Antitumor effects of the benzophenanthridine alkaloid sanguinarine in a rat syngeneic model of colorectal cancer.


Abstract

To evaluate the in-vivo preclinical antitumor activity of sanguinarine in a rat syngeneic model of colorectal cancer. The effects of sanguinarine on DHD/K12/TRb colorectal adenocarcinoma cells were first evaluated in vitro by means of H-thymidine incorporation, 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) assay, and terminal transferase dUTP nick end labeling (TUNEL) microscopy. For the in-vivo studies, DHD/K12/TRb cells (1.5×10 cells/0.3 ml of sterile saline/animal) were injected subcutaneously in syngeneic BDIX rats, which were chronically treated with sanguinarine (5 mg/kg/day per os) or control diluent. Tumor growth, body weight, hematologic, and clinical chemistry measurements were monitored in individual animals at defined time intervals. After killing, subcutaneous tumors were explanted from experimental animals for histopathological examination. In vitro, micromolar concentrations of sanguinarine inhibited dose-dependently DHD/K12/TRb cell proliferation and metabolism and induced cell death by apoptosis. In vivo, oral administration of sanguinarine induced a significant inhibition of tumor growth (P<0.01 vs. untreated controls), in the absence of any toxic or side effects. Marked apoptosis and reduced peritumoral vascularization were observed in tumors from sanguinarine-treated rats as compared with the controls. Additional basic studies are needed to fully characterize the mechanism/s underlying the inhibitory effects of sanguinarine on angiogenesis and tumor growth as well.
as the pharmacological and safety profile of this drug in experimental tumor models. Overall, findings from this study suggest that sanguinarine is a likely candidate for further evaluation in cancer therapy.

PMID:

21849887