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Biological properties in relation to health promotion effects of *Garcinia mangostana* (queen of fruit)

A short report

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Abstract

Purpose – For the prevention and cure of disease, patient use various types of chemical and drug agents. Along with their curative effect, almost all drugs have some destructive effects and side-effects. Due to the minimal and/or none of unwanted side-effect, recently, the use of herbal remedy as the drug of choice becomes the preference choice. The mangosteen, *Garcinia mangostana*, contains various types of polyphenols. It has been used as a traditional medicine from the ancient times till present days. The purpose of this paper is to investigate the biological properties of mangosteen in relation to health promotion effects.
Design/methodology/approach – Several research papers from well-known database (such as PubMed, Google scholar, Scopus and Sciencedirect) were reviewed without considering publication-times to understand the biological properties of mangosteen.
Findings – Mangosteen and its xanthone exerted diverse biological activities such as anti-oxidant, anti-inflammatory, anti-allergy, anti-bacteria, anti-fungal, anti-malaria, anticancer and anti-diabetes.
Originality/value – Based on these studies, mangosteen is beneficial dietary supplement of overall human health.

Keywords *Garcinia mangostana*, Xanthones, Biological properties
Paper type Short report

Introduction

The mangosteen, *Garcinia mangostana* (GM), which defines as "queen of fruits"[1], is native plant mainly found in the tropical rainforest areas of South-Asian countries, e.g., Myanmar, Thailand, Indonesia, Malaysia, Philippines, Sri-Lanka, etc. It belongs to the Guttiferae Family. GM has known and being used as traditional medicine to treat various types of diseases such as diarrhea, abdominal pain, dysentery, wound-infections and chronic ulcer[1]. According to various studies, GM extracts possess potent anti-oxidant[2], anti-tumoral[3], anti-allergic[4], anti-inflammatory[5] anti-bacterial[6] and anti-fungal activities[7]. Mangostana is famous for its tasty fruit named as mangosteen fruit. It is a dark purple/reddish color fruit with white soft and delicious consumable pulp. This pulp is little bit acidic and sweet in flavor with charming smell. Products containing mangosteen juice/extract are highly demandable in the beverage market; and in the USA, the sales of mangosteen products exceeded up to $200m in 2008. A variety of secondary metabolites have been isolated from GM, xanthone is one of them[8]. Mangosteen fruit contains 160 aromatic compounds (epicarp) and 105 compounds (endocarp) evaluated by gas chromatography–mass spectral analysis[9].

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Tang *et al.*[10], in their randomized, double-blind, placebo-controlled trial, reported that, mangosteen intake for 30 days enhanced human immune responses compared to placebo controls. Udani *et al.*[11] found that intake of blended mangosteen juice by obese subjects for eight-weeks ameliorated the inflammation compared to placebo group. Another randomized, double-blind, placebo-controlled trial by Kudiganti *et al.*[12] revealed that consumption of meratrim (contained GM fruit rinds) for 16 weeks by healthy overweight subjects, significantly reduced the body weight, BMI, hip size and serum lipid profile compared to the placebo control. After ingestion of 60 mL mangosteen juice by healthy adult subjects with high-fat breakfast, xanthone were detected in serum approximately 762–4,030 nM/L/h and 0.9-11.1 μM in 24 hours urine indicate the well-absorbtion of xanthone when taken with high-fat-diet[13]. Chang *et al.*[14] unveiled that acute administration of 250 mL mangosteen juice one hour before cycle ergometer exercise, does not have impact on exercise-mediated physical fatigue. The acute toxicity study of ethyl-acetate fraction shows no toxicity to the experimental rat evaluated by physical changes and mortality[15]. Therefore, GM and its isolated xanthones are safe for people.

Xanthone from GM

Xanthone (known as xanthen-9H-ones), an active compound, is an important element of oxygenated heterocycles group. It is the secondary metabolites obtained from higher plant family, fungi and lichen. It has been classified into five major groups: simple oxygenated xanthone, xanthone glycosides, prenylated xanthone, xanthone-lignoids and miscellaneous xanthone[8]. Maruganadan *et al.*[16] revealed that around 1,000 different xanthones have been isolated from the natural source. During the year of 2000 to 2004, about 278 new xanthones have been obtained from 20 higher plant families[17]. Mangostin (known as α-mangostin) is the first xanthone and was first isolated in 1855. Currently, 54 xanthones were isolated from the GM's pericarp, e.g., β-mangostin, γ-mangostin, mangostenol, 1-isomangostin, 1-isomangostin hydrate, etc.[8].

