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Critical Evaluation of Modified-Release Formulation Containing Silybum Marianum Herb Extract for Oral Application

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1. Introduction

The herbal drug silymarin is used in medicine for curing or preventing liver and gall diseases for thousands of years. Silymarin has a low solubility and permeability, which is the main limitation of its clinical use. Current pharmacotherapy means conventional dosage forms such as capsules, which results in low bioavailability. [1] In this research our aim was to formulate sustained release tablets to enhance the bioavailability of silymarin, offering a better alternative than the conventional therapy by this. We used four different Carbopols as matrix-forming polymers: Carbopol 71G, 971 PNF, 974 PNF, and Noveon. The complexation of silymarin with four different β-cyclodextrins was intended to increase the solubility of the active ingredient.

2. Methods

We carried out MTT assay to examine the cytotoxicity of Carbopols to intestinal cells. [2] Tablet ingredients were homogenized in mortar, and the tablets were compressed by a manual bench-top press. Silymarin-cyclodextrin complexes were made by physical mixture method. [3] Composition of the tablets can be seen in Table I. We carried out weight uniformity, tablet friability, and hardness test, according to Ph. Hg. VIII. For the dissolution tests, we used artificial gastric juice in the first 60 minutes and artificial intestinal juice for 360 minutes more as medium. Samples were taken from the medium during the tests, and the dissolution curves were displayed using the absorbances of the samples.

Table 1 *Composition of the tablets*

	Quantity (mg)
Silymarin	70
Cyclodextrin	189
Carbopol	150
Mg-stearate	15
Talc	5
Ca-phosphate dibasic	10
Ludipress	Ad 500 mg (61 mg)

3. Results

The MTT essays proved the biocompatibility of the carriers (***Figure 1***). According to the pharmaceutical tests, our tablets were proper. The dissolution curves allowed us to evaluate the different compositions.

In case of every composition, the release of silymarin was elongated and sustained.

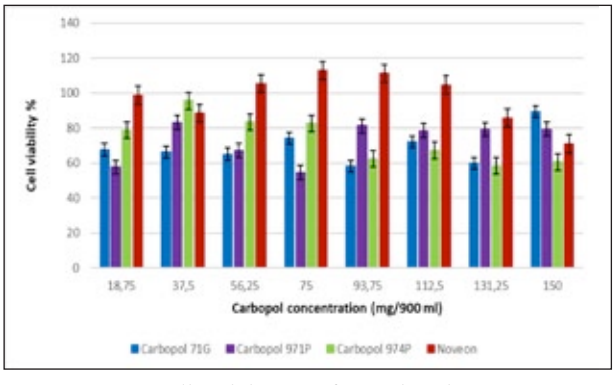

Figure 1 *MTT cell viability test for Carbopols*

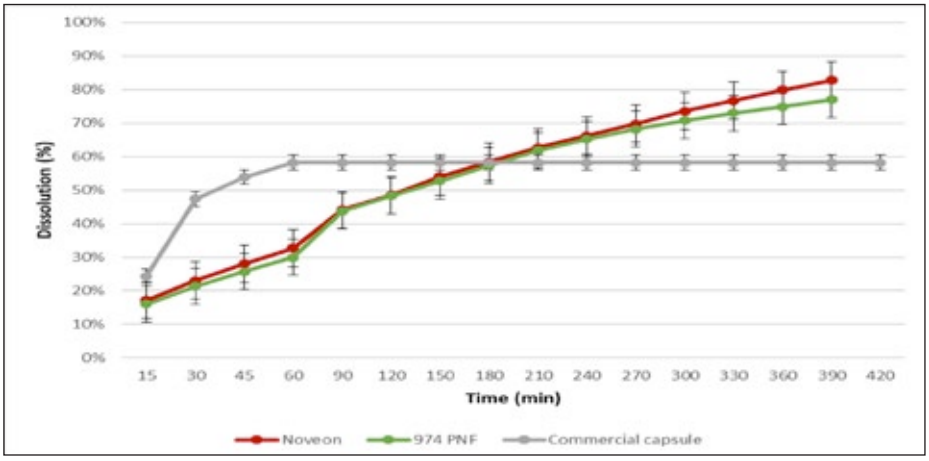

Figure 2 *Dissolution of a commercial silymarin capsule and the Noveon and Carbopol 974 PNF based matrix tablets containig silymarin complexed with Methylated ß – cyclodextrin in altered medium*

4. Conclusions

With the Carbopol-based matrix technology, we achieved sustained release of the active ingredient. The solubility of the silymarin was increased by the cyclodextrin complexation. After the comparison of our results, we could select the Carbopol-cyclodextrin combination with the optimal drug release. The Methylated β – cyclodextrin enhanced the drug release the most, while Noveon and Carbopol 974 PNF proven to be the most proper polymers for sustained release. The technology provided enhanced bioavailability compared to the conventional silymarin therapy.

5. Acknowledgements

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