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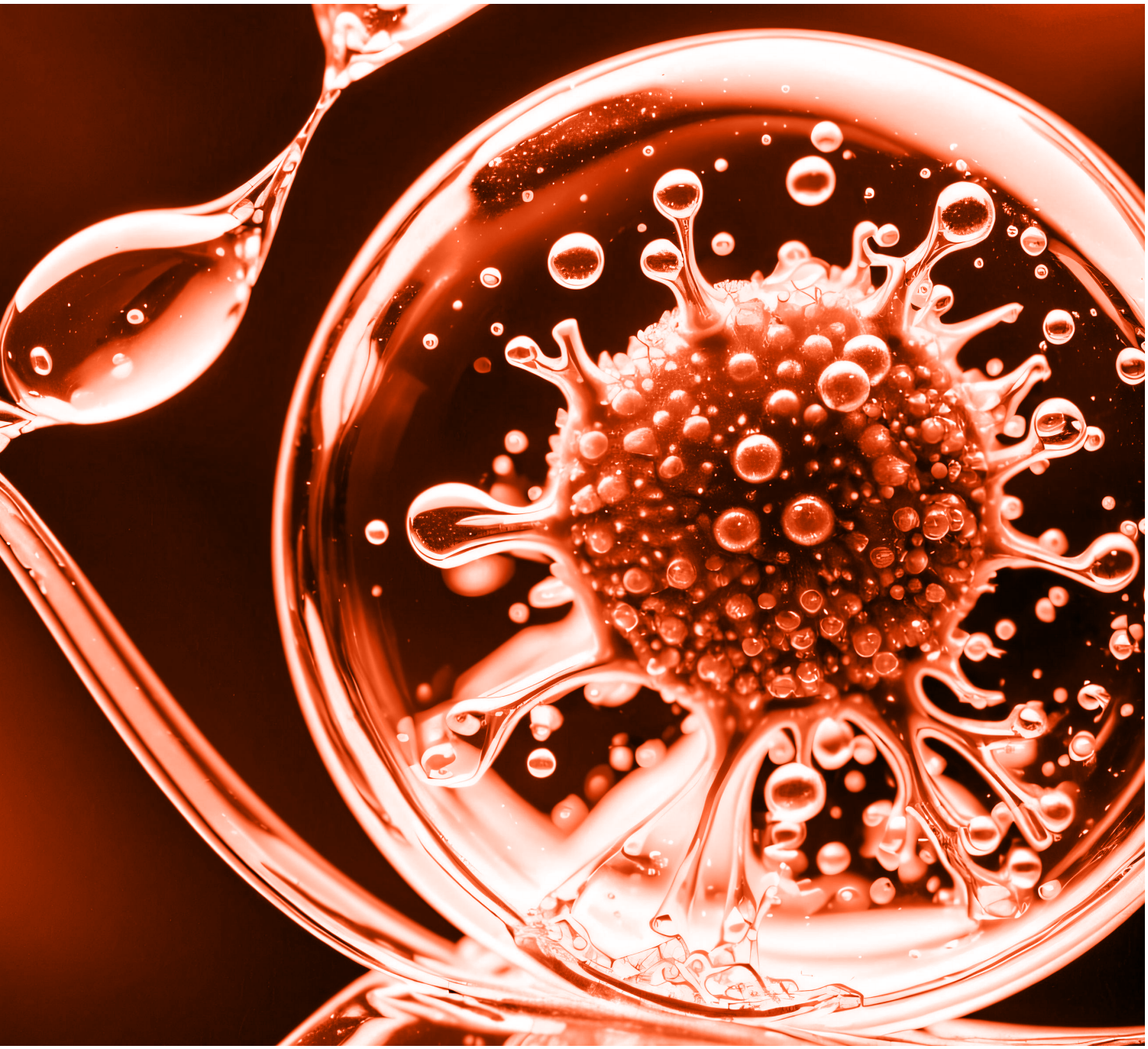
CANXIDA REMOVE

WHITE PAPER



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The aim of this whitepaper is to provide a comprehensive overview of Candida, Candida infections, and treatment using CanXida Remove (RMV). Within this, the most up-to-date scientific evidence will be reviewed, highlighting the key studies and information underlying the mechanisms of Candida infection and the formulation design of CanXida RMV.

