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Combination of sulfamethoxazole and selenium in anticancer therapy: a novel approach

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Abstract Sulfonamides have been reported to possess substantial antitumor activity as they act as carbonic anhydrase inhibitors. In addition, selenium appears to have a protective effect at various stages of cancer due to its antioxidant property, enhanced carcinogen detoxification, inhibition of cell invasion, and by inhibiting angiogenesis. Here, in the present study we aimed to evaluate and synergize the cytotoxic activity of sulfonamide and selenium (SM+SE) as effective therapy in the treatment of DENA-induced HCC. Hepatocarcinogeneis was induced by a single intraperitoneal injection of diethylnitrosamine (DENA) (200 mg/kg) in phosphate buffer. 30 Male Wistar rats used in this study were divided randomly into five equal groups ($n = 6$). DENA-administered animals showed significant alteration ($p < 0.001$) in liver-specific enzymes—glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), alkaline phosphatase (ALP), and Alpha fetoproteins (AFP), and also induced severe histopathological changes in the hepatic tissues. Interestingly, treatment with (SE+SE) (SM 30 mg/kg + SE 3 mg/kg) significantly reduced ($P < 0.001$, $P < 0.001$, $P < 0.001$, $P < 0.001$) the elevated AFP, SGOT, SGPT, and ALP levels, respectively, suggesting that combination therapy of SM+SE has a potential to treat DENA-induced liver damage.

Keywords DENA · HCC · Sulfonamide · Selenium · Histopathology · Anticancer

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Introduction

Hepatocellular carcinoma (HCC) is a primary malignancy of the liver. Worldwide, the incidence of HCC in developing nations is twice than that in developed countries [1]. In 2000, the age-adjusted incidence of HCC in men was 17.43 per 100,000 population in developing countries compared with only 8.7 per 100,000 population in the United States. In high-income countries the number of liver incidence accounts 2.7 % of 285,804 global economic burden [2]. Patients with Non-alcoholic fatty liver disease (NAFLD) can progress to fibrosis, cirrhosis, and now HCC [3].

Diethylnitrosamine (DENA) is frequently used to induce hepatocarcinogenesis in experimental animals [4] possibly by causing oxidative stress and cellular injury with enhanced formation of detrimental free radicals. DENA metabolizes to its active ethyl radical, which can interact with DNA causing mutation and subsequent oncogenesis [5, 6].

Selenium is an essential dietary component for animals including humans, and there is increasing evidence for the efficacy of certain forms of selenium as cancer-