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PHARMACOLOGICAL ACTIVITY *Garcinia mangostana* LINN : A REVIEW

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A B S T R A C T

Garcinia mangostana Linn. (GML) is a tropical tree from Southeast Asia has a distinctive taste and is known as "the queen of fruits". The spread of mangosteen plants in India, Myanmar, Malaysia, Philippines, Sri Lanka, and Thailand. The main phytochemicals present in this species are xanthone isoprenylation, a secondary metabolite class with many reports of biological effects. In Ayurvedic medicine, mangosteen is used as antidiarrhea, anti-inflammatory, cholera and dysentery medications. Traditional Thai medicine has also used a mangosteen pericarp to treat skin infections, wounds, and diarrhea for many years. Based on several studies have shown that the xanthon contained in the mangosteen fruit has extraordinary biological activity. Among others are antimicrobial, antimalarial, anti-inflammatory, antitumor, anticancer, antioxidant and antidiabetic.

INTRODUCTION

One of the best tropical fruits is mangosteen (*Garcinia mangostana* L.) GML and is known as "the queen of fruits". The mangosteen fruit isdark purple or reddish, soft, with white and pulp that is easily edible with a slightly acid and sweet flavor and a pleasant aroma (Jung *et al*., 2006). Distribution of mangosteen plants in India, Myanmar, Malaysia, Philippines, Sri Lanka, and Thailand. This tropical tree can reach 6 - 25 m and has leaves that are leathery and is slow to grow (Morton, 1987). In Ayurvedic medicine, the antidiarrheal activity, anti-inflammatory (Balasubramanian and Rajagopalan, 1988), treatment of cholera and dysentery (Sen *et al*., 1980) are found in the pericarp of the mangosteen fruit. Traditional Thai medicine has also used a mangosteen pericarp to treat skin infections, wounds, and diarrhea for many years (Martin *et al*., 1980; Mahabusarakam *et al*., 1987; Moongkarndi *et al*., 2004).

Figure 1 *Garcinia mangostana* Linn.

Scientific classification of mangosteen plants based on United States Department of Agriculture (USDA):

Kingdom : Plantae
Subkingdom : Tracheobionta
Superdivision : Spermatophyta
Division : Magnoliophyta
Class : Magnoliopsida
Subclass : Dilleniidae
Ordo : Theales
Family : Clusiaceae / Guttiferae
Genus : *Garcinia* L.
Species : *Garcinia mangostana* L.

Chemical Constituents

This plant is plentiful in xanthones and is known to have the type of natural polysaccharides (Bennett and Lee, 1989). Govindachari and Muthukumaraswamy (1971), Sultanbawa (1980), Peres *et al* (2000) attest to the presence of various secondary metabolites such as xanthones prenylated and oxygenated in mangosteen.

Xanthones of the whole fruit, stems, branches, and leaves of GML. There are three new xanthones isolated from the whole mangosteen: manggenon C, D and E (Suksamrarn *et al*., 2006). In total, 18 xanthones isolated from the whole mangosteen fruit. In addition, 21 xanthones isolated from GML trunks and branches (Holloway and Scheinmann, 1975; Nilar *et al*., 2005; Nilar and Harrison, 2002; Ee *et al*., 2006) (Table 4). On the other hand, 1,6-dihydroxy-3-methoxy-2-isoprenyl-xanthone, 1-hydroxy-6-acetoxy-3-methoxy-2-isoprenylxanthone and gartanin

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isolated from mangosteen leaf (Parveen and Khan, 1988). Chin *et al*. (2008) isolate and identify two new compounds of 1.2-dihydro-1,8,10-trihydroxy-2- (2-hydroxypropane-2-yl) -9- (3-methylbut-2-enil) furo [3,2-a] xanthen-11-one and 6-deoxy-7-demethylmangostanin.

Pharmacological Activity

Antimicrobial Activity

Evaluation of antibacterial activity by Chomnawang *et al* (2005) in *Staphylococcus epidermis* and *Propionibacterium acnes*, which a pus-forming bacterium and triggered inflammation in acne, was done by 19 medicinal plants from Thailand getting good results. The strongest effect for both bacteria with MIC value 0.039 μg / mL came from growth inhibition activity by GML. Furthermore, the minimum bactericidal concentration of GML, ie the lowest concentration to kill bacteria, was 0.039 and 0.156 μg / mL against *P. acnes* and *S. epidermidis*. In addition, a significant reduction in TNF-α production resulting from peripheral blood of mononuclear cells by stimulating *P. acnes* is also an activity produced by GML ethanol extract.

