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Candida albicans in the Oral Cavity: A Critical Review of Taxonomy, Virulence Factors, Host Interactions, Diagnosis, and Modern Therapeutic Strategies

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المبيضات البيضاء (Candida albicans) في التجويف الفموي: مراجعة نقدية للتصنيف، وعوامل الضراوة، والتفاعلات مع المضيف، والتشخيص، والاستراتيجيات العلاجية الحديثة

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Abstract

Candida albicans is a prevalent member of the oral mycobiome and the principal cause of oral candidiasis, yet its detection does not by itself establish disease. This review critically integrates fungal taxonomy, oral ecology, virulence, mucosal immunology, diagnostic reasoning, antifungal therapy, and emerging interventions. A targeted structured update of PubMed-indexed and publisher-indexed literature was combined with a supplied bibliographic corpus; mechanistic studies, clinical cohorts, diagnostic evaluations, guidelines, and recent translational evidence were prioritized. The evidence supports a threshold model in which candidiasis emerges from convergence of fungal fitness, ecological disruption, and impaired host containment. Adhesins and morphogenetic circuits enable stable colonization and hyphal invasion; biofilm extracellular matrix and metabolic plasticity promote persistence; and the Ece1-derived toxin candidalysin links hyphal growth to epithelial injury and danger signaling. Protection is site-specific and depends on salivary function, epithelial pattern-recognition, neutrophils, and IL-17-dominant immunity, while bacterial–fungal interactions can either restrain or amplify pathogenicity. Diagnosis remains primarily clinicopathological: microscopy and culture are confirmatory, species identification is useful when treatment failure or epidemiological risk makes it consequential, and molecular or mass-spectrometric methods

improve identification but cannot independently distinguish colonization from infection. Established treatment pairs correction of predisposing factors and oral reservoirs with topical or systemic antifungals selected according to severity, host status, prior azole exposure, species, and—when indicated—susceptibility testing. Biofilm tolerance, efflux, target alteration, and sterol-pathway remodeling complicate recurrent disease. Photodynamic therapy, probiotics, anti-biofilm materials, nanoparticles, vaccines, and host-directed or anti-candidalysin strategies are promising but unevenly mature. Future studies require standardized case definitions, lesion-targeted sampling, clinically anchored fungal-load thresholds, longitudinal multi-omics, and trials that measure recurrence and patient-reported outcomes rather than culture clearance alone.

Keywords: Candida albicans; oral candidiasis; oral mycobiome; biofilm; candidalysin; IL-17; MALDI-TOF MS; antifungal resistance; photodynamic therapy; precision dentistry.

الملخص

تُعد (Candida albicansالمبيضات البيضاء (أحد الأعضاء الشائعة في الميكوبايوم الفموي، كما أنها السبب الرئيس لداء المبيضات الفموي. ومع ذلك، فإن مجرد الكشف عنها لا يُثبت بحد ذاته وجود المرض. تدمج هذه المراجعة بصورة نقدية بين علم تصنيف الفطريات، والبيئة الفموية، وعوامل الضراوة، والمناعة المخاطية، والمنطق التشخيصي، والعلاج المضاد للفطريات، والتدخلات العلاجية الناشئة.

وقد جرى الجمع بين تحديث موجّه ومنظم للأدلة العلمية المفهرسة في PubMed والمصادر المفهرسة لدى الناشرين وبين مجموعة المراجع الببليوغرافية المقدمة، مع إعطاء الأولوية للدراسات الآلية، والدراسات السريرية، وتقييمات الاختبارات التشخيصية، والإرشادات العلاجية، والأدلة الحديثة ذات الصلة بالترجمة من البحث إلى التطبيق السريري.

وتدعم الأدلة نموذجًا عتبيًا لحدوث المرض، بحيث يظهر داء المبيضات الفموي نتيجة تضافر عدة عوامل، تشمل اللياقة الفطرية، واضطراب البيئة الميكروبية، وضعف قدرة المضيف على احتواء الفطر .وتمكّن جزيئات الالتصاق والدوائر المنظمة للتحول المورفولوجي الفطر من الاستعمار المستقر والغزو الخيطي للأنسجة، في حين تسهم المصفوفة خارج الخلوية للأغشية الحيوية والمرونة الأيضية في تعزيز استمرار الفطر ومقاومته للظروف المعادية.

ويربط السم الكانديداليسين(Candidalysin) ، المشتق من بروتين Ece1، بين النمو الخيطي للفطر وإصابة الخلايا الظهارية وتنشيط إشارات الخطر المناعية. وتعتمد الحماية المناعية على الموقع التشريحي، وتشمل دور إفراز اللعاب، والتعرف على الأنماط الجزيئية بواسطة الظهارة، والعدلات، والمناعة السائدة بوساطة .IL-17 كما يمكن للتفاعلات بين البكتيريا والفطريات أن تحد من القدرة الإمراضية أو، على العكس، أن تعززها.

ولا يزال التشخيص يعتمد بصورة أساسية على التقييم السريري والمرضي؛ إذ يمكن استخدام الفحص المجهري والزراعة كوسائل تأكيدية، في حين يكون تحديد النوع الفطري مفيدًا عندما يكون فشل العلاج أو المخاطر الوبائية ذات أهمية سريرية. كما تعمل الطرق الجزيئية وتقنيات مطيافية الكتلة على تحسين عملية تحديد الأنواع، إلا أنها لا تستطيع بمفردها التمييز بين الاستعمار الفطري والعدوى المرضية.

ويرتكز العلاج المعتمد على تصحيح العوامل المهيئة للمرض والسيطرة على خزانات الفطر الفموية، بالتزامن مع استخدام مضادات الفطريات الموضعية أو الجهازية التي يتم اختيارها وفقًا لشدة المرض، وحالة المضيف، والتعرض السابق لمضادات الآزول، ونوعCandida ، وعند الحاجة، نتائج اختبار الحساسية.

وتزيد قدرة الأغشية الحيوية على تحمل مضادات الفطريات، وآليات طرد الدواء، وتغير الأهداف الدوائية، وإعادة تشكيل مسار الستيرول من تعقيد حالات المرض المتكرر. وتُعد العلاج الضوئي الديناميكي، والبروبيوتيك، والمواد المضادة للأغشية الحيوية، والجسيمات النانوية، واللقاحات، والاستراتيجيات الموجهة للمضيف، والاستراتيجيات المضادة للكانديداليسين من التدخلات الواعدة، إلا أن مستوى نضج الأدلة الخاصة بها لا يزال متفاوتًا.
وتحتاج الدراسات المستقبلية إلى تعريفات موحدة للحالات المرضية، وأخذ عينات موجهًا نحو الآفات، وحدود كمية للحمل الفطري مرتبطة بالنتائج السريرية، ودراسات متعددة الأوميكس طولية، بالإضافة إلى تجارب سريرية تقيس معدلات النكس ونتائج المرضى المبلغ عنها ذاتيًا بدلًا من الاعتماد على التخلص من الفطر بالزراعة وحدها.

الكلمات المفتاحية: داء المبيضات الفموي؛ الميكوبايوم الفموي؛ الأغشية الحيوية؛ الكانديداليسين؛ IL-17؛ مطيافية الكتلة MALDI-TOF MS؛ مقاومة مضادات الفطريات؛ العلاج الضوئي الديناميكي؛ طب الأسنان الدقيق.

1. Introduction

Oral candidiasis is often described as a simple overgrowth infection, but that shorthand obscures a more informative biological problem: C. albicans is simultaneously a normal colonizer, an ecosystem engineer, and a context-dependent pathogen. The World Health Organization places C. albicans in the critical-priority group of fungal pathogens because of its health impact, antifungal resistance, and research needs, while emphasizing that mucosal candidiasis differs fundamentally from invasive disease [1,2]. In the mouth, the practical challenge is not merely to detect the organism but to determine when fungal activity has crossed from carriage into tissue-associated disease.

