Technical Report

Significance of Caprylic Acid in CanXida Remove (Formula RMV)

Caprylic acid is often recognized as an alternative antibiotic for gut pathogens. Scientific and clinical evidence support these claims through consistent and repetitively positive outcomes. It also has a strong influence on the gut microbiome and restores immune functions and gastrointestinal defenses.

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Executive Summary

Caprylic acid is emerging as an effective treatment option for pathogens causing pathological conditions in the gut. Its therapeutic efficacy against biofilm-forming bacteria and fungi makes it an attractive therapeutic ingredient in formulations such as CanXida Remove (Formula RMV). It has a high affinity for binding with the lipid bilayer of cell membranes and penetrating within the cells of pathogens, inactivating proteins and enzymes, and even inducing cell death by membrane lysis. Due to this distinct antimicrobial action, it is also effective against pathogens that are resistant to antibiotics.

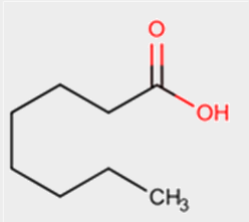
Besides antimicrobial activity, it also modulates the immune system by influencing the gut microbiome. It maintains a healthy balance between Firmicutes and Bacteroidetes group of probiotic bacteria and helps in relieving symptoms associated with inflammatory diseases of the gastrointestinal tract such as Small Intestinal Bacterial Overgrowth (SIBO). It also prompts intestinal cells to release antibacterial peptides such as defensins and restore microbial barriers to avoid systemic infections. It plays a vital role in CanXida Remove formulation to impart not only antimicrobial properties but also restore the normal gut microbiome.

1. Introduction

Caprylic acid belongs to a very unique group of fatty acids called medium-chain fatty acids (MCFA). It is often recognized as "Nutraceutical" due to its immense benefits in health, medicinal applications, and food supplements. A food or its bioactive compound is regarded as a nutraceutical if it can be used in the treatment and prevention of diseases. It is only found in limited natural sources such as coconut oil and palm oil. It is also present naturally in human breast milk and provides antimicrobial and immuno-protective effects in the gut of newborns. It has the unique ability to denature proteins but leaves antibodies unaffected. Hence, it neutralizes protein toxins secreted from the bacteria or protozoa, kills pathogens by rendering the structural proteins dysfunctional, and helps the immune system perform its function without interruption. It destabilizes the proteins on the cell membrane of bacteria, and fungi, leading to a weakened pathogen that is easy to eliminate by the immune system. It can penetrate inside the pathogens and bind with the enzymes ultimately killing the pathogen.

Dr. Carl Fischer, working as a research fellow in Microbiology at the University of Iowa, USA, published a report along with her colleagues demonstrating that caprylic acid can be used as an alternative to antibiotics for

Caprylic Acid



Generic Name:	Caprylic Acid
Drug Bank Accession Number:	DB04519
Drug Bank Status:	Approved
Drug Category:	Fatty Acids, Acyclic Inhibitors
FDA UNII:	OBL58JN025
WHO Approval Date:	1998
Other Names:	Octanoic acid, 1-heptane carboxylic acid
Chemical Formula:	$C_8H_{16}O_2$
Molecular Weight:	144.2 g/mol
Melting Point:	16.3 °C

bacterial pathogens in the gut (Fischer et al 2012). Her results were validated by other researchers as well (Nejrup et al. 2017) It also possesses strong antioxidant properties and plays an anti-inflammatory role during the healing and regeneration of the gut wall.

2. Therapeutic Potential

Caprylic acid has strong antifungal and antibacterial properties. It works as an inhibitor of enzymes or proteins which are directly involved in the virulence of the pathogen. It also promotes the growth of probiotic bacteria and fungi in the gut to maintain immune balance.

2.1. Antifungal Properties

Caprylic acid is a multi-targeting antifungal agent. A report published in the Journal of Medicinal Foods reported that caprylic acid controls the virulence of *Candida albicans* by reducing its adhesion to the gut wall, its maturation (morphogenesis), and biofilm formation. Biofilms are clusters of pathogens formed on the surface of the gut wall and protected by a resistant coating secreted by pathogens that protect *Candida* from attacks by the immune system as well as antibiotics. It was observed that caprylic acid also interferes with the hyphal growth of pathogenic and opportunistic fungi. Similar results were also reported elsewhere demonstrating the efficacy of caprylic acid in combating pathogenic fungi by eradicating fungal biofilms (Rosenblatt et al 2015)

Dr Bhattacharyya and colleagues from Vyome Therapeutics Ltd., India, published a report in the Frontier in Microbiology showing that caprylic acid is effective against different drug-resistant fungi including *Candida albicans, Malassezia furfur, Trichophyton rubrum, and Trichophyton mentagrophytes* (Bhattacharya et al 2020). The results showed that caprylic acid disrupts the lipid bilayer in the cell membrane of pathogenic fungi. Similar results were also reported by Bae and colleagues showing that caprylic acid treats pathogenic C. albicans by membrane disruption (Bae et al. 2019).