The antituberculosis potential of the prenylated xanthones obtained from the pericarp of the mangosteen fruit, including α-, and β-mangostin and garcinone B showed the strongest inhibitory effect on *Mycobacterium tuberculosis*, with MIC 6.25 μg / mL; while demethylcalabaxanthone and trapezifolixanthone had MIC values of 12.5 μg / mL and γ mangostin, garcinone D, mangostanin, mangostenone A and tovophyllin B had a MIC value of 25 μg / mL. Xanthones activity antituberculosis low potential are mangostenol and mangostanol with MIC values of 100 μg / mL and 200 μg / mL. (Suksamrarn *et al*., 2003)

The ability to inhibit MRSA from 35 hospitals was studied Voravuthikunchai and Kitpipit (2005) from ethanol extracts and water extracts obtained from 10 traditional Thai medicinal plants. Nine Thai plants have activity against this bacteria. The ethanol extract from GML, *Punica granatum* and *Quercus infectoria* was highly efficient in inhibiting bacterial growth, with MIC values of 0.05, 0.2 to 0.4 and 0.1 to 1.6 μg / mL.

Antimalarial Activity

Riscoe *et al* (2005) demonstrated invitro antimalarial activity to*Plasmodium falciparum* from xanthone isolates of β-mangostin and α-mangostin showed comparable IC_{50} values (7 and 5.1 μM respectively), while mangiferine, xanthone-glucoside, IC_{50} value is higher than 50 μM. Another indicator of IC_{50} value is 17 μM to P. Falciparum (Mahabusarakan *et al*., 2006).

Antiinflammatory Activity

Chen *et al*. (2008) showed that α- and γ-mangostin significantly inhibited lipopolysaccharide - stimulated $NO^{\cdot}$ production and cytotoxicity against RAW cells 264,7. $NO^{\cdot}$ production amounts at 3 to 25 μM are continuously measured, and IC_{50} values are 12.4 and 10.1 μM for α- and γ-mangostin. α- and γ-mangostin also significantly reduced the production of PGE2 in lipopolysaccharide - activated RAW cells 264,7 with IC_{50} values of 11.08 and 4.5 μM. The effect of this xanthone is investigated by measuring inducible nitric oxide synthase (iNOS) and COX enzyme expression. Both xanthones depend on the iNOS induction concentration. RAW cells 264,7 activated with lipopolysaccharide (1 μg / mL) for 12 hours and treatment with α- or γ-mangostin (5 μg / mL) for 24 h inhibited weak iNOS activity and activated RAW 264,7 macrophages.

The anti-inflammatory effects of α- and γ-mangostin evaluated by carrageenan-induced paw edema in mice. Treatment of α-mangostin and sulindac (reference compound) showed inhibition of pH edema potential at 3 h and 5 h. The mangostin results are faster than sulindac. However, γ-mangostin did not significantly inhibit paw edema in mice. This suggests that in vivo α-mangostin has better anti-inflammatory activity than γ-mangostin. In addition, Deschamps *et al*. (2007) showed that α-mangostin inhibited 12-LOX with IC_{50} 0,58 μM.

Antitumor Activity

Suppression of synergistic growth in cells with combination of treatment with 2,5 μM mangostin and 2,5 μM 5-fluorouracil (5-FU), chemotherapy agent for additive adenocarcinoma. They showed that the growth of cell counts decreased with the administration of 20 μM mangostin. The cytotoxic effects of 20 μM α-mangostin are found to be due to apoptosis. This α-mangostin evaluation was performed on in vitro cytotoxicity of DLD-1 cells (Nakagawa *et al*., 2007).

The antiproliferative effect of 4 xanthones prenylated (α, β, and γ-mangostin and methoxy-β-mangostin) in human colon cancer cells DLD-1. The results showed that three xanthones strongly inhibited cell growth at 20 μM at 72 hours and its antitumor efficacy correlated with the number of hydroxyl groups except methoxy-β-mangostin. Apoptosis is associated with the antiproliferative effects of α and γ-mangostin, but not from β-mangostin. The expression of cyclins cdc2 and p27 influencing cell-cycle is associated with antiproliferative effects of α, β (phase G1) and γ-mangostin (phase S) (Matsumoto *et al*., 2005).
Activity of their antitumoral properties in prenoplastic lesions induced 7,12-dimethylbenz [a] anthracene (DMBA) in rat organ cultures. α-mangostin inhibits the DMBA-induced prenoplastic lesion with IC_{50} 1,0 μg / mL (2,44 μM). They isolated from the two new xanthone maize pericarp (8-hydroxycudraxanthone G and mangostinone) and 12 other known xantones compounds (Jung *et al*., 2006).