The oral cavity presents multiple microhabitats—tongue dorsum, keratinized and non-keratinized mucosa, saliva, dental plaque, carious dentine, and prosthetic or orthodontic surfaces. These niches vary in oxygen tension, pH, shear, nutrient availability, and microbial partners. Saliva continuously disperses organisms while supplying mucins, antimicrobial peptides, immunoglobulins, and nutrients. Consequently, fungal burden is dynamic, and a sample from saliva does not necessarily represent activity at an erythematous palatal lesion or a non-wipeable plaque. This spatial mismatch explains part of the wide variation in reported carriage and disease estimates [6–8].

The supplied source document appropriately emphasized taxonomy, colonization, classic virulence factors, culture media, germ-tube testing, molecular identification, orthodontic appliances, and regional evidence from Libya. However, its thesis-specific aims and extensive pomegranate section did not match the new review question. The present manuscript therefore retains the scientifically relevant foundation but reconstructs it around five linked questions: how C. albicans should be classified and named; how it transitions to pathogenicity; how host and microbiome responses contain or promote it; how clinicians should interpret tests; and where established and emerging therapies fit within an evidence hierarchy.

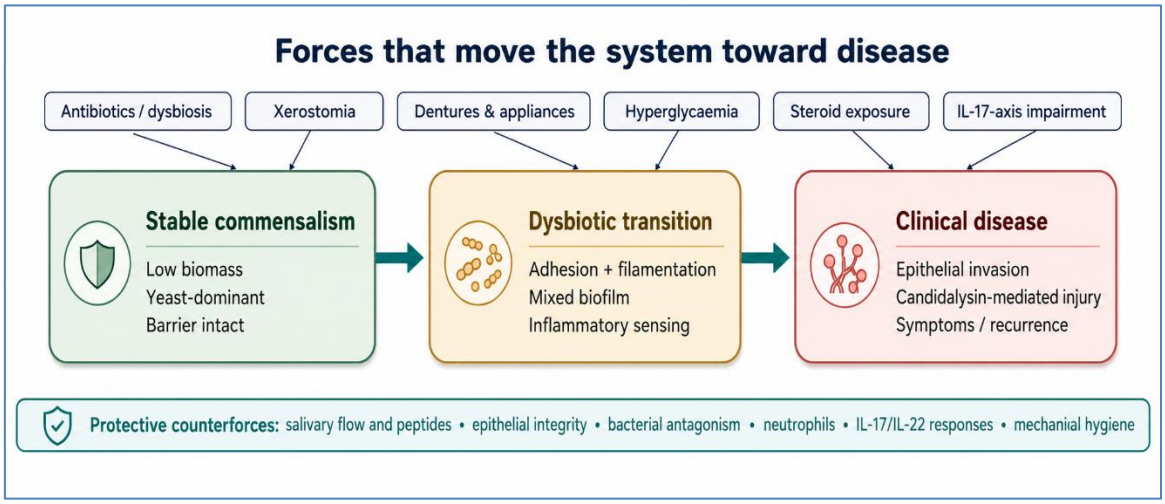

Figure 1. *Conceptual commensal-to-pathogen continuum in the oral cavity. The figure is a mechanistic synthesis, not a quantitative risk model. Disease emerges when ecological and host disruptions permit fungal biomass, filamentation, biofilm formation, and tissue injury to exceed protective containment.*

2. Review approach and interpretive framework

This article is a critical narrative review with a targeted structured update, not a registered systematic review or meta-analysis. The starting corpus was the supplied Chapter 1, Chapter 2, and reference list. An update search was then performed through 22 July 2026 using combinations of Candida albicans, oral candidiasis, taxonomy, nomenclature, oral biofilm, candidalysin, epithelial response, IL-17, oral microbiome, diagnosis, PCR, MALDI-TOF, antifungal susceptibility, photodynamic therapy, probiotics, vaccines, and resistance. Priority was given to primary mechanistic studies, clinical cohorts, diagnostic evaluations, current authoritative guidance, and recent systematic syntheses when they were necessary to appraise treatment evidence.

Evidence was interpreted by question rather than pooled across incompatible designs. Murine and organotypic models were used to infer mechanism, not human effect size. Culture and molecular studies were assessed in relation to their sampling frame and clinical phenotype. Treatment claims were graded conceptually as established, adjunctive, translational, or experimental. No PRISMA flow diagram or numerical study count is reported because the search was targeted and iterative; presenting such counts would imply exhaustiveness that was not achieved. This transparency is important in a field where terminology, taxonomic names, susceptibility standards, and clinical endpoints continue to evolve.

Three interpretive rules guide the review. First, association is not equivalent to causation: a higher oral fungal load in diabetes, denture use, or immunosuppression can reflect both a causal contribution and a marker of disrupted ecology. Second, in vitro susceptibility does not fully predict biofilm response or mucosal outcome. Third, eradication of C. albicans is neither feasible nor desirable in most hosts; the therapeutic goal is restoration of a stable, asymptomatic ecosystem while preventing tissue damage and recurrence.

3. Taxonomy, nomenclature, and biological identity

3.1 Phylogenetic placement

C. albicans is an ascomycetous budding yeast in the subphylum Saccharomycotina, class Saccharomycetes, order Saccharomycetales, and family Debaryomycetaceae. It belongs to the

CUG-Ser1 clade, whose members translate the CUG codon predominantly as serine rather than leucine. Comparative genomics demonstrates that pathogenicity is not a single innovation but a product of lineage-specific expansions, cell-surface diversification, regulatory plasticity, and host adaptation [9–11]. C. albicans remains the accepted name; this stability contrasts with clinically important former Candida species that have moved to Nakaseomyces, Pichia, Meyerozyma, and other genera.

The historical genus Candida was polyphyletic: morphologically similar yeasts without an observed sexual state were grouped together even when phylogenetically distant. Modern nomenclature seeks one name for one fungus and increasingly reflects genome-scale relationships. That creates a clinical communication problem. A laboratory may report Nakaseomyces glabratus while a guideline or clinician still uses Candida glabrata. Dual reporting of the current name followed by the familiar synonym is therefore safer during the transition, particularly where intrinsic or frequent resistance phenotypes differ by species [9,10].

Table 1. Taxonomic and clinically relevant nomenclature in oral Candida work

Organism	Current taxonomic point	Oral relevance	Reporting implication
Candida albicans	Name retained; CUG-Ser1 clade	Dominant oral pathogenic yeast; yeast–hypha plasticity	Report directly; distinguish infection from carriage
Candida dubliniensis	Closely related to C. albicans	May be recovered in immunocompromised hosts; germ-tube positive	Use molecular/MALDI confirmation when distinction matters
Candida tropicalis	Name retained	Oral colonizer and opportunistic pathogen	Species identification matters in high-risk or refractory disease
Candida parapsilosis complex	Species complex	Occasional oral carriage; device and hand-associated epidemiology	Complex-level reports may conceal susceptibility differences
Nakaseomyces glabratus	Formerly C. glabrata	Yeast-form oral opportunist; reduced azole susceptibility is common	Dual-name reporting improves recognition
Pichia kudriavzevii	Formerly C. krusei	Less frequent oral isolate	Intrinsic fluconazole resistance is clinically important
Meyerozyma guilliermondii	Formerly C. guilliermondii	Uncommon oral isolate	Confirm identification; avoid assuming C. albicans behavior

Taxonomic names should be checked against the laboratory's current validated database. Legacy names remain common in clinical guidance and are shown to reduce communication error [9,10].

3.2 Morphological and phenotypic plasticity

C. albicans occupies several cell states, including budding yeast, pseudohyphae, true hyphae, white and opaque states, chlamydospores under specific conditions, and gastrointestinally adapted states. These are not merely microscopic labels. Yeast cells disseminate efficiently and may favor commensal persistence, whereas hyphae express a distinct surface and secretory program that promotes tissue penetration, biofilm architecture, and damage. Nevertheless, the binary claim that yeast equals commensal and hypha equals pathogen is too simple: hyphae can occur without disease, and pathogenicity depends on tissue context, fungal load, and immune state [12–15].

