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Formation of phytosome containing silymarin using thin layer-hydration technique aimed for oral delivery

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Silymarin is a unique flavonoid complex isolated from milk thistle (Silybum marianum) and has been widely used as hepatoprotective agent. Orally administered silymarin will be absorbed rapidly and only 20-50% of silymarin will be absorbed through gastrointestinal tract, resulting on its low bioavailability. Those limitations are due to its poorly soluble either in water and oil and its low intestinal permeability. This study was aimed to develop silymarin-loaded phytosomes to improve silymarin bioavailability with sufficient safety and stability. This system consists of silymarin-phospholipid complex prepared by solvent evaporation method, which was incorporated to formed phytosome shape vesicles using thin layer method with various concentration and molar ratio of silymarin and phospholipid. Phytosome vesicles size was reduced using probe sonication. The result demonstrated that formula with 2% silymarin-phospholipid complex and molar ratio of 1:5 showed the best physical properties with mean vesicle diameter of 133.53±8.76 nm, polydispersity index of 0.34±0.08, entrapment efficiency of 97.17±2.41 %, loading capacity of 12.18±0.30%, and good stability after freeze thaw stability test. Analysis of FTIR spectroscopy and DSC was confirmed the presence of physical and chemical interactions between silymarin and phospholipid complex. Well formed and discrete vesicles of phytosome were revealed by Transmission Electron Microscopy, drug content, and freeze thaw stability test.

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siRNA-based targeted gene therapies in cancer: Targeting EF2-kinase in solid tumors

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After recent discovery, the use of small interfering RNA (siRNA) has rapidly become a powerful tool for silencing oncogenes and holds promise as a novel class of therapeutics in cancer. siRNA based therapeutic intervention can be uses especially for those targets that cannot be targeted by small inhibitors or for "non drugable" targets. However, successful clinical applications and *in vivo* delivery of the siRNA-based therapeutics to primary and metastatic tumors remains as a great challenge. We recently identified eEF2-kinase in solid tumorssuch as breast and pancreatic cancer developed tumor targeting nanoliposomes that can target siRNA *in vivo* into tumor cells more effectively than regular liposomes, leading to significant and robust target gene silencing for about a week in breast, ovarian and prostate cancers animal models. Overall, our preclinical studies demonstrated that highly specific targeting of genes promoting cell proliferation, survival, tumor growth, invasion ad progression including EF2-kinase (Ef2K) and Bcl-2, EphA2 genes by liposomal siRNA nanotherapeutics significantly inhibited tumor growth in breast, ovarian and prostate cancers, respectively, as well as hematological tumor models such as lymphoma. Our data suggest that siRNA based nanotherapies have potential as novel class of systemic therapies for various cancers and provide the proof of concept and the impetus for translational studies for Phase I clinical trials in patients.

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