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Review

Medicinal properties of mangosteen (*Garcinia mangostana* L.): A comprehensive update

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ABSTRACT

Garcinia mangostana L. (Clusiaceae) is a tropical tree native to Southeast Asia known as mangosteen which fruits possess a distinctive and pleasant taste that has granted them the epithet of "queen of the fruits". The seeds and pericarps of the fruit have a long history of use in the traditional medicinal practices of the region, and beverages containing mangosteen pulp and pericarps are sold worldwide as nutritional supplements. The main phytochemicals present in the species are isoprenylated xanthones, a class of secondary metabolites with multiple reports of biological effects, such as antioxidant, pro-apoptotic, anti-proliferative, antinociceptive, anti-inflammatory, neuroprotective, hypoglycemic and anti-obesity. The diversity of actions displayed by mangosteen xanthones shows that these compounds target multiple signaling pathways involved in different pathologies, and place them as valuable sources for developing new drugs to treat chronic and degenerative diseases. This review article presents a comprehensive update of the toxicological findings on animal models, and the preclinical anticancer, analgesic, neuroprotective, antidiabetic and hypolipidemic effects of *G. mangostana* L. extracts and its main isolates. Pharmacokinetics, drug delivery systems and reports on dose-finding human trials are also examined.

Contents

1. Introduction

Mangosteen (*Garcinia mangostana* L.) is an evergreen tropical tree belonging to the Clusiaceae family that grows in Southeast Asia, and is cultivated mainly as a source of its highly palatable fruit,

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consisting of a fragrant white internal pulp divided in septa, contained in a dark purple rind. Early reports of the traditional uses of infusions and decoctions of its peels and seeds to treat gastrointestinal and urinary tract infections, and as anti-scorbutic, laxative and anti-fever agent, date from almost two hundred years ago (Descourtilz et al., 1821; Lilly and Colman, 1833; Pardo de Tavera and Thomas, 1901). Modern uses of the species comprise the alleviation of infection-related symptoms, such as diarrhea, abdominal pain, and fever, and also complains linked to inflammatory and immunological diseases, like acne, food allergies and arthritis (Wang et al., 2017). Nowadays, fruit derivatives demand has increased exponentially (as suggested by the numerous commercial brands of supplements offered in web sites), especially between people living with metabolic illnesses, in particular obesity and diabetes, and among who suffer cancer or neurodegenerative disorders, as multiple claims about mangosteen beneficial health properties have arisen, conferring it inherent safety and pharmacological effects that have not been fully elucidated and corroborated using adequate preclinical and clinical evaluations. Moreover, a poor correlation between the traditional uses of mangosteen and its chemical composition has been described (Genovese et al., 2016). Indeed, prenylated xanthones, dibenzo-γ-pyrone derivatives, are the main compounds present in the fruit, and they possess a plethora of activities *in vitro*, such as antioxidant, antibacterial, cytotoxic, and anti-proliferative, being α-, β- and γ-mangostins; gartanin; 8-deoxygartanin; and garcinones C and D the most abundant and therefore the most studied (Pedraza-Chaverri et al., 2008). At least 68 xanthones have been isolated from *G. mangostana* L., and there are numerous reports on dimeric and cage xanthones discovered on several families and genera; the biosynthesis, isolation and chemical characterization of these compounds are reviewed elsewhere (Anantachoke et al., 2012; Negi et al., 2013; Obolskiy et al., 2009).

In this review we focused in providing an updated and comprehensive report on the toxicological, pharmacodynamics and pharmacokinetics investigations of *G. mangostana* L. extracts and isolates, considering that its constituent phytochemicals exhibit polyvalence, an attribute by which a single component of the species can interact with multiple biological targets, and by which several components of an extract may improve solubility and absorption, and in consequence, enhance bioavailability and efficacy (Wagner and Ulrich-Merzenich, 2009). The review comprises the effects of mangosteen extracts and its main prenylated xanthones (Figs. 1–4) on cell-based and animal models of cancer and pain, as well as inflammatory, neurological, and metabolic disorders, examining the molecular pathways proposed and the biochemical parameters described to explain the effects observed. Findings on human trials and drug delivery improvements are also herein discussed.