4. Oral ecology: from carriage to candidiasis

Oral carriage varies with sampling method, age, dentition, geography, medication exposure, salivary function, and the definition of a positive sample. This heterogeneity makes universal prevalence percentages misleading. Concentrated oral rinse surveys usually recover more yeast than a single swab; lesion-targeted sampling improves anatomical specificity; molecular assays detect non-viable or low-abundance DNA that culture may miss. The clinically useful distinction is therefore not carrier versus non-carrier but stable low-impact colonization versus a symptomatic, tissue-associated state.

Local risk factors change the physical niche. Dentures and removable orthodontic appliances provide protected, irregular surfaces that support adherent mixed biofilms and reduce shear. Poor fit causes microtrauma, while overnight wear and inadequate decontamination sustain reinoculation. Xerostomia reduces clearance and salivary antimicrobial activity. Inhaled corticosteroids create local immune suppression when mouth rinsing and device technique are suboptimal. High fermentable-carbohydrate exposure and low pH can favor acid-tolerant consortia, although diet alone should not be presented as a sufficient cause.

Systemic factors act through different mechanisms. Hyperglycaemia can increase salivary glucose, impair neutrophil performance, and associate with xerostomia. Broad-spectrum antibiotics remove bacterial competitors. Advanced HIV infection, chemotherapy, transplantation, corticosteroids, primary IL-17-pathway defects, extremes of age, nutritional deficiency, and head-and-neck radiotherapy alter immune containment or mucosal integrity. The strongest inference arises when a plausible mechanism, temporal exposure, compatible lesion, and response to correction converge; cross-sectional carriage studies alone cannot establish causality [2,6–8].

Table 2. Predisposing factors and mechanistic links to oral candidiasis.

Domain	Examples	Mechanistic effect	Actionable assessment
Salivary	Xerostomia; Sjögren syndrome; radiotherapy; anticholinergic burden	Reduced clearance, buffering, mucins, and antimicrobial proteins	Review medications; measure/estimate flow; manage dry mouth
Iatrogenic	Antibiotics; inhaled/systemic steroids; chemotherapy	Loss of bacterial restraint; local/systemic immune suppression	Confirm indication, duration, inhaler technique, and mouth rinsing

Metabolic	Poorly controlled diabetes; malnutrition	Altered nutrients, epithelial repair, and phagocyte function	Assess glycaemic control and nutritional status
Mechanical	Dentures; removable appliances; trauma; overnight wear	Biofilm reservoir, sheltered surface, microtrauma	Inspect fit and hygiene; sample mucosa and device when needed
Immune	Advanced HIV; neutropenia; IL-17-axis disorders; immunosuppressants	Impaired epithelial/neutrophil containment	Risk-stratify; lower threshold for species identification and follow-up
Behavioral	Smoking; high-frequency sugar exposure; poor hygiene	Ecological stress and persistent plaque	Use non-stigmatizing prevention and cessation support

Risk factors are neither necessary nor sufficient individually. Their effect depends on intensity, duration, co-exposures, and host response.

5. Virulence mechanisms

5.1 Adhesion and invasion

Adhesion establishes residence on epithelium, enamel-associated plaque, acrylic, silicone, and orthodontic polymers. The agglutinin-like sequence (Als) family, Hwp1, Eap1, and other cell-wall proteins bind host proteins, cadherins, abiotic surfaces, and microbial partners. Als3 and Ssa1 can promote induced endocytosis by host cells, whereas extending hyphae also penetrate actively. In oral epithelia both routes may operate, and their relative contribution changes with cell type and model architecture [12,20]. Adhesion is therefore both a virulence function and a commensal requirement; pathogenic interpretation depends on what follows it.

5.2 Morphogenesis and candidalysin

Temperature, neutral-to-alkaline pH, serum signals, N-acetylglucosamine, carbon dioxide, amino acids, hypoxia, and nutrient status feed into overlapping regulators including Efg1, Cph1, Nrg1, Brg1, and Ume6. Hyphal development reorganizes the surface proteome and induces ECE1. Proteolytic processing of Ece1 releases candidalysin, a 31-amino-acid amphipathic peptide that damages epithelial membranes and activates danger signaling. Deletion and complementation experiments established candidalysin as a critical driver of mucosal damage rather than a passive correlate of filamentation [18]. Biophysical work subsequently showed that the peptide can polymerize and form membrane pores [19].

Candidalysin illustrates the duality of virulence. It injures epithelial cells and facilitates invasion, yet the same damage signal activates EGFR/MAPK pathways, cytokine production, neutrophil recruitment, and type-17 immunity. Excessive or poorly regulated inflammation can contribute to symptoms, while a competent response limits fungal expansion. Therapeutic blockade of candidalysin therefore requires caution: reducing tissue damage without weakening protective alarm signaling is a more demanding objective than simple neutralization.

5.3 Biofilm formation

Biofilm development proceeds through attachment, proliferation, filamentation, extracellular-matrix accumulation, maturation, and dispersal. The mature matrix contains polysaccharides, proteins, lipids, and extracellular DNA. It restricts drug penetration, sequesters some agents,

supports metabolically heterogeneous cells, and creates microenvironments of hypoxia and nutrient limitation. Persister-like subpopulations and stress responses further reduce killing. Cells released during dispersion may be transcriptionally primed for colonization, connecting a local reservoir to recurrence [16,17].

Oral biofilms are rarely monospecies. C. albicans can provide a scaffold for streptococci; streptococcal glucosyltransferases and fungal adhesins stabilize coaggregation; lactate and oxygen consumption reshape local metabolism. Conversely, bacterial products can suppress filamentation. Enterococcus faecalis EntV, for example, inhibits hyphal morphogenesis and biofilm virulence in experimental systems [27–31]. These findings caution against labelling the entire bacterial microbiome as either protective or pathogenic. Interaction is strain-, site-, nutrient-, and time-dependent.

5.4 Hydrolytic enzymes, nutrient acquisition, and stress adaptation

Secreted aspartyl proteases, phospholipases, lipases, and other enzymes degrade host substrates and remodel the fungal surface. Their contribution is context-dependent and partly redundant, which explains why high enzyme activity in vitro does not always predict mucosal severity. Iron, zinc, and carbon acquisition systems support persistence in nutrient-limited niches. C. albicans can switch among glucose, lactate, amino acids, and alternative carbon sources, adapt to acidic or alkaline pH, resist reactive oxygen species, and remodel its cell wall. These responses link metabolism to immune evasion because carbon source and stress alter β-glucan exposure and phagocyte recognition.

5.5 Phenotypic heterogeneity and immune evasion

Within a genetically similar population, cells differ in growth rate, morphology, stress state, and drug tolerance. White–opaque switching alters mating competence, antigen presentation, and host interaction. The fungal wall masks or exposes β-glucan dynamically; complement regulators can be recruited to the surface; antioxidant systems counter phagocyte-derived reactive oxygen species; and hyphae can damage or escape phagocytes. These strategies do not render the organism invisible. Rather, they shift the timing and intensity of recognition, which can determine whether containment occurs before tissue injury.

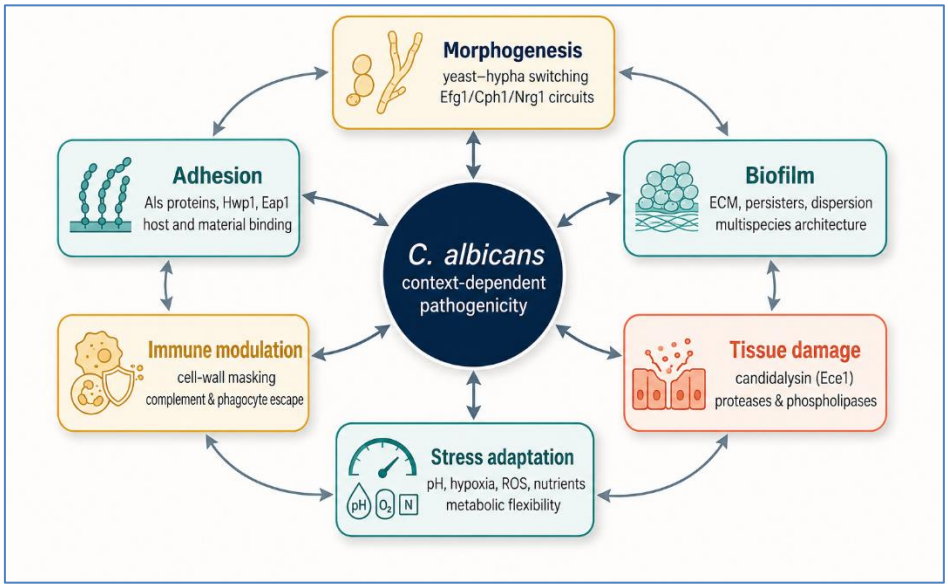

Figure 2. *Integrated virulence network of C. albicans. Bidirectional arrows emphasize that adhesion, morphogenesis, biofilm, damage, stress adaptation, and immune modulation are mutually reinforcing. Gene examples are illustrative, not exhaustive [12–19].*

