Journal of Medicinal and Chemical Sciences 7 (2024) 275-286

Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Review Article

Alpha-Mangostin as an Antiviral Candidate: A Mini Review

Arif Nur Muhammad Ansori[1,2,3,4], Ahmad Affan Ali Murtadlo[3,4,5], Viol Dhea Kharisma[3,4,5], Bayyinatul Muchtaromah[6], Muhammad Badrut Tamam[3,7], Dora Dayu Rahma Turista[3,8], Imam Rosadi[9], Vikash Jakhmola[2], Maksim Rebezov[10,11], Rahadian Zainul*[12,13]

[1]*Postgraduate School, Universitas Airlangga, Surabaya, Indonesia*
[2]*Uttaranchal Institute of Pharmaceutical Sciences, Uttaranchal University, Dehradun, India*
[3]*Generasi Biologi Indonesia Foundation, Gresik, Indonesia*
[4]*Division of Research and Development, CV Jalan Tengah, Pasuruan, Indonesia*
[5]*Faculty of Science and Technology, Universitas Airlangga, Indonesia*
[6]*Master Program of Biology, Universitas Islam Negeri Maulana Malik Ibrahim, Malang, Indonesia*
[7]*Department of Biology, Faculty of Science, Technology and Education, Universitas Muhammadiyah Lamongan, Lamongan, Indonesia*
[8]*Department of Biology Education, Faculty of Teacher Training and Education, Mulawarman University, Samarinda, Indonesia*
[9]*Department of Biology, Faculty of Mathematics and Natural Sciences, Mulawarman University, Samarinda, Indonesia*
[10]*Department of Scientific Research, V. M. Gorbatov Federal Research Center for Food Systems, Moscow, Russian Federation*
[11]*Faculty of Biotechnology and Food Engineering, Ural State Agrarian University, Yekaterinburg, Russian Federation*
[12]*Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Negeri Padang, Padang, Indonesia*
[13]*Center for Advanced Material Processing, Artificial Intelligence, and Biophysic Informatics (CAMPBIOTICS), Universitas Negeri Padang, Padang, Indonesia*

ARTICLE INFO

Article history

Receive: 2023-09-11
Received in revised: 2023-10-08
Accepted: 2023-10-11
Manuscript ID: JMCS-2309-2288
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Fatima Ramezani
Editor who approved publication:
Dr. Majid Darroudi

DOI:10.26655/JMCHEMSCI.2024.2.1

KEYWORDS

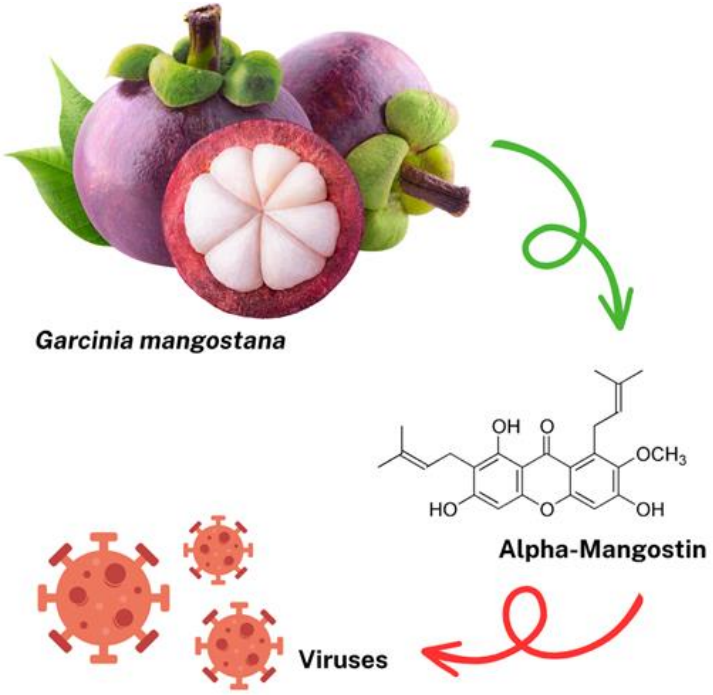
Alpha-mangostin
Antiviral
Garcinia mangostana
Mechanism of action
Viral infections

ABSTRACT

This mini review aims to explore the potential of alpha-mangostin as an antiviral candidate. Alpha-mangostin is a natural compound found in the fruit of the *Garcinia mangostana* tree. Over the years, it has attracted considerable attention due to its diverse pharmacological properties, including antiviral activity. This review provides an overview of the current literature on the antiviral effects of alpha-mangostin, focusing on its mechanisms of action and its efficacy against various viral infections. The potential application of alpha-mangostin as a therapeutic agent against viral diseases is discussed, along with future research directions and challenges in the development of alpha-mangostin-based antiviral therapies.

* Corresponding author: Rahadian Zainul
✉ E-mail: rahadianzmsiphd@fmipa.unp.ac.id

GRAPHICAL ABSTRACT



Introduction

Viral infections continue to pose a significant global health threat, with limited treatment options available for many viral diseases. The search for novel antiviral agents from natural sources has gained considerable attention in recent years. Among the numerous natural compounds under investigation, alpha-mangostin has emerged as a promising candidate with potential antiviral properties. Alpha-mangostin is a xanthone derivative primarily found in the fruit of the *Garcinia mangostana* tree, native to Southeast Asia [1-3]. Alpha-mangostin has been the subject of extensive research due to its diverse pharmacological activities, including antimicrobial, antioxidant, anti-inflammatory, and anticancer effects. In recent years, the focus has shifted towards exploring its antiviral potential. Various studies have demonstrated that alpha-mangostin exhibits significant inhibitory effects against a wide range of viruses, including DNA and RNA viruses. These findings have sparked interest in investigating alpha-mangostin as a potential therapeutic agent against viral infections [4-6]. The mechanisms underlying the antiviral activity of alpha-mangostin are multifaceted. Studies have shown that it can inhibit viral entry into host cells by interacting with viral envelope proteins or cellular receptors. Additionally, alpha-mangostin has been reported to interfere with different stages of the viral replication cycle, such as viral attachment, genome replication, protein synthesis, and virion assembly. Furthermore, it possesses immunomodulatory properties, influencing the host immune response against viral infections [7-9]. The antiviral effects of alpha-mangostin have been evaluated against a wide array of viruses, including herpesviruses, influenza viruses, human immunodeficiency virus (HIV), dengue virus, and hepatitis viruses, among others. *In vitro* and *in vivo* studies have demonstrated promising results, indicating the potential of alpha-mangostin as a broad-spectrum antiviral agent. Furthermore, recent studies have explored its efficacy against emerging viral infections, such as Zika virus and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [10-12].

