al. conducted a similar study on 2 groups of patients using Ginger mouthwash and nystatin suspension. They showed that nystatin was more effective than Ginger mouthwash at all three measurement times (days 7, 14, and 21). The study included 25 participants in each experimental group**,** and measurements were made using graph paper and a copy pencil. In contrast, the present study used the open-source image processing software ImageJ 2.0 in addition to the medication used in the previous study in the third group**,** and the group size was 20 samples. Both studies were otherwise completely consistent in terms of other conditions, and the results of the previous study are consistent with the results of our study [12].

However, the results of another similar study by Eslami et al. were less consistent with the findings of the present study. In this study, a significant difference in the length and width of the erythema area in denture stomatitis was observed between the two experimental groups only on the day 20 measurement. This study was conducted on two groups of 15 patients with denture stomatitis .they used (1-VO) ginger mouthwash and nystatin suspension. Measurements were taken on days 0, 5, 15, and 20 using calibrated calipers, the data measured were the length and width of the erythema area. In contrast, in the present study, the data measured were the area of the erythematous region, and the measuring tool was the open-source image processing software ImageJ 2.0. In addition to the two mouthwashes mentioned above, the mouthwash Ginger and Yarrow (2-

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IR) was also used in the third group of the study. The group size in the both studies were different. The prescribed dose in the present study was 5 ml 4 times a day, while in the study by Eslami et al. it was 20 ml 3 times a day [9].

Azizi et al. investigated the efficacy of ginger oil spray for eliminating *C. albicans* adhered to acrylic plates. In this invitro study, 120 acrylic disc plates made in the dental clinic were infected with *C. albicans* .the groups were randomly divided into four main: ginger oil spray group, nystatin as positive control group, distilled water as negative control group, and a group with no treatment. The (MIC) of ginger oil and nystatin was determined using the microdilution test. The persistence of *C. albicans* was measured by culturing samples from the treated acrylic plates and comparing the mean number of remaining colonies. The MIC for ginger oil was 1560 µg/ml and for nystatin was 4 µg/ml. Both sprays significantly reduced the number of fungal colonies, but the effect was greater for nystatin, although this was not statistically significant. This paper

Ghods et al. compared the effect of ginger mouthwash on the growth of *C. albicans* strain in a laboratory study with the effect of nystatin. They showed that both drugs had a positive effect on preventing the growth of *C. albicans* fungal strain, and nystatin had a significant advantage over ginger mouthwash, which is similar with our results [8].

Khan et al. studied fluconazole-resistant (FLZ) strains of vulvovaginal *C. albicans*. This study compared the effect of a combination of methanolic ginger extract and fluconazole with fluconazole alone. It was shown that the diameter of the inhibition zone for the wells containing fluconazole, ginger extract, and the combination of extract and fluconazole (with extract concentrations of 250 and 500) was 0, 10, 30, and 35 mm, respectively. The antifungal MIC of FLZ for *C. albicans* strain was 64 µg/ml. The MIC for ginger extract was 512 µg/ml. The MIC for the combination of FLZ and ginger extract was significantly reduced to 16 µg/ml and 1 µg/ml, respectively. These findings show a significant and synergistic effect of ginger on *C. albicans*. In another study, Khan et al. tested the drug developed in the laboratory study on mice with vaginal candidiasis and observed that although high doses of oral fluconazole had a positive effect on reducing the vaginal candidal load, this effect was associated with kidney toxicity, while the use of methanol ginger extract alone had a greater dose-dependent effect on reducing the candidal load and was simultaneously without toxic effect on the kidneys. However, the greatest effect on reducing vaginal candidal load was the synergistic effect of both drugs together. The former study are consistent with the our findings on the positive effect of ginger extract on inhibiting *Candida* strains, although the concentration used in the Khan et al. study is different and human samples were not used [14].

Alp Avci et al. investigated the antimicrobial and antioxidant effects of ginger and galangal in a *in vitro* setting. Both plants are from the ginger family. Aqueous and ethanol hand-made solutions with a concentration of 80 g soluble per 1 kg solvent were prepared. It was shown that according to the Pillai method [15], both interventions had weak to moderate antifungal activity in both disk diffusion and agar diffusion methods. The findings are inconsistent with the present study, which describes the effect of ginger solution as equivalent to or slightly less than nystatin suspension. This difference could be due to the lower concentration used in the Alp Avci et al. study (about 8 % versus 25 % in our study) [16].