INTRODUCTION

Candida is a species of pathogenic fungi that colonizes multiple sites in the human body including the gastrointestinal (GI) tract, the genitourinary tract, and the skin, without causing infection[1]. However, changes in host immunity, stress, resident microbiota, and other factors can lead to Candida overgrowth and infection[1].

Candida infections can range from superficial mucosal infections to severe hematogenously disseminated candidiasis, and are responsible for the majority of globally reported deaths caused by fungi[1]. Candida infections, particularly from the most prevalent species Candida albicans, are a growing concern due to a lack of antifungal drugs, increased use in the immunocompromised population, and antifungal resistance[1].

UNDERSTANDING *CANDIDA*

Of the 150 different species of Candida, C. albicans, C. glabrata, C. tropicalis, C. parapsilosis, and C. krusei are responsible for more than 90% of Candida-related infections[2].

Of these, the most common cause of candidiasis is C. albicans, which is also the most extensively researched Candida species[2].

According to the Centers for Disease Control and Prevention (CDC), approximately 25,000 cases of candidemia (the presence of Candida species in the blood) occur in the USA every year. In the UK, this is estimated at around 5000 cases, and global yearly incidence is thought to be in excess of 160,000 cases[3]. The incidence of Candida infections is increasing worldwide[2].

Mortality rates among patients with invasive candidiasis or candidemia generally range between 40% and 60%, depending on underlying conditions, and in certain patient populations, mortality can exceed 70%[2].

Candida overgrowth can cause multiple different types of candidiasis and different symptoms can manifest depending on the site of infection. Candidiasis can occur in the mouth, throat, esophagus, vagina (known as vaginal thrush) and gastrointestinal (GI) tract. A general overview of Candida infection and candidiasis symptoms is presented below[4]:

- Gas, Cramps, And Bloating.
- Unexplained Constipation, Diarrhea, And Nausea.
- Stomach Or Abdominal Pain.
- Vaginal Thrush Symptoms, Including Itching And/or Burning, Vaginal Discharge, Redness And/or Swelling, And A Yeasty Smell.
- Recurring Urinary Tract Infections (Utis) And Associated Symptoms.
- Fungal Infections, Particularly Of The Skin Or Nails.
- Oral Yeast Infection Symptoms Such As White Tongue, And/or Redness And Soreness Of
- The Tongue And Mouth.
- Lack Of Energy, Fatigue, And Tiredness.
- Joint Pain.


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An overgrowth of Candida in the oral cavity leads to oral candidiasis. Oral candidiasis can occur at any age but is more prevalent in infants, elderly individuals, and those with underlying medical conditions like diabetes mellitus or immunosuppression[5]. Risk factors include impaired salivary gland function, dentures, a high carbohydrate diet, smoking, and certain medications[5].

Candida UTIs commonly occur in hospitalized patients, particularly those with risk factors including diabetes mellitus, indwelling urinary catheters, urinary obstruction, or admission to intensive care units[6]. Candida UTIs can be caused by hematogenous spread following candidemia or retrograde infection via the urethra. Risk factors for invasive Candida infection in critically ill patients include demographics (e.g., age), comorbidities (e.g., HIV), and medical interventions (e.g., broad-spectrum antibiotics, blood transfusions)[6].

Small intestinal fungal overgrowth (SIFO) is characterized by excessive fungal organisms (such as Candida species) in the small intestine that lead to the GI symptoms listed above[7]. It is well understood that Candida species cause GI symptoms in immunocompromised individuals or those receiving steroids or antibiotics[7]. It has also been reported that immunocompetent subjects can experience SIFO-related symptoms, caused by high levels of intestinal Candida[7]. Although there are limited studies exploring this, it appears that the presence of fungi (especially C. albicans) in the small intestine causes abdominal pain or diarrhea in otherwise healthy subjects, which can be resolved after antifungal treatment[7].

Vulvovaginal candidiasis (VVC) is a common infection worldwide and is also known as vaginal thrush. It is primarily caused by C. albicans, but other species (including C. glabrata) can also be involved[8]. Symptoms of VVC include itching, burning, redness, and discharge[8]. Risk factors for VVC include antibiotic use, intercourse, humid weather, and use of hygiene products[8]. The majority of VVC cases are self-diagnosed and cured with over-the-counter medications. However, physician-diagnosed cases tend to achieve higher symptom relief rates and recurrent VVC may require long-term antifungal maintenance therapy[8].