Table 3. Virulence modules, evidence, and critical interpretation

Module	Representative components	Functional consequence	Critical caveat
Adhesion	Als1/Als3; Hwp1; Eap1; Ssa1	Binding to epithelium, proteins, devices, and bacteria	Essential for colonization as well as disease
Morphogenesis	Efg1/Cph1; Nrg1; Brg1; Ume6	Hyphal invasion, surface remodeling, tissue penetration	Hyphae are neither necessary nor sufficient for every phenotype
Candidalysin	Ece1-derived peptide	Membrane injury and epithelial danger signaling	Damage and protective immune activation are coupled
Biofilm	Bcr1 network; ECM; persister-like cells	Reservoir formation, tolerance, and dispersal	In vitro biomass does not directly equal clinical resistance
Hydrolytic enzymes	Sap proteins; phospholipases; lipases	Substrate degradation and invasion support	Families are redundant and expression is niche-specific
Metabolic/stress adaptation	pH sensing; oxidative stress; alternative carbon use	Survival under saliva, hypoxia, nutrient, and immune stress	Laboratory media can misrepresent oral conditions
Immune modulation	β-glucan masking; complement binding; antioxidant defenses	Delayed recognition and phagocyte survival	Often increases fitness rather than causing injury directly

Strongest causal evidence comes from genetically controlled loss- and gain-of-function experiments in relevant epithelial or animal models; clinical association alone is weaker.

6. Host–fungus–microbiome interactions

6.1 Epithelial sensing and barrier responses

Oral keratinocytes are active immune sentinels. They recognize fungal cell-wall components and damage through pattern-recognition receptors and receptor-kinase networks, including dectin-associated pathways and EphA2. EphA2 recognizes exposed fungal β-glucan and contributes to epithelial signaling; it also participates in neutrophil antifungal function in experimental oropharyngeal infection [21,22]. The epithelial response is graded: low-level yeast contact can be tolerated, whereas sustained hyphal growth and candidalysin activate MAPK pathways, chemokines, antimicrobial peptides, and alarmins. This discrimination helps explain why colonization does not cause chronic inflammation in most carriers.

6.2 Neutrophils and type-17 immunity

Neutrophils restrict hyphae through phagocytosis, oxidative and non-oxidative mechanisms, extracellular traps, and coordinated recruitment. At the oral mucosa, IL-17 receptor signaling is central. Mice deficient in IL-17RA or upstream IL-23 pathways develop greater susceptibility to oropharyngeal candidiasis, while human disorders affecting IL-17 production or signaling predispose to chronic mucocutaneous candidiasis [23,24]. IL-17 drives chemokines, granulopoiesis, β-defensins, and epithelial repair. The pathway is therefore a mechanistic bridge between clinical immunodeficiency phenotypes and experimental oral infection.

IL-22 supports barrier integrity and antimicrobial programs, but its role is not interchangeable with IL-17. Emerging work suggests that non-canonical IL-22-receptor signaling and epithelial metabolic memory may reshape later responses to mucosal fungal exposure. These findings are

biologically important but not yet a basis for routine host-directed treatment. Therapeutic amplification of type-17 pathways could improve clearance while also risking inflammatory injury; patient selection and tissue-specific delivery will be essential.

6.3 Saliva, IgA, and innate soluble defenses

Saliva imposes shear and supplies histatins, defensins, lysozyme, lactoferrin, peroxidases, mucins, and secretory IgA. Histatin 5 has direct candidacidal activity but is sensitive to proteolysis, ionic conditions, and binding within oral biofilms. Secretory IgA agglutinates organisms and limits epithelial attachment; experimental evidence indicates that mucosal IgA helps prevent commensal C. albicans from driving dysbiosis [25]. Reduced flow therefore removes several defenses simultaneously, which is why xerostomia is more informative than any single salivary analyte.

6.4 Cross-kingdom ecology

Streptococcus oralis, S. gordonii, S. mutans, Actinomyces, Fusobacterium, Enterococcus, lactobacilli, and anaerobes can alter C. albicans adhesion, morphology, metabolism, and immune effects. S. oralis–C. albicans biofilms exhibit enhanced mucosal pathogenicity in organotypic and animal models, including disruption of epithelial junctions [27–30]. In contrast, lactobacillus-derived acids or metabolites and Enterococcus EntV can suppress fungal growth or filamentation. The direction of effect is not taxonomically fixed: a 'beneficial' genus may behave differently by strain and niche.

A 2026 longitudinal pilot study of primary oral candidiasis found residual bacterial-community shifts after clinical antifungal response, but the cohort included only 16 patients, seven follow-up samples, and seven controls [37]. The study is hypothesis-generating rather than definitive. It nevertheless exposes a clinically relevant possibility: symptom resolution and fungal suppression may not immediately restore ecosystem resilience, helping to explain recurrence. Future work should combine fungal, bacterial, metabolite, salivary, and host-response measurements at lesion and control sites.

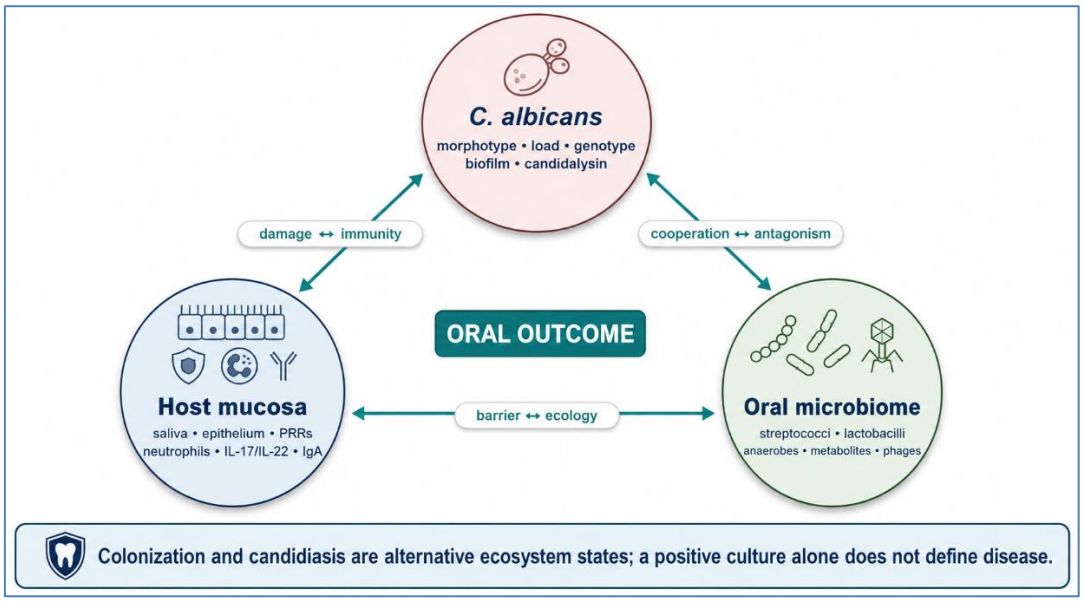

Figure 3. *The host–fungus–microbiome triad. Oral outcome is produced by reciprocal interactions among fungal state, mucosal defense, and bacterial ecology. The model explains why the same C. albicans strain can remain commensal in one host or niche and cause disease in another [21–31].*

7. Clinical phenotypes and differential diagnosis

Pseudomembranous candidiasis presents with creamy white plaques that can usually be wiped away, leaving erythematous or bleeding mucosa. Erythematous candidiasis may affect the palate or dorsal tongue and can follow antibiotics or inhaled steroids. Denture stomatitis typically appears as erythema beneath a prosthesis and may be classified by distribution, although visible inflammation reflects a mixed mechanical, microbial, and host process. Angular cheilitis often involves Candida with Staphylococcus aureus and is promoted by maceration, reduced vertical dimension, nutritional deficiency, or saliva pooling [8,40,41].