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Geraldi et al. [17] investigated the antifungal properties of tropical medicinal plants found in Indonesia .they showed that among the 11 types of extracts prepared, even at a concentration of 25 mg/ml, turmeric and common ginger showed a larger inhibition zone than 100,000 IU nystatin in disk diffusion. It was also shown that the higher the concentration of these two solutions (up to 500 mg/ml), the greater their inhibitory power, although it did not exceed moderate power on the Pillai scale [15].

Khalaf et al. used the well diffusion method to measure the sensitivity of 120 samples collected from the mouths of patients to different concentrations of alcoholic ginger extract. They deternined that even a concentration of 50 mg/ml ginger extract had a larger inhibition zone than the 100,000 IU/ml nystatin used .The results of these two different studies are inconsistent with the results of the present study. The findings of the present study showed that the performance of the Ginger (1-VO) used was never better than that of an equal volume of 100,000 IU suspension [18].

Bohlouli et al. investigated the preventive effect of soluble ginger tablets on the prevention of *Candida* colony formation on dentures. In this *in vitro* study, 81 acrylic resin dentures were prepared and divided into 3 groups, then infected with *C. albicans*, *C. glabrata*, and *C. krusei* fungi, respectively. Each group was then divided into 3 subgroups and immersed in solutions containing effervescent ginger tablets, Nystatin (as a positive control group), and distilled water (as a negative control group). Fungal culture was performed from dentures at different time: 30, 60, and 180 minutes then, the condition of fungal colonies in the study groups was examined. In general, the mean number of fungal colonies in the Nystatin group was lower than the ginger tablet group. The antifungal effect of nystatin started earlier than ginger tablets**;** the number of fungi decreased to zero after 60 minutes with nystatin, while this occurred after 180 minutes in the effervescent ginger tablet solution. In this research, the concentration of ginger tablets was 25 % and the amount of nystatin used was 40 drops per sample. Although the exact volume and amount of the solution mentioned in this study are not exactly specified, it is noteworthy that the concentration of ginger used is the same as the concentration used in the present study, and the results obtained are consistent with the findings of the present study [19].

Maxwell et al. conducted a study on fenugreek and ginger rhizome extracts .they compared their effects with the antifungal drugs nystatin, fluconazole against *Candida* species and the synergistic effects of these drugs with each other. They performed the disc diffusion method. The results showed that the combination of fluconazole and each of the fenugreek and ginger rhizome extracts had a larger inhibition zone, followed by nystatin. Each of these two drugs alone resulted in an inhibition zone approximately half the size of the nystatin inhibition zone. This is somewhat consistent with the findings of the present study that nystatin is more successful in the final treatment of *candidiasis* lesions. However, the article does not mention the exact amount of the active ingredients used (ginger and fenugreek) anywhere, and only mentions the extraction method and the amount of solvents used [20].

Rashed et al. extracted the active ingredient gingerol from ginger rhizome .they investigated its effect on *C. albicans* and *C. tropicalis* samples extracted from the vagina of patients using the disc diffusion method. They observed that a 30 mg/ml gingerol tablet created an inhibition zone with a diameter almost twice

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that of a 50-unit nystatin tablet. This result suggests a strong contradiction with the present study [21].

Mazhar et al. [22] on biofilm formation and the inhibitory effect of ginger extract, and Prastiyanto et al. [23] on the antifungal activity of plants in the ginger family, both provided positive results in laboratory studies indicating the effect of ginger on inhibiting the growth of *C. albicans* the limitations of both articles were a control group and did not compare them to conventional drugs.

Rashidi Meybodi et al. in their laboratory study investigated the effect of ginger (1-VO) mouthwash and nystatin on the growth of *C. albicans* strain .they found that the effect of nystatin, even when diluted 264 times, was much better than the effect of the above mouthwash. The results of this study showed that the diameter of the growth inhibition zone in the nystatin group was 8.04 mm, while in the ginger (1-VO) mouthwash group it was 1.16 mm. This result is consistent with the findings of the present study. However, since a sample of fungus from a cell bank was used in this study instead of clinical swab samples, the results of this study cannot be generalized [6].

