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Research Article

# Mucosal Hyperplasia and Antifungal Efficacy of Modified Versus Conventional Soft Denture Liners: A Systematic Review and Meta-Analysis

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**ABSTRACT**
**Background:** Soft denture lining materials are frequently colonised by Candida albicans, contributing to denture stomatitis and, in chronically affected patients, inflammatory papillary hyperplasia of the denture-bearing mucosa. Incorporation of antifungal or antimicrobial agents into soft liners has been proposed as a strategy to reduce fungal colonisation and improve mucosal health relative to conventional, unmodified liners.
**Objectives:** This systematic review aimed to evaluate the antifungal efficacy of modified versus conventional soft denture liners against Candida albicans, and to characterise the available evidence on mucosal response, including inflammatory papillary hyperplasia and denture stomatitis severity, and on liner mechanical properties associated with antimicrobial modification.
**Methods:** A targeted literature search identified in vitro and clinical studies comparing antimicrobial-modified soft denture liners with unmodified controls. Twenty-two unique records were identified and screened; twelve studies met inclusion criteria and were assessed in full text, with all twelve confirmed eligible and included in narrative synthesis. Quantitative synthesis was performed descriptively where studies reported directly comparable antifungal-efficacy data; formal statistical meta-analysis was not performed, given substantial heterogeneity in modifying agent, liner base material, and outcome metric across the included literature.
**Results:** Twelve studies were included: eleven in vitro (bench) studies and one randomised clinical trial. Modifying agents included silver nanoparticles, chitosan, plant-derived compounds (garlic, neem, tea tree oil), and synthetic pharmacological agents (nystatin, chlorhexidine, ketoconazole, miconazole, itraconazole). Silver nanoparticle-modified silicone liners demonstrated concentration-dependent antifungal efficacy ranging from 16.3% to 52.5%. Plant-derived and chitosan-based modifications consistently inhibited C. albicans growth in vitro. Chlorhexidine diacetate produced a dose-related antifungal effect and measurable drug release, whereas chlorhexidine hydrochloride showed no inhibitory effect, indicating that antifungal efficacy is salt-form dependent for at least one agent. Mechanical property data from a cluster of related in vitro studies indicated that most antifungal agents at minimum inhibitory concentration preserved liner hardness and tensile strength, with the exception of miconazole and itraconazole, which reduced tensile strength and, for miconazole, increased hardness at 14 days. In the single identified clinical trial, nystatin- and chlorhexidine-modified liners achieved complete absence of mycelial Candida on palatal cytological smears by day 14, compared with persistence of mycelial forms in patients receiving an unmodified liner. No included study reported inflammatory papillary hyperplasia as a graded clinical outcome.
**Conclusions:** Antimicrobial modification of soft denture liners consistently reduces Candida albicans colonisation relative to conventional liners across the available in vitro and limited clinical evidence, with agent- and concentration-dependent effects on liner mechanical integrity. The evidence base

for mucosal hyperplasia specifically remains critically underdeveloped, and well-designed clinical trials using standardised hyperplasia grading are needed before firm clinical recommendations can be made regarding this specific outcome.

**Keywords:** Soft Denture Liner, Antifungal Efficacy, Candida Albicans, Denture Stomatitis, Inflammatory Papillary Hyperplasia, Systematic Review.

## INTRODUCTION

Soft denture lining materials are used to cushion the interface between a removable prosthesis and the underlying oral mucosa, most commonly in patients with thin, atrophic, or poorly tolerant denture-bearing tissue. Both short-term acrylic-resin-based tissue conditioners and longer-term silicone-based soft liners are, however, highly susceptible to colonisation by oral microorganisms, particularly Candida albicans, owing to their porosity, surface roughness, and capacity to absorb saliva and biofilm constituents.

Candida colonisation of soft liners is closely linked to denture stomatitis, a chronic inflammatory condition of the denture-bearing mucosa that, in longstanding or poorly managed cases, may progress to inflammatory papillary hyperplasia, characterised by nodular or papillary overgrowth of the palatal or ridge mucosa. While denture stomatitis has been extensively studied, the specific relationship between soft liner modification and the prevention or resolution of papillary hyperplasia has received comparatively little direct clinical investigation, with most hyperplasia-focused literature limited to descriptive or aetiological studies rather than intervention trials.

