

Studying silibinin effect on human endothelial and hepatocarcinoma cell lines

N. Vakili¹, M. Nakhjavani¹, H. Mirzayi², F. H. Shirazi^{3,*}

¹*Department of Pharmacology and Toxicology, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

²*Shohada General Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

³*Pharmaceutical Sciences Research Center, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

Background and Aims: Silibinin is a natural flavonoid from milk thistle herb, famous for its healing effects on liver. Several suggested mechanisms including maintaining normal rate of protein synthesis in liver, membrane stabilizing and antioxidant effects share influences on its hepatoprotection. These effects together with its proposed anti-angiogenic effect, has made silibinin a good candidate for liver cancer investigations.

Methods: In this project, cytotoxicity (trypan blue assay), cell membrane integrity (trypan blue assay), mitochondrial (MTT assay), apoptotic (LDH assay and fluorescence microscopy) and proliferative (trypan blue assay) effects of silibinin on human hepatocarcinoma cell line (HepG2) and human umbilical vein endothelial cell line (HUVEC) were investigated.

Results: The IC₅₀ of 24-hour exposure of silibinin to HepG2 and HUVEC cell lines were calculated 150 µg/ml and 150 µg/ml, respectively (P<0.05). A dose-response correlation on the growth induction has been shown up to 100 µg/ml. Silibinin exposure to either of HepG2 or HUVEC cells raised LDH leakage of these cells from 30% to 45% at different concentrations.

Conclusions: Cell growth was significantly reduced after exposure to silibinin in a dose-dependent manner. There was a significant difference between Silibinin effect on growth depression of HepG2 and HUVEC cells. LDH release confirmed a necrotic mode of death in these cell lines due to Silibinin. In contrary to previous thought, Silibinin did not present any specific proliferative effects on the endothelial cells compare to the liver one, within the range of exposure in this investigation model. Further studies to investigate silibinin's intracellular molecular effects, as well as its tissue specificity are recommended.

Keywords: Silibinin; HepG2; HUVEC