

Preparation, physico-chemical characterization and in vitro test of a Silybin–phospholipid complex encapsulated into liposomes.

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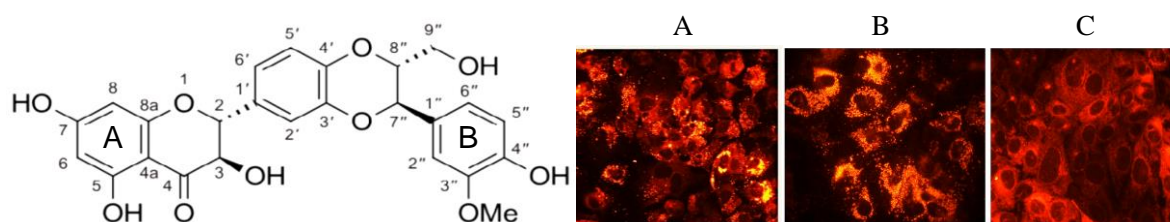
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Silybin is the main polyphenolic component of silymarin, a flavonoid complex extracted by the milk thistle plant *Silybum marianum*. Silybin possesses many health-promoting activities, such as antioxidation, anticancer and hepatoprotective [1]. However, the benefits are curtailed by its extremely poor water solubility [2]. Consequently, the bioavailability and therapeutic effective of silybin is also limited. Nanotechnology is an available approach to solving these issues. Currently, the efficacy of natural extracts may be improved through their incorporation into liposome, thanks to their versatility to load and protect unstable/photosensitive molecules having different structure and molecular weight, and their ability to facilitate and control the delivery of the loaded drug to the target. Here, we tested a formulation based on the encapsulation of a silybin-phospholipid complex, commercially available with the trade name Siliphos™, into liposomes to yield a new type of supramolecular aggregates, also called *Phyto-Liposomes* [3].

First, we set up a simple preparation protocol through the reverse-phase evaporation method and investigated the physico-chemical properties of the obtained liposomal suspensions. A careful investigation of host-guest interactions was carried out by performing UV–vis, spectrofluorimetry and NMR experiments both in aqueous and non-polar solvents to probe the influence of phospholipids on the electronic properties of silybin and its propensity to engage H-bonding with the lipid headpolar groups. Then, it was demonstrated the ability of phyto-liposomes to be internalized in human hepatoma Huh7.5 cells, being 2.4 fold more efficient than the pristine silybin. Finally, the new formulation was tested on cell systems supporting HCV replication and infection, and its spectrum of pharmacological activities was compared with that of the active principle dissolved in DMSO revealing a three hundreds fold more potent pharmacological activity [4]. A striking anti-viral effect was also manifested by empty liposomes used as control. We suspect that the presence of a minor non-phospholipidic component in the raw lecithin used to produce liposomes might be responsible for the inhibitory activity observed by naïve vesicles.

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Left: Molecular structure of silybin. **Right:** Fluorescent microphotographs at 40X of Huh7.5 human hepatoma cellular monolayers incubated at 37°C for 72 h with (A) Liss-Rhod-PE labelled phyto-liposomes loaded with silybin; (B) Liss-Rhod-PE labelled empty liposomes; (C) free red-emitting Liss-Rhod-PE labelled phospholipid.

References.

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