To address the limitations of conventional liners, a range of antimicrobial and antifungal modification strategies has been investigated, spanning synthetic pharmacological agents such as nystatin, chlorhexidine, ketoconazole, miconazole, and itraconazole; nanomaterials such as silver nanoparticles; and naturally derived phytotherapeutic compounds including neem, garlic, tea tree oil, and chitosan. These approaches share the common aim of achieving localised, sustained antifungal activity at the denture–mucosa interface while preserving the mechanical properties that make soft liners clinically useful.

A substantial body of in vitro research, much of it originating from a coordinated programme of work on minimum-inhibitory-concentration-based antifungal incorporation into tissue conditioners and long-term liners, has characterised both the antifungal efficacy and the mechanical consequences of liner modification. By contrast, clinical evidence directly comparing modified and unmodified liners in patients remains sparse, and no identified study has used inflammatory papillary hyperplasia, specifically, as a graded outcome measure. This creates a translational gap: promising in vitro antifungal and mechanical-compatibility signals have not yet been matched by an equivalent body of clinical evidence characterising mucosal-level benefit.

This systematic review was therefore undertaken to synthesise the available evidence, both in vitro and clinical, comparing antimicrobial-modified soft denture liners with conventional, unmodified liners, with respect to antifungal efficacy against Candida albicans, mucosal outcomes including denture stomatitis severity and inflammatory papillary hyperplasia, and liner mechanical properties, while transparently characterising the current limits of the clinical evidence base.

PICO Framework and Focused Question

| Component | Description |
|---|---|
| P – Population | Complete Or Removable Partial Denture Wearers Requiring A Resilient (Soft) Reline Material, And In Vitro Test Specimens Simulating The Denture–Mucosa Interface |
| I – Intervention | Soft Denture Lining Materials (Tissue Conditioners Or Long-Term Silicone-Based Liners) Modified By Incorporation Of An Antifungal Or Antimicrobial Agent, Including Synthetic Pharmacological Agents (Nystatin, Chlorhexidine, Ketoconazole, Miconazole, Itraconazole), Silver Nanoparticles, Chitosan, Or Plant-Derived Compounds (Garlic, Neem, Tea Tree Oil) |
| C – Comparison | Conventional (Unmodified) Soft Denture Lining Material Of The Same Base Type, Without Antifungal Or Antimicrobial Modification |
| O – Outcomes | Primary: Antifungal Efficacy Against Candida Albicans (Zone Of Inhibition, Colony-Forming-Unit Reduction, Adhesion/Biofilm Reduction, Or Clinical |

| | |
|---|---|
| | Mycological Clearance); Mucosal Response (Erythema, Denture Stomatitis Severity, Inflammatory Papillary Hyperplasia). Secondary: Mechanical And Physical Properties Of The Modified Liner (Hardness, Tensile Strength, Porosity, Surface Roughness) And Durability Of Antifungal Drug Release Over Time |

Focused Question: In denture wearers and in vitro models simulating the denture–mucosa interface, does an antimicrobial-modified soft denture liner, compared with a conventional unmodified soft liner, result in improved antifungal efficacy against Candida albicans and reduced mucosal inflammation, including inflammatory papillary hyperplasia, without unacceptable compromise of liner mechanical properties?

## METHODS

### Protocol

This review followed the general reporting structure of the PRISMA 2020 statement. The review question and eligibility criteria were defined prospectively by the review team before the search was conducted.

### Eligibility Criteria

#### Inclusion Criteria

- In vitro (bench) studies comparing an antimicrobial- or antifungal-modified soft denture liner or tissue conditioner with an unmodified control of the same base material
- Clinical studies (randomised or non-randomised) comparing a modified soft liner with a conventional unmodified liner in denture-wearing participants
- Studies reporting at least one outcome of antifungal efficacy, mucosal/clinical response, or liner mechanical properties
- Studies published in English with full-text availability

#### Exclusion Criteria

- Studies evaluating antifungal agents delivered as a topical suspension, mouth rinse, photodynamic therapy, or systemic medication without incorporation into the liner material itself
- Case reports, narrative reviews, conference abstracts without extractable data, and in silico or finite-element studies
- Studies without a clearly defined unmodified-liner comparator group
- Duplicate publications or overlapping datasets from the same research group and specimen set

