

MANGIFERIN EXTRACTION PROCESSES AND THEIR ANTIMICROBIAL PROPERTIES

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ABSTRACT

Mangiferin (MGF), derived from *Mangifera indica*, is a bioactive compound with potent antioxidant, anti-inflammatory, and antimicrobial properties. This review explores advanced extraction methods designed to reduce reliance on organic solvents, utilizing technologies such as ultrasonic, supercritical fluid, ionic liquid, and microwave-assisted extraction to enhance efficiency and sustainability. *In vitro* studies confirm the efficacy of MGF against pathogens, underscoring its potential as a natural antimicrobial agent. Optimizing extraction techniques and exploring novel nanoformulations could significantly improve the bioavailability and therapeutic effectiveness of MGF. These advancements not only promote eco-friendly extraction processes, but also suggest the potential of MGF as a viable treatment for antibiotic-resistant infections and other biotechnological challenges.

Keywords: Mangiferin. Green sources. Antimicrobial activity. Biomolecule extraction. Purification.

1 INTRODUCTION

Currently, there is significant interest in the use of plants for pharmaceutical and biotechnological applications, many of which have been utilized throughout history. This renewed interest is partly driven by the increasing resistance of microbes to numerous antibiotics, highlighting the need for alternative therapeutic agents. Consequently, the exploration and use of extracts and bioactive compounds from natural sources have surged¹. Among these natural compounds, mangiferin (MGF, as highlighted in **Figure 1**) has emerged as a particularly promising candidate. MGF is a naturally occurring, crystalline, yellow-colored glucosylxanthone found in various plants (notably from *Mangifera indica*). It has demonstrated a wide range of biological activities, including significant antimicrobial properties². Extensive research has also highlighted MGF's therapeutic potential, including its antioxidant, anti-inflammatory, and antitumor properties³. Given the pressing need for new antimicrobial agents and the promising profile of MGF, this work focuses on reviewing eco-friendly processes for extracting MGF and its potential antimicrobial activity. By understanding these aspects, we can better appreciate the value of MGF in developing new pharmaceutical and biotechnological products.

Eco-friendly extraction of mangiferin (MGF) from green sources (*Mangifera indica* L.)

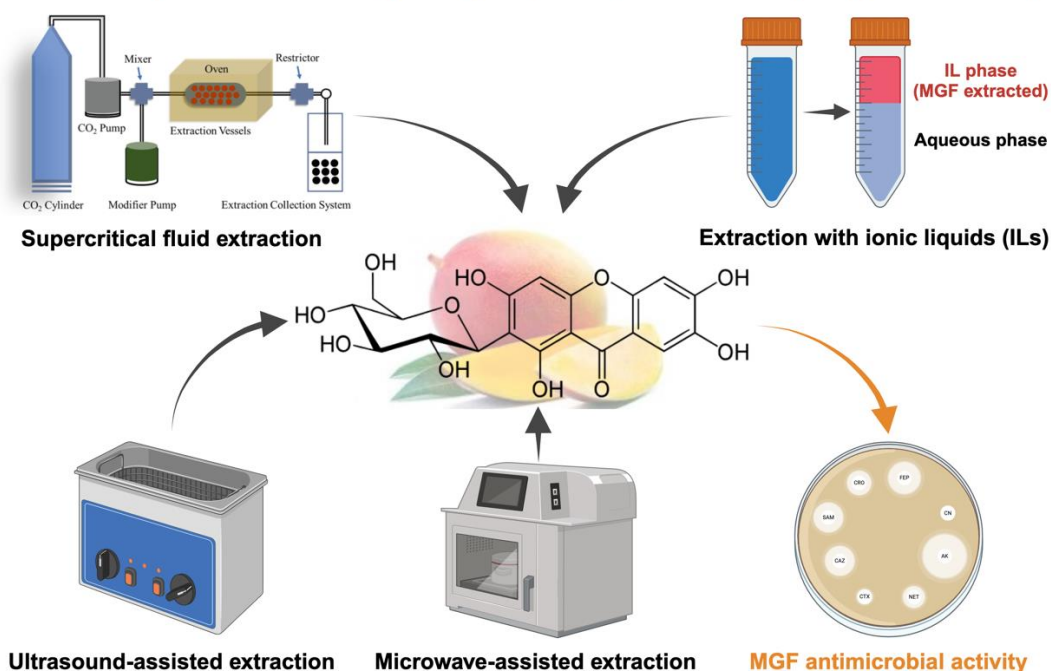


Figure 1. Main processes employed in the mangiferin extraction.