Caprylic acid is also effective against oral yeast infections and multi-drug-resistant Candida strains. It effectively inhibited the growth of fungus in *in-vitro* studies and in pre-clinical models.

2.2. Antibacterial Properties

Caprylic acid has well-established antibacterial properties against Gram-positive and Gram-negative bacteria residing in the gut and oral cavity. One of the common intestinal pathogens is *Salmonella* which often showcases multi-drug resistance. It causes around 1.2 million infections with 450 deaths every year in the US. A report published by Maijankattil and colleagues demonstrated in an in vitro study that caprylic acid significantly reduces the bacterial count of *Salmonella* (Manjankattil et al. 2021). Another study demonstrated that caprylic acid is effective against a range of intestinal bacteria such as *Salmonella*, *Escherichia coli*, *Listeria monocytogenes,* and *Staphylococcus aureus*.

Caprylic acid is effective in eradicating food-borne pathogenic bacteria which are associated with infecting the gut wall and interfering with nutrition absorption. It can act on bacteria not only in the small intestine but also in the posterior parts of the large intestine such as the caecum. It can help reduce infections and symptoms associated with diarrhea and regulate bowel movements. Its effectiveness against various pathogenic

strains of bacteria such as *Clostridium, Campylobacter*, and *Staphylococcus* species.

2.3. Small intestinal bacterial overgrowth (SIBO)

SIBO or small intestinal bacterial overgrowth is a medical condition characterized by increased growth of bacteria in the small intestine, especially the jejunum. Its symptoms include abdominal pain, cramping, bloating, constipation, and low vitamin B12 levels in the blood. This often leads to more serious and life-threatening ailments such as irritable bowel syndrome. A clinical trial by Dr. Nathan Morris, MD at Good Medicine Clinic, Oxford, Ohio (clinical trial ID NCT03420976) is undergoing a Phase I interventional study to investigate the effect of a diet containing caprylic acid in the treatment of SIBO. Current treatment options have limited efficacy and clinicians often use alternative therapy including dietary supplements such as CanXida RMV.

2.4. Immune System Modulation

Caprylic acid belongs to medium-chain fatty acids which are known to interact with cells, both immune cells and non-immune cells by binding to receptors called G-protein coupled receptors (GPCR). These receptors are found on immune cells such as macrophages, monocytes, granulocytes, and lymphocytes (B-cells and T-cells) as well as on the cells of the liver, spleen, and colon. The binding of caprylic acid to GPCR activates the immune cells at the site of infection by a process called chemotaxis which then recruits T-cells to kill the pathogens (Haghikia et al. 2015).

It also binds with immature T-cells in the lymph nodes present in the gut to gain pathogen-specific maturity. Mature T-cells

***Table 1**: List of clinical trials using caprylic acid as an active ingredient in disease treatment and prevention.*

NCT Number	Study Status	Activity	Study Type
NCT01793883	Completed	Antivral	INTERVENTIONAL
NCT02397577	Completed	Bowel Movement	INTERVENTIONAL
NCT01510223	Completed	Digestive Health	INTERVENTIONAL
NCT01226134	Unknown	Bowel Movement	INTERVENTIONAL
NCT02522000	Unknown	Digestive Health	OBSERVATIONAL
NCT03467659	Completed	Bowel Movement	INTERVENTIONAL
NCT01244945	Completed	Functional Constipation	INTERVENTIONAL
NCT03420976	Unknown	Small Intestinal Bacterial Overgrowth	INTERVENTIONAL

are primed for specific pathogens and can develop active immunity to future infections as well.

Caprylic acid has a unique effect on the host immune system by encouraging it to produce special peptides that not only act as antibacterial but also improve the gut microbial barrier. These specialized peptides are called defensins. Defensins are known to be effective against bacteria and protozoa by lysing the cell membranes. These peptides are normally produced by the human innate immune system located along the mucosa of the intestine. Caprylic acid activates those cells to produce sufficient quantities of these peptides to combat pathogens responsible for ulcers and damage to the gut wall (Wang et al 2018).