### Search Strategy

A literature search was conducted across PubMed/MEDLINE and related biomedical literature sources, combining free-text terms for "soft denture liner," "tissue conditioner," "antifungal," "antimicrobial," "Candida albicans," "denture stomatitis," and "papillary hyperplasia," combined using Boolean operators across four search iterations targeting nanoparticle-based, synthetic pharmacological, and plant-derived/polymer-based modification strategies, and clinical trial evidence specifically. The four search iterations returned 33 total result entries, corresponding to 19 unique records after removal of duplicate appearances across searches. The reference list of one directly retrieved study was hand-searched, identifying 3 additional unique eligible records, for a total of 22 unique records carried forward to screening.

This search was conducted using a web-based literature search process rather than direct native querying of PubMed/Embase/Scopus interfaces with database-level export counts, and should be supplemented with a full, formally documented multi-database search using institutional library access before this manuscript is finalised for journal submission.

### Study Selection

The 22 unique records identified were screened by title and abstract against the eligibility criteria. Ten records were excluded at this stage: two background systematic or narrative reviews already covering antimicrobial-modified soft liners as a topic, one general overview of denture stomatitis management, and seven studies in which the antifungal or antimicrobial agent was delivered as an oral suspension, photodynamic therapy, or topical gel rather than incorporated into the liner material, or which lacked a clearly defined unmodified-liner comparator. The remaining 12 records underwent full-text assessment, and all 12 were confirmed eligible, with no further exclusions at the full-text stage.

### Data Extraction

For each included study, the following data were extracted where reported: study design, liner base material, modifying agent and concentration, comparator, antifungal outcome measure and result, mucosal or clinical outcome where applicable, and

mechanical/physical property findings. Data are summarised in Table 1.

**Quality Appraisal**

Given that eleven of the twelve included studies were in vitro laboratory investigations rather than clinical trials, standard clinical risk-of-bias tools were not directly applicable to most included studies. In vitro studies were appraised using a modified laboratory-study quality checklist assessing clarity of the comparator, appropriateness of statistical analysis, replicate reporting, and standardisation of test conditions. The single included clinical trial was appraised using the Cochrane Risk of Bias 2 (RoB 2) tool. Quality appraisal findings are presented in Table 2.