2 ANTIMICROBIAL ACTIVITY

MGF has demonstrated significant antimicrobial activity against various pathogens (**Figure 1**). *In vitro* studies have shown MGF's effectiveness against bacteria such as *Staphylococcus aureus* and *Escherichia coli*, as well as fungi like *Candida albicans* ^{4,5}. Beyond its antimicrobial properties, MGF also exhibits potent antioxidant and anti-inflammatory effects⁶, which may further enhance its antimicrobial action. The promising results from these studies suggest that MGF could serve as a natural alternative to conventional antimicrobial drugs for treating various infectious diseases⁷. However, it is important to recognize that many of these studies have been conducted solely *in vitro*. Therefore, more research is needed to establish the efficacy and safety of MGF as an antimicrobial treatment in humans⁷. Another important consideration is the extraction and purification processes of MGF. The downstream processes of MGF can be challenging, and optimizing these methods is crucial to fully harness the antimicrobial potential of this special molecule.

3 MANGIFERIN EXTRACTION METHODS

MGF can be obtained from various parts of the mango plant, including leaves, peels, and green fruits. Natural sources of MGF are increasingly valued in the biopharmaceutical, food, and cosmetic industries due to their potent antioxidant and anti-inflammatory properties. The method of extraction and the processing conditions used significantly impact the quantity and quality of the extracted MGF⁷. Traditional techniques for MGF extraction, such as maceration, reflux extraction, solid-phase microextraction, and hydrodistillation, often lack cost-effectiveness and environmental sustainability⁸. In response to these limitations, recent advancements have led to the development of innovative extraction methods that are faster, more efficient, and eco-friendly. These advanced methods include ultrasonic, supercritical fluid, ionic liquid, and microwave, which are highlighted in **Figure 17**. These approaches aim to minimize the use of volatile organic compounds (VOCs) and reduce the generation of toxic waste discarded into industrial effluents compromising the ecosystem.

In particular, ultrasonic extraction applies cavitation effects that enhance the penetration of the solvent into the plant tissue, increasing the contact surface between the solid and liquid phases. This technique facilitates rapid solute diffusion from the solid phase into the solvent, leading to efficient extraction⁹. Supercritical fluid extraction employs supercritical CO₂ as a solvent to obtain a pure extract free of impurities. Under specific conditions of temperature and pressure, CO₂ acts as an effective solvent, resulting in higher yields and more efficient extraction processes^{6,10}. Ionic liquid (ILs) extraction are an organic salt in the liquid state that consists of an organic cation paired with an organic or inorganic anion. ILs possess the ability to dissolve and extract bioactive compounds from plants efficiently¹¹. This method is particularly advantageous due to the low volatility and high thermal stability of ILs. Microwave-assisted extraction leverages high-frequency electromagnetic waves to selectively heat the solvents. This technique offers the benefit of obtaining better yields in a reduced time frame while consuming less solvent¹². The selective heating mechanism allows for efficient energy transfer, resulting in enhanced extraction efficiency. Additionally, sustainable novel processes for MGF extraction are being developed. One such process with great potential is platforms based on aqueous biphasic systems. This method can be used to purify and concentrate MGF samples, and besides that can also provide MGF within nanostructures formed by phase separation ^{13,14}

4 FUTURES PERSPECTIVES

The significant antimicrobial properties of MGF highlight its potential as a natural alternative to conventional antimicrobial agents. While *in vitro* studies have demonstrated promising results, future research should focus on *in vivo* studies and clinical trials to establish the efficacy and safety of MGF in human treatments. Additionally, optimizing extraction and formulation techniques will be crucial to enhancing the bioavailability and therapeutic effectiveness of MGF. Investigating synergistic effects with existing antimicrobial drugs could also pave the way for novel combination therapies. Addressing these research gaps will be essential for fully harnessing the potential of MGF in the biotechnological and pharmaceutical industries, offering new solutions for combating antibiotic-resistant infections and other health challenges. Furthermore, the possibility of developing novel nanoformulations could significantly advance MGF's application. Nanoformulations can improve drug solubility, stability, and targeted delivery, thereby enhancing the bioavailability and efficacy of MGF. This innovation could not only facilitate controlled release, but also mitigate potential side effects associated with conventional drug formulations. Integrating these advanced delivery systems with optimized extraction processes (e.g., based on aqueous biphasic systems) would represent a transformative approach to maximizing the therapeutic benefits of MGF, positioning it as a versatile tool in modern bioengineering.

