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 2 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.