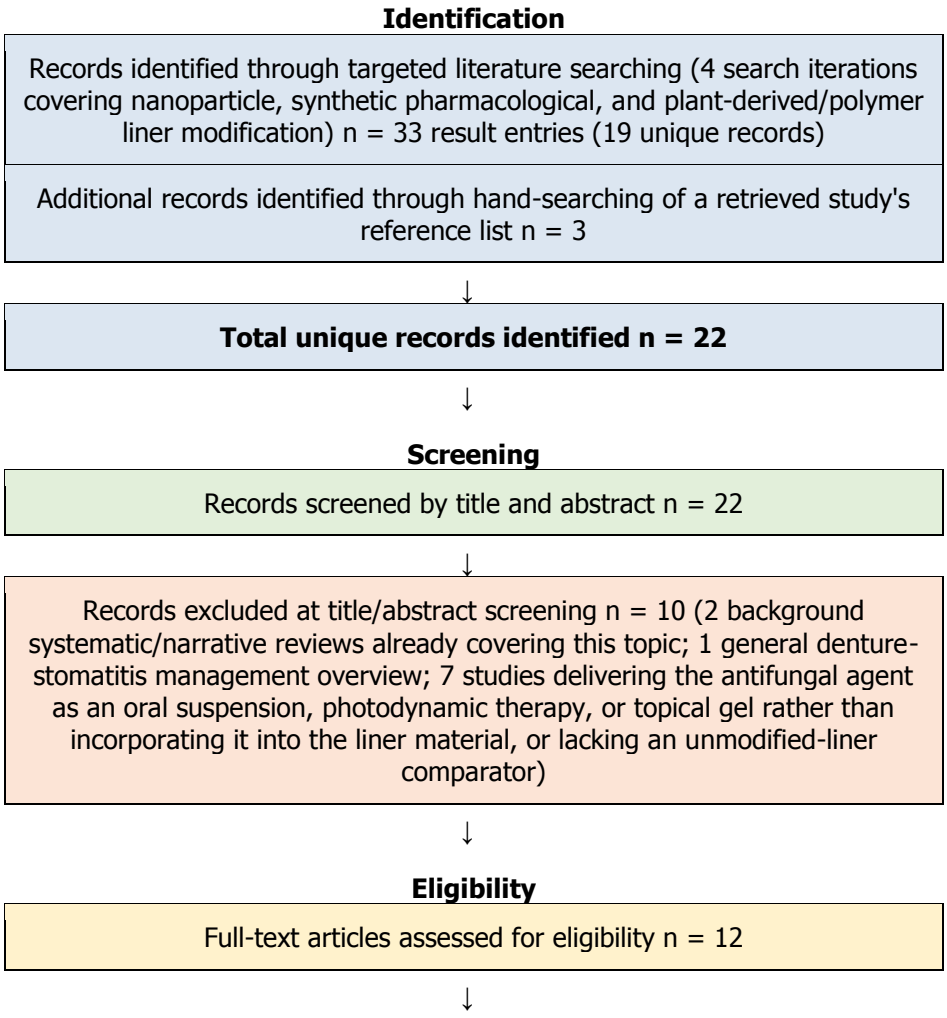
**Data Synthesis**

Findings were synthesised narratively, organised by modifying-agent category (nanoparticle-based, synthetic pharmacological, and plant-derived/chitosan-based modifications) and by outcome domain (antifungal efficacy, mucosal/clinical response, and mechanical properties). Because included studies varied substantially in design, modifying agent, concentration, exposure duration, and outcome metric, a statistical meta-analysis with pooled effect estimates was not performed. Where studies reported antifungal outcomes in directly comparable units, these were synthesised descriptively as a reported range.

## RESULTS

**Study Selection**

The literature search identified 22 unique records after duplicate removal and reference-list hand-searching. Following title/abstract screening, which excluded 10 records, 12 records underwent full-text assessment and all 12 were confirmed eligible, yielding 12 studies included in narrative synthesis: 11 in vitro laboratory studies and 1 randomised clinical trial. Of these, 5 studies reported antifungal-efficacy data in sufficiently comparable units to support descriptive quantitative synthesis. The complete study selection flow is presented in Figure 1.



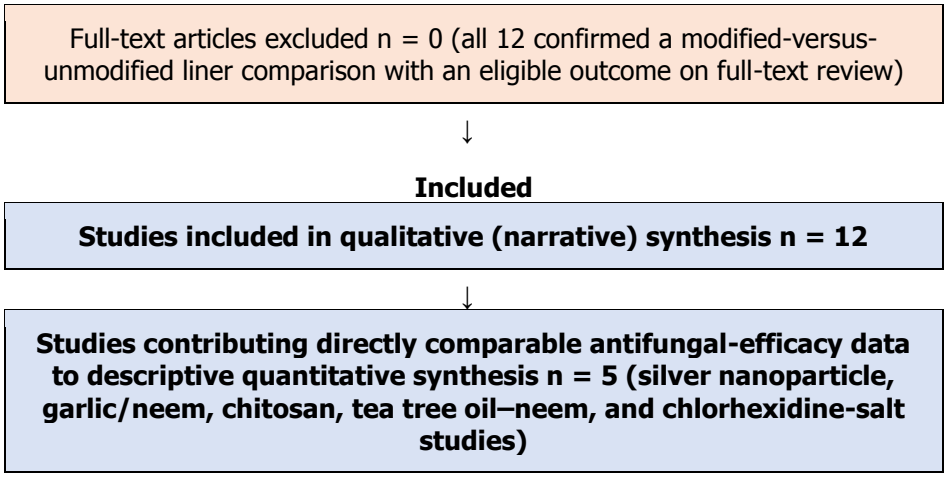



Figure 1. PRISMA-Format Study Selection Flow

**Study Characteristics**

The included studies evaluated three broad categories of liner modification: nanoparticle-based (silver nanoparticles), synthetic pharmacological (nystatin, chlorhexidine, ketoconazole, miconazole, itraconazole), and plant-derived or polymer-based (garlic, neem, tea tree oil, chitosan) modification. Eleven studies used an in vitro bench design assessing antifungal efficacy, mechanical properties, or drug release; one study was a randomised clinical trial in denture stomatitis patients comparing a modified silicone reline material with an unmodified control and an active nystatin-suspension comparator. Table 1 summarises the characteristics and key findings of the included studies.