Chronic hyperplastic candidiasis is clinically important because a non-wipeable white plaque may contain epithelial dysplasia or mimic leukoplakia. Candida can colonize pre-existing lesions, so fungal detection cannot establish that the lesion is primarily candidal. Biopsy is appropriate when a plaque is persistent, indurated, non-wipeable, atypical, or unresponsive to initial management. Median rhomboid glossitis and linear gingival erythema require contextual interpretation rather than automatic antifungal labeling.

Symptoms include burning, soreness, altered taste, dysgeusia, discomfort with spicy or acidic foods, and occasionally dysphagia. Dysphagia or odynophagia in an immunocompromised patient raises concern for oesophageal involvement, which is outside the scope of purely local treatment. Important mimics include coated tongue, frictional keratosis, lichen planus, leukoplakia, oral hairy leukoplakia, geographic tongue, mucous-membrane pemphigoid, contact reactions, aphthous disease, nutritional glossitis, and squamous neoplasia.

Table 4. Major oral presentations, sampling strategy, and differential diagnosis

Phenotype	Typical findings	Best confirmatory sample	Key mimics / caution
Pseudomembranous	Wipeable white plaques; erythematous base	Firm swab or scraping from active plaque/base	Coated tongue; debris; chemical burn
Erythematous	Red, sore mucosa; palate or tongue	Lesion-targeted swab/scrape	Erythroplakia; trauma; nutritional or drug-related glossitis
Denture stomatitis	Erythema matching denture-bearing area	Palatal mucosa plus denture surface when recurrence matters	Contact reaction; trauma; poor fit; bacterial biofilm
Angular cheilitis	Fissuring and maceration at commissures	Swab fissure; consider bacterial culture	S. aureus coinfection; iron/B-vitamin deficiency; irritant dermatitis
Chronic hyperplastic	Persistent non-wipeable white plaque	Biopsy with PAS/GMS ± culture	Leukoplakia and dysplasia; do not rely on antifungal response alone
Oesophageal concern	Odynophagia or dysphagia in high-risk host	Clinical pathway beyond oral swab; endoscopic assessment when indicated	Reflux, pill injury, viral oesophagitis, malignancy

The presence of Candida in a specimen supports but does not independently prove that it is the cause of a lesion.

8. Diagnosis: from phenotype to clinically meaningful identification

8.1 Clinical diagnosis and sampling

For a typical first episode in an immunocompetent patient, diagnosis is often clinical. Laboratory confirmation becomes more valuable when the lesion is atypical, recurrent, severe, associated with significant immunosuppression, or unresponsive to appropriate therapy. Sampling should occur before a major change in antifungal exposure when feasible. A swab is convenient, scraping yields material for direct microscopy, imprint culture maps a lesion, concentrated oral rinse estimates broader carriage, and biopsy evaluates tissue invasion or dysplasia. The method must match the question [32].

Pre-analytical variation is a major source of error. Eating, toothbrushing, mouthwash, denture removal, recent antifungal use, collection pressure, transport delay, and sampled site all influence yield. Reports should specify the site and method. Quantitative colony counts can support comparison within a protocol but lack a universal diagnostic threshold because background carriage and sampling recovery vary. The same caution applies to qPCR copy number.

8.2 Microscopy, culture, and phenotypic identification

Direct KOH, Gram stain, or fluorescent stains can rapidly demonstrate budding yeasts, pseudohyphae, or hyphae. Finding tissue-associated hyphae in a compatible lesion is more persuasive than recovering sparse yeast by culture. Culture on Sabouraud agar increases sensitivity and allows further identification; chromogenic media can presumptively separate common species and reveal mixed cultures. Germ-tube formation is a rapid presumptive test for C. albicans but also occurs in C. dubliniensis, and atypical isolates can mislead. Cornmeal morphology and carbohydrate assimilation are now mainly useful where more definitive methods are unavailable.

8.3 MALDI-TOF MS, sequencing, and molecular tests

MALDI-TOF mass spectrometry identifies cultured yeasts rapidly when the reference database contains high-quality spectra. In a Senegalese evaluation spanning oral and other clinical samples, MALDI-TOF identified 214 of 218 recovered Candida isolates to species level, but performance was assessed after culture and depended on the database [34]. It therefore shortens identification, not specimen-to-answer time. Closely related or newly renamed species may require database updates or sequence confirmation.

PCR and qPCR can detect and differentiate Candida directly from oral rinse, swabs, or tissue, while ITS or D1/D2 sequencing resolves uncommon isolates. These methods are sensitive, but DNA from non-viable cells and asymptomatic carriage reduces clinical specificity. A 2023 tissue study demonstrated species-specific real-time PCR in oral biopsies, illustrating analytical feasibility rather than a stand-alone candidiasis test. Amplicon or shotgun metagenomics can characterize the mycobiome, yet extraction bias, low fungal biomass, database limitations, and lack of validated clinical thresholds currently restrict routine use [33,36,37].

8.4 Susceptibility testing

Antifungal susceptibility testing is most useful for refractory or recurrent disease, prior azole exposure, immunocompromised hosts, non-albicans species, or epidemiological concern. CLSI and EUCAST broth microdilution provide standardized reference approaches, but breakpoints are species–drug specific and are absent for some oral topical agents [43,44]. Biofilm susceptibility is not captured by standard planktonic MICs. A result should be interpreted with species, drug exposure, adherence, lesion reservoir, and clinical response rather than treated as a binary explanation of failure.

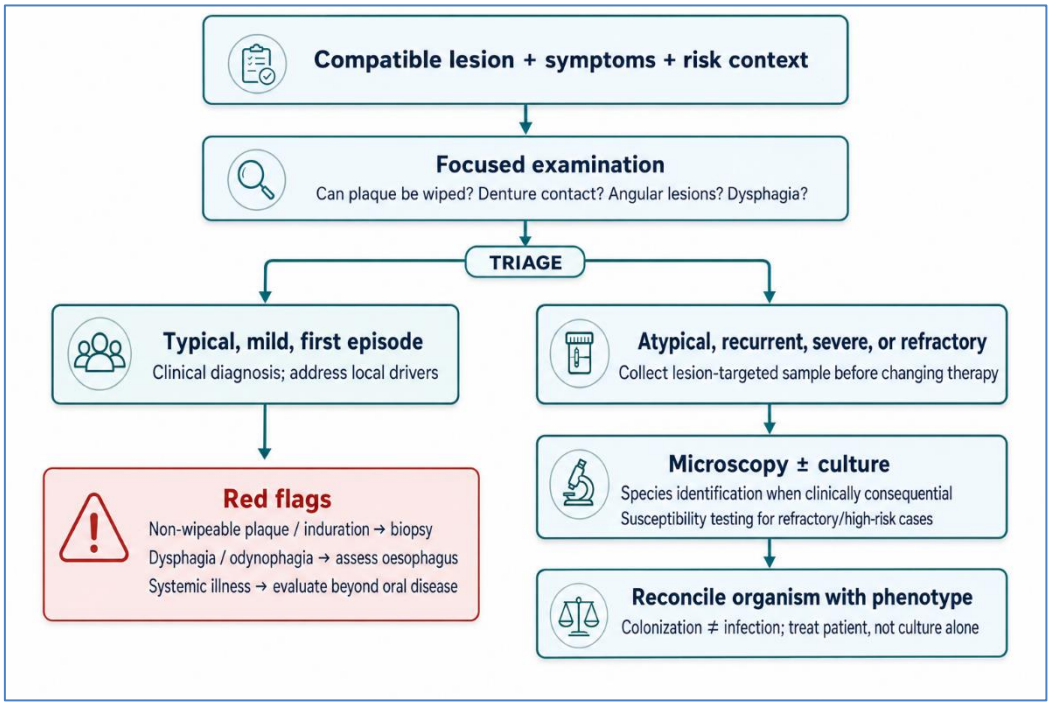

Figure 4. *Diagnostic workflow for suspected oral candidiasis. The algorithm prioritizes clinical phenotype and red flags, then uses microscopy, culture, identification, and susceptibility testing when they can change management [4,5,32,42].*