While the antiviral activity of alpha-mangostin is promising, several challenges and questions remain. The bioavailability and pharmacokinetic properties of alpha-mangostin need to be further elucidated to determine suitable dosage regimens and formulations for clinical applications. Safety considerations and potential toxicity profiles also require comprehensive evaluation. In addition, the synergistic effects of alpha-mangostin in combination with other antiviral agents should be investigated to enhance its therapeutic potential [13-15]. In this mini review, we aim to provide an overview of the current literature on alpha-mangostin as an antiviral candidate. We will discuss the mechanisms of action underlying its antiviral effects, summarize its activity against different viral infections, and explore its potential applications as an adjunct therapy or prophylactic agent. Furthermore, we will address the challenges and future perspectives in the development of alpha-mangostin-based antiviral therapies. By consolidating the available knowledge, this review seeks to contribute to the understanding of alpha-mangostin's antiviral potential and guide further research in this promising field.

Source and Extraction

The primary natural source of alpha-mangostin is the fruit of the *Garcinia mangostana* tree, commonly known as the mangosteen. The mangosteen tree is native to tropical regions of Southeast Asia, including countries such as Indonesia, Thailand, and Malaysia. The fruit is highly valued for its delicious taste and has been consumed traditionally for centuries [16-18].

The extraction of alpha-mangostin from the mangosteen fruit involves a multi-step process. The initial step typically involves the removal of the pericarp, which is the thick outer rind of the fruit. The pericarp contains high concentrations of alpha-mangostin compared to other parts of the fruit. Once the pericarp is separated, it is dried and ground into a fine powder [19-21]. Various extraction methods have been employed to isolate alpha-mangostin from the powdered pericarp. Solvent extraction methods, such as maceration, reflux, or Soxhlet extraction, are commonly used. Organic solvents such as ethanol, methanol, or ethyl acetate are frequently employed due to their ability to effectively dissolve and extract alpha-mangostin from the plant material [22-24]. After extraction, the solvent is evaporated under reduced pressure to obtain a crude extract containing alpha-mangostin. Further purification steps, such as column chromatography or crystallization, may be employed to isolate and obtain a pure form of alpha-mangostin. The purity of the extracted compound can be assessed using analytical techniques like high-performance liquid chromatography (HPLC) or mass spectrometry (MS) [25-27].

It is worth noting that alternative methods, including supercritical fluid extraction, ultrasound-assisted extraction, and microwave-assisted extraction, have also been explored for the extraction of alpha-mangostin. These methods offer advantages such as shorter extraction times, reduced solvent consumption, and enhanced extraction efficiency, but their application in large-scale production and commercial settings requires further investigation [28-30].

The availability and abundance of mangosteen trees and the extraction yield of alpha-mangostin can vary depending on factors such as geographical location, climate, and cultivation practices.

Therefore, efforts have been made to explore sustainable cultivation techniques and improve extraction processes to ensure a reliable and consistent supply of alpha-mangostin for further research and potential pharmaceutical development [31-33]. To sum up, alpha-mangostin is primarily sourced from the fruit of the *Garcinia mangostana* tree. The pericarp of the fruit, which contains high concentrations of alpha-mangostin, is extracted using solvent-based methods. Further purification steps are often employed to obtain a pure form of alpha-mangostin. Continued research in extraction techniques and cultivation practices will contribute to the sustainable production of alpha-mangostin and facilitate its potential use as an antiviral candidate [34, 35].

Chemical structure and properties

Alpha-mangostin, chemically known as $C_{24}H_{26}O_6$, belongs to the class of xanthone derivatives. It is a yellowish crystalline compound with a molecular weight of 410.47 g/mol. The chemical structure of alpha-mangostin consists of a xanthone core, which comprises two aromatic benzene rings linked by a pyran ring [36, 37]. The xanthone core of alpha-mangostin is decorated with various functional groups, including hydroxyl (-OH) and methoxy (-OCH3) groups. These functional groups contribute to its overall chemical properties and biological activities. The presence of multiple hydroxyl groups renders alpha-mangostin a polyphenolic compound, contributing to its antioxidant potential. Alpha-mangostin exhibits lipophilic characteristics due to the presence of long hydrocarbon chains attached to the xanthone core. This lipophilicity facilitates its interaction with cellular membranes and biological targets, potentially influencing its antiviral activity [38, 39]. Furthermore, the chemical stability of alpha-mangostin is influenced by environmental factors such as light, heat, and pH. It is relatively stable under acidic conditions, but degradation may occur under alkaline conditions. The sensitivity of alpha-mangostin to degradation by light and heat necessitates appropriate storage and handling conditions to maintain its stability and potency [40, 41]. The physicochemical properties of alpha-mangostin contribute to its solubility characteristics, which in turn impact its formulation and delivery. Alpha-mangostin is sparingly soluble in water, but exhibits good solubility in organic solvents such as ethanol, methanol, and ethyl acetate. The low aqueous solubility poses challenges for its systemic administration, necessitating the development of appropriate solubilization strategies such as nanoemulsions, nanoparticles, or inclusion complexes [42]. Therefore, alpha-mangostin is a xanthone derivative with a distinct chemical structure. Its polyphenolic nature, lipophilicity, and functional groups contribute to its biological activities, including its potential antiviral effects. Understanding the chemical properties of alpha-mangostin is crucial for its formulation, delivery, and optimization as an antiviral candidate [33, 38]. Further investigations into its structure-activity relationship will shed light on its interaction with viral targets and aid in the design of more potent derivatives or analogs.