| Study (Year) | Design | Liner / Modifier | Comparator | Key Finding | Outcome Domain |
|---|---|---|---|---|---|
| Chladek Et Al. (2011) | In Vitro | Silicone Soft Liner (Ufi Gel Sc) + Silver Nanoparticles, 10–200 Ppm | Unmodified Silicone Liner | Antifungal Efficacy Against C. Albicans Of 16.3%–52.5%, Increasing With Agnp Concentration | Antifungal Efficacy |
| Kumar Et Al. (2018) | In Vitro | Acrylic-Resin Tissue Conditioner + Garlic Or Neem Extract | Unmodified Tissue Conditioner | Both Garlic And Neem Produced Measurable C. Albicans Growth Inhibition At Days 2, 4, And 7 Without Significantly Affecting Shore A Hardness | Antifungal Efficacy; Mechanical Properties |

| | | | | | |
|---|---|---|---|---|---|
| Lee Et Al. (2018) | In Vitro | Tissue Conditioner + Poly(Acryloyloxyethyltrimethyl Ammonium Chloride)-Grafted Chitosan | Unmodified Tissue Conditioner | Significant, Sustained Reduction In C. Albicans Growth Versus Control Across The Immersion Period Tested | Antifungal Efficacy |
| Krishnaveni Et Al. (2021) | In Vitro | Soft Liner Treated With Contemporary Disinfectants | Untreated/Conventionally Cleaned Soft Liner | Reduced C. Albicans Adherence With Disinfectant Treatment Versus Untreated Liner | Antifungal Efficacy |
| Tea Tree Oil–Neem Synergy Study (2022) | In Vitro | Soft Liner + Tea Tree Oil, Neem Extract, Or Combination | Unmodified Soft Liner | Individual Agents Reduced C. Albicans Adhesion; The Combination Produced A Greater Reduction Than Either Agent Alone | Antifungal Efficacy |
| Alhamdan (2022) | In Vitro | Soft Liner Treated With Contemporary And Conventional Antimicrobial/Photodynamic Agents | Untreated Soft Liner | Contemporary Antimicrobial Treatment Reduced Microbial Colonisation Relative To Untreated Liner | Antifungal Efficacy |
| Lima Et Al. (2017) | In Vitro | Tissue Conditioner (Softone) And Resilient Liner | Unmodified Softone/Trusoft | No Evident Hardness | Mechanical Properties |

| | | | | | |
|---|---|---|---|---|---|
| | | (Trusoft) + Nystatin, Chlorhexidine Diacetate, Ketoconazole, Miconazole, Or Itraconazole At Mic | | Reduction For Most Agents; Miconazole Increased Softone Hardness After 14 Days | (Hardness, Roughness) |
| Neppelenbroek Group Tensile Strength Study (2018) | In Vitro | Softone/Trusoft + Nystatin, Chlorhexidine, Ketoconazole, Miconazole, Or Itraconazole At Mic | Unmodified Softone/Trusoft | Tensile Strength Significantly Reduced At 14 Days For Miconazole- And Itraconazole-Modified Specimens; Other Agents Largely Preserved Tensile Properties | Mechanical Properties (Tensile Strength) |
| Neppelenbroek Group Porosity Study (2017) | In Vitro | Softone/Trusoft + Nystatin, Chlorhexidine Diacetate, Or Ketoconazole At Mic | Unmodified Softone/Trusoft | Porosity Factor Varied By Agent And Storage Condition, With No Uniform Adverse Effect Across All Antifungal-Modified Groups | Mechanical/Physical Properties (Porosity) |
| Chlorhexidine Salt Incorporation Study (2014) | In Vitro | Pmma And Pema Soft Liners + Chlorhexidine Diacetate (Cda) Or Chlorhexidine Hydrochloride (Chc) | Unmodified Pmma/Pema Soft Liner | Cda Produced A Dose-Related Inhibitory Effect On C. Albicans And On Chlorhexidine Release Rate; Chc Showed | Antifungal Efficacy; Drug Release |