There are two major groups of defensins, classified into β-defensins 1 and β-defensins 2 and caprylic acid induces increased expression of both of these peptides. This is a particularly important aspect of caprylic acid in controlling pathogens that damage the intestinal wall, cause bloody diarrhea, and compromise the intestinal barrier leading to systemic infections. Pathogens in this category include enterohemorrhagic bacteria such as *E. coli*.

3. Gut Health and Microbiome

The gut microbiome is divided into two diverse groups of bacteria called Gram-negative Bacteroidetes and Gram-positive Firmicutes. Both of these probiotic groups ferment complex indigestible carbohydrates into digestible fatty acids with implications for health and disease. It is a well-established fact that the ratio of Firmicutes and Bacteroidetes in the intestine is associated with several intestinal disorders including inflammatory bowel disease and irritation of the intestinal wall. A report published in the International Journal of Molecular Science demonstrated that caprylic acid was

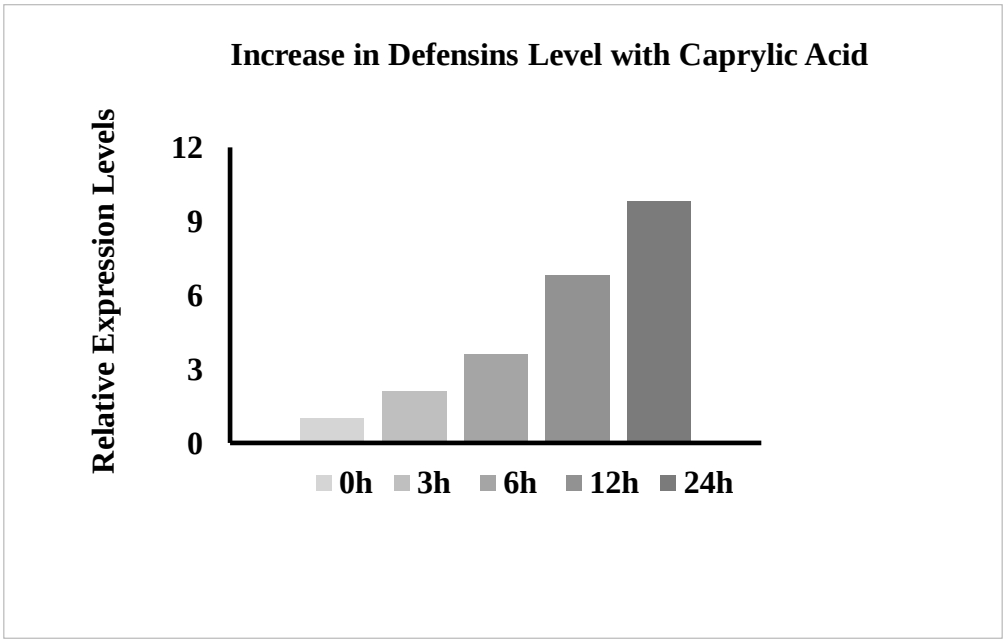


***Figure 1**: Increase in defensin secretion from the gut cells after incubation with caprylic acid for 24 hours. Source: Wang et al 2018.*

significantly associated with maintaining a physiologically healthy ratio of Bacteroidetes and Firmicutes. Its effect on the growth rate of Firmicutes is less pronounced as compared to the growth of Bacteroidetes with an overall result of increased Bacteroidetes growth. In some cases, it was even associated with decreased growth rates of Firmicutes which resulted in relieved symptoms of inflammatory bowel disease (Machate e al 2020). An overview of different probiotic bacteria in relation to caprylic acid activity is provided in Table 2.

***Table 2**: The effect of caprylic acid on gut microbiome of animal models. HFD: High Fat Diet.*

DIETS	MAIN OUTCOMES GUT MICROBIOTA
Virgin coconut oil with a caprylic acid content of 6.57%; for 16 weeks	*Bifidobacterium* (Actinobacteria)↑ *Allobaculum* and *Lactobacullum* (Firmicutes)↑
HFD (50 or 95%) of virgin coconut oil with 5.22% caprylic acid for 10 weeks	*Bacteroides and Prevotella* (Bacteroidetes)↑ *Bifidobacterium* (Actinobacteria)↑ *Lactobacullum and Enterococcus* (Firmicutes)↑ *Clostridium histolyticum* (Firmicutes)↓
HFD containing medium chain fatty acids for 8 weeks	*Allobaculum, Staphylococcus, Clostridium, F16, YS2, Lactobacillus* (Firmicutes)↑ *Deltaproteobacteria* (Proteobacteria)↑ *Bacteroidetes*↓