Antiviral mechanisms of alpha-mangostin

The antiviral mechanisms of alpha-mangostin are diverse and multifaceted, contributing to its potential efficacy against various viral infections. Understanding these mechanisms is essential for elucidating its mode of action and optimizing its use as an antiviral candidate. Several key mechanisms of action have been proposed based on experimental evidence:

Inhibition of viral entry

Alpha-mangostin has been reported to interfere with viral entry into host cells. It can inhibit viral attachment to cellular receptors, thereby preventing viral fusion and internalization. Studies have demonstrated that alpha-mangostin can directly interact with viral envelope proteins, such as glycoproteins or spike proteins, hindering their binding to host cell receptors. By blocking the initial steps of viral entry, alpha-mangostin limits viral infection and replication within host cells [43].

Viral replication suppression

Another crucial mechanism by which alpha-mangostin exerts its antiviral activity is through the suppression of viral replication. Alpha-mangostin has been shown to inhibit key steps in the viral replication cycle, such as viral genome replication and protein synthesis. It can interfere with viral enzymes involved in replication, transcription, or translation processes, thereby inhibiting viral replication and reducing the production of infectious viral particles [44].

Modulation of host immune response

Alpha-mangostin possesses immunomodulatory properties that can influence the host immune response against viral infections. It has been demonstrated to modulate the production of pro-inflammatory cytokines, such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and

interferons (IFNs). By regulating the immune response, alpha-mangostin may contribute to the control of excessive inflammation and promote a balanced immune environment conducive to viral clearance [45].

Inhibition of viral protease activity

Many viruses rely on specific proteases for their replication and maturation. Alpha-mangostin has shown inhibitory effects on viral proteases, such as the HIV protease or the proteases involved in the processing of viral polyproteins. By blocking viral protease activity, alpha-mangostin interferes with viral maturation and the generation of infectious virions [46].

Disruption of viral protein-protein interactions

Alpha-mangostin has also been reported to disrupt critical protein-protein interactions essential for viral replication. It can interfere with the formation of viral protein complexes, preventing the proper assembly and function of viral replication complexes. By disrupting these interactions, alpha-mangostin hinders the efficient replication of viral genomes and the production of infectious progeny [47]. These mechanisms collectively contribute to the antiviral potential of alpha-mangostin. It is important to note that the specific mechanisms of action may vary depending on the virus under investigation, highlighting the broad-spectrum nature of alpha-mangostin's antiviral activity. Further research is necessary to fully elucidate the detailed molecular interactions between alpha-mangostin and viral targets, providing insights into its precise mode of action and enabling the development of more targeted antiviral strategies [48].

Antiviral activity of alpha-mangostin

The antiviral activity of alpha-mangostin has been investigated against a wide range of viruses, including both DNA and RNA viruses. Numerous *in vitro* and *in vivo* studies have provided valuable insights into its efficacy against various viral infections [13, 14, 21, 23]. The following subsections highlight the antiviral activity of alpha-mangostin against different viral families:

Alpha-mangostin against DNA viruses

Alpha-mangostin has demonstrated potent antiviral effects against DNA viruses, including herpesviruses such as herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2), varicella-zoster virus (VZV), and human cytomegalovirus (HCMV). Studies have shown that alpha-mangostin inhibits viral replication, reduces viral gene expression, and impedes the formation of infectious viral particles. Furthermore, it has exhibited antiviral activity against other DNA viruses such as adenoviruses and papillomaviruses [49, 50].

Alpha-mangostin against RNA viruses

Alpha-mangostin has also shown promising antiviral activity against RNA viruses. It has been reported to inhibit the replication of RNA viruses belonging to different families, including flaviviruses (e.g., dengue virus, Zika virus), coronaviruses (e.g., SARS-CoV, MERS-CoV), and influenza viruses. Alpha-mangostin has been found to reduce viral RNA synthesis, impede viral protein expression, and inhibit the release of infectious viral particles. These effects suggest its potential utility as an antiviral agent against a broad spectrum of RNA viruses [10, 11, 15].

Alpha-mangostin against emerging viral infections

In addition to its efficacy against well-known viral pathogens, alpha-mangostin has shown promise against emerging viral infections. For instance, studies have investigated its antiviral activity against the Zika virus, which emerged as a significant public health concern. Alpha-mangostin has demonstrated inhibitory effects on Zika virus replication, viral protein expression, and the production of infectious viral particles. Furthermore, recent investigations have explored its potential against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of the ongoing COVID-19 pandemic. Preliminary studies have indicated that alpha-mangostin may exhibit inhibitory effects on SARS-CoV-2 replication, although further research is needed to evaluate its efficacy and potential synergistic effects with other antiviral agents [20, 22].

The antiviral activity of alpha-mangostin can vary depending on factors such as the specific virus, viral strain, cell type, and experimental conditions. While promising, it is important to note that most studies evaluating its antiviral activity have been conducted *in vitro* or in animal models, and further research is needed to assess its effectiveness in human clinical settings [23]. Thus, alpha-mangostin has demonstrated broad-spectrum antiviral activity against DNA and RNA viruses, including both well-established pathogens and emerging viral infections. Its ability to inhibit viral replication, reduce viral gene expression, and disrupt viral particle formation highlights its potential as a therapeutic agent against viral diseases. Further studies, including clinical trials, are necessary to determine the full extent of its antiviral efficacy, evaluate its safety profile, and optimize its formulation and delivery for potential clinical applications.

