

Abstract:

Introduction: Various risk factors such as chemical carcinogens contribute to development of liver cancer. N-ethyl-n-nitrosourea (ENU) as a n-nitrosamine and alkylating agent, ubiquitous within living cells and in the environment can act as a full carcinogen and induce tumor cells in various tissues such as liver. In this study, gallic acid loaded chitosan nanoparticles (GANPs) were synthesized using the ionic gelation method and evaluated its chemopreventive effect against ENU-induced hepatotoxicity and mortality in rat.

Materials and Methods: Twenty-four male Wistar rats were divided into 4 groups. Rats in Group 1 were used as a control and received normal saline orally for 30 days. In Group 2, as a positive control (ENU), liver carcinogenesis was induced in rats through the intraperitoneal injection of single doses of 50 mg/kg body weight, on the 31st day of study (group II). Groups 3 (GA +ENU) and 4 (GANPs +ENU) received GA 50 mg/kg and GANPs (50 mg/kg) respectively, for 30 days and the same treatment in Group 2 on the 31st day of study. Weight change and mortality were monitored during 30 days, and then the animals were sacrificed and alpha-fetoprotein (AFP) as a tumor marker, liver function tests (ALT, AST and ALP), oxidative stress markers (GSH and MDA), mitochondrial toxicity parameters and histopathological abnormalities were evaluated.

Results: Except AFP and MDA, ENU caused significant elevated liver enzymes, mitochondrial ROS formation, collapse of mitochondrial membrane potential (MMP), depletion of GSH, histopathological abnormalities and mortality in rat. Our data showed that GANPs significantly increased the survival of rats up to 66%, delay in death time and prevented weight changes after exposure to ENU. Moreover, GANPs restored liver enzymes level, ROS formation, mitochondrial dysfunction, GSH amount, and histopathological abnormalities towards normal.

Discussion: Our significances recognized that GANPs revealed a potential impact against deadly toxicity induced by ENU as a full carcinogen in liver tissue. Our results demonstrated that GANPs has promise for chemopreventive treatment of alkylating agents-induced carcinogenicity and toxicity in liver tissue.

Key words: N-nitrosamines; Alkylating Agents; Chemical Carcinogens; Antioxidants; Liver Cancer