Side effect of GM

There are few scientific reports published about mangosteen side-effect. Daily consumption of mangosteen juice for a long time may produce type-B lactate acidosis in chronic kidney disease patient and metabolic syndrome. This may be due to the releasing of cytochrome-c, by the α-mangostin, cytosol from the mitochondria and directly impair the mitochondrial electron transport that leads to lactic acidosis[18]. Liu *et al.*[19] found that α- and γ-mangostin from GM can inhibit platelet aggregation and induce cytolysis, therefore it should be avoided before any surgery.

Biological properties of GM

Anti-oxidant properties

Many scientists reported that GM and its isolated xanthone exhibited potent anti-oxidant properties[20–23]. In the cisplatin-induced nephrotoxic rats, the α-mangostin from GM exerted renoprotective effect by reducing cisplatin-induced renal oxidative/nitrosative stress[2]. Tjahjani *et al.*[20] evaluated the anti-oxidant activity of the different fraction of mangosteen rind, and found that the ethyl-acetate fraction exerted higher anti-oxidant than other fractions. The GM's pericarp extract also inhibited the formation of pentosidine and reduced advanced glycation end-products accumulation in the skin, which suppressed the glycation stress and improve skin conditions[21]. Xie *et al.*[22] found that drinking 245 mL mangosteen contained beverage by healthy populations enhanced the plasma anti-oxidant capacity (maximum 60 percent after one hour). A clinical study reported that oral administration of polar fraction extract from mangosteen pericarp to human subjects for 24-weeks enhanced the anti-oxidant activity without producing potential side-effect[23].

Anti-allergy and anti-inflammatory properties

Anti-allergy and anti-inflammatory properties of GM have been proved by various scientific evidence. The GM's pericarp inhibited the histamine- and serotonin-induced isolated thoracic rabbit aorta contractions, and blocked the histamine and serotonin receptor, respectively[4]. In RBL-2H3 cell line, 40 percent ethanol extract of mangosteen was found to inhibit the histamine release and prostaglandin E2 (PGE2) synthesis activities[24]. The 18 hours treatment of γ-mangostin suppressed the continuous PGE2 release and cyclooxygenase-2 (COX-2) gene expression in the C6 rat glioma cells in concentration-dependent manners[5]. The extracted isogarcinol from GM exhibited anti-inflammatory activity by suppressing the CD4 T-cells regulation in the murine model[25]. The combination of Garcinia with cocoa, coffee and green tea significantly reduced the lipid content from serum and liver in a dose-dependent manner. It also improved homeostasis model by assessing insulin resistance index and pro-inflammatory cytokines (TNF-α, IL-6)[26].

Anti-bacterial and anti-fungal properties

A number of studies described anti-bacterial and anti-fungal properties of xanthone extracts from GM[6–7, 27–30]. It was reported that the polysaccharides compound obtained from mangosteen fruit increased polymorphonuclear phagocytic cell activity against *Salmonella enteritidis*[27]. Prenylated xanthone from GM's pericarp has potential effect on tuberculosis, showed potent anti-bacterial activity by inhibiting *Mycobacterium tuberculosis*[28]. Sakagami *et al.*[6] found that α-mangostin inhibited the vancomycin-resistant *Enterococci* (VRE) and MRSA (MIC value 6.25 and 12.5 μg/ml). Different xanthones (α-, γ-mangostin, gartanin, garcinone D, BR-xanthone and euxanthone) isolated from mangosteen exhibited the anti-fungal activity against phytopathogenic fungi (e.g. *Fusarium oxysporum vasinfectum*, *Alternaria tenuis,* and *Dreschlera oryzae*, etc.) by showing potent inhibitory activity[7]. Moreover, ethanol and chloroform extract of mangosteen demonstrated anti-bacterial activity, evaluated by colony formation and zone of inhibition of the *E. coli*, streptococcus and lactobacillus bacteria[29, 30].