Pharmacokinetics and toxicity profile

To fully explore the potential of alpha-mangostin as an antiviral candidate, an understanding of its pharmacokinetics and toxicity profile is essential. These aspects provide valuable insights into its absorption, distribution, metabolism, excretion, as well as its safety considerations [17-19]. The following subsections provide an overview of the current knowledge regarding the pharmacokinetics and toxicity profile of alpha-mangostin:

Absorption, distribution, metabolism, and excretion

Limited studies have focused specifically on the pharmacokinetics of alpha-mangostin. It is known to exhibit low aqueous solubility, which can influence its absorption and bioavailability. Efforts have been made to enhance its solubility and oral bioavailability through formulation approaches such as nanoemulsions, solid lipid nanoparticles, and self-microemulsifying drug delivery systems. These strategies aim to improve the dissolution and absorption of alpha-mangostin in the gastrointestinal tract [31, 32]. Once absorbed, alpha-mangostin undergoes distribution throughout the body. It has been detected in various tissues and organs, indicating its ability to penetrate biological barriers. However, further research is required to elucidate its specific distribution patterns and tissue concentrations [37, 45]. The alpha-mangostin metabolism has been investigated to a limited extent. In *in vitro* studies using liver microsomes, it was found to undergo metabolism primarily through cytochrome P450 enzymes. The identification of specific metabolites and their pharmacological activities requires further investigation [4, 6, 7]. The excretion pathways of alpha-mangostin have not been extensively studied. It is anticipated that alpha-mangostin and its metabolites are eliminated primarily through biliary and renal routes. However, comprehensive studies on its excretion kinetics, including the characterization of major metabolites and their elimination pathways, are needed to gain a comprehensive understanding of its pharmacokinetic profile [47, 48].

Safety and toxicological considerations

The safety profile of alpha-mangostin is an important aspect to consider for its development as an antiviral candidate. Overall, it has shown a favorable safety profile in preclinical studies. Acute and subchronic toxicity studies in animal models have indicated a lack of significant adverse effects at therapeutic doses. However, long-term toxicity studies and comprehensive safety evaluations are required to assess its chronic toxicity and potential cumulative effects. Investigations into the cytotoxicity of alpha-mangostin have demonstrated varying results depending on the cell type and concentration used. While it exhibits selective cytotoxicity towards cancer cells, further studies are needed to evaluate its impact on normal cells and tissues [32, 50]. Toxicological studies have also evaluated the genotoxicity and mutagenicity of alpha-mangostin. In general, it has shown no genotoxic potential in bacterial mutagenicity assays and *in vitro* micronucleus tests. Nevertheless, additional genotoxicity studies are necessary to fully assess its safety profile [23, 27]. The pharmacokinetics of alpha-mangostin,

including its absorption, distribution, metabolism, and excretion, are still areas of ongoing research. Efforts to enhance its solubility and bioavailability have been explored through various formulation approaches. Moreover, alpha-mangostin has demonstrated a favourable safety profile in preclinical studies, showing limited acute and subchronic toxicity. However, further studies are required to comprehensively evaluate its chronic toxicity, genotoxicity, and potential adverse effects. Continued investigation into the pharmacokinetics and toxicology of alpha-mangostin is crucial to determine appropriate dosage regimens, optimize its formulation, and ensure its safety in potential clinical applications as an antiviral candidate [37, 39, 41, 42].

Potential therapeutic applications

Alpha-mangostin as an adjunct therapy

Alpha-mangostin holds potential as an adjunct therapy in combination with existing antiviral agents. The synergistic effects of alpha-mangostin with conventional antiviral drugs have been investigated in several studies. Combination therapy can offer advantages such as increased antiviral efficacy, reduced drug resistance, and expanded antiviral spectrum. Alpha-mangostin's unique mechanisms of action, such as viral entry inhibition and modulation of host immune response, may complement the modes of action of existing antiviral agents, leading to improved treatment outcomes [19, 23, 24].

Alpha-mangostin as a prophylactic agent

Given its broad-spectrum antiviral activity, alpha-mangostin also holds promise as a prophylactic agent against viral infections. Prophylaxis aims to prevent viral infection in individuals at high risk or in specific populations. Alpha-mangostin's ability to inhibit viral entry and replication suggests it could be used as a preventive measure to reduce the risk of viral transmission. Further research is needed to determine appropriate dosing regimens and administration routes for prophylactic use [27, 28]. The potential applications of alpha-mangostin extend beyond direct antiviral effects. Its immunomodulatory properties may have implications in enhancing host immune responses, which could be beneficial in individuals with compromised immune systems. Furthermore, alpha-mangostin's antioxidant and anti-inflammatory activities may contribute to alleviating viral-induced oxidative stress and inflammation, potentially mitigating tissue damage associated with viral infections [20, 21]. Despite its potential therapeutic applications, challenges remain in the development of alpha-mangostin-based antiviral therapies. The optimization of its formulation, enhancement of its bioavailability, and determination of appropriate dosing regimens are critical for effective clinical translation. Moreover, rigorous preclinical and clinical studies are required to evaluate its safety, efficacy, and potential drug interactions in diverse populations [37, 45]. Alpha-mangostin holds promise as both an adjunct therapy and a prophylactic agent in the fight against viral infections. Its synergistic effects with existing antiviral drugs, broad-spectrum antiviral activity, and immunomodulatory properties make it an attractive candidate for further investigation. Continued research efforts are necessary to uncover its full therapeutic potential, optimize its formulation, and evaluate its safety and efficacy in clinical settings [44, 46].

Challenges and future perspectives

Formulation and delivery systems

One of the primary challenges in utilizing alpha-mangostin as an antiviral therapy lies in its formulation and delivery systems. As a compound with limited aqueous solubility, developing efficient delivery methods to enhance its bioavailability and target specific sites of viral infection is crucial. Strategies such as nanoformulations, liposomes, or prodrug approaches may be explored to improve its solubility, stability, and targeted delivery to infected cells or tissues. Moreover, the development of suitable dosage forms, including oral, topical, or intravenous formulations, would contribute to its clinical feasibility and efficacy [29, 31].

Clinical trials and regulatory considerations

The translation of alpha-mangostin from preclinical studies to clinical trials poses another challenge. Conducting well-designed clinical trials with appropriate endpoints, patient populations, and rigorous methodologies is necessary to evaluate its safety, efficacy, and optimal dosing regimens. Furthermore, regulatory considerations and guidelines need to be addressed to ensure compliance with ethical and legal standards for the development and approval of alpha-mangostin-based antiviral therapies [18, 19].

