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# Xanthones as Promising Anti-Infective Agents: Mechanisms and Therapeutic Potential

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## Abstract

Infectious diseases remain a major global health burden, further intensified by antimicrobial resistance (AMR) and the lack of effective treatments for viral and parasitic infections. Xanthones, a class of oxygenated heterocyclic compounds mainly derived from *Garcinia mangostana* and other medicinal plants, have emerged as promising broad-spectrum antimicrobial agents. These compounds exhibit potent antibacterial, antiviral, antifungal, and antiparasitic activities through mechanisms such as bacterial membrane disruption, viral replication inhibition, mitochondrial dysfunction induction in fungi, and interference with parasite metabolism. Notably, α-mangostin shows strong efficacy against *Staphylococcus aureus*, including MRSA strains, while synthetic derivatives have demonstrated activity against *Mycobacterium tuberculosis*. Xanthones also exhibit inhibitory effects on HIV, Dengue virus, and Hepatitis B virus, highlighting their potential in antiviral drug development. Despite their therapeutic promise, poor aqueous solubility, limited in vivo validation, and suboptimal pharmacokinetics pose significant barriers to clinical application. Future studies should prioritize structural modification, mechanism-based target identification, and comprehensive preclinical evaluation. Overall, xanthones represent a valuable scaffold for the development of next-generation anti-infective therapies targeting resistant and emerging pathogens.

**Keywords:** Xanthones, Antimicrobial resistance, Antibacterial agents, Antiviral compounds, Drug development

## Introduction

Xanthones are a structurally diverse class of polyphenolic compounds distinguished by their unique dibenzo-γ-pyrone scaffold. Naturally occurring in various higher plants, fungi, and lichens-particularly abundant in the pericarps of *Garcinia mangostana* (mangosteen)-xanthones have garnered increasing scientific interest due to their wide range of biological activities, including antioxidant, anti-inflammatory, anticancer, and notably, anti-infective effects. In the face of escalating global challenges such as antimicrobial resistance (AMR) and the emergence of novel viral and parasitic pathogens, the discovery of new therapeutic agents is both urgent and essential. Natural compounds, especially those with broad-spectrum potential, represent a valuable source for drug development. Xanthones have demonstrated potent antibacterial, antiviral, antifungal, and antiparasitic properties through diverse mechanisms of action. These include disruption of microbial membranes, inhibition of nucleic acid synthesis, and interference with pathogen-specific metabolic pathways. Given these promising bioactivities, a comprehensive understanding of the structural diversity of xanthones and their corresponding antimicrobial mechanisms is critical for guiding future drug discovery and development. This study aims to explore the structure-activity relationships of xanthones, highlight key examples of their anti-infective potential, and identify current limitations and future directions in their therapeutic application.

## Structural Classifications and Their Anti-Infective Activity

Xanthones can be categorized into several structural subclasses, including simple xanthones, prenylated xanthones, caged

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xanthones, hydroxylated xanthones, glycosylated xanthones, and synthetic derivatives. Each subclass is defined by specific chemical modifications that confer unique physicochemical properties and biological activities. For instance, prenylated xanthones often exhibit enhanced lipophilicity and membrane permeability, contributing to potent antibacterial and antiparasitic effects. Caged xanthones, characterized by their rigid three-dimensional architecture, are particularly noted for their cytotoxic and anticancer activities. Hydroxylated and glycosylated xanthones typically possess improved antioxidant capacity and may influence bioavailability and metabolic stability. Meanwhile, synthetic xanthone derivatives allow for targeted structural modifications aimed at optimizing pharmacokinetic profiles and enhancing selectivity toward microbial or viral targets. These structural variations play a pivotal role in modulating xanthones' pharmacological profiles, influencing not only their potency and spectrum of action but also their solubility, stability, and biodistribution. Understanding the relationship between structural features and biological activity is therefore essential for guiding the rational design and development of xanthone-based therapeutics (Figure 1, Table 1).