REFERENCES

1. Dzotam, J. K. & Kuete, V. Antibacterial and Antibiotic-Modifying Activity of Methanol Extracts from Six Cameroonian Food Plants against Multidrug-Resistant Enteric Bacteria. *Biomed Res Int* **2017**, 1–19 (2017).
2. Yehia, R. S. & Altwaim, S. A. An Insight into In Vitro Antioxidant, Antimicrobial, Cytotoxic, and Apoptosis Induction Potential of Mangiferin, a Bioactive Compound Derived from *Mangifera indica*. *Plants* **12**, 1539 (2023).
3. Lum, P. T., Sekar, M., Gan, S. H., Pandey, V. & Bonam, S. R. Protective effect of mangiferin on memory impairment: A systematic review. *Saudi J Biol Sci* **28**, 917–927 (2021).

4. Cardenas, V., Mendoza, R., Chiong, L. & del Aguila, E. Comparison of the Antibacterial Activity of the Ethanol Extract vs Hydroalcoholic Extract of the Leaves of *Mangifera indica* L. (Mango) in Different Concentrations: An In Vitro Study. *J Contemp Dent Pract* **21**, 202–206 (2020).
5. Jiang, T., Han, F., Gao, G. & Liu, M. Mangiferin exert cardioprotective and anti-apoptotic effects in heart failure induced rats. *Life Sci* **249**, 117476 (2020).
6. Morozkina, S. N., Nhung Vu, T. H., Generalova, Y. E., Snetkov, P. P. & Uspenskaya, M. V. Mangiferin as New Potential Anti-Cancer Agent and Mangiferin-Integrated Polymer Systems—A Novel Research Direction. *Biomolecules* **11**, 79 (2021).
7. Yehia, R. S. & Altwaim, S. A. An Insight into In Vitro Antioxidant, Antimicrobial, Cytotoxic, and Apoptosis Induction Potential of Mangiferin, a Bioactive Compound Derived from *Mangifera indica*. *Plants* **12**, 1539 (2023).
8. Zou, T.-B. *et al.* Ultrasound-Assisted Extraction of Mangiferin from Mango (*Mangifera indica* L.) Leaves Using Response Surface Methodology. *Molecules* **19**, 1411–1421 (2014).
9. Rostagno, M. A., Palma, M. & Barroso, C. G. Ultrasound-assisted extraction of soy isoflavones. *J Chromatogr A* **1012**, 119–128 (2003).
10. Baldino, L., Scognamiglio, M. & Reverchon, E. Supercritical fluid technologies applied to the extraction of compounds of industrial interest from *Cannabis sativa* L. and to their pharmaceutical formulations: A review. *J Supercrit Fluids* **165**, 104960 (2020).
11. Chen, J.-K. *et al.* α -Glucosidase Inhibitory Phytochemical Components of Chinese Endemic Plant *Whitfordiodendron filipes* var. *tomentosum*. *Plants* **13**, 692 (2024).
12. Segatto, M. L., Schnarr, L., Olsson, O., Kümmerer, K. & Zuin, V. G. Ionic liquids vs. ethanol as extraction media of algicidal compounds from mango processing waste. *Front Chem* **10**, (2022).
13. Kurnik, I. S. *et al.* Separation and purification of curcumin using novel aqueous two-phase micellar systems composed of amphiphilic copolymer and cholinium ionic liquids. *Sep Purif Technol* **250**, 117262 (2020).
14. Kurnik, I. S. *et al.* Separation and purification of curcumin using novel aqueous two-phase micellar systems composed of amphiphilic copolymer and cholinium ionic liquids. *Sep Purif Technol* **250**, 117262 (2020).

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