Beyond the antibiotic effect of caprylic acid on pathogenic fungi and bacteria, its role in regulating the growth of probiotic bacteria and fungi is prominent in the maintenance of gut health and immune physiology. Medium-chain fatty acids including caprylic acid promote the growth of the probiotic bacterium *Lactobacillus* in the intestine in animal models. *Lactobacillus* and *Bifidobacterium are* predominantly present during early life and the growth is maintained and encouraged by caprylic acid coming from breast milk. These bacteria produce acetic acid and lactic acid which inhibit toxic agents secreted from gut pathogens. Similarly, caprylic acid also has the ability to precipitate and deactivate toxic proteins such as those of S*almonella* and *Escherichia coli*.

It is evident that caprylic acid along with other medium-chain fatty acids plays a significant role in modifying the gut microbiota which is then associated with improved health of the host or relieving the symptoms associated with gastrointestinal disorders.

4. Mechanism of Action

The antimicrobial activity of caprylic acid is its ability to multi-target pathogens including cell surface, cell proteins and enzymes, cell membranes, and cellular structures and organelles.

4.1. Cell Membrane Penetration

Caprylic acid is a fatty acid and has a high affinity for penetrating the lipid bilayer pathogen cell membranes and altering its structure and fluidity. This hinders the pathogen's ability to adhere to the gut wall and hence reduce virulence. Sometimes it also accelerates cell membrane lysis leading to the death of pathogens, especially fungi.

4.2. Protein Inactivation

Caprylic acid is a strong protein precipitating agent which leads to inactive proteins. Although antibodies are also proteins, caprylic acid does not have any effect on antibodies. This unique mechanism is vital in providing antibiotic activity to breast milk during infancy when the immune system is still maturing.

Another effect on proteins and enzymes is the inhibitory action. It deactivates enzymes involved in cellular respiration and energy metabolism such as dehydrogenase enzymes in *Candida albicans*. As a result, energy-deprived pathogens cannot survive for long. The lack of energy also arrests the growth and cell division of the pathogen. In fungal pathogens, it stops cell maturation and development of hyphae (fungal cells).

4.3. Biofilms Instability

Caprylic acid is known to be effective against bacteria that make biofilms on the intestinal wall, making them resistant to the immune system and antibiotics. Biofilms are generally composed of a complex mixture of polysaccharides, similar to bacterial cell walls. These biofilms are rendered by specific proteins called Mrk A which forms a matrix and holds the structure together even under shear stress. Another protein that is found in bacterial fimbria, is GalF. Fimbriae are specialized cell extensions that are used by pathogen bacteria to adhere to the gut wall. Dr Gupta and colleagues from the Centre for Research in Infectious Disease, India, reported that caprylic acid binds and inhibits both of these proteins (Gupta et al. 2019).

Caprylic acid also inhibits the formation of new biofilms and the restoration of old ones. This makes it possible to eradicate drug resistance and biofilm-making bacteria which are otherwise hard to eradicate.

5. Pharmacokinetics & Biosafety Profile

Caprylic acid is a nutrient, so it is digested and metabolized in the body like other nutrients. It is a medium-chain saturated fatty acid. Unlike long-chain fatty acids which are absorbed through lymphatic ducts and stored in adipose tissues (leading to obesity), caprylic acid absorption and metabolism are different altogether. It is absorbed through portal veins and is directly transported to the liver where it is oxidized completely to generate energy. Other fatty acids are often recycled to produce other lipids or stored in adipose tissue after metabolism, but caprylic acid does not undergo those modifications.

WHO and FDA classify caprylic acid as a GRAS (generally recognized as safe) substance. It is virtually non-toxic even in higher quantities. The human body also produces caprylic acid as a defense mechanism and it is secreted through the skin to impart its antimicrobial properties and maintain the skin microbiome.

Caprylic acid can stay in plasm for an appreciable time. It can also cross the blood-brain barrier and nervous tissue can directly use it as an energy source.

6. Effective Targets

Considering its role in gut health, caprylic acid is effective against a wider range of bacteria and fungi causing gastrointestinal infections.

The **Fungal Targets** of Caprylic acid are:

Candid albicans: Candida belongs to a group of fungi called yeast. These fungi are single-celled pathogens and can rapidly grow through budding. Candida infecting the gut and oral cavity are often drug-resistant and anti-fungal anti-biotics are ineffective against it. Caprylic acid has been extensively studied and proved effective against all strains of Candida including drug-resistant and multi-drug-resistant.