THE TRIPLE THREAT: ANTIFUNGAL, ANTIBACTERIAL, ANTI-PARASITIC TREATMENT

CanXida RMV is an advanced, 12-ingredient formula that has been developed using natural ingredients with scientifically-proven health benefits. CanXida RMV is designed to eliminate Candida infections, treat related symptoms, and restore normal, healthy gut function*. The formulation has antifungal properties that enable it to effectively eliminate all common Candida species including C. albicans, C. tropicalis, and C. krusei, as well as over 150 other types of yeast including Aspergillus, Trichsporon, and Rhodotorula.

In addition, it has antibacterial properties that render it effective against over 800 species of harmful bacteria, including the common infection-causing bacteria Escherichia coli. Finally, its antiparasitic properties ensure it eliminates a broad spectrum of parasites including Giardia duodenalis, Entamoeba histolytica, and Trichomonas vaginalis.

The antifungal, antibacterial, and anti-parasitic effects mean that CanXida RMV is not only effective at tackling the causes of infection (Candida overgrowth) but can also help to improve the associated symptoms, including:

- ✕ Severe gas and bloating*
- ✕ Unexplained constipation and diarrhea*
- ✕ Stomach or abdominal pain caused by indigestion*
- ✕ Symptoms of VVC (discharge and yeasty smell)*
- ✕ Oral candidiasis symptoms such as white tongue*
- ✕ Sugar cravings (often caused by Candida)*
- ✕ Severe lack of energy, fatigue and tiredness*
- ✕ Inability to lose weight*
- ✕ Persistent itchy skin rashes (caused by Candida overgrowth)*
- ✕ Symptoms attributed to IBS (irritable bowel syndrome), SIBO (small intestine bacterial overgrowth), and leaky gut syndrome*

Additionally, the “triple threat” antimicrobial properties of CanXida RMV make it an effective therapy against other intestinal problems, including irritable bowel syndrome (IBS) symptoms, small intestine bacterial overgrowth (SIBO), and leaky gut syndrome.

*These statements have not been evaluated by the FDA


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CANXIDA RMV: KEY INGREDIENTS

The formulation of CanXida RMV has been informed by scientific research into Candida overgrowth, candidiasis, and the removal of pathogenic fungi from the human body. Each of the 12 ingredients included in CanXida RMV has a key role to play in the treatment of Candida, and has been selected based on the supporting scientific literature.

GRAPEFRUIT SEED EXTRACT (GSE)

GSE has powerful antifungal properties and has been proven to effectively destroy yeast by mitochondria-dependent apoptosis[9]. This enables GSE to inhibit the growth of yeast cells, reducing biofilm formation, and disrupting the synergism between different species of pathogens involved in GI tract and oral infections[9,10]. GSE efficacy has previously been tested against 43 different strains of Candida, with a substantial reduction in C. albicans load measured after 5 days[10].

GSE also contributes to the antibacterial properties of CanXida RMV. GSE disrupts bacterial membranes and liberates the cytoplasmic contents of a wide range of gram-negative and gram-positive bacteria after 15 minutes of contact, even at dilute concentrations[11].

BERBERINE CONCENTRATE HCL

Berberine is a herb that has natural, broad-spectrum antimicrobial properties, with a long-documented history as a therapy against GI infections[12]. The underlying mechanism of action for the antifungal and antibacterial ability of berberine lies in the production of reactive oxygen species (ROS)[13]. ROS attack cell walls, cell membranes, DNA, RNA, and proteins, inducing cell cycle arrest and apoptosis[13].

Berberine also potentiates the activity of other antifungals and antibiotics, enhancing their inhibitory effects[12,13]. The effects of this synergistic behavior have been demonstrated using Candida cultures. It was found that a combination of berberine and terbinafine (an antifungal agent) showed enhanced antifungal potency against C. albicans, potentially reducing the dosage needed for treatment[14].

CLOVE

Eugenol is a bioactive phenylpropene compound extracted from cloves and has several pharmacological activites[15]. In a study examining the effects of eugenol on C. albicans, the compound was found to encourage cell leakage, causing the release of cellular material, and increasing cell permeability[15]. This shows that eugenol disrupts the cell wall of C. albicans[15], highlighting the potential of clove as an effective antifungal agent.