Table 5. Diagnostic modalities for oral Candida: performance logic and appropriate use

Method	Approximate time	Strength	Limitation	Best use
Clinical examination	Immediate	Integrates lesion, symptoms, and risk	Observer-dependent; mimics overlap	Typical first episode; triage and red flags
KOH / Gram / PAS smear	Minutes–hours	Shows fungal morphology at lesion	Sensitivity depends on sample and reader	Rapid confirmation; hyphae support tissue activity
Culture ± chromogenic agar	1–3 days	Viable isolate; mixed species; enables AST	Carriage reduces specificity; some species look similar	Atypical, recurrent, refractory, or high-risk disease
Germ-tube / biochemical panel	Hours–1 day	Low-cost presumptive identification	C. dubliniensis overlap; lower resolution	Resource-limited workflows with confirmatory plan
MALDI-TOF MS	Minutes after growth	Fast species identification from colony	Requires culture, instrument, and database	Clinically consequential species-level identification

PCR / qPCR	Hours	Sensitive; direct detection and quantitation	Detects carriage/non-viable DNA; thresholds unstandardized	Selected difficult specimens; research; confirm unusual species
ITS/D1-D2 sequencing	1–3 days	High taxonomic resolution	Cost, contamination, and reference-quality dependence	Discordant or uncommon isolates
Biopsy + histopathology	Days	Assesses invasion, dysplasia, and mimics	Invasive; focal sampling	Persistent non-wipeable or suspicious lesions

Times are workflow-dependent and exclude transport or batching. AST = antifungal susceptibility testing.

Table 6. Selected empirical anchors and what they do—and do not—show

Study	Design / sample	Key observation	Interpretive limit
Moyes et al., 2016 [18]	Genetic, epithelial, and mucosal infection models	Ece1-derived candidalysin is causally required for major mucosal damage	Mechanistic effect size is model-dependent
Sow et al., 2015 [34]	734 clinical specimens; 218 Candida isolates	MALDI-TOF identified 214/218 isolates to species level after culture	Mixed specimen types; database and laboratory dependent
Alkhars et al., 2023 [39]	114 C. albicans isolates from mother–infant dyads	MIC ranges: nystatin 0.25–8, fluconazole 0.25–1, caspofungin 0.016–0.25 µg/mL	Small cohort; no validated nystatin clinical breakpoint
Azizan et al., 2026 [37]	16 cases, 7 follow-ups, 7 controls	Residual bacterial dysbiosis after clinical antifungal response	Exploratory sample; causality and recurrence unproven
Haghani et al., 2026 [38]	270 patients with β-thalassaemia major	17 oral candidiasis and 22 colonization cases; non-albicans species were clinically relevant	Single high-risk population; not general prevalence

Values are retained to show the scale and constraints of representative primary studies. They should not be pooled across incompatible populations or methods.

9. Therapeutic perspectives

9.1 Correct the ecosystem and the reservoir

Successful management begins with confirmation of the phenotype and correction of drivers. Dentures and removable appliances should be mechanically cleaned, disinfected with a material-compatible method, removed overnight when clinically appropriate, and assessed for fit. Oral hygiene, tongue cleaning, salivary management, inhaler technique and post-dose

rinsing, glycaemic control, nutrition, smoking cessation, and review of unnecessary antibiotics or corticosteroids reduce recurrence. Treating mucosa while leaving a contaminated prosthesis unchanged invites reinoculation.

9.2 Established antifungals

Topical agents such as nystatin, clotrimazole, or miconazole are commonly used for limited mild disease because systemic exposure is low. Contact time, dosing frequency, sugar content, denture reservoirs, and adherence strongly influence effectiveness. Miconazole has clinically important drug interactions, including with warfarin. Fluconazole is the standard systemic option for appropriately selected moderate-to-severe oropharyngeal candidiasis, but pregnancy, hepatic risk, QT effects, interactions, prior exposure, and species susceptibility must be considered. Current HIV opportunistic-infection guidance continues to recommend fluconazole for oropharyngeal candidiasis, while IDSA guidance provides alternatives for refractory disease [4,5].

This review is not a prescribing guideline. Regimens should be checked against the patient's age, pregnancy status, renal and hepatic function, interacting medicines, immune state, lesion severity, and current local recommendations. Echinocandins and intravenous amphotericin B are not routine solutions for uncomplicated oral disease; they are reserved for specific refractory or systemic contexts. Repeated empiric azole courses without diagnostic reassessment can select less susceptible organisms and delay recognition of a mimic.

Table 7. Antifungal options and stewardship considerations

Class / example	Mechanism	Oral role	Important limitations
Polyene: nystatin	Binds ergosterol and disrupts membrane	Topical option for mild localized disease	Frequent dosing/contact time; formulation acceptability; no robust species-specific breakpoints
Imidazole: clotrimazole / miconazole	Inhibits ergosterol synthesis	Topical troche or mucoadhesive/oral formulation where available	Interactions; formulation availability; adherence
Triazole: fluconazole	Inhibits lanosterol 14α-demethylase (Erg11)	Systemic standard for appropriate moderate–severe OPC	Resistance, interactions, pregnancy considerations, hepatic/QT risk
Other triazoles	Ergosterol synthesis inhibition	Selected fluconazole-refractory disease	Cost, interactions, absorption/formulation, stewardship
Echinocandins	Inhibit β-1,3-glucan synthase	Parenteral rescue in selected refractory/systemic contexts	Not convenient for localized disease; biofilm and species context
Amphotericin B	Polyene membrane disruption	Selected refractory or systemic settings	Toxicity for IV use; oral suspension availability varies

OPC = oropharyngeal candidiasis. Detailed dose and duration should follow current patient-specific guidance [4,5].

9.3 Resistance and tolerance

Azole resistance can arise through ERG11 mutation or overexpression, activation of transcriptional regulators such as Tac1 or Mrr1, increased Cdr1/Cdr2 or Mdr1 efflux, altered sterol flux, aneuploidy, and stress-response adaptation. Polyene resistance is less common and may involve reduced or altered ergosterol. Echinocandin resistance is associated mainly with hotspot mutations in FKS genes. Biofilm-associated recalcitrance is broader than inherited resistance: matrix sequestration, slow growth, persister-like cells, hypoxia, and stress pathways create tolerance even when planktonic MICs appear susceptible [39,45–47].

The primary clinical response to suspected resistance should be diagnostic discipline. Confirm exposure and adherence; inspect dentures and other reservoirs; repeat lesion-targeted sampling; identify the species; evaluate for non-infectious mimics or deeper disease; and request standardized susceptibility testing when it can guide therapy. A longitudinal mother–infant study found changing MICs in a subset of oral isolates, but its sample was small and the results are not population resistance estimates [39]. This distinction is visualized in Figure 5.