Combination therapies and synergistic effects

Exploring combination therapies involving alpha-mangostin and other antiviral agents represents a promising avenue for future research. Synergistic effects may be achieved by combining alpha-mangostin with existing antiviral drugs or other natural compounds with complementary mechanisms of action. Combination therapies could lead to enhanced antiviral activity, reduced drug resistance, and broader efficacy against a range of viral infections. However, comprehensive studies are needed to investigate the compatibility, optimal dosing, and potential interactions of alpha-mangostin with other therapeutic agents [11-13].

Pharmacogenomics and personalized medicine

Concerning the inter-individual variability in response to antiviral therapies, pharmacogenomic studies could provide valuable insights into the efficacy and safety of alpha-mangostin. Identifying genetic factors that influence individual responses to alpha-mangostin could aid in the development of personalized treatment approaches. Moreover, understanding the pharmacogenomics of alpha-mangostin could help optimize its dosing regimens, minimize adverse effects, and improve treatment outcomes [34, 35].

Sustainability and commercial production

As the interest in alpha-mangostin as an antiviral candidate grows, ensuring sustainable and environmentally friendly methods of production is vital. Exploring eco-friendly cultivation practices, optimizing extraction processes, and implementing scalable production methods will contribute to a reliable supply of alpha-mangostin for pharmaceutical development. Collaborations between researchers, industry partners, and local communities can foster sustainable practices and promote the responsible utilization of natural resources [47, 49]. While alpha-mangostin shows great promise as an antiviral candidate, several challenges must be addressed for its successful development. Formulating optimal delivery systems, conducting robust clinical trials, and considering combination therapies are critical for advancing alpha-mangostin-based antiviral therapies. Additionally, the integration of pharmacogenomic approaches and sustainable production practices will enhance its therapeutic potential and support its responsible utilization [50-52].

Conclusion

In conclusion, alpha-mangostin shows immense potential as an antiviral candidate. Its diverse mechanisms of action, broad-spectrum antiviral activity, and natural origin make it a promising therapeutic option in the fight against viral infections. Continued research efforts, collaboration between academia and industry, and regulatory support are necessary to further explore its antiviral efficacy, optimize its formulation and delivery, and pave the way for its translation into clinical practice. Alpha-mangostin stands as a promising natural compound that holds the potential to contribute significantly to the development of novel antiviral therapies and the mitigation of viral diseases in the future.

Disclosure Statement

No potential conflict of interest was reported by the authors.

Funding

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the article and agreed to be responsible for all the aspects of this work.

ORCID

Arif Nur Muhammad Ansori
https://orcid.org/0000-0002-1279-3904
Ahmad Affan Ali Murtadlo
https://orcid.org/0000-0002-7942-875X
Viol Dhea Kharisma
https://orcid.org/0000-0001-9060-0429
Bayyinatul Muchtaromah
https://orcid.org/0000-0001-9968-8295
Muhammad Badrut Tamam
https://orcid.org/0000-0001-7527-9606
Dora Dayu Rahma Turista
https://orcid.org/0000-0001-7527-9606
Imam Rosadi
https://orcid.org/0000-0001-6988-3495
Vikash Jakhmola
https://orcid.org/0000-0002-8108-006X
Maksim Rebezov
https://orcid.org/0000-0002-1683-2501
Rahadian Zainul
https://orcid.org/0000-0002-3740-3597

References

[1]. a) Mohamed G.A., Al-Abd A.M., El-Halawany A.M., Abdallah H.M., Ibrahim S.R.M. New xanthones and cytotoxic constituents from Garcinia mangostana fruit hulls against human hepatocellular, breast, and colorectal cancer cell lines. *Journal of ethnopharmacology*, 2017, **198**:302 [Crossref], [Google Scholar], [Publisher]; b) Milani Fard A.M., Milani Fard M. Evaluation of Office Stones in Kidney Patients and How to form and Treat Them. *Eurasian Journal of Science and Technology*, 2022, **2**:111 [Crossref], [Publisher]; c) Motaharian E.S., Sadeghi, Z., Sharif Mousavi L.S., Maleki R., Rigi Z., Milani Fard M., Milani Fard A.M., Nomiri F. A Systematic Review of the Literature, Management of Nursing Human Resources in Covid-19 Pandemics Period. *Eurasian Journal of Science and Technology*, 2022, **2**:152 [Crossref], [Publisher]; d) Sangy S., Miryousefiata S.F. The Effects of Physical Exercise on the Immune System. *Eurasian Journal of Science and Technology*, 2021, 1:252 [Crossref],], [Publisher]; e) Lakshmidevi V.R., Reeja D., Rajan A.R., Vinod B. Advanced Spectrum of Imidazole Derivatives in Therapeutics: A Review. *Journal of Chemical Reviews*, 2023, **5**:241 [Crossref], [Publisher]; f) Mehrdana L., Safari H., Maher A. Crisis Management in the Face of Covid-19 to Control Drug Chemistry for Cancer Patients in Different Countries: A Review Study. *Journal of Chemical Reviews*, 2021, **3**:232 [Crossref], [Publisher]

[2]. Suksamrarn S., Suwannapoch N., Phakhodee W., Thanuhiranlert J., Ratananukul P., Chimnoi N., Suksamrarn A., Antimycobacterial activity of prenylated xanthones from the fruits of Garcinia mangostana, *Chemical and pharmaceutical bulletin*, 2003, **51**:857 [Crossref], [Google Scholar], [Publisher]

[3]. Janhom P., Dharmasaroja P., Neuroprotective effects of alpha-mangostin on MPP+-induced apoptotic cell death in neuroblastoma SH-SY5Y cells, *Journal of toxicology*, 2015, **2015**:[Crossref], [Google Scholar], [Publisher]

[4]. Chen G., Li Y., Wang W., Deng L., Bioactivity and pharmacological properties of α-mangostin from the mangosteen fruit: a review, *Expert opinion on therapeutic patents*, 2018, **28**:415 [Crossref], [Google Scholar], [Publisher]

[5]. Pothitirat W., Chomnawang M.T., Supabphol R., Gritsanapan W., Comparison of bioactive compounds content, free radical scavenging and anti-acne inducing bacteria activities of extracts from the mangosteen fruit rind at two stages of maturity, *Fitoterapia*, 2009, **80**:442 [Crossref], [Google Scholar], [Publisher]