The considerable antifungal activities of clove essential oil have been demonstrated against clinically-relevant Candida, Aspergillus, and Dermatophyte strains, including antifungal-resistant strains[16]. A high incidence of drug-resistant Candida strains has been identified in VVC[17]. Research into this particular type of candidiasis revealed that Syzygium aromaticum (clove) extracts exhibited high antifungal activity at low concentrations, highlighting it as a natural source of potential antifungals[17].

GARLIC

Garlic (Allium sativum) is another plant that has been used as a traditional herbal medicine because of its antimicrobial properties[18]. The bioactive ingredient in garlic is allicin, a well-researched and potent antimicrobial agent that has been proven to effectively kill numerous strains of yeast and bacteria[18,19]. This includes C. albicans - allicin was found to be effective at reducing the mean survival time of C. albicans both in vitro and in animal models, suggested that garlic could be a safe and accessible option in the treatment of Candida[18,19].

The antifungal effects of Allium sativum along with another garlic extract, Allium hirtifolium, on C. tropicalis were also investigated both in vivo and in vitro[20]. A significant reduction in C. tropicalis load was observed, highlighting the potential of garlic extracts to be used as an adjuvant therapy in the management of Candida infection[20].

CAPRYLIC ACID

Caprylic acid is a medium-chain fatty acid that has been investigated for its potential therapeutic effects against Candida overgrowth. Caprylic acid treatment showed a significant reduction in intractable medical problem symptoms (frequent urination, incontinence, tooth infection), caused by mixed infections of C. albicans, H. pylori, Cytomegalovirus, and other microorganisms[21]. Within in vitro and murine models of oral candidiasis, caprylic acid and other fatty acids were also found to inhibit C. mycelia growth and improve symptoms[22].

Looking specifically at C. albicans infection, a fatty acid modification of an antimicrobial peptide (CGA-N9) was highlighted as a promising candidate for the defense against infection and resolving drug resistance[23]. Caprylic acid supplements and dietary modifications explored as a treatment for intestinal candidiasis also resulted in increased immunological activity and an improvement in symptoms[24].

UNDECYLENIC ACID

Undecylenic acid is a monounsaturated fatty acid, primarily extracted from castor bean oil, which has been investigated for its antifungal activity[25]. Undecylenic acid has been identified as being particularly useful at disrupting C. albicans biofilm formation[25,26]. While lower dosages are effective at inhibiting biofilm formation, higher dosages are also able to completely eliminate the morphological transition from yeast cells to the filamentous phase[26].

BETAINE HCL

Betaine HCl is the hydrochloride salt of betaine that increases the production of stomach acid and thereby decreases stomach pH. 1500mg of betaine HCl has been shown to reduce the pH of the stomach to less than pH 3 in approximately 6 minutes[27]. This mechanism is important in tackling Candida infections as Candida overgrowth has been shown to be inhibited by pancreatic enzymes and HCl production, which prevents the yeast from entering the small intestine's absorbent surfaces[28].

BLACK WALNUT HULL EXTRACT

Black walnut is a traditional medicinal plant that has been used because of its many therapeutic qualities including antimicrobial, antioxidant, and anti-inflammatory activity[29]. The principal bioactive compound in black walnut is juglone, which shows strong antifungal and antimicrobial activity[29].

Several studies have demonstrated the antifungal potential of black walnut against multiple Candida strains, including C. albicans[30,31]. In a rat model of VVC, black walnut husk extract was found to effectively suppress the growth of C. albicans after one week of treatment[32].

PAU D'ARCO

Pau d'arco (Tabebuia avellanedae) is a traditional South American medicinal plant that has been used because of its strong antimicrobial and antifungal properties. Pau d'arco has previously been identified as having one of the highest antifungal activities amongst Paraguayan plants used in traditional medicine[33]. Methanol extract from Pau d'arco was found to inhibit the activity of multiple Candida species, indicating its potential as an alternative agent for the prevention of candidiasis[34].

