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Review Article

# ACTIVE COMPOUND SUBSTANCE AND ANTICANCER ACTIVITY OF MANGOSTEEN RIND EXTRACT: A REVIEW

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**ABSTRACT**

Recent research on the mangosteen rind was more focused on the content of active substance. This review explored the active substance that had anticancer activity. Review showed that the derivatives of xanthone from mangosteen rind extract containing α-mangosteen, γ-manggosteen, panaxhantone, and garcinon E. Anticancer mechanism of those xanthons derivates were in antiproliferation and apoptosis. α-mangosteen was effective for breast-cancer and leukemia, whereas garcinon E was effectively used as an anticancer of liver.

**Key words**: *Garcinia mangostana* L., α-mangosteen, γ-mangosteen, panaxhantone, garcinon E, anticancer

## INTRODUCTION

Plants of mangosteen (*Garcinia mangostana* L.) live on a shady tropical forests in Southeast Asia, including Indonesia and Malaysia. Garcinia is a genus of the family Guttiferae and known by the name manggisan[1]. Some research has been done on the benefits of traditional medicine from rind extracts of mangosteen fruit. On a review of this article will discuss the activity of extract of mangosteen rind as anticancer drugs, from a variety of studies on the activity.

### Mangosteen (*Garcinia mangostana* L.)

The content of the active compounds from rind extract, mangosteen fruit, namely phenol compounds: xanthone, benzophenone, and flavonoids[1]. The xanthone compounds is the major activity as anticancer drugs. There are two compounds namely 1,3,6-trihydroxy-7-methoxy-2,8-bis(3-methyl-2-buthenyl)-9Hxanten-9-on and 1,3,6,7-tetrahydroxy-2,8-bis(3-methyl-2-buthenyl)-9Hxanten-9-on. The synonym is α-mangosteen and γ-mangosteen[2]. The tree of *G. mangostana* L., mangosteen fruit with the rind, and chemical structure of mangosteen can be seen in figure 1. Ho, *et al.* reported that a xanthone compounds results in isolation, there was the mangosteen rind compound garcinon E which showed anticancer activity[4]. Jung, *et al*. managed to identify the content of xanthone extracts from mangosteen rind that was soluble in dichloromethane, namely xanthone oxygenate prenylated and twelve other xanthones[5].

### Mechanism of anticancer mangosteen rind extract

Mangosteen rind utilization has been used empirically. Mangosteen fruit rind was used on different treatment in different countries, among others, in Thailand, Myanmar, and Sri Lanka[6]. Thailand community utilizing the rind of mangosteen for diseases treatment such as aphthous ulcers, cystitis, dysentery, diarrhea, gonorrhea, and eczema[7].

The advanced research about the mangosteen rind lead to anticancer activity[4]. Mechanism of anticancer activity of extract of mangosteen rind more cytotoxic effect on directional and apoptosis of cancer cells[8]. To know the characteristics of anticancer compounds that were present in the extract of mangosteen rind, Monajjemi *et al*. conducted a study in silico. The results suggest that α- mangosteen, γ-mangosteen, and deoxygartanin have a side of the active form of functional groups OH, phenyl, Br, F, and ethyl, which can be used as anticancer[9]. Ho *et al.* managed to isolate some of the xanthone compounds and to test the effects of the cytotoxicity on the cell line HEp 3B, HCC36, TONG, HA22T, SK-Hep-1 of liver cancer. Based on such research, the compound garcinon E showed the activity of the cytotoxicity[4]. In the meantime, Moongkarndi *et al*. reported that the methanol extract of mangosteen rind indicated very high activity in inhibiting the proliferation of SKBR3 breast cancer cells and showed the activity of apoptosis[10]. Matsumoto, *et al*. researching on antiproliferation activity and apoptosis in HL60 human leukemia cell growth. The results suggest that α-mangosteen showed highest activity between other xanthone compounds. And then, they continued such research to study the mechanism of apoptosis of α-mangosteen[11]. Continuing the findings above, Nabandith, *et al*. conducted a study in vivo activity of chemo preventive from α-mangosteen on a preneoplastic lesion putative carsinogenesis involved in the colon of rats, induced by 1,2-dimethylhydrazine (DMH). The granting of the compound for four to five weeks, inhibits the induction and development of aberrant crypt foci (ACF), lowering the dysplastic foci (DF) and betacatenin accumulated crypts (BCAC). In the cell nucleus antigen labeling undergoes proliferation, these compounds decrease the occurrence of focal lesions and colonic epithelium of rats[12].