Suksamrarn *et al*. (2006) determined the cytotoxic properties of three different human cancer cell lines: oral epidermoid carcinoma (KB), breast cancer (BC-1), and small cell lung cancer (NCI-H187). Three new prenylated xanthones (mangostenone C, D and E) and 16 identified xanthones isolated from the pericarp of the mangosteen fruit. The cytotoxic properties of this xanthone determined against Mangostenone C show cytotoxic effects on three proven cell lines, with IC_{50} values of 2,8; 3,53; and 3,72 μg / mL. However, α-mangostin showed the strongest effect on BC-1 cells with IC_{50} values of 0,92 μg / mL, a greater activity than standard ellipticine (IC_{50} = 1,46 μg / mL); α-mangostin also has cytotoxic effects on KB cells

(IC_{50} = 2,08 µg / mL); and gartanin is able to inhibit the growth of NCI-H187 (IC_{50} = 1,08 µg / mL).

Antioxidant Activity

Antioxidant activity was evaluated by DPPH method using 1, 10, 50 and 100 µg / mL of each extract. Water extract and ethanol (50%) showed high antioxidant activity (inhibitory concentrations of 50% each (IC50) = 34.98 ± 2.24 and 30.76 ± 1.66 µg / mL). Then the antioxidant activity of this extract was tested on neuroblastoma cells (NG108-15) exposed to hydrogen peroxide (H_2O_2); Both of these extracts showed neuroprotective activity when they used a concentration of 50 µg / mL. 50% ethanol extract had higher neuroprotective activity than water extract (Weecharangsan *et al*., 2006)

Based on research Chomnawang *et al* (2007) showed that GML ethanol extract has significant antioxidant activity, as measured by inhibition of DPPH radical formation up to 50%. This extract showed IC_{50} of 6,13 µg / mL compared with ethanol extract from *Houttuynia cordata*, *Eupatorium odoratum* and *Senna alata* (IC_{50}value 32,53; 67,55 and 112,46 µg / mL).

HO capture activity of some xanthones isolated from GML fruit powder. Only γ-mangostin of 16 xanthones tested showed HO capture activity (IC_{50} = 0,2 µg / mL) (Chin *et al*., 2008). In addition, Chin *et al*. (2008) tested the same xanthones for quinone reductase induction (phase enzymatic enzyme QR, phase II), using murine hepatoma cells (Hepa 1c1c7) in vivo.

Antidiabetic Activity

A single dose of 100 mg / kg of ethanol extract from the pericarp fruit (whose main compound is α-mangostin, γ-mangostin, and gartanin) reduces postprandial glycaemia addition after oral maltose tolerance test. Pure compounds exhibit a α-glucosidase inhibitor, being a potentially reversible α-mangostin inhibitor type mixture (Ryu *et al*., 2011).

Taher *et al* (2016) in his study explained that chronic administration of 28 days of ethanol extract from pericarp fruit (50, 100, and 200 mg / kg po) in diabetic rats not only showed hypoglycemic effects, but also reduced serum triglycerides, and density lipoproteins very low (LDL and VLDL), serum glutamate oxaloacetic and pyruvic transaminases (SGOT, SGPT), urea and creatinine, while increasing high-density lipoprotein (HDL) and total protein. The most important finding documented in the study the ability of the extract to increase the number of β-pancreatic cells (Taher *et al*., 2016).

Daily α-mangostin supplementation in diabetic mice (200 mg / kg included in diet, 8 weeks) triggered significant hypoglycemic and insulinotropic effects, decreased plasma glycolate hemoglobin and decreased serum and cholesterol triglyceride (Jariyapongskul *et al*., 2015).

CONCLUSION

Based on several studies have shown that xanthones contained in mangosteen fruit have biological activities such as antimicrobial, antimalarial, anti-inflammatory, antitumor, anticancer, antioxidant, antidiabetes. This suggests the possibility of therapeutic applications associated with GML. However, further research needs investigate the effects of GML extract on humans.

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