Abstract

Cancer is a multifaceted disease with a non-uniform complex burden across the globe. Liver cancer, the sixth most common cancer worldwide, is an aggressive kind of tumor that originates in the liver, frequently in the context of chronic liver ailment and cirrhosis, making it a severe health concern globally. At present, the available treatment options for liver cancer, such as liver transplantation, chemotherapy, surgical resection, percutaneous ablation, radiotherapy, and transarterial and systemic therapies have limited efficacy, high cost, and adverse side effects including chemoresistance and recurrence. Cruciferous plants like *Raphanus sativus* (red radish) possess antitumor and antioxidant properties due to their bioactive components (such as isothiocyanates, sulforaphene, glucosinolates, sinigrin, saponin, gibberellins coumarins, and phenolics). Particularly, *Raphanus sativus* conjugated silver nanoparticles have been shown to have cytotoxic effect against hepatocellular carcinoma *in vitro*. The current study was designed to evaluate the anticancer potential of *Raphanus sativus* conjugated silver nanoparticles against HCC in *in vivo* model. Diethylnitrosamine (DEN) was employed for the induction of HCC in animal models. *R.sativus* conjugated were synthesized using the green synthesis method. The synthesized nanoparticles underwent characterization through the utilization of UV-Vis spectrophotometry and Fourier Transform Infrared (FTIR) analysis. Swiss male albino mice were divided in 11 groups (n=5 in each group). The treatment groups G1,G2A,G2B,G2C,G2D,G3,G4,G5,G6,G7, and G8 were treated with Saline, DEN, Cisplatin (Treatment), *R.sativus* extract (Treatment), *R.sativus* conjugated silver nanoparticles (Treatment), Cisplatin (Toxicity), *R.sativus* extract (Toxicity), *R.sativus* extract conjugated silver nanoparticles (Toxicity), DEN+Cisplatin (Prevention), DEN+*R.sativus* extract and DEN+*R.sativus* conjugated silver nanoparticles (Prevention) respectively. The biochemical parameters were evaluated to analyze the HCC status in mice. The histopathology of liver was also examined. The outcomes of the present study highlight that the application of the treatment resulted in significant reduction in levels of serum biomarkers in contrast to the DEN-treated group. However, *R.sativus* conjugated silver nanoparticles (150mg/kg) showed the most significant results as follows: AFP (47.8±1.5 ng/ml), AST (284.6±6.0 U/L), ALT (126.2±5.2 U/L), ALP (225.0±6.7 U/L), LDH (522.6±7.9 U/L), GGT (30.0±1.2 U/L), bilirubin (5.7±0.1 mg/dl) and MDA (5.2±0.1 mmol/l). A reduction in levels of antioxidant enzymes levels was found in DEN-treated group. These levels were elevated in treatment groups but highlysignificant levels were observed in *R.sativus* conjugated silver nanoparticles (150mg/kg) treated group as follows: GSH (2.8±0.1 µmol/l) and CAT (139.0±3.2 mmol/l). The histopathological study of liver tissues showed alteration in liver architecture in the DEN treated group but restoration in the treatment groups. Therefore, the anticancer potential of *R.sativus* conjugated silver nanoparticles was evident and could be used as treatment against HCC as it successfully reinstated the normal liver structure, serum biomarker and oxidative marker levels.