

Effects of curcumin analogue, 2, 6-bis (2, 5-dimethoxybenzylidene) cyclohexanone (BDMC33) on the activities of drug-metabolizing enzymes in cultured Caco-2 cell model

ABSTRACT

Poor systemic delivery of curcumin outside the gut due to its rapid metabolism has severely limited its application to many chronic diseases. Previously, our research group synthesized curcumin analogues 2, 6-bis (2, 5-dimethoxybenzylidene) cyclohexanone (BDMC33) that has potent anti-inflammatory activities. Therefore, the aim of this study is to evaluate the effects of curcumin analog (BDMC33) on the activities of drug metabolizing enzymes in Caco-2 cells, which was compared with that of curcumin and 3-(2-Fluoro-benzylidene)-5-(2-fluorocyclohexylmethylene)-piperidin-4-one (EF-24). BDMC-33 was synthesized through the appropriate reaction of the aromatic aldehyde with cyclohexanone, under base catalyzed aldol condensation, at the ratio of ketone: aldehyde (1:2). Activity of drug metabolizing enzymes such as NADPH-cytochrome p450 reductase (CPR), UDP-glucuronosyltransferase (UGT), glutathione-S-transferase (GST) and Sulfotransferase (SULT) in Caco-2 cells were evaluated upon exposure to 50 μ M of BDMC33, curcumin, and EF-24, separately, for 4 hours. The BDMC33, EF-24, and curcumin treatments did not affect the activities of UGT, GST, SULT, and CPR in respect to their controls (29.45, 27.18, 23.64 and 2.08 μ mol/mg), respectively, at all periods of incubation. Hence, BDMC33 was able to maintain the activities of both phases I and II drug metabolizing enzymes, and therefore it could be a potential lead, anti-inflammatory agents.

Keyword: Caco-2 cells; Curcumin; Drug metabolizing enzymes; Glutathione-S-transferase; NADPH-cytochrome c reductase; Sulfotransferase; UDP-glucuronosyltransferase