**ABSTRACT**

**Background & Objectives:**

Over the past 10 years, research for new drugs to be used in oncology has refocused on natural products, which led to the finding of some new compounds such as taxanes and camptothecins. Sea buckthorn (Hippophae rhamnoides L.) is thorny nitrogen fixing deciduous shrub and is primarily valued for its very rich content of vitamin A, B1, B12, C, E, K and P; flavonoids, lycopene, carotenoids and phytosterols. There arescientific reports on various pharmacologic activities of Hippophae rhamnoides L., but antitumour activity for seeds is not reported. Hence, we investigated anticanceractivity of hydroalcoholic extract of Hippophae rhamnoides L. seeds alone and in combination with cyclophosphamide.

**Methods:** HL-60 (Human promyelocytic leukemia) cell lines and BHK-21 cell lines were obtained from NCCS, Pune and were cultured in RPMI-1640 and DMEM growth medium respectively, supplemented with 10% FBS. The cytotoxic and antiproliferative effect of Hippophae rhamnoides L. in the doses of 50-500 μg/ml on HL-60 cancer cells and BHK-21 normal cell lines was determined by using MTT assay, Trypan blue exclusion method, DNA fragmentation and Clonogenic assay. HEHR was used in the doses of 285.7 mg/kg and 666.6 mg/kg body weight of mice for Glutathione and Catalase estimation. Mutagenicity of HEHR on Salmonella typhimurium TA98 and TA100 Strains was determined by AMES assay.

**Results:** HEHR produced significant (p<0.01) and time dependent anti-proliferative effect in terms of percentage cell viability and inhibition of colony growth, on both cancer (HL-60 cells) and normal cells (BHK-21 cells) but cytotoxicity was observed only on HL-60 cells. The cytotoxic effects of HEHR showed time-dependent action against HL-60 cells, with IC50 value of 70.67±6.8 and 50.0±4.9 μg/ml after treatmentwith HEHR for 48 and 72 h respectively. HEHR very significantly (p<0.01) inhibited ocolony growth of HL-60 and BHK-21 cell lines. HL-60 cells treated with HEHR (500 μg/ml) for 72 h produced maximum DNA fragmentation as indicated by the lessamount of DNA in the agarose gels which is hallmark of apoptosis induced by HEHR. HEHR (500 μg/plate) very significantly (p<0.01) produced mutagenic effect on TA98 and TA100 strains, with and without S9 liver mix and mutagenic effect was more onTA98 strain (frame-shift mutations) compared to TA100 strain (base-pair substitutions). The level of GSH significantly decreased in all treated groups compared to tumour induced control group on 6th, 10th and 15th day of cancer induction.

**Conclusion:**

 The anti-proliferative effect of Hippophae rhamnoides Linn. due to its interference with the cell kinetics was indicated with the reduction in the GSH levels and colony growth. The cytotoxic effect of HEHR is produced by apoptosis mechanism which involved DNA fragmentation and mutagenic effect. The antiproliferative and cytotoxic effect of HEHR seeds may be due to the presence of very rich phytoconstituents such as vitamin-E, sterol, carotenoides (β-carotene and lycopene etc.), flavonoides, vitamin-K etc.