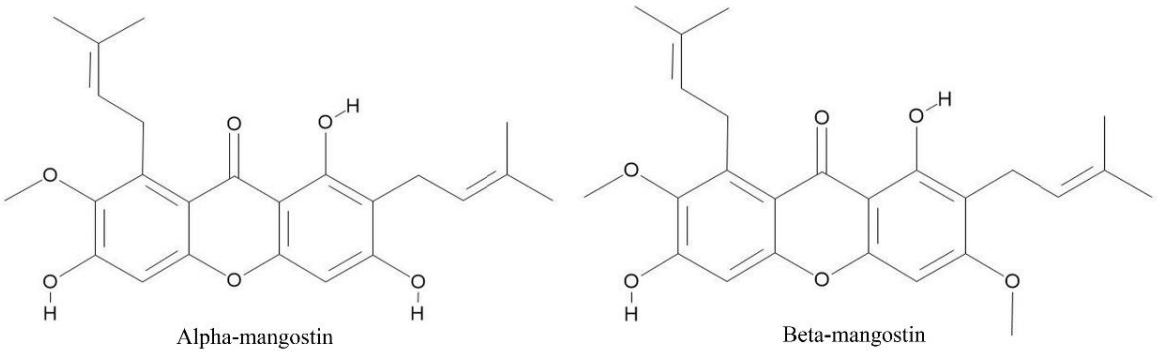
The intestinal efflux transporter inhibition activity of xanthones from Mangosteen pericarp: An in silico, in vitro and ex vivo approach

The capacity of α-mangostin (α-MG) and β-mangostin (β-MG) from mangosteen pericarp on P-glycoprotein (Pgp) in silico, in vitro, and ex vivo was investigated in this study. Screening with the ADMET Predictor™ program predicted the two compounds to be both a Pgp inhibitor and Pgp substrate. The compounds tended to interact with Pgp and inhibit Pgp ATPase activity. Additionally, bidirectional transport on Caco-2 cell monolayers demonstrated a significantly lower efflux ratio than that of the control (α-(44.68) and β-(46.08) MG versus the control (66.26); $p < 0.05$) indicating an inhibitory effect on Pgp activity. Test compounds additionally revealed a downregulation of MDR1 mRNA expression. Moreover, an ex vivo absorptive transport in everted mouse ileum confirmed the previous results that α-MG had a Pgp affinity inhibitor, leading to an increase in absorption of the Pgp substrate in the serosal side. In conclusion, α- and β-MG have the capability to inhibit Pgp and they also alter Pgp expression, which makes them possible candidates for reducing multidrug resistance. Additionally, they influence the bioavailability and transport of Pgp substrate drugs.



Chemical structure of α-mangostin and β-mangostin
The two-dimensional structure of α-mangostin (α-MG) and β-mangostin (β-MG) drawn in the MedChem Designer™ program.

Reference:

Dechwongya P, Limpisood S, Boonnak N, Mangmool S, Takeda-Morishita M, Kulsirirat T, Rukthong P, Sathirkul K. The intestinal efflux transporter inhibition activity of xanthones from Mangosteen pericarp: An in silico, in vitro and ex vivo approach. Molecules. 2020;25:5877. doi: 10.3390/molecules25245877.

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