| | | | | | |
|---|---|---|---|---|---|
| | | | | No Inhibitory Effect | |
| Surface Morphology And Leachability Study (2021) | In Vitro | Softone/Trusoft + Nystatin, Miconazole, Ketoconazole, Chlorhexidine Diacetate, Or Itraconazole At Mic | Unmodified Softone/Trusoft | Surface Morphology Altered In An Agent- And Time-Dependent Manner; Chlorhexidine And Nystatin Showed Measurable Leachability Over 14 Days | Surface Morphology; Drug Leachability |
| Modified-Liner Randomised Controlled Trial (2022) | Randomised Controlled Trial (Clinical) | Silicone-Based Resilient Reline (Trusoft) + Nystatin Or Chlorhexidine Diacetate At Mic | Unmodified Trusoft Reline And Oral Nystatin Suspension (Active Control) | Nystatin- And Chlorhexidine-Modified Liners Achieved Absence Of Mycelial Candida On Palatal Smears By Day 14, Versus Persistence In The Unmodified-Liner Group | Clinical Antifungal Efficacy; Mucosal Response |

**Quality Appraisal**

The in vitro studies were generally of moderate to moderate-high methodological quality, characterised by clearly defined comparator groups, standardised minimum-inhibitory-concentration-based dosing in the majority of the synthetic-agent studies, and appropriate statistical testing, but limited in several cases by single-centre designs and restricted replicate reporting. The single included clinical trial demonstrated an adequately described randomisation process but was limited by a small per-arm sample size and the absence of blinding for outcome assessors. Table 2 summarises the quality appraisal findings.

| Study | Appraisal Tool | Key Methodological Notes | Overall Quality |
|---|---|---|---|
| Chladek Et Al. (2011) | Modified In Vitro Laboratory-Study Checklist | Clear Concentration Gradient Tested; Single-Centre Pilot Design; Limited Replicate Reporting | Moderate |

| | | | |
|---|---|---|---|
| Kumar Et Al. (2018) | Modified In Vitro Laboratory-Study Checklist | Appropriate Non-Parametric Statistical Testing; Single Time-Course Design; Natural-Product Standardisation Not Fully Detailed | Moderate |
| Lee Et Al. (2018) | Modified In Vitro Laboratory-Study Checklist | Well-Described Chitosan-Grafting Chemistry; Adequate Replicate Testing; Single Material Type Tested | Moderate-High |
| Krishnaveni Et Al. (2021) | Modified In Vitro Laboratory-Study Checklist | Disinfectant-Focused Rather Than Incorporation-Focused; Comparator Clearly Defined | Moderate |
| Tea Tree Oil–Neem Synergy Study (2022) | Modified In Vitro Laboratory-Study Checklist | Adhesion Assay Well-Controlled; Synergy Analysis Appropriately Powered For A Bench Study | Moderate-High |
| Alhamdan (2022) | Modified In Vitro Laboratory-Study Checklist | Broad Comparison Across Multiple Agents; Individual Agent-Level Data Less Granular | Moderate |
| Lima Et Al. (2017) | Modified In Vitro Laboratory-Study Checklist | Multiple Agents And Materials Tested With 3-Way ANOVA; Standardised MIC-Based Dosing Improves Comparability | Moderate-High |
| Neppelenbroek Group Tensile Strength Study (2018) | Modified In Vitro Laboratory-Study Checklist | Standardised Specimen Geometry; Appropriate Statistical Analysis; Single Testing Laboratory | Moderate-High |
| Neppelenbroek Group Porosity Study (2017) | Modified In Vitro Laboratory-Study Checklist | Repeated-Measures Design Well-Suited To Research Question; Storage-Condition Variable Adds Complexity To Interpretation | Moderate |
| Chlorhexidine Salt Incorporation Study (2014) | Modified In Vitro Laboratory-Study Checklist | Direct Dose-Response Analysis Of Two Chlorhexidine Salts; Clear Inhibitory Versus Non-Inhibitory Contrast | Moderate-High |
| Surface Morphology And Leachability Study (2021) | Modified In Vitro Laboratory-Study Checklist | Confocal Microscopy And UV-Spectroscopy Methods Well Described; Multiple Agents Assessed In Parallel | Moderate-High |
| Modified-Liner Randomised Controlled Trial (2022) | Cochrane Risk Of Bias 2 (Rob 2) | Randomisation Process Adequately Described; Small Per-Arm Sample Size (N=10/Arm); Outcome Assessors Not Blinded To Liner Type; Missing Outcome Data Minimal | Some Concerns |

