

## Synthesis of PEGylated zinc protoporphyrin conjugated with folate: For targeted cancer therapy

M. Tebarzad<sup>1\*</sup>, H. Rouhani<sup>2</sup>, M. Amini<sup>3</sup>, R. Dinarvand<sup>3</sup>

<sup>1</sup>Novel Drug Delivery System, Faculty of pharmacy, Teharn university of medical sciences, Tehran, Iran

<sup>2</sup>Medicinal Chemistry, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup>Medical Nanotechnology Research Center, Faculty of pharmacy, Teharn university of medical sciences, Tehran, Iran

**Background and Aims:** In the last two decades studies have shown that Reactive Oxygen Species (ROS) have an important role in all stages of cancer development and relation between cancer and oxidative stress has always been a case of study . According to the toxic effect of ROS and lack of sufficient antioxidant enzymes in tumor cells ,this novel strategy has been revealed that induction of ROS in large amounts in tumor cells which lead to oxidative therapy as a potent anticancer treatment . Heme oxygenase (HO) is a key enzyme in heme metabolism; This enzyme oxidatively degrades heme to biliverdin ,that is subsequently reduced to form bilirubin, a potent antioxidant . Zinc protoporphyrin (ZnPP) is a strong HO-1 inhibitor which is introduced as new anticancer agent by oxidative stress mechanism, but its direct intravenously administration for cancer therapy is limited because of low water solubility characteristic .Previous studies suggested ZnPP conjugated with poly (ethyleneglycol) (PEG-ZnPP) to enhance water solubility and better HO-1 inhibitory effect in tumor cells. In addition targeted delivery of this compound to tumor tissues is an important issue to consider , because its nonspecific HO-1 inhibition results in oxidative stress and adverse reactions in normal cells.

**Methods:** Accordingly in this study we conjugated PEG to folate as a targeting agent and then in the second step, conjugated this PEG-folate to protoporphyrin .Finally by chelating the zinc ion by PP-PEG-Folate we synthesized pegylated ZnPP targeted to folate.

**Results:** Fourier transform infrared spectroscopy (FTIR) showed the conjugation of PEG to folate was done successfully .This information was confirmed by H-NMR spectra .Achievements in synthesis of zinc chelated PP-PEG-Folate was demonstrated by Ultraviolet UV spectrophotometry.

**Conclusions:** Base of our results, we successfully synthesized ZnPP-PEG targeted with folate ligand which can be evaluated for its promising efficacy by consequent in-vivo and in-vitro studies.

**Keywords:** Heme oxygenase; Reactive oxygen species; Targeted anticancer therapy; Zinc Protoporphyrin