2. Acute and chronic toxicity

Several *in vivo* evaluations involving mangosteen fruit derivatives and/or its pure compounds have determined their lack of acute or chronic toxicity in the models and dose ranges tested. In this type of experiments, death, central nervous (related to

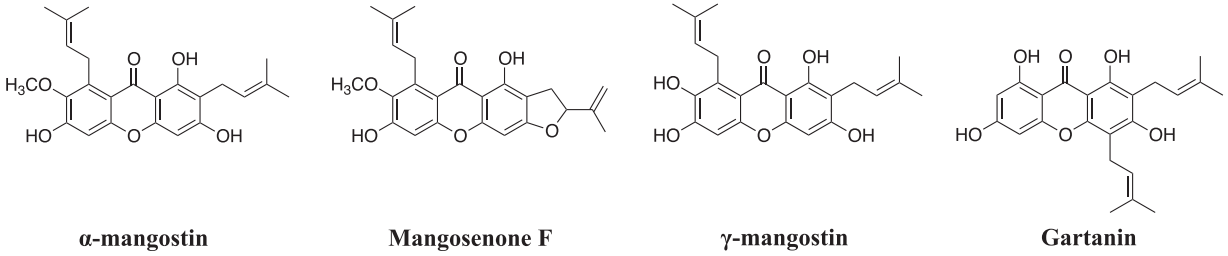

Fig. 1. Chemical structures of *G. mangostana* L. xanthones with antineoplastic activities.

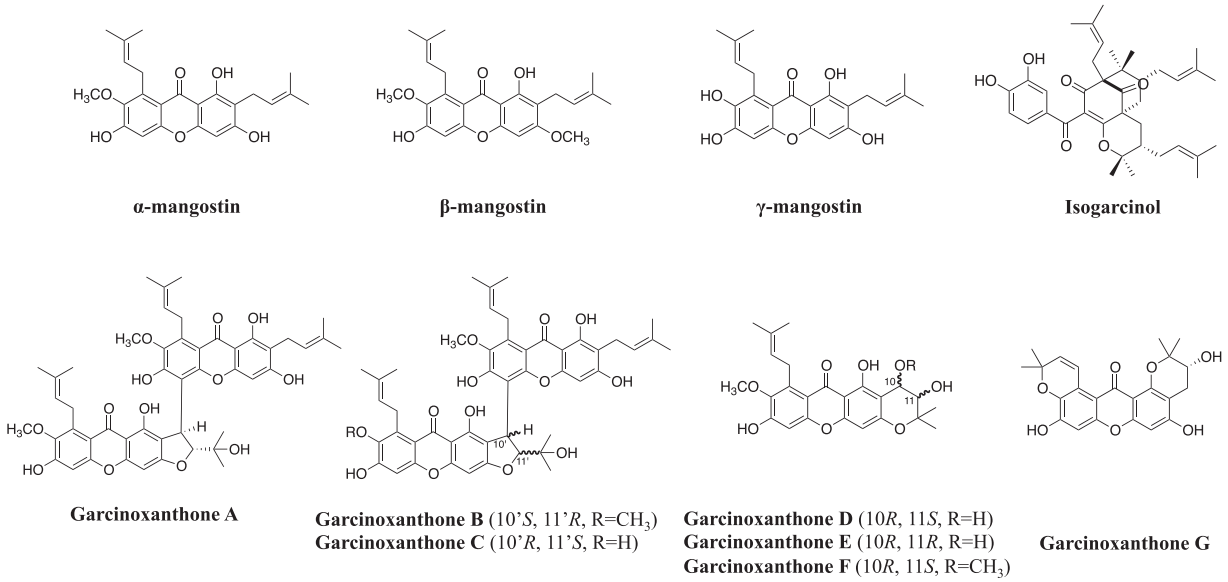

Fig. 2. Chemical structures of *G. mangostana* L. xanthones with antinociceptive and anti-inflammatory activities.