[6]. Wang J.J., Sanderson B.J., Zhang W., Cytotoxic effect of xanthones from pericarp of the tropical fruit mangosteen (Garcinia mangostana Linn.) on human melanoma cells, *Food and Chemical Toxicology*, 2011, **49**:2385 [Crossref], [Google Scholar], [Publisher]

[7]. Tang Y.Q., Jaganath I.B., Manikam R., Sekaran S.D., Inhibition of MAPKs, Myc/Max, NFκB, and hypoxia pathways by Phyllanthus prevents proliferation, metastasis and angiogenesis in human melanoma (MeWo) cancer cell line, *International Journal of Medical Sciences*, 2014, **11**:564 [Crossref], [Google Scholar], [Publisher]

[8]. Soetikno V., Andini P., Iskandar M., Matheos C.C., Herdiman J.A., Kyle I.K., Suma M.N.I., Louisa M., Estuningtyas A., Alpha-Mangosteen lessens high-fat/high-glucose diet and low-dose streptozotocin induced-hepatic manifestations in the insulin resistance rat model, *Pharmaceutical Biology*, 2023, **61**:241 [Crossref], [Google Scholar], [Publisher]

[9]. Balunas M.J., Su B., Brueggemeier R.W., Kinghorn A.D., Xanthones from the botanical dietary supplement mangosteen (Garcinia mangostana) with aromatase inhibitory activity, *Journal of natural products*, 2008, **71**:1161 [Crossref], [Google Scholar], [Publisher]

[10]. Matsumoto K., Akao Y., Kobayashi E., Ohguchi K., Ito T., Tanaka T., Iinuma M., Nozawa Y., Induction of apoptosis by xanthones from mangosteen in human leukemia cell lines, *Journal of natural products*, 2003, **66**:1124 [Crossref], [Google Scholar], [Publisher]
[11]. Suhandi C., Alfathonah S.S., Hasanah A.N., Potency of Xanthone Derivatives from Garcinia mangostana L. for COVID-19 Treatment through Angiotensin-Converting Enzyme 2 and Main Protease Blockade: A Computational Study, *Molecules*, 2023, **28**:5187 [Crossref], [Google Scholar], [Publisher]
[12]. Shan T., Ma Q., Guo K., Liu J., Li W., Wang F., Wu E., Xanthones from mangosteen extracts as natural chemopreventive agents: potential anticancer drugs, *Current molecular medicine*, 2011, **11**:666 [Crossref], [Google Scholar], [Publisher]
[13]. Quan X., Wang Y., Ma X., Liang Y., Tian W., Ma Q., Jiang H., Zhao Y., α-Mangostin induces apoptosis and suppresses differentiation of 3T3-L1 cells via inhibiting fatty acid synthase, *PloS one*, 2012, **7**:e33376 [Crossref], [Google Scholar], [Publisher]
[14]. Díaz L., Bernadez-Vallejo S.V., Vargas-Castro R., Avila E., Gómez-Ceja K.A., García-Becerra R., Segovia-Mendoza M., Prado-Garcia H., Lara-Sotelo G., Camacho J., The Phytochemical α-Mangostin Inhibits Cervical Cancer Cell Proliferation and Tumor Growth by Downregulating E6/E7-HPV Oncogenes and KCNH1 Gene Expression, *International Journal of Molecular Sciences*, 2023, **24**:3055 [Crossref], [Google Scholar], [Publisher]
[15]. Choy C.S., Hu C.M., Chiu W.T., Lam C.S.K., Ting Y., Tsai S.H., Wang T.C., Suppression of lipopolysaccharide-induced of inducible nitric oxide synthase and cyclooxygenase-2 by Sanguis Draconis, a dragon's blood resin, in RAW 264.7 cells, *Journal of Ethnopharmacology*, 2008, **115**:455 [Crossref], [Google Scholar], [Publisher]
[16]. Moongkarndi P., Kosem N., Kaslungka S., Luanratana O., Pongpan N., Neungton N., Antiproliferation, antioxidation and induction of apoptosis by Garcinia mangostana (mangosteen) on SKBR3 human breast cancer cell line, *Journal of Ethnopharmacology*, 2004, **90**:161 [Crossref], [Google Scholar], [Publisher]
[17]. Chen Y.L., Chen Y.C., Xiong L.A., Huang Q.Y., Gong T.T., Chen Y., Ma L.F., Fang L., Zhan Z.J., Discovery of phenylcarbamoyl xanthone derivatives as potent neuroprotective agents for treating ischemic stroke, *European journal of medicinal chemistry*, 2023, **251**:115251 [Crossref], [Google Scholar], [Publisher]
[18]. Trinh B.T., Quach T.T., Bui D.N., Staerk D., Nguyen L.H.D., Jäger A.K., Xanthones from the twigs of Garcinia oblongifolia and their antidiabetic activity, *Fitoterapia*, 2017, **118**:126 [Crossref], [Google Scholar], [Publisher]
[19]. Kalick L.S., Khan H.A., Maung E., Baez Y., Atkinson A.N., Wallace C.E., Day F., Delgadillo B.E., Mondal A., Watanapokasin R., Mangosteen for malignancy prevention and intervention: Current evidence, molecular mechanisms, and future perspectives, *Pharmacological Research*, 2022, 106630 [Crossref], [Google Scholar], [Publisher]
[20]. Ibrahim M.Y., Hashim N.M., Omer F.A.A., Abubakar M.S., Mohammed H.A., Salama S.M., Jayash S.N., Potential Antitumor Effect of α-Mangostin against Rat Mammary Gland Tumors Induced by LA7 Cells, *International Journal of Molecular Sciences*, 2023, **24**:10283 [Crossref], [Google Scholar], [Publisher]
[21]. Adisakwattana S., Jiphimai P., Prutanopajai P., Chanathong B., Sapwarobol S., Ariyapitipan T., Evaluation of α-glucosidase, α-amylase and protein glycation inhibitory activities of edible plants, *International Journal of Food Sciences and Nutrition*, 2010, **61**:295 [Crossref], [Google Scholar], [Publisher]
[22]. Tantra I., Rizqiawan A., Sumarta N.P.M., Kamadjaja D.B., Soesilowati P., Rahman M.Z., Pramono C., Effect of α-Mangostin on Interleukin-11 and Runt-related Transcription Factor-2 Gene Expression on Cell Line Osteoblast Cultures Induced with Lipopolysaccharide, *Contemporary Clinical Dentistry*, 2023, **14**:68 [Crossref], [Google Scholar], [Publisher]
[23]. Kim S.E., Yin M.Z., Roh J.W., Kim H.J., Choi S.W., Wainger B.J., Kim W.K., Kim S.J., Nam J.H., Multi-target modulation of ion channels underlying the analgesic effects of α-mangostin in dorsal root ganglion neurons, *Phytomedicine*, 2023, **115**:154791 [Crossref], [Google Scholar], [Publisher]
[24]. Park S.Y., Lee J.H., Ko S.Y., Kim N., Kim S.Y., Lee J.C., Antimicrobial activity of α-mangostin against Staphylococcus species from companion animals in vitro and therapeutic potential of α-mangostin in skin diseases caused by S. pseudintermedius, *Frontiers in Cellular and Infection Microbiology*, 2023, **13**:1203663 [Crossref], [Google Scholar], [Publisher]
[25]. Nauman M.C., Won J.H., Petiwala S.M., Vemu B., Lee H., Sverdlov M., Johnson J.J., α-Mangostin Promotes In Vitro and In Vivo Degradation of Androgen Receptor and AR-V7 Splice Variant in Prostate Cancer Cells, *Cancers*, 2023, **15**:2118 [Crossref], [Google Scholar], [Publisher]
[26]. Yue P.Y.K., Mak N.K., Cheng Y.K., Leung K.W., Ng T.B., Fan D.T.P., Yeung H.W., Wong R.N.S., Pharmacogenomics and the Yin/Yang actions of ginseng: anti-tumor, angiomodulating and steroid-like activities of ginsenosides, *Chinese medicine*, 2007, **2**:1 [Crossref], [Google Scholar], [Publisher]