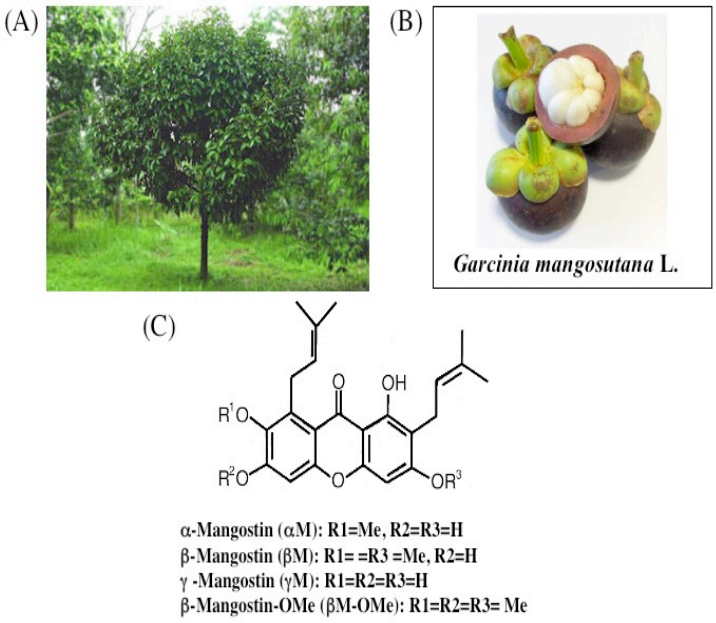


**Figure 1: The tree of *G. mangostana* L.(A), mangosteen fruit with the rind(B), and chemical structure of mangosteen(C)[3]**

**Breast Anticancer Activity**

Moongkarndi, *et al*. tested pure methanol extracts activity of the crap fruit mangosteen by in vivo, with cell line SKBR3 method using human breast cancer, showed antiproliferation activity against cancer cells, with MTT assay[10]. This statement was further analyzed by Doi, *et al*. by doing a in vivo study taking action against rats who suffered from breast cancer cells. The rats were given of panaxanthone (75-85% α-mangosteen and 5-15% γ-mangosteen) as much as 2500 ppm, for three weeks experienced a decrease in volume tumor cell significantly (from 1.749±461 $mm^3$ become 939±197 $mm^3$). After further examined, it turns out that panaxanthone works by apoptosis inducing and inhibits DNA synthesis of tumor cells in the G1 phase[13].

**Liver Anticancer Activity**

According to Shankaranarayan, *et al*. Garcinon E can be used as chemotherapy cancer cells of the liver and lungs[14]. Garcinon E according to research Ho, *et al.* give LD50 range 0.1-5.4 µM and cytotoxic potential of having multiple cells line the heart (HEp 3B, HCC36, TONG, HA22T, SK-Hep-1). Garcinon E when compared with Taxol was less effective, but more effective compared to methotrexate, myxtoxantron, cis-Pt, 5-Fu, and vincrystin, as an anticancer compounds that come from other plants[4].

**Anticancer Activity of Blood (Leukemia)**

Matsumoto *et al*. succeeded in isolating the α-mangosteen from the crap of the mangosteen, which was then examined and deliver results that at concentrations of 5-10 µM α-mangosteen, inhibit the growth of leukemia cells by 50%[8]. In vitro tests showed that the inhibition of leukemia cells (cell line HL60) by α-mangosteen happens through the mediation of the mitochondrial pathway in the induction apoptosis of cancer cells. Parameters the existence of mitochondrial dysfunction, including the mitochondrial swelling, loss of membrane potential, intracellular ATP, decreased the accumulation of ROS, and expenses of c/AIF, one to two hours after administering α-mangosteen11.

**DISCUSSION**

Methanol extract of mangosteen rind has a lot of xanthone content and its derivation, tested, either in vitro or in vivo anticancer activity. Xanthone compounds have applications in between, α-mangosteen, β-mangosteen, γ- mangosteen, garcinon E and panaxanthone. Anticancer mechanism of action of the extract of mangosteen rind works as antiproliferation and apoptosis. α-mangosteen had work against breast cancer cells, liver, and leukemia, panaxanthone provided in the breast, and garcinon E had the highest activity than the other as anticancer. Garcinon E when compared with Taxol was at second place, but more effective compared to methotrexate, mixtoxanthrone, cis-Pt, 5-Fu, and vincristine, as an anticancer compounds that come from other plants.

**CONCLUSION**

Study of in silico, in vitro, and in vivo showed that α- mangosteen, γ-mangosteen, panaxanthone, and garcinon E contained in the mangosteen rind had activity as anticancer drugs. α-mangosteen had work against breast cancer cells, liver, and leukemia, panaxanthone provided in the breast, and garcinon E had the highest activity than the other as anticancer.

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