Mangostin

Mangostin is a natural xanthonoid, a type of organic compound isolated from various parts of the mangosteen tree (Garcinia mangostana). It is a yellow crystalline solid with a xanthone core structure. Mangostin and a variety of other xanthonoids from mangosteen have been investigated for biological properties including antioxidant, anti-bacterial, anti-inflammatory, and anticancer activities.

The ATP-binding cassette (ABC) drug transporter ABCG2 can actively efflux a wide variety of chemotherapeutic agents out of cancer cells and subsequently reduce the intracellular accumulation of these drugs. Therefore, the overexpression of ABCG2 often contributes to the development of multidrug resistance (MDR) in cancer cells, which is one of the major obstacles to successful cancer chemotherapy. Moreover, ABCG2 is highly expressed in various tissues including the intestine and blood-brain barrier (BBB), limiting the absorption and bioavailability of many therapeutic agents. For decades, the task of developing a highly effective synthetic inhibitor of ABCG2 has been hindered mostly by the intrinsic toxicity, the lack of specificity, and complex pharmacokinetics. Alternatively, considering the wide range of diversity and relatively nontoxic nature of natural products, developing potential modulators of ABCG2 from natural sources is particularly valuable. α-Mangostin is a natural xanthone derived from the pericarps of mangosteen (Garcinia mangostana L.) with various pharmacological purposes, including suppressing angiogenesis and inducing cancer cell growth arrest. In this study, we demonstrated that at nontoxic concentrations, α-mangostin effectively and selectively inhibits ABCG2-mediated drug transport and reverses MDR in ABCG2-overexpressing MDR cancer cells. Direct interactions between α-mangostin and the ABCG2 drug-binding site(s) were confirmed by stimulation of ATPase activity and by inhibition of photolabeling of the substrate-binding site(s) of ABCG2 with [125I]iodoarylazidoprazosin. In summary, our findings show that α-mangostin has great potential to be further developed into a promising modulator of ABCG2 for reversing MDR and for its use in combination therapy for patients with MDR tumors [1)].

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Wu CP, Hsiao SH, Murakami M, Lu YJ, Li YQ, Huang YH, Hung TH, Ambudkar SV, Wu YS. Alpha-Mangostin Reverses Multidrug Resistance by Attenuating the Function of the Multidrug Resistance-Linked ABCG2 Transporter. Mol Pharm. 2017 Aug 7;14(8):2805-2814. doi: 10.1021/acs.molpharmaceut.7b00334. Epub 2017 Jul 5. PubMed PMID: 28641010.