## Integrative Assessment of the Novel Radioprotective Efficacy of Cardamonin: A Comprehensive in vitro and in silico Analysis

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Current radiobiology research focusses to identify radioprotective agents that can protect normal tissues from radiation-induced injury due to accidental exposures. Recently, cardamonin has gained interest for its potential antioxidant, anti-inflammatory, anticancer activity and biosafety properties. The main purpose of this project is to decipher the novel radioprotective effects of cardamonin by computational evaluations and in vitro experiments. Clone 9 and WI-38 cells were exposed to 8 Gy gamma irradiation after treatment with or without cardamonin (5 µM). Cell morphology and intracellular ROS generation were assessed. Further studies were done in clone 9 cells. Gene and protein expression of antioxidant enzymes were studied. Apoptosis was measured by live cell imaging using caspases 3/7 stain. Cancer cells were used to study the selective effects of cardamonin. Molecular docking studies were done with Discovery studio and Autodock-vina computational docking software. Pretreatment with cardamonin significantly prevented cell death, and reduced intracellular ROS levels after irradiation. Cardamonin pretreated cells significantly upregulated transcription factor Nrf2 and maintained antioxidant status, which protected the cells against radiation injury. Apoptosis was significantly prevented by inhibiting the activation of caspases. Cardamonin had differential effects in cancer cells. Docking studies revealed the potent anti-apototic, anti-inflammatory and anti-fibrotic efficacy of cardamonin. In conclusion, this project provided significant evidence that cardamonin may serve as a promising radiation countermeasure to mitigate radiation injury and sensitize cancer cells for radiotherapy.