**Table 1:** Structural Classifications for xanthone subclasses and their anti-infective activities.

| Xanthone Type | Representative Compounds | Structural Features | Anti-Infective Activities | Pathogenic Targets |
|---|---|---|---|---|
| **Simple Xanthones** | α-Mangostin, β-Mangostin | Few substituents, unbridged tricyclic core | Antibacterial, antifungal | MRSA, *Candida albicans* |
| **Prenylated Xanthones** | Gambogic acid, γ-Mangostin | Contains prenyl side chains, lipophilic | Antiviral, antiparasitic, anti-TB | HIV, HBV, *Mycobacterium tuberculosis* |
| **Caged Xanthones** | Gambogin, Morellic acid | Complex tricyclic "caged" structure | Broad-spectrum antibacterial, antiviral | SARS-CoV-2, Gram-positive bacteria |
| **Glycosylated Xanthones** | Mangiferin | Contains sugar moieties, better solubility | Antiviral, immunomodulatory | Dengue virus, HSV-1 |
| **Hydroxylated Xanthones** | Norathyriol, Bellidifolins | Multiple hydroxyl groups, an antioxidant | Anti-inflammatory, antibacterial | *E. coli, Salmonella typhi* |
| **Synthetic Derivatives** | DMXAA-like, XAA-amides | Chemically modified for targeting | Effective against MDR pathogens | *Pseudomonas aeruginosa,* VRE |

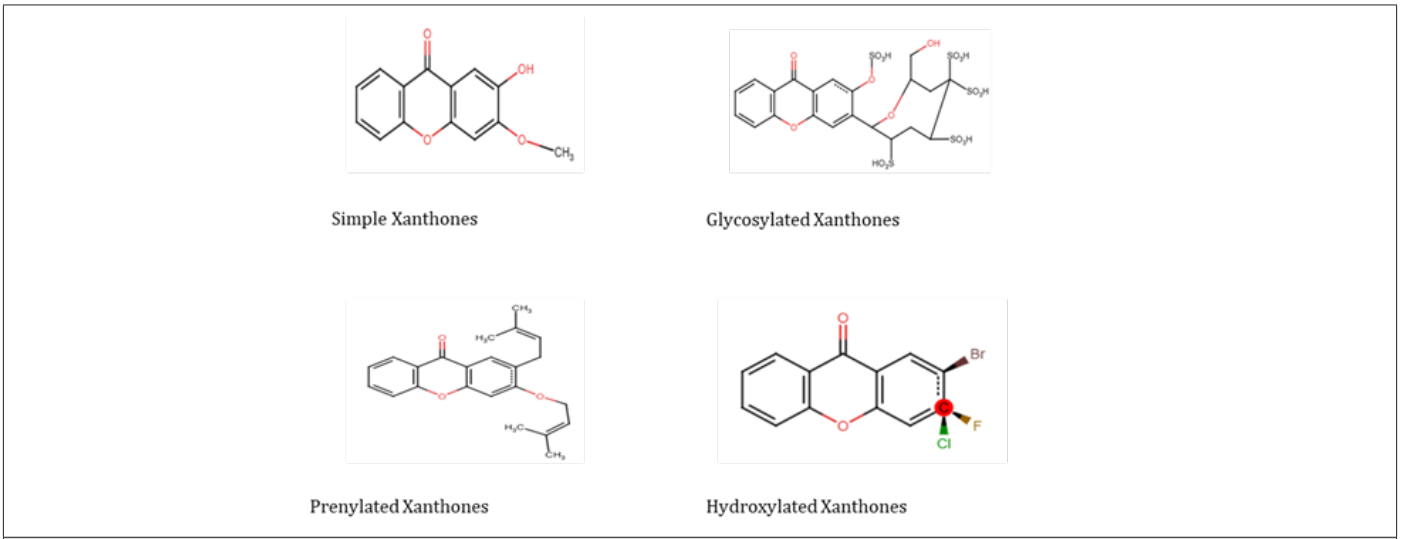


**Figure 1:** Representative chemical structures of key xanthone subclasses.

## Challenges and Therapeutic Potential

While xanthones show high in vitro potency, there are limitations to their clinical application:

i. Bioavailability and Solubility Issues: Bioavailability remains a challenge due to poor solubility and metabolic instability.

ii. Toxicological and Safety Concerns: Toxicity profiles for certain xanthones (e.g., gambogic acid) require further evaluation in vivo.

iii. Need for Standardization and Optimization: Standardization of extraction, synthesis, and formulation is essential for therapeutic development.

Taken together, to overcome these hurdles, researchers have synthesized xanthone derivatives with enhanced solubility, stabil-

ity, and pathogen selectivity. For example, xanthone-amide hybrids have shown activity against multidrug-resistant Pseudomonas aeruginosa and vancomycin-resistant Enterococcus [1-8].

## Conclusion and Future Outlook

Xanthones represent a rich and underexplored class of anti-infective agents with promising mechanisms targeting both bacteria and viruses. Future research should focus on structure-activity relationship (SAR) studies, formulation development (e.g., nano-carriers), and in vivo efficacy testing. With proper optimization, xanthone-based compounds may play a vital role in the next generation of anti-infective therapeutics, particularly against resistant and emerging pathogens.

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## Conflict of Interest

The authors declare no conflict of interest.

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