Dietary administration of berberine or Phellodendron amurense extract inhibits cell cycle progression and lung tumorigenesis.

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Abstract

Phellodendron amurense extract is a Chinese herbal remedy that has recently been studied for its antitumor, antimicrobial and other biological activities. It is previously unknown if these agents are bioavailable and effective against tumors when delivered as a dietary component. It is also unknown if the anti-tumorigenic properties of berberine, an isoquinoline alkaloid component of P. amurense, is equally effective when administered alone. There are contrasting reports on the cellular processes involved in anti-tumorigenesis by P. amurense and berberine. Here we find that berberine, when administered orally through the diet, inhibits in vivo tumorigenesis of both p53 expressing and p53 null lung tumor xenografts equally whether administered in its pure form or as a part of P. amurense extract. We also show that berberine induces G1 cell cycle arrest, inhibits proliferative kinase signaling and arrests the growth of lung tumor cells in culture. Berberine administered in the diet was detectable by HPLC in the lungs of mice fed P. amurense or equivalent doses of berberine at concentrations of 455 and 518 ng/ml respectively and inhibited the growth of xenografted A549 cell tumors, which grew to 9.4 and 6.4 mm³ respectively, compared to 58.9 mm³ in control mice (P < 0.001). Phosphorylation of Akt, CREB and MAPK was inhibited in A549 cells by P. amurense. Demonstration of oral bioavailability and anti-tumorigenic efficacy of dietary berberine, as well as further demonstration of signaling pathway modulation and cell-cycle arrest, implicate this relatively safe, natural compound as a potentially important therapeutic and chemopreventive agent for lung cancer.