

Supercritical antisolvent (SAS) assisted thymoquinone liposomal formulation for radioprotection

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Exposure of ionizing radiation (IOR) can be through various diagnostic and therapeutic processes or inadvertently through nuclear accidents. Lethality of IOR is predominantly linked with generation of reactive oxygen species (ROS), apart from direct deleterious effects on antioxidants and antioxidant enzymes. ROS can readily react with cellular lipids, proteins and DNA to cause irreversible cellular damage and cascading pathogenesis. Thymoquinone (TQ) or 2-Isopropyl-5-methyl-1,4-benzoquinone, obtained from seeds of *Nigella sativa* (Ranunculaceae) has strong antioxidant effect and is proven to defend against oxidative damage. Moreover, *in vivo* studies also highlighted the potential of *Nigella sativa* extract against radiation induced injuries. Nevertheless, due to poor aqueous solubility and rapid elimination rate, the full potential of TQ is not exploited. This study was to develop SAS assisted TQ loaded PEGylated liposome for enhanced blood circulation, improved bioavailability and greater radioprotection. Supercritical antisolvent (SAS) process was optimized by QbD approach and characterized. The radioprotective efficacy of the developed formulation was compared with pure drug solution and amifostine (FDA approved radioprotector) administered through i.v. route post gamma radiation exposure on Swiss albino strain 'A' mice. SAS process (Temperature=35°C; pressure=140 bar and solution flow rate=0.18 mL/min, phospholipid=7.5 mMole, cholesterol= 0.75 mMole and TQ=1 mMole, 5% DSPE-mPEG-2000) produced spherical optimized liposome (FV-17B) with particle size of 231.3±6.74 nm and entrapment efficiency of 89.4±3.69%. *In vivo* study showed that non-significant body weight change, increased survival probability, normalization of hematological parameters, spleen index and frequency of micronucleus cells in bone marrow apart from least DNA damage was observed after administration of FV-17B post 7Gy of whole body irradiation as compared to irradiation control as well as amifostine group. Thus, the developed formulation could be a suitable non-toxic alternative against damage during radiotherapy.

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