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A triterpenoid (corosolic acid) ameliorated AOM-mediated aberrant crypt foci in rats: modulation of Bax/PCNA, antioxidant and inflammatory mechanisms

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Abstract

Corosolic acid (CA) is a well-known natural pentacyclic triterpene found in numerous therapeutic plants that can exhibit many bioactivities including anti-inflammatory and anti-tumor actions. The current investigation explores the chemoprotective roles of CA against azoxymethane (AOM)-induced colonic aberrant crypt foci (ACF) in rats. Thirty Sprague-Dawley rats were grouped in 5 cages; Group A, normal control rats inoculated subcutaneously (sc) with two doses of normal saline and fed orally on 10% tween 20; Groups B–E received two doses (sc) of azoxymethane in two weeks and treated with either 10% tween 20 (group B) or two intraperitoneal injections of 35 mg/kg 5-fluorouracil each week for one month (group C), while group D and E treated with 30 and 60 mg/kg, respectively, for 3 months. The toxicity results showed lack of any behavioral abnormalities or mortality in rats ingested with up to 500 mg/kg of CA. The present AOM induction caused a significant initiation of ACF characterized by an increased number, large in size, and well-matured tissue clusters in cancer controls. AOM inoculation created a bizarrely elongated nucleus, and strained cells, and significantly lowered the submucosal glands in colon tissues of cancer controls compared to 5-FU or CA-treated rats. CA treatment led to significant suppression of ACF incidence, which could be mediated by its modulatory effects on the immunohistochemical proteins (pro-apoptotic (Bax) and reduced PCNA protein expressions in colon tissues). Moreover, CA-treated rats had improved oxidative stress-mediated cytotoxicity indicated by increased endogenous antioxidants (SOD and CAT) and reduced lipid peroxidation indicators (MDA). In addition, CA ingestion (30 and 60 mg/kg) suppressed the inflammatory cascades, indicated by decreased serum TNF- α and IL-6 cytokines and increased anti-inflammatory (IL-10) cytokines consequently preventing further tumor development. CA treatment maintained liver and kidney functions in rats exposed to AOM cytotoxicity. CA could be a viable alternative for the treatment of oxidative-related human disorders including ACF.

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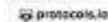
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