Indian Journal of Experimental Biology
Vol. 62, October 2024, pp. 802-809
DOI: 10.56042/ijeb.v62i10.371

Taurine reduces cholesterol through CYP7A1 in a calcineurin-dependent manner

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Received 06 April 2023; revised 19 December 2023

Taurine (2-aminoethanesulfonic acid) could reduce serum and liver cholesterol concentrations via regulating expression and the activity of cholesterol 7α-hydroxylase (CYP7A1). To investigate the possible role of calcineurin in taurine upregulating CYP7A1 expression in HepG2 cells under high cholesterol conditions. High cellular cholesterol conditions were achieved using 0.2 mM cholesterol in HepG2 cells. Calcineurin was decreased by FK506 and was depleted in CnAβ-/- cells. HepG2 cells were cultured in a taurine-containing medium for 24 or 48 h. The levels of total intracellular cholesterol were determined by an enzymatic method, and the expression levels of calcineurin, CYP7A1, and key transcriptional regulatory molecules were detected by western blotting. High-cholesterol resulted in increased CYP7A1 and calcineurin expressions. Taurine exhibited cholesterol-lowering effects regardless of low/high cholesterol conditions or calcineurin status. Taurine induced the expression of CYP7A1, which was abolished by inhibiting or deleting calcineurin. Taurine suppressed MEK1/2, p-c-Jun, and SHP-1, key molecules in one inhibitory pathway of CYP7A1 transcription. In contrast, suppression of MEK1/2 but not p-c-Jun or SHP-1 was reversed after completely knocking down calcineurin. Calcineurin is required for taurine's upregulation of CYP7A1 expression through inhibiting MEK1/2, which was partly responsible for taurine's cholesterol-lowering effect.

Keywords: Calcineurin, Cholesterol, CYP7A1, MEK1/2, Taurine

addition to clinical studies, numerous animal