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BIOAVAIBILITY α - MANGOSTIN : A REVIEW

Rosita Irianti Dehi., Muchtaridi Muchtaridi and Aliya Nur Hasanah

Department of Medicinal Chemical and Chemical Analysis, Faculty of Pharmacy, Padjadjaran University, Indonesia

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A B S T R A C T

α-Mangostin, the main xanthone isolated from mangosteen fruit (Garcinia mangostana Linn), Mangosteen (Garcinia mangostana L.) is a tropical tree native of Southeast Asia that produces pericarp fruit which contains tricyclic isoprenylated polyphenols called xanthones. Many in vitro studies have shown that xanthones have anti-oxidants, anti-proliferative, pro-apoptosis, anti-inflammatory and anti-carcinogenic activities. Bioavailability of α-MG has been reported to several recent studies. In mice, alpha-mangostin is well tolerated with several doses as high as 200 mg / kg and is not associated with specific toxicity. Pharmacokinetic studies in rats identified two attributes of alpha-mangostin. First, alpha-mangostin is less absorbed under certain conditions. Second, the metabolism of alpha-mangostin is fast with most of the metabolism occurring within the first 30-60 minutes. In 94.2 mg of healthy human volunteers xanthone, including an unknown amount of alpha-mangostin, given as juice, reaches a peak plasma concentration of 3.42 ng / mL. There are also several reports that discuss xanthones bioavailability in human subjects. Healthy subjects consume 59 mL of xanthones-rich mangosteen juice products containing 94.2 mg of xanthones. The maximum plasma concentration of α-MG (3.12 ± 1.47 ng / mL) is achieved within 1 hour

INTRODUCTION

Mangosteen (Garcinia mangostana L.) is a fruit commonly found in Southeast Asia. Mangosteen is very well known because it is one of the best tropical fruits. The fruit is dark purple or reddish, with white, soft and slightly sour taste and sweet taste with a pleasant aroma. Mangosteen is one such super fruit produced by Garcinia mangostana L. The genus Garcinia is native to Asia and Africa and includes more than 300 different species from several families of bioactive compounds namely xanthones, flavonoids, triterpenoids, and benzophenone has been isolated and characterized (Chin and Kinghorn, 2008) Mangosteen has been used as a traditional medicine for the treatment of diarrhea, trauma, skin infections and wounds (Zhao *et al*., 2016). Research has shown that mangosteen contains various primary secondary metabolites such as xanthones and oxygenated xanthones (Govindacharit, 1971). Isolate compounds from the mangosteen peel contain xanthones abundantly, for example: α-mangostin, β-mangostin, γ-mangostin, gartanin, 8-deoxygartanin, and mangostanol (Nilar and Harrison, 2002).

α-Mangostin is one of the main xanthones (total xanthone content in total 78%) [11] and isolated from mangosteen pericopes. A number of studies have shown that a-mangostin has anti-inflammatory and antitumor activity (Krajarng *et al*., 2012).

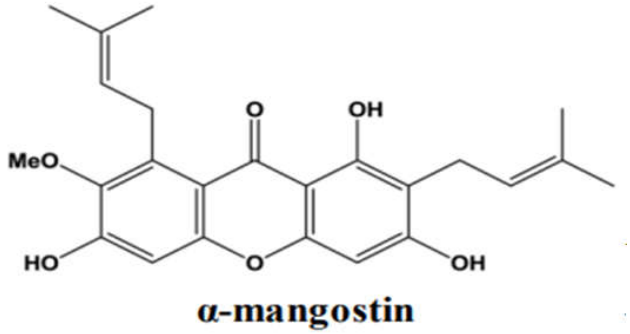
Xanthones mangostana are increasingly in demand because of their remarkable pharmacological effects, including not only anticancer], but also analgesic, antioxidant, anti-inflammatory (Chen, Yang and Wang, 2008) allergic, anti microbial, anti tuberculosis, antifungal, antiviral, cytotoxic, cardio protective (Weecharangsan *et al*., 2006), neuroprotective, and immunomodulation effects (Zhao *et al*., 2016)

Structure

α-Mangostin (1,3,6-Trihydroxy-7-methoxy-2,8-bis (3-methyl-2-butenyl) -9H-xanthhen-9-one, see Fig. 1) is a naturally occurring xanthone found in Mangosteen (Garcinia mangostana) fruit and many are reported to have many health promoting properties. Like other xanthone derivatives, alpha-mangostin has a tricyclic aromatic ring system and a mixture of hydroxyl and isoprenyl groups, which makes it highly hydrophobic. In Southeast Asia the cure for the use of mangosteen fruit has long been known

Corresponding author:* **Rosita Irianti Dehi
Department of Medicinal Chemical and Chemical Analysis, Faculty of Pharmacy, Padjadjaran University, Indonesia

for time and has become a popular dietary supplement and juice drink. For this reason, alpha-mangostin has received increasing attention by scientists and consumers for its potential to promote health property (Pedraza-Chaverri *et al*., 2008)



α-mangostin

Method Analysis

α-mangostin represents most of the clinical benefits of this herbal drug, it makes sense and logical to determine the concentration of α-α-mangostin as a chemical marker for quality control of G. mangostana and its products, which is usually the only amount of xanthone-marked material on the label. However, there is little information about determining the quality and quantity of α-mangostin in mangosteen (Yodhnu, Sirikatitham and Wattanapiromsakul, 2009).