NEEM

The neem plant (Azadirachta indica) has seen extensive investigation because of its potential antimicrobial, antioxidant, and anti-inflammatory properties. The antifungal potential of several neem extracts was evaluated against human pathogenic fungi (C. albicans and Aspergillus species), with nimonol and ethyl acetate identified as compounds with strong antifungal effects[35]. Further in vitro studies have also highlighted the robust antimicrobial activity of neem leaf, seed, and bark extracts against C. albicans, members of the Aspergillus family, and multiple strains of bacteria[36,37].

BIOTIN

Biotin is an essential cofactor for carboxylase enzymes and is integral to metabolic processes like gluconeogenesis and amino acid metabolism[38].

OREGANO OIL

Oregano oil (Origanum vulgare) has been used in traditional medicine for respiratory and gastrointestinal disorders, due to its potential antimicrobial properties. Within Candida research, oregano oil has been shown to be effective against the biofilm adhesion and formation of Candida species, including dual biofilms with Staphylococcus aureus[39,40].

Oregano essential oil has also been shown to have activity against C. albicans in vitro. It was found that the oil inhibited the growth and activity of C. albicans more effectively than clotrimazole, a commonly used antifungal drug[41].

SYNERGISTIC EFFECT

On top of the beneficial effects each ingredient has been shown to have on its own, multiple studies have been performed exploring the synergistic effects of combining different ingredients together. The first of these measured the fungicidal effects of neem and clove individually, and in combination, against Aspergillus, Candida, and Penicillium strains[42]. Neem and clove extracts were prepared using ethanolic and acetone solvents - both neem extracts showed a higher potency and greater efficacy[42]. Although this showed that neem had greater fungicidal activity than clove, the study also showed a synergistic effect that further increased fungicidal activity when combining neem and clove together[42].

The combined antimicrobial effect of oregano essential oil and caprylic acid was also investigated against Salmonella serovars, Escherichia coli, Staphylococcus aureus, and Listeria monocytogenes[43]. This study demonstrated the synergistic effect of oregano essential oil and caprylic acid in the inhibition of these pathogenic microbes[43]. More recently, the antimicrobial activity of several essential oils in combination with caprylic acid was assessed, highlighting a potentially enhanced activity against E. coli[44].

The synergistic effects of clove and other essential oils were also explored against C. albicans and A. niger[45]. It was found that the extracted bioactive components of the oils were more effective than total essential oils and showed synergistic effects when combined[45]. A combination of essential oil components could also lead to decreased side effects and be used to treat various fungal infections[45]. Finally, fresh garlic extract and black seed extract (from the plant Nigella Sativa) were also found to have a synergistic inhibitory effect against C. albicans[46].


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SUSTAINED-RELEASE ADDITIVES

CanXida RMV also contains several additives designed to formulate a sustained release in the GI tract (Table 1).

Table 1. CanXida RMV Sustained-Release Additives.

ADDITIVE	PROPERTIES
Hydroxypropyl methylcellulose	Hydrophilic carrier with high swellability. Delays the breakdown of CanXida RMV in the GI tract.
Magnesium stearate	Functions as a binder and lubricating agent.
Dicalcium phosphate	Odor remover that sanitizes CanXida RMV. Adds a fresh scent and an additional source of calcium. Can aid in the reduction of dentinal hypersensitivity

CONCLUSION

Candida is a form of yeast that typically grows on skin and in their GI tracts. Candida overgrowth can lead to infections, various complications and symptoms, including vulvovaginal candidiasis, and invasive candidiasis.

CanXida RMV is an advanced, 12-ingredient formula that has been developed using natural ingredients with scientifically-proven health benefits. CanXida RMV is designed to eliminate Candida infections, treat related symptoms, and restore normal, healthy gut function. The formulation has antifungal properties that enable it to effectively eliminate all common Candida species. In addition, it has antibacterial properties that render it effective against over 800 species of harmful bacteria. Finally, its antiparasitic properties ensure it also eliminates a broad spectrum of parasites.

The formulation of CanXida RMV has been informed by scientific research into Candida overgrowth, candidiasis, and the removal of pathogenic fungi from the human body. Each of the 12 ingredients included in CanXida RMV has a key role to play in the treatment of Candida, and has been selected based on the supporting scientific literature. This assists in regulating the amounts of Candida and pathogenic yeast in the body, detoxifying the gut and restoring normal and healthy function.

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