[27]. Ardakanian A., Rahbardar M.G., Omidkhoda F., Razavi B.M., Hosseinzadeh H., Effect of alpha-mangostin on olanzapine-induced metabolic disorders in rats, *Iranian Journal of Basic Medical Sciences*, 2022, **25**:198 [Crossref], [Google Scholar], [Publisher]
[28]. Eisvand F., Imenshahidi M., Ghasemzadeh Rahbardar M., Tabatabaei Yazdi S.A., Rameshrad M., Razavi B.M., Hosseinzadeh H., Cardioprotective effects of alpha-mangostin on doxorubicin-induced cardiotoxicity in rats, *Phytotherapy research*, 2022, **36**:506 [Crossref], [Google Scholar], [Publisher]
[29]. Alam M., Rashid S., Fatima K., Adnan M., Shafie A., Akhtar M.S., Ganie A., Eldin S.M., Islam A., Khan I., Biochemical features and therapeutic potential of α-Mangostin: Mechanism of action, medicinal values, and health benefits, *Biomedicine & Pharmacotherapy*, 2023, **163**:114710 [Crossref], [Google Scholar], [Publisher]
[30]. Esmaeelpanah E., Razavi B.M., Vahdati Hasani F., Hosseinzadeh H., Evaluation of epigallocatechin gallate and epicatechin gallate effects on acrylamide-induced neurotoxicity in rats and cytotoxicity in PC 12 cells, *Drug and Chemical Toxicology*, 2018, **41**:441 [Crossref], [Google Scholar], [Publisher]
[31]. Matsumoto K., Akao Y., Yi H., Ohguchi K., Ito T., Tanaka T., Kobayashi E., Iinuma M., Nozawa Y., Preferential target is mitochondria in α-mangostin-induced apoptosis in human leukemia HL60 cells, *Bioorganic & medicinal chemistry*, 2004, **12**:5799 [Crossref], [Google Scholar], [Publisher]
[32]. Lohiya N., Goyal R.B., Antifertility investigations on the crude chloroform extract of Carica papaya Linn. seeds in male albino rats, *Indian journal of experimental biology*, 1992, **30**:1051 [Google Scholar], [Publisher]
[33]. Salem H., Mazen D.Z., Emad N., Hassan H., Omran B., Abdelmajed M.A., Green micellar spectrofluorimetric determination of α-mangostin as antioxidant and other biological activities beneficial to human health found in herbal products, *Luminescence*, 2023, [Crossref], [Google Scholar], [Publisher]
[34]. Ghobakhlou F., Eisvand F., Razavi B.M., Ghasemzadeh Rahbardar M., Hosseinzadeh H., Evaluating the effect of alpha-mangostin on neural toxicity induced by acrylamide in rats, *Environmental Science and Pollution Research*, 2023, **30**:95789 [Crossref], [Google Scholar], [Publisher]
[35]. Nakatani K., Atsumi M., Arakawa T., Oosawa K., Shimura S., Nakahata N., Ohizumi Y., Inhibitions of histamine release and prostaglandin E2 synthesis by mangosteen, a Thai medicinal plant, *Biological and Pharmaceutical Bulletin*, 2002, **25**:1137 [Crossref], [Google Scholar], [Publisher]
[36]. Oka N., Matsubara H., Imai T., Yoshioka Y., Katsuki J., Fujii S., Nakamura S., Shimazawa M., Hara H., Sakurai K., Protective effects of alpha-mangostin encapsulated in cyclodextrin-nanoparticle on cerebral ischemia, *Journal of Controlled Release*, 2023, **353**:216 [Crossref], [Google Scholar], [Publisher]
[37]. Xie Y., Gong C., Xia Y., Zhou Y., Ye T., Mei T., Chen H., Chen J., α-Mangostin Suppresses Melanoma Growth, Migration, and Invasion and Potentiates the Anti-tumor Effect of Chemotherapy, *International Journal of Medical Sciences*, 2023, **20**:1220 [Crossref], [Google Scholar], [Publisher]
[38]. Yiu C.Y., Chen S.Y., Yang T.H., Chang C.J., Yeh D.B., Chen Y.J., Lin T.P., Inhibition of Epstein-Barr virus lytic cycle by an ethyl acetate subfraction separated from Polygonum cuspidatum root and its major component, emodin, *Molecules*, 2014, **19**:1258 [Crossref], [Google Scholar], [Publisher]
[39]. Wang S., Sun H., Wang S., Ren Q., Dai Y., Zhu M., Zhang Y., Kang H., Li J., Xiao J., α-Mangostin Exhibits a Therapeutic Effect on Spinal Cystic Echinococcosis by Affecting Glutamine Metabolism, *Antimicrobial agents and chemotherapy*, 2023, e00098 [Crossref], [Google Scholar], [Publisher]
[40]. Suhandi C., Wilar G., Lesmana R., Zulhendri F., Suharyani I., Hasan N., Wathoni N., Propolis-Based Nanostructured Lipid Carriers for α-Mangostin Delivery: Formulation, Characterization, and In Vitro Antioxidant Activity Evaluation, *Molecules*, 2023, **28**:6057 [Crossref], [Google Scholar], [Publisher]
[41]. Nithitanakool S., Pithayanukul P., Bavovada R., Antioxidant and hepatoprotective activities of Thai mango seed kernel extract, *Planta medica*, 2009, **75**:1118 [Crossref], [Google Scholar], [Publisher]
[42]. Gopalakrishnan G., Banumathi B., Suresh G., Evaluation of the antifungal activity of natural xanthones from Garcinia mangostana and their synthetic derivatives, *Journal of natural products*, 1997, **60**:519 [Crossref], [Google Scholar], [Publisher]
[43]. Suksamrarn S., Suwannapoch N., Phakhodee W., Thanuhiranlert J., Ratananukul P., Chimnoi N., Suksamrarn A., Antimycobacterial activity of prenylated xanthones from the fruits of Garcinia mangostana, *Chemical and pharmaceutical bulletin*, 2003, **51**:857 [Crossref], [Google Scholar], [Publisher]
[44]. Dang T.H., Kim J.Y., Kim H.J., Kim B.J., Kim W.K., Nam J.H., Alpha-Mangostin: A Potent Inhibitor of TRPV3 and Pro-Inflammatory Cytokine Secretion in Keratinocytes, *International Journal of Molecular Sciences*, 2023, **24**:12930 [Crossref], [Google Scholar], [Publisher]
[45]. Eltahir H.M., Elbadawy H.M., Alalawi A., Aldhafiri A.J., Ibrahim S.R., Mohamed G.A., Shalkami A.G.S.,

