Abstract

Luteolin is an important flavonoid with a potential anticancer effect. Luteolin, usually occurs in its glycosylated form in celery, green pepper, perilla leaf, and camomile tea, etc., and much as an aglycone in perilla seeds. Recently, a potent anticancer effect of luteolin has been shown in several experiments in vitro. A great amount of data have indicated the therapeutic benefits of luteolin against cancer. However, it remains unclear whether these benefits are similar and equally effective in both the early and advanced stages of cancer or carcinogenesis. In this study, the effects of luteolin in the advanced stages of hepatocarcinogenesis has been reported using N-nitrosodiethylamine (DEN)-induced hepatocellular carcinoma (HCC) in male Wistar rats. For this experiment, rats were categorised into four groups. The rats which developed HCC, i.e., 15-16 weeks after DEN administration (post-HCC) were treated with luteolin and compared to untreated HCC-bearing rats. The levels of cancer marker enzymes viz., α-fetoprotein and CEA which are the known serum markers for HCC and other serum and liver marker enzymes were found to decrease upon luteolin treatment compared to untreated HCC-bearing rats. Luteolin stabilizes and restores the antioxidant defense system viz., GSH, CAT, SOD, GPx and GST. These antioxidant enzymes protect cells from ROS damage in DEN-induced HCC. Luteolin protects the activities of liver injury and tumor markers by decreasing MDA. The antioxidant potential was further confirmed by the non-enzymatic antioxidants such as Vitamin-C, Vitamin E, GSH and MDA levels. The DEN induced treated group showed significantly decreased levels of Vitamin-C, Vitamin-E, GSH and MDA. The non-enzymatic antioxidants in the DEN induced luteolin treated rats were found to be similar to that of control (normal) rats. These findings indicated that luteolin reduces the DEN induced increased ROS generation during hepatocarcinogenesis and promotes the enzymatic and non-enzymatic antioxidant defense system and has potentiality in chemoprevention. Haematoxylin and Eosin staining of liver tissues showed an alteration and / or transformation of liver parenchymatous tissue in DEN-induced HCC. Luteolin treatment to DEN induced HCC rats showed a marked difference in the tissue architecture compared to untreated HCC. Argyrophillic nucleolar organizing regions (AgNORs) are a set of nucleolar proteins that are necessary for ribosomal biogenesis. Luteolin treatment significantly reduced the amount of AgNORs, when compared with tumor-induced animals suggesting that its treatment inhibited the cell proliferation induced by DEN. Mast cells are involved in invasion and angiogenesis and in the present study
investigations on the role of luteolin on mast cell density (MCD) in DEN induced HCC revealed that the increase in MCD was inhibited by treatment with Luteolin. In recent decades, many in silico studies have been done to predict protein functional sites based on protein structures including methods for prediction of protein–protein interaction sites and protein–ligand binding sites. The molecular docking of HCC receptors with the luteolin strongly proved it as a potent anticancer drug. The findings of the study have indicated that administration of luteolin either at the early or advanced stages of hepatocarcinogenesis is equally effective and involves the activation of the apoptotic pathway in male Wistar rats.