There are recent reports using high pressure liquid chromatography with photodiode array detectors (HPLC-PDA) at 320 nms to detect and measure α-mangostin and five other xanthones from G. mangostana (Ji, Avula and Khan, 2007).

Thus the speed of analysis is suitable for the measurement routine α-mangostin in not only product preparation, but also in the raw extract from G. mangostana. The study described the easy and feasible method for purification of alpha-mangostin from Garcinia mangostana rind, Identification and by TLC, UV-Vis Spectrophotometer and HPLC. The purity of purified abamangostin was confirmed by the standard standard of Alpha-mangostin. Purification and quantification are much more efficient and faster and produce higher compounds Alpha-mangostin which is the main component (according to the literature) responsible for various beneficial pharmacological activities (Garcinia, 2016)

Bioavaibility α – Mangostin

Bioavailability of α-MG has been reported on several recent studies with laboratory mice. Previously it was reported that injections of α-MG (2 mg / kg) in mice were slowly removed from the blood and quickly distributed to tissues with a maximum concentration of 17.9 μg / mL. Oral bioavailability given α-MG (20 mg / kg dose) dissolved in an aqueous solution containing 2% ethanol and 2% Tween 80 is estimated to be only 0.4% (Li *et al*., 2011). Maximum plasma concentration (4.8 μg / mL) is achieved in 63 minutes (Gutierrez-Orozco and Failla, 2013).

In mice, alpha-mangostin is well tolerated with several doses as high as 200 mg / kg and is not associated with specific toxicity. Pharmacokinetic studies in rats identified two attributes of alpha-mangostin (Ramaiya *et al*., 2012). First, alpha-mangostin is less absorbed under certain conditions. Second, the metabolism of alpha-mangostin is fast with most of the metabolism occurring within the first 30-60 minutes. In healthy human volunteers 94.2 mg xanthone, including an unknown amount of alpha-mangostin, is given as juice, reaching a peak plasma concentration of 3.42 ng / mL (Udani *et al*., 2009). It is important to note that alpha-mangostin is well tolerated without serious adverse effects.

There are also several reports that discuss xanthones bioavailability in human subjects. Healthy subjects consume 59 mL of xanthones-rich mangosteen juice products containing 94.2 mg of xanthones. Maximum plasma concentration of α-MG (3.12 ± 1.47 ng / mL) is achieved within 1 hour (Gutierrez-Orozco and Failla, 2013).

This study was limited by the fact that plasma samples were only collected for 6 hours after ingestion of mangosteen products and xanthone metabolites were not considered in the analysis. Plasma antioxidant capacity as measured by oxygen radical absorption capacity, ORAC, in this subject increased by 18% after consumption of mangosteen products compared to subjects swallowing a placebo product. However, the contribution to α-MG to the increase in ORAC valued is unknown because the drink also contains green tea, aloe vera, and supplements including minerals, and vitamins A, B, C, D and E (Ondo *et al*., 2009).

In more recent human studies, xanthones from 100% mangosteen fruit juice (containing pericarp fluid and particles) were found to be absorbed and partly conjugated by healthy adults who took a single dose (60 mL) of mangosteen juice (containing 130 mg of xanthones) with high fat. Both free and glucuronidated / sulfate xanthones (α- and γ-MG, garcinones D and E, 8-deoxygatanin and gartanin) are detected in serum and urine. Maximum variability in the concentration of α-MG in serum (113 ± 107 nmol / L), as well as in time to maximum concentration (3.7 ± 2.4 hours), was recorded for 10 subjects. Urinary excretion of xanthones is obtained 2% of the dose taken (Chitchumroonchokchai *et al*., 2012). Xanthones still present in plasma 24 hours after consumption of juice indicated slow a turnover as reported on mice after oral administration (Ramaiya *et al*., 2012).

CONCLUSION

Research on α-mangostin has been reported as follows: anti-inflammatory response, bioaccessibility, biotransformation and metabolic methods. However, in fact, α-mangostin has limited bioavailability (Bumrungpert *et al*., 2009). This is one of the most abundant prenylations of xanton present in mangosteen and has been reported to have a lot of bioactivity, providing it to use mangosteen products as nutraceuticals, functional foods and dietary supplements. Therefore, an effective method of increasing the bioavailability of α-mangostin is needed for further development and utilization.

bioavailability of very low pure a-mangostin after oral administration in mice could be associated with the first intensive metabolic pass. Pharmacokinetic studies are known to play an increasingly important role in the discovery and development of drug processes, from toxicity and clinical studies to optimization of candidate drugs (Sun *et al*., 2009). Pharmacokinetic studies of bioactive components can help us understand in vivo action and explain various events related to the efficacy and toxicity of relevant herbs or herbal preparations where these constituents are found (Lv *et al*., 2011). Therefore, it is clinically important to explore in vivo pharmacokinetic profile of a-mangostin in mice. In pre-clinical settings, rats are the most popular model and our knowledge there have been no reports on the pharmacokinetic profile of α-mangostin in rats. We choose a dose that when translated using FDA guidelines on dose translation can be achieved in humans by consuming 486 to 615 mg (Ramaiya *et al*., 2012).

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