Aghazadeh et al. evaluated the antifungal properties of ginger extract against *Candida* species and the effect of the extract on biofilm formation. The MIC of ginger extract for the strains evaluated was 10 and 5 mg/mL for *C. albicans* and *C. krusei*, respectively. Ginger extract successfully prevented biofilm formation by *C. krusei* and *C. albicans* no comparison was made between the inhibition zone of the extract under study and nystatin or azole group drugs, and only the lower MIC of ginger extract compared to fluconazole and nystatin drugs in vitro was mentioned. Also, only one strain of *C. albicans* and *C. krusei* was used for the test, and in this respect, it is similar to the study by Rashidi Meybodi et al. Concentrations between 0.625 mg/ml and 5 mg/ml had the highest anti-biofilm and antifungal effects. This result, however, contradicts newer research showing that increasing the concentration and dose has a positive effect on the antifungal effect of ginger extract [24].

Fattahi et al. investigated the antifungal effect of methanolic extracts and essential oils obtained from five plants. The medicinal plants were: (*Salvadora persica*, *Mentha spicata*, *Achillea millefolium*, *Matricaria chamomilla*, and *Zingiber officinale*) against 25 clinical isolates of *C. albicans* collected from patients with denture stomatitis. Antifungal susceptibility was assessed using broth microdilution as the primary method, with agar diffusion assays performed to provide complementary visual confirmation. Nystatin was determined as a reference control. Across the tested samples, essential oils consistently showed stronger antifungal effects than the corresponding methanolic extracts. Notably, *Z. officinale* essential oil exhibited the highest level of activity, inhibiting 15 out of 25 isolates and, in several cases, demonstrating efficacy comparable to or exceeding that of nystatin. Chemical profiling by GC–MS indicated that the ginger essential oil was dominated by sesquiterpene and monoterpene hydrocarbons, with zingiberene (21.49 %) being the major constituent, followed by *β*-sesquiphellandrene, *α*-curcumene, sabinene, and *α*-citral. This terpene-rich composition may contribute to the observed antifungal activity, potentially through the disruption of fungal cell membrane integrity. These results suggest that *Z. officinale* essential oil represents a promising natural antifungal agent, candidate for the treatment of denture stomatitis *C. albicans* infections [25].

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In this research, a review of two topical herbal medicines as a treatment modalities for oral *candidiasis* is conducted. In today's healthcare landscape, Herbal medicines are gaining recognition as new and viable treatment options. They offer several advantages, including greater patient acceptance, renewable sources, and cost-effectiveness. As a result, research is being conducted to further explore the quality and safety of these medicines in comparison with standard antifungal treatment [26, 27].

As the demand for natural alternatives to antibiotics grows in the Iranian population, ginger may continue to play a significant role in the future of oral health care, offering a natural, effective, and sustainable treatment option for oral infections in oral medicine knowledge. The lack of standardized ginger formulations and limited research on the long-term effects of this herb on oral tissues highlight areas requiring further study. New clinical trials are crucial to validate the efficacy of different ginger formulations in real-world settings and to assess potential adverse effects. The optimal formulation, dosage, and clinical application of ginger for various oral infections remain unclear. It needs new clinical trial designing [28].

5. Conclusion

The results of this study support the effect of both ginger and yarrow and ginger mouthwashes in combating denture stomatitis. However, the extent of this effect is less than that of nystatin suspension.

The difficulty of finding suitable meant that some dropped out of treatment after the first week. This study used a new method with ImageJ software that can be implemented on smartphones. It is suggested that a similar study be conducted using using ginger constituents instead of ready-made compounds.

The Claude AI was used for English language editing of the manuscript.

Supplementary Materials

Table 1: Distribution of patients by prosthetic age, age, and gender. Table: Distribution of patients by mouthwash flavor satisfaction. Table 3: Changes in erythema area (mm^2) between groups. Table 4: Erythema on days 0, 7, 14, and 21 after receiving ginger and yarrow mouthwash. nystatin mouthwash.and ginger mouthwash. Chart 1. Erythema area before and after treatment according to drug type and measurement day.

Authors contributions

Conceptualization: AA. Methodology: L.S., A.A. Formal analysis: L.S., A.A. Investigation: M.SMZ. Resources: M.SMZ. Writing - original draft preparation: M.SMZ. Writing - review and editing: A.A. Visualization: A.A. Supervision: A.A., L.S. Project administration: A.A. Funding acquisition: none. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that the study was carried out without any commercial or financial relationships that could be interpreted as a potential conflict of interest.

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