Anti-malarial properties

The α-mangostin from GM exhibited *in-vitro* anti-malarial activity (IC_{50} values 17 ± 1 μM) against *Plasmodium falciparum* compared to chloroquine standard drug (IC_{50} values 0.59 ± 0.02 μM), evaluated on *P. falciparum*-infected erythrocytes[31]. Laphookhieo and his team isolated four xanthone (5-O-methylcelebixanthone, celebixanthone, cochinchinone C and β-mangostin) from the root of *Cratoxylum cochinchinensem*, and found that β-mangostin exerted better *in-vitro* anti-malarial effect (IC_{50} value 7.2) than other compound (IC_{50} values 3.2, 4.9 and 2.6 mg/ml, respectively), when they were evaluated via [3 H]-hypoxanthine uptake by *P. falciparum*[32]. An *in-vivo* study exposed that α-mangostin ($IC_{50} = 0.2 \pm 0.01$ μM) showed more effective anti-malarial activity than γ-mangostin ($IC_{50} = 121.2 \pm 1.0$ μM) against chloroquine resistant strain *of P. falciparum* on the malarial murine model[33]. In addition, different fraction of mangosteen exerted synergistic anti-malarial activity with artemisinin drug against *Plasmodium falciparum* 3D7 clone[34].

Anti-tumoral properties

Several studies revealed the anticancer activities of xanthones derivative from GM[35–41]. In HL60 cell line, six xanthones (α-, β-, γ-mangostin, mangostinone, garcinone E and 2-isoprenyl-1, 7-dihydroxy-3-methoxy xanthone) possessed the cytotoxic effect by inhibiting cell growth, while the α-mangostin exerted the highest inhibitory activity than others[3]. The α-mangostin also induced the mitochondrial dysfunction in the early phase through activating caspases-3/-9, ROS production, and cytochrome-c release[35]. Nakagawa *et al.*[36]

unveiled that the α-mangostin exerted *in-vitro* cytotoxic effect against DLD-1 cell line. In HeLa cell line, encapsulation of GM with methyl-cellulose and ethyl-cellulose nanoparticles showed two-fold higher better anticancer activity than the encapsulation of GM with ethyl-cellulose[37]. The α-mangostin exhibited the most potent mammalian DNA polymerase inhibition, evaluated by the inhibition of human DNA topoisomerases I and II activities (IC_{50} values 15.0 and 7.5 μM). It also suppressed the HCT116 cell proliferation (LC_{50} value 18.5 μM)[38]. In prostate cancer, gartanin xanthone bind with androgen receptors (AR) and enhance AR degradation[39]. Manimekalai *et al.*[40] revealed that mangosteen showed anticancer activity on HepG2 cell line evaluated by the cell viability assay. A total of 14 isolated compounds from chloroform fraction of mangosteen exerted anticancer activity against different cancer cell line, e.g., HepG2, HCT116 and MCF7[41].

Anti-diabetic properties

Different fractions of the GM's pericarp and isolated xanthone showed an anti-diabetic effect by inhibiting α-amylase and α-glucosidase enzyme activities[42, 43]. Ethanolic extract of GM showed the anti-diabetic effect against streptozotocin-induced diabetic rats by lowering high blood glucose, biochemical parameters, hepatic architectures and increased the HDL and total protein levels, compared to the control group[44]. While, in high-fat-diet- and streptozotocin-induced diabetic mice, mangosteen vinegar rind from GM, lowered the hyperglycemia, hyperlipidemia, oxidative stress marker, hepatic damage marker and improved the glycogen contents and anti-oxidant markers[45]. In similar model, isolated xanthone from GM demonstrated the nephroprotective effect by reducing the body weight, high glucose level, kidney hypertrophy, kidney damage marker and MDA level of plasma and kidney tissue[46].

Conclusion

Recently, the increasing awareness on the negative impacts of nutrition and diets, such as causing obesity, development of chronic diseases, cardiovascular disease, diabetes, cancer and other disease, was quite alarming as well as obvious especially in the western countries. A large number of bioactive compounds have already been identified in foods and drinks, contain high percentage of polyphenolic compounds (e.g. xanthone, lignans, phenolic acids, etc.).

The GM possesses potential biological properties without producing noticeable side-effect. It boosts up immune systems, reduced metabolic syndromes and its associated diseases, respectively. The GM's xanthone was found to associate with health beneficial effects by lowering oxidative stress, reducing inflammation, managing and controlling obesity and diabetes, inhibiting the growth of cancer cells as well as showing anti-allergic, anti-bacterial, anti-fungal and anti-malarial properties.

However, most of investigations on GM mentioned in this report were conducted either in cell-free, cell-type or animal model and none of them was on humans. Therefore, the further studies of health effects on human subjects are crucial and needed.

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