

FORMULATION STUDIES OF SYLIBUM MARIANUM SEED EXTRACTS

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INTRODUCTION

Sylimarin, the active substance of *Sylibum Marianum* has a well-known hepatoprotective effect (1). The result of extraction process of the *Sylibum Marianum* seed were 25% oil and a dry, water insoluble sylimarin extract. The aim of the study was to prepare sylimarin formulations with high bioavailability for the treatment of acute hepatotoxicity. Water miscible self micro emulsifying drug delivery systems (SMEDDS) (2) of the oil and water soluble formulations of sylimarin were produced which are suitable for further *in vitro* and *in vivo* examinations.

MATERIALS AND METHODS

Materials

Sylibum Marianum seed oil and sylimarin were originated from *Sylibum Marianum* seeds. Hydroxypropyl- β -cyclodextrin (HPBCD), randomly methylated β -cyclodextrin (RAMEB) and 2,6-di-O-methyl β -cyclodextrin (DIMEB) were the product of Cyclolab Ltd. (Hungary), Labrasol[®] was a kind gift of Gattefosse (France), while all other reagents purchased from Sigma.

Methods

Sylibum Marianum seed oil was incorporated into SMEDDS, using Labrasol. Cyclodextrin-sylimarin complexes were produced by kneading method (3). The weight ratio of cyclodextrins and sylimarin was 10:1 in the

mixtures. The UV-spectra of the solutions were recorded by Shimadzu UV-1601 spectrophotometer.

RESULTS AND DISCUSSION

To increase the bioavailability of *Sylibum Marianum* seed oil we produced different SMEDDS compositions. The emulsifying agent (Labrasol) content and the oil content of SMEDDS varied between 60-80% and 10-30% respectively. Each system remained stable in 10, 100 and 1000 times dilutions in water. The diameter of the dispersed oil phase was in micrometer range as confirmed by microscopic investigation.

Excess amount of cyclodextrin-sylimarin mixtures were dissolved in water until equilibrium is reached between the unsolved and dissolved phases and the UV-spectra of the filtered solutions were recorded. All of the cyclodextrins (HPBCD, RAMEB and DIMEB) were able to solubilise sylimarin, but DIMEB had the greatest ability for the complexation (Fig. 1.)

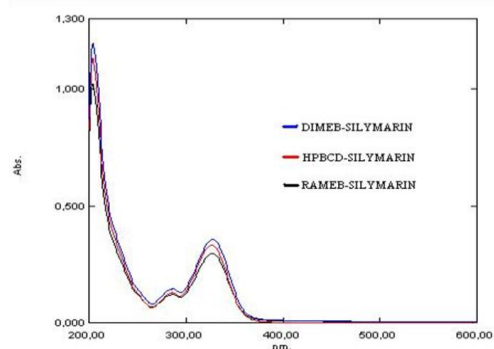


Fig. 1: UV-spectra of different cyclodextrin-silymarin complexes.

CONCLUSIONS

Stable *Silybum Marianum* seed oil SMEDDS; HPBCD, RAMEB and DIMEB water soluble silymarin complexes were produced. The products are suitable for further safety and effectiveness examinations.

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