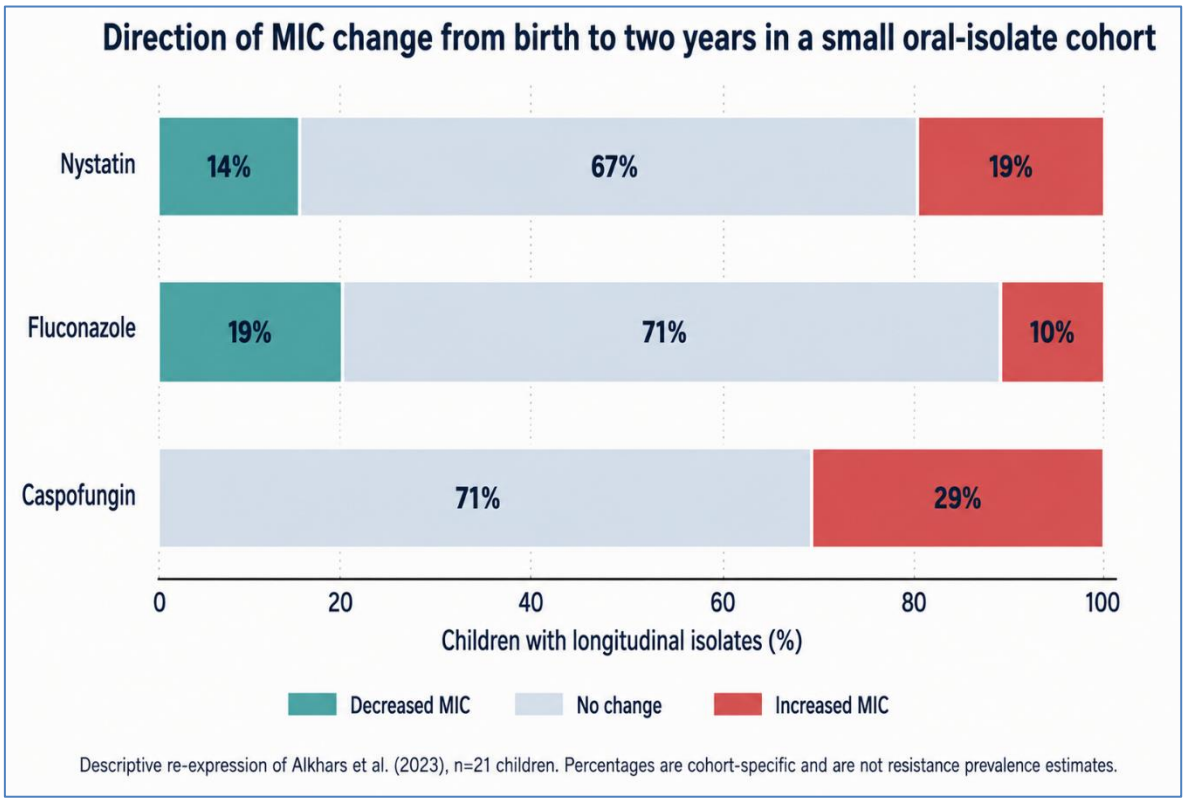

Figure 5. *Longitudinal direction of MIC change in 21 children with serial oral C. albicans isolates. Percentages are a descriptive re-expression of Alkhars et al. [39]; 'no change' is the remainder after reported increases and decreases. The figure illustrates within-host variability and must not be interpreted as resistance prevalence.*

Table 8. Mechanisms of reduced antifungal response

Mechanism	Typical association	How it affects response	Clinical implication
ERG11 alteration / overexpression	Azoles	Reduced target binding or increased target abundance	Species identification and MIC may guide alternative therapy
CDR1/CDR2 or MDR1 efflux	Azoles; multidrug effects	Lower intracellular drug exposure	Repeated azole exposure can select resistant subpopulations
Sterol-pathway remodeling	Azoles / polyenes	Changes target pathway or ergosterol abundance	Cross-resistance patterns may be complex
FKS hotspot mutation	Echinocandins	Reduced glucan-synthase inhibition	Use standardized species-specific interpretation
Biofilm matrix	Multiple classes	Sequestration, diffusion limitation, protected niches	Remove/decontaminate devices; planktonic MIC may underestimate recalcitrance
Persister-like and stress states	Multiple classes	Phenotypic survival without stable high MIC	Recurrence may occur despite apparent susceptibility
Wrong diagnosis or reservoir	All therapies	Apparent failure unrelated to microbial resistance	Reassess phenotype, adherence, device, and differential diagnosis first

Resistance is heritable reduced susceptibility; tolerance and persistence describe survival dynamics that may occur without a resistant MIC.

10. Emerging and adjunctive therapies

10.1 Photodynamic therapy

Antimicrobial photodynamic therapy combines a photosensitizer, light of an appropriate wavelength, and oxygen to generate reactive species. Clinical studies in denture stomatitis and oral candidiasis suggest that photodynamic therapy can reduce colony counts and improve lesions, sometimes comparably to topical antifungals. A 2025 evidence synthesis found broadly comparable overall efficacy between photodynamic and antifungal therapy and a possible benefit of combination treatment, but protocols varied in photosensitizer, wavelength, fluence, session number, and endpoint [50–52]. It should therefore be considered a promising adjunct rather than a standardized replacement.

10.2 Probiotics, postbiotics, and ecological therapy

Selected Lactobacillus and Bifidobacterium preparations can reduce oral Candida carriage in some elderly or denture-wearing populations [48,49]. Plausible mechanisms include competitive adhesion, acidification, bacteriocins, hydrogen peroxide, immune modulation, and suppression of hyphal signaling. However, ‘probiotic’ is not a single intervention. Strain identity, viability, dose, delivery vehicle, host population, baseline carriage, and endpoint vary widely. Culture-count reduction without lesion resolution or recurrence data is insufficient to establish therapeutic equivalence.

10.3 Natural products and pomegranate-derived compounds

The supplied thesis emphasized Punica granatum peel, which contains ellagitannins and other phenolics with in vitro anti-Candida activity. Experimental studies report membrane and

morphological effects and synergy with fluconazole; a small in vivo comparison with nystatin also suggested activity [53,54]. These findings justify standardized pharmacological research, not substitution for established therapy. Extract composition changes with cultivar, solvent, processing, and assay. Cytotoxicity, oral retention, taste, stability, interaction with restorative materials, and reproducible minimum effective concentration require definition before clinical recommendations are defensible.

10.4 Nanotechnology, peptides, and anti-biofilm materials

Silver, zinc oxide, chitosan, polymeric nanoparticles, liposomes, and nanostructured delivery systems can improve local retention, disrupt biofilms, or co-deliver antifungals. Antimicrobial peptides and histatin analogues offer rapid membrane activity, while surface modifications seek to reduce fungal adhesion to acrylic and silicone. Most evidence remains in vitro. Translation requires testing under saliva, protein pellicles, mixed biofilms, mechanical wear, and clinically realistic exposure. Cytotoxicity and environmental release are not secondary issues; an impressive reduction in laboratory biomass is not sufficient for oral use.

10.5 Vaccines and host-directed therapy

The Als3-based NDV-3A vaccine generated human safety and immunogenicity data and reduced recurrent vulvovaginal candidiasis in a subgroup, while preclinical studies show interference with adhesion and biofilm [55,56]. Direct evidence for prevention or treatment of oral candidiasis in humans is lacking. Other strategies include β-glucan or cell-wall antigens, trained immunity, epithelial-memory pathways, IL-17-axis modulation, and candidalysin neutralization. These approaches are biologically attractive but must respect site-specific immunity and the commensal role of C. albicans.

10.6 New systemic antifungal classes

The broader antifungal pipeline includes agents with new targets or formulations, such as glucan-synthase inhibitors, Gwt1 inhibitors, and long-acting echinocandins. Their development is important for invasive candidiasis and resistant fungi, but approval or efficacy in one syndrome cannot be extrapolated to uncomplicated oral candidiasis. Oral bioavailability, salivary exposure, topical retention, microbiome effects, interaction burden, and resistance selection must be evaluated in syndrome-specific trials [57,58].