Malassezia: These fungi are common on the skin but develop infection in the gut if the normal microbiome is disturbed. These fungi are responsible for inflammatory bowel disease (IBD). These are opportunistic fungi and normally don't infect healthy individuals. However, a weakened immune system in the gut lets these fungi grow with detrimental consequences.

Trichophyton: These fungi are responsible for athlete's foot and other infections of skin, and toes.

The **Bacterial Targets** of caprylic acid are diverse. Some of the clinically significant pathogenic targets are as follows:

Salmonella: Salmonella bacteria (*Salmonella enterica* and *Salmonella bongori*) are intestinal pathogens that cause stomach cramps, fever, and diarrhea due to toxins produced by these bacteria.

Clostridium difficile: This bacterium grows in the intestinal tract of those people who have been using antibiotics too long or have improper use of antibiotics. This bacterium is antibiotic-resistant and can transfer the drug-resistant traits to other bacteria as well. It causes diarrhea.

Campylobacter jejuni: It is a gastrointestinal pathogen associated with food poisoning and inflammation in the gut wall.

Listeria monocytogenes: This pathogen causes infection of the intestinal wall by penetrating inside the cells. It causes cramps, abdominal pain, cramps, and diarrhea.

Vibrio cholerae: It is an intestinal pathogen infamous for fatal diarrhea. It produces lethal toxins. Caprylic acid is effective in this bacterium.

The **Probiotic Targets** are microbiota of the intestine which are influenced by caprylic acid activity. Caprylic acid restores the following probiotic bacteria:

Lactobacillus: This group of bacteria is found in the human gut, oral cavity, and vagina. It is the most common group of probiotic bacteria and is associated with maintaining gut health and normal immune function.

Bifidobacterium: This bacterium is solely found in the intestine and stomach and plays a vital role in maintaining a balance between infectious strains and commensal strains of the bacteria. For example, it discourages the growth of *Helicobacter pylori* in the stomach which causes ulcers.

Deltaproteobacteria*:* These bacteria have the unique ability to produce antibacterial substances to control the pathogenic strains of the bacteria. It uses taurine amino acid as

its substrate to produce antibacterial compounds. Taurine is normally present in bile. Caprylic acid has a positive effect on the growth and maintenance of this group of bacteria in the intestine.

7. Significance of Caprylic acid in CanXida Remove (Formula RMV)

CanXida Remove (Formula RMV) holds the promise to combat gastrointestinal pathogens including fungi and bacteria. It is also designed to restore normal gut microbiome for a long-lasting effect. Caprylic acid contributes significantly to CanXida Remove formulation in combating pathogens and restoring gut microbiome.

It has been proven and validated through repeated scientific research that caprylic acid can be used as an alternative antibiotic (Dai et al. 2020). Its antibacterial and antifungal activity is well-established for pathogenic species in the human gastrointestinal tract. It provides a vital contribution to removing pathogenic fungi and bacteria in the gut. It also acts synergistically with other ingredients for effective and efficient eradication of a wide range of pathogens, including drug-resistant pathogens of bacterial or fungal origin.

Its prominent efficacy in removing resistant pathogens comes from its ability to destabilize colonies of bacteria and fungi which usually make biofilms. Caprylic acid in CanXida Remove (Formula RMV) acts as an effective and scientifically validated ingredient to eliminate drug-resistant and multi-drug-resistant pathogens. Its positive impact is also more pronounced as it is a natural nutraceutical.

It is worth mentioning that the gut microbiome plays a crucial role in the disease and health of an individual. Although it is well established that gut microbiota maintains normal gut health and immune function, it is little understood that a balance between different microbial species of probiotic bacteria is also important. Even if the gut is equipped with a probiotic microbiome, it can still develop abnormal physiology due to an imbalance in the microbiome. Caprylic acid is one of the unique ingredients of CanXida Remove (Formula RMV) which restores a healthy gut microbiome and has a proven track record of improving symptoms of SIBO (small intestinal bacterial overgrowth) and intestinal inflammatory bowel disease.

8. Conclusion

A wide range of scientific literature and clinical data provides conclusive evidence demonstrating that caprylic acid is a natural way to manage inflammatory symptoms of the bowel as well as eradicate microbial pathogens. Its role is well aligned with the CanXida Remove (Formula RMV) formulation to eliminate microbial pathogens in general and specifically drug-resistant ones as well as restore gut health and immune defenses.

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