

Abstract

Disrupting Androgen Receptor Functionality with Xanthones from the Mangosteen (*Garcinia mangostana*) Fruit †

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† Presented at the 3rd International conference on Natural Products for Cancer Prevention and Therapy, Kayseri, Turkey, 18–20 December 2019.

Published: 3 March 2020

Abstract: The Southeast Asian mangosteen (*Garcinia mangostana*) contains a class of phytochemicals known as xanthones that possess extensive biological activity. Applications of xanthones, including the most prominent, alpha-mangostin, have been shown to possess anti-cancer, anti-oxidant, and anti-proliferation properties. To confirm the anti-cancer activity of xanthones we have evaluated 9 xanthones for decreasing cellular proliferation of cancer cells. These xanthones include alpha-mangostin, gartanin, 9-hydroxycalabaxanthone, garcinone C, garcinone D, and others. Using this approach, we have focused on understanding the ability of xanthones to disrupt androgen receptor in prostate cancer cells with a combination of cell free and cell-based assays. In addition, we have performed pharmacokinetic studies in mice with alpha-mangostin to characterize the optimal dosing strategy. Taken together, we have identified individual xanthones as capable of disrupting kinases, including CDK4, using cell free biochemical models and cell-based animal models. These results have been further validated in an in vivo xenograft model. Taken together, we have begun to describe the anti-cancer potential of xanthones for prostate cancer.

Keywords: mangosteen; *Garcinia mangostana*; mangostin; prostate cancer; androgen receptor



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