Almikhlafi M.A., Albadrani M., Alahmadi Y., Alpha-Mangostin ameliorates acute kidney injury via modifying levels of circulating TNF-α and IL-6 in glycerol-induced rhabdomyolysis animal model, *Acta Biochimica Polonica*, 2023, **70**:277 [Crossref], [Google Scholar], [Publisher]

[46]. Deng X., Xu H., Li D., Chen J., Yu Z., Deng Q., Li P., Zheng J., Zhang H., Mechanisms of Rapid Bactericidal and Anti-Biofilm Alpha-Mangostin Activity against, *Polish Journal of Microbiology*, 2023, **72**:199 [Crossref], [Google Scholar], [Publisher]

[47]. Felix L., Mishra B., Khader R., Ganesan N., Mylonakis E., In vitro and in vivo bactericidal and antibiofilm efficacy of alpha mangostin against Staphylococcus aureus persister cells, *Frontiers in Cellular and Infection Microbiology*, 2022, **12**:898794 [Crossref], [Google Scholar], [Publisher]

[48]. Sivaranjani M., Prakash M., Gowrishankar S., Rathna J., Pandian S.K., Ravi A.V., In vitro activity of alpha-mangostin in killing and eradicating Staphylococcus epidermidis RP62A biofilms, *Applied microbiology and biotechnology*, 2017, **101**:3349 [Crossref], [Google Scholar], [Publisher]

[49]. Koh J.J., Qiu S., Zou H., Lakshminarayanan R., Li J., Zhou X., Tang C., Saraswathi P., Verma C.,Tan D.T., Rapid bactericidal action of alpha-mangostin against MRSA as an outcome of membrane targeting, *Biochimica et Biophysica Acta (BBA)-Biomembranes*, 2013, **1828**:834 [Crossref], [Google Scholar], [Publisher]

[50]. Suksamrarn S., Komutiban O., Ratananukul P., Chimnoi N., Lartpornmatulee N., Suksamrarn A., Cytotoxic prenylated xanthones from the young fruit of Garcinia mangostana, *Chemical and pharmaceutical bulletin*, 2006, **54**:301 [Crossref], [Google Scholar], [Publisher]

[51]. Pramana T.Y., Wasita B., Widyaningsih V., Cilmiaty R., Suroto S., Mudigdo A., Purwanto B., The ethanol extract of Garcinia mangostana L peel reduces the isoniazid-induced liver damage in rats, *Bali Medical Journal*, 2021, **10**:156 [Crossref], [Google Scholar]

[52]. Indharty S., Japardi I., Siahaan A.M., Tandean S., Mangosteen extract reduce apoptosis via inhibition of oxidative process in rat model of traumatic brain injury, 2019 [Crossref], [Google Scholar], [Publisher]

HOW TO CITE THIS ARTICLE

Arif Nur Muhammad Ansori, Ahmad Affan Ali Murtadlo, Viol Dhea Kharisma, Bayyinatul Muchtaromah, Muhammad Badrut Tamam, Dora Dayu Rahma Turista, Imam Rosadi, Vikash Jakhmola, Maksim Rebezov, Rahadian Zainul*, Alpha-Mangostin as an Antiviral Candidate: A Mini Review. *J. Med. Chem. Sci.*, 2024, 7(2) 275-286.
DOI: https://doi.org/10.26655/JMCHEMSCI.2024.2.1
URL: https://www.jmchemsci.com/article_182189.html