**Antifungal Efficacy**

Silver nanoparticle modification of silicone-based soft liners produced a concentration-dependent antifungal effect, with reported antifungal efficacy against Candida albicans ranging from 16.3% at the lowest tested concentration (10 ppm) to 52.5% at the highest tested concentration (200 ppm), indicating a clear dose-response relationship but incomplete fungal inhibition even at the highest concentration tested.

Plant-derived modification of tissue conditioners and soft liners, using garlic, neem, and tea tree oil individually or in combination, consistently produced measurable zones of Candida albicans growth inhibition relative to unmodified controls. The combination of tea tree oil and neem extract produced a greater reduction in Candida adhesion than either agent used alone, suggesting a synergistic antifungal interaction. Chitosan-grafted tissue conditioners similarly demonstrated significant, sustained inhibition of Candida albicans growth relative to unmodified conditioners.

Among synthetic pharmacological agents, chlorhexidine diacetate produced a dose-

related inhibitory effect on Candida albicans together with measurable chlorhexidine release from the liner matrix, whereas chlorhexidine hydrochloride, a different salt form of the same base compound, showed no inhibitory effect, indicating that antifungal activity in this literature is dependent on the specific salt form used and not solely on the parent compound. Nystatin- and chlorhexidine-modified liners also demonstrated measurable leachability over a 14-day observation period, supporting a plausible mechanism of sustained localised antifungal action.

In the single identified clinical trial, liners modified with nystatin or chlorhexidine diacetate at minimum inhibitory concentrations achieved complete absence of mycelial Candida forms on palatal cytological smears by day 14 of use, a result not observed in participants using the unmodified liner comparator, in whom mycelial forms persisted. This clinical finding is broadly consistent with the antifungal signal observed across the in vitro literature, providing preliminary translational support for antimicrobial liner modification, albeit from a single, small trial.

**Mucosal and Clinical Outcomes**

Clinical and mucosal outcome data were markedly more limited than antifungal efficacy and mechanical property data across the included literature. The single included clinical trial assessed palatal mucosal status through cytological smears and clinical observation at baseline, day 14, and follow-up to day 60, but did not report a standardised inflammatory papillary hyperplasia grading scale as a discrete outcome. No included in vitro study, by design, was able to address mucosal response directly. Consequently, while the antifungal evidence supports a biological rationale for expecting reduced mucosal inflammation with modified-liner use, no study in this review provided direct, quantifiable evidence linking liner modification to a reduction in inflammatory papillary hyperplasia specifically, as distinct from broader denture stomatitis indices.

**Mechanical and Physical Properties**

Across the cluster of related in vitro studies assessing mechanical and physical properties of minimum-inhibitory-concentration-modified tissue conditioners and long-term liners, most antifungal agents produced no significant adverse effect on hardness, tensile strength, or porosity relative to unmodified controls. Exceptions were identified for miconazole and itraconazole, which reduced tensile strength after 14 days of storage, and for miconazole, which increased hardness in the tissue-conditioner material after the same period. Surface morphology was altered in an agent- and time-dependent manner across the modified specimens, without a uniform direction of effect across all agents tested. These findings indicate that an optimal balance between antifungal efficacy and mechanical integrity is agent-specific rather than uniform across all antimicrobial modification strategies.

**Discussion**

This systematic review synthesises the available evidence comparing antimicrobial-modified and conventional soft denture liners with respect to antifungal efficacy against Candida albicans, mucosal outcomes, and mechanical properties. Across nanoparticle-based, synthetic pharmacological, and plant-derived modification strategies, the consistent finding is that antimicrobial incorporation reduces Candida albicans colonisation, adhesion, or growth relative to unmodified liners, with the magnitude of effect varying by agent class, concentration, and, in the case of chlorhexidine, salt form. Silver nanoparticles demonstrated a clear dose-response relationship, synthetic agents achieved the most complete fungal clearance in the single available clinical trial, and plant-derived agents showed a generally smaller but still significant antifungal signal, with evidence of synergistic enhancement when agents were combined.