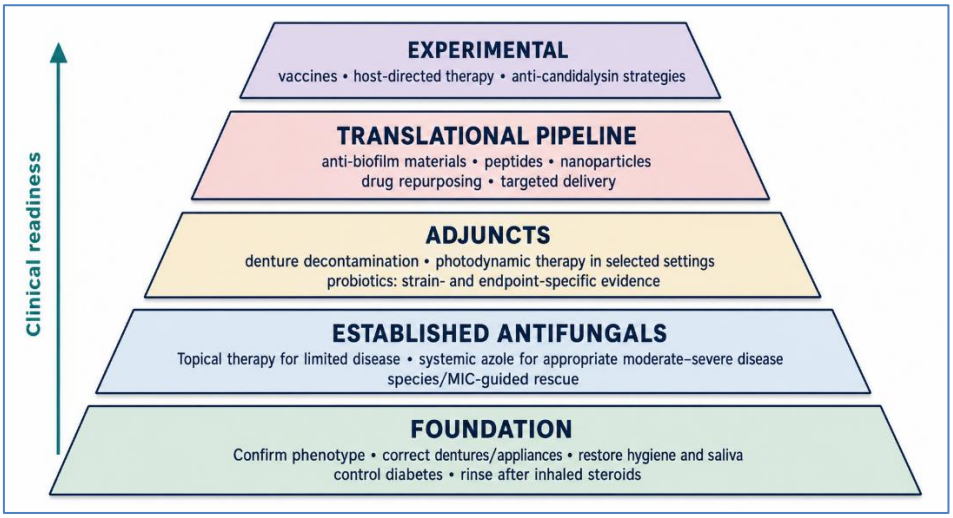

Figure 6. *Therapeutic evidence pyramid. Clinical readiness decreases from correction of drivers and established antifungals toward host-directed and vaccine strategies. Placement is qualitative and reflects current oral-candidiasis evidence, not a ranking of biological promise.*

Table 9. Emerging interventions: promise, maturity, and decisive next experiment

Strategy	Current signal	Maturity for oral candidiasis	Decisive evidence needed
Photodynamic therapy	Clinical lesion and CFU improvement; protocol heterogeneity	Adjunctive / selected clinical use	Standardized, adequately powered RCT with recurrence and safety
Probiotics/postbiotics	Some reduction in carriage and symptoms	Adjunctive, strain-specific	Strain-defined trials with clinical—not only microbiological—endpoints
Pomegranate/plant phenolics	In vitro activity and limited in vivo signals	Preclinical / early translational	Standardized extract, pharmacokinetics, mucosal safety, controlled trial
Nanoparticles / targeted delivery	Strong biofilm disruption in vitro	Preclinical	Saliva/mixed-biofilm models followed by toxicology and dose-finding
Anti-adhesion / device coatings	Reduced attachment on model materials	Preclinical to translational	Durability, wear, microbiome neutrality, and clinical device trial
Vaccines	Human immunogenicity in non-oral syndrome; preclinical oral protection	Experimental for oral disease	Oral-candidiasis prevention trial in a defined high-risk population
Host-directed / anti-candidalysin	Compelling mechanistic rationale	Experimental	Show less damage without impairing protective mucosal immunity

RCT = randomized controlled trial; CFU = colony-forming units.

11. Critical gaps and a research agenda

The field's main limitation is not a lack of candidate mechanisms but weak alignment between mechanism, sampling, and clinical outcome. Studies use oral rinse, unstimulated saliva, tongue swab, palatal swab, plaque, denture sonicate, or tissue, often without reporting recent food, hygiene, or antifungal exposure. 'Oral candidiasis' may be defined by clinical appearance, culture threshold, clinician diagnosis, or response to treatment. These are not equivalent case definitions.

A minimum core protocol should record lesion type and site, symptoms, immune status, diabetes control, salivary status, denture or appliance exposure, recent antibiotics and steroids, antifungal history, sampling method, species, and whether fungal forms are seen in direct microscopy or tissue. Trials should include clinical resolution, pain/burning, functional

outcomes, adverse effects, adherence, recurrence at a prespecified interval, and culture or molecular outcomes. Culture clearance alone rewards eradication of a commensal rather than restoration of health.

Longitudinal lesion-resolved multi-omics is a high priority. Paired lesion and contralateral control samples can distinguish local activity from global carriage. Metatranscriptomics and metabolomics can identify which organisms are active, while host transcriptomics and salivary proteomics can capture containment or injury. Yet prediction models must be externally validated and designed for clinical decisions. A molecular signature that distinguishes groups after diagnosis is less useful than a tool that changes management at the first visit.

Table 10. Prioritized research agenda

Priority	Current problem	Recommended design	Clinically meaningful output
Case definition	Incompatible clinical and culture criteria	Consensus core outcome set with lesion phenotyping	Comparable incidence, recurrence, and treatment effects
Sampling	Site and method heterogeneity	Paired lesion/control plus standardized timing and metadata	Clinically anchored fungal load and morphology
Host–microbiome dynamics	Mostly cross-sectional associations	Longitudinal multi-kingdom and host profiling before/during/after therapy	Predictors of transition and recurrence
Biofilm response	Planktonic MIC poorly captures device disease	Material-specific mixed-biofilm testing linked to clinical outcomes	Actionable reservoir and decontamination strategy
Diagnostics	Sensitive detection without infection specificity	Prospective diagnostic-accuracy studies using expert phenotype + histology where appropriate	Rule-in/rule-out value and management impact
Therapeutic trials	Small, heterogeneous, short follow-up	Pragmatic RCTs with optimized conventional-care comparator	Symptoms, function, recurrence, safety, resistance
Equity and geography	Underrepresentation of Africa and resource-limited settings	Regional surveillance and low-cost diagnostic implementation studies	Locally valid species and susceptibility guidance

The agenda prioritizes decision-changing evidence over additional descriptive carriage surveys.

12. Clinical synthesis

A rational oral-candidiasis pathway can be summarized in six steps. First, define the lesion and symptoms. Second, identify local and systemic drivers. Third, look for red flags that require biopsy, oesophageal evaluation, or systemic assessment. Fourth, use lesion-targeted microscopy and culture when the phenotype is uncertain or risk is high. Fifth, pair antifungal therapy with correction of reservoirs and exposures. Sixth, if response is inadequate, reassess the diagnosis before escalating, then obtain species and susceptibility data where they can change treatment.

This pathway avoids two symmetrical errors: undertreating genuine mucosal disease in a vulnerable host and overtreating asymptomatic colonization or a non-fungal lesion. It also reframes stewardship. The objective is not merely to use less antifungal drug, but to use the right diagnostic evidence, correct modifiable ecology, and reserve broader or repeated exposure for patients likely to benefit.

13. Limitations of this review

This review used a supplied thesis bibliography plus a targeted structured update rather than a reproducible database-by-database systematic search. Publication selection may therefore be incomplete, and no risk-of-bias instrument or quantitative synthesis was applied. Several mechanistic conclusions derive from murine, epithelial monolayer, organotypic, or in vitro biofilm systems. These models are essential for causal inference but do not provide direct clinical effect sizes. Recent 2026 clinical studies were included to capture emerging evidence, yet their small or specialized cohorts require cautious interpretation.

Treatment guidance changes over time and differs by country, formulation availability, age, pregnancy status, immune condition, and resistance epidemiology. The therapeutic section should be read as an evidence framework and checked against current local prescribing guidance. Finally, taxonomic databases may adopt names at different speeds; dual nomenclature was used where it improves clinical clarity.

14. Conclusions

C. albicans is best understood as a flexible oral pathobiont whose behavior emerges from a three-way interaction among fungal state, mucosal defense, and microbiome ecology. Adhesion and morphogenesis enable access to protected niches; biofilm and stress adaptation support persistence; and candidalysin couples hyphal activity to epithelial damage and immune alarm. IL-17-centered mucosal immunity, neutrophils, salivary defenses, and bacterial partners normally contain this potential.

The central diagnostic principle is equally clear: organism detection is not disease diagnosis. Clinical phenotype and tissue context should determine when microscopy, culture, species identification, molecular testing, biopsy, or susceptibility testing adds value. Established antifungals remain effective when matched to severity and combined with correction of prosthetic, salivary, metabolic, and medication-related drivers. Emerging interventions are scientifically promising, but most require standardized protocols, clinically meaningful endpoints, and longer follow-up before they can displace optimized conventional care.

Progress will depend less on cataloguing additional virulence factors than on integrating them into longitudinal, lesion-resolved human studies. The most useful future tools will distinguish damaging activity from harmless carriage, predict recurrence, and guide the least disruptive effective therapy.

Declarations and submission notes

Data availability: No new primary dataset was generated. The review synthesizes the supplied document corpus and published literature.

Ethics approval: Not applicable to this literature review.

Author metadata: Institutional affiliation, corresponding-author address, funding statement, conflict-of-interest declaration, and author-contribution statement should be completed and verified by the author before journal submission.

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Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.