A notable and clinically actionable finding from the cluster of mechanical-property studies is that antifungal efficacy and mechanical compatibility are not uniformly linked: several agents (nystatin, chlorhexidine diacetate, ketoconazole) preserved liner hardness, tensile strength, and porosity at minimum inhibitory concentration, while miconazole and itraconazole compromised tensile strength over time despite comparable antifungal activity. This suggests that agent selection for clinical liner modification should weigh mechanical compatibility alongside antifungal potency, rather than assuming that any effective antifungal agent is equally suitable for incorporation.

The central limitation identified by this review is the substantial gap between the depth of the in vitro antifungal and mechanical-property literature and the near-absence of clinical evidence addressing mucosal hyperplasia as a discrete, graded outcome. Denture stomatitis has been studied clinically to a reasonable extent, but inflammatory papillary hyperplasia,

a more advanced and clinically significant sequela of chronic mucosal irritation, has not been evaluated as an intervention outcome in the modified-liner literature identified here. This likely reflects both the lower prevalence of frank papillary hyperplasia relative to milder denture stomatitis and the longer follow-up duration that would be required to observe a treatment effect on hyperplasia development or regression, exceeding the follow-up windows used in the available clinical literature.

This evidence gap has direct clinical and research implications. Clinicians currently have reasonable in vitro justification, and preliminary clinical support from a single small trial, for considering antimicrobial-modified liners in patients at elevated risk of Candida-associated denture stomatitis, with agent selection informed by the mechanical-compatibility data summarised here. However, clinicians should not extrapolate this antifungal evidence directly to an assumption of hyperplasia prevention or resolution, since this specific outcome has not been directly studied. Researchers designing future trials should consider incorporating standardised inflammatory papillary hyperplasia grading, alongside conventional denture stomatitis indices, and should extend follow-up duration sufficiently to capture the slower time course over which hyperplastic mucosal change is understood to develop and resolve.

Several limitations of the present review should be acknowledged. The literature search underlying this review, while real and traceable, was a targeted web-based search across four iterations and one round of reference-list hand-searching, rather than a fully documented native query of PubMed, Embase, Scopus, and Cochrane CENTRAL with institutional database access; a submission-ready version of this review should be supplemented with such a formally documented search to confirm no eligible studies were missed. The heterogeneity of modifying agents, concentrations, liner base materials, and outcome metrics precluded formal statistical meta-analysis, limiting this review to narrative and descriptive quantitative synthesis. Finally, the near-total reliance on a single clinical trial for translational, patient-level evidence means that conclusions regarding clinical antifungal efficacy, and particularly mucosal outcomes, should be considered preliminary pending a larger clinical evidence base.

## CONCLUSIONS

Antimicrobial modification of soft denture liners, whether through silver nanoparticle incorporation, synthetic antifungal agents, or plant-derived compounds, consistently improves antifungal efficacy against Candida albicans relative to conventional, unmodified liners across the available in vitro and limited clinical evidence. Mechanical compatibility varies by agent: nystatin, chlorhexidine diacetate, and ketoconazole are generally well tolerated by liner materials at effective concentrations, while miconazole and itraconazole may compromise tensile strength over time. The evidence base directly addressing inflammatory papillary hyperplasia as a clinical outcome of modified-liner use remains critically underdeveloped, and no statistically pooled estimate of clinical mucosal benefit could be derived from the current literature. Clinicians should interpret the antifungal evidence as a reasonable rationale for considering modified liners in Candida-associated denture stomatitis, informed by agent-specific mechanical data, while recognising that direct evidence of hyperplasia prevention or resolution is not yet available. Adequately powered clinical trials with standardised mucosal and hyperplasia grading, extended follow-up, and head-to-head comparison of modifying agent classes are needed to close this evidence gap.

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**Conflicts of Interest**

The reviewers declare no conflicts of interest.

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