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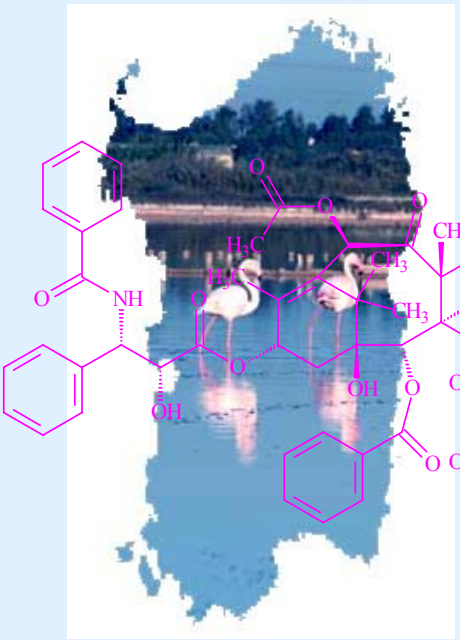

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IN VITRO AND IN VIVO STUDIESOF ARTICHOKE EXTRACT (*CYNARA SCOLYMUS* L.)AS KETOPROFEN SKIN PENETRATION ENHANCER

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The most difficult aspect of transdermal delivery system is to overcome the barrier of stratum corneum. Various skin permeation enhancers have been screened for their effects on ketoprofen skin permeability [1]. Terpenes, monoterpenes as well as larger terpene molecules, sesquiterpenes, have also been evaluated as enhancers for molecules permeating human skin membranes [2]. The artichoke leaves present a high content of sesquiterpene lactones among which cynaropicrin is the principal (3).
In this study, the enhancing effect of artichoke extract containing cynaropicrin on the *in vitro* and *in vivo* percutaneous absorption of ketoprofen from gels has been investigated.

Artichoke leaves have been extracted by a Soxhlet using methylene chloride; after evaporation, the residue obtained has been dissolved into a solution of water–methanol, washed using ether and then evaporated to obtain finally a dried green extract. The cynaropicrin content was determined as follows: an exact amount of extract has been dissolved in methanol and injected in HPLC to find the amount of cynaropicrin.

Fastum® gel (A) is an Italian commercial product; it has been used as comparison and as the base for the preparation of the other different gels (B-E). It contains 2.5% (w/w) of ketoprofen. Gels B-D have been obtained from A to which 1.0, 2.0 or 3.0 % (w/w) of extract has been added respectively. Gel E has been prepared by incorporation of 0.5% (w/w) of cynaropicrin standard to A.

The *in vitro* permeation studies have been performed by Franz diffusion cells, using phosphate buffer (pH 7.4, 37°C, magnetic stirring) as receptor fluid. At set time points (from 0 to 3.5 h) the amount of ketoprofen permeated has been determined by UV spectrophotometer at 254 nm.
The *stripping test* has been employed to perform the *in vivo* studies. The formulations A, B and E have been chosen on the basis of the previous results. The drug penetrated through the stratum corneum has been determined spectrophotometrically.

The extraction method employed is suitable to obtain an extract rich in cynaropicrin (45% w/w).

The *in vitro* results demonstrate that the cumulative amount of the ketoprofen permeated is dependent on the composition of the formulation and particularly on the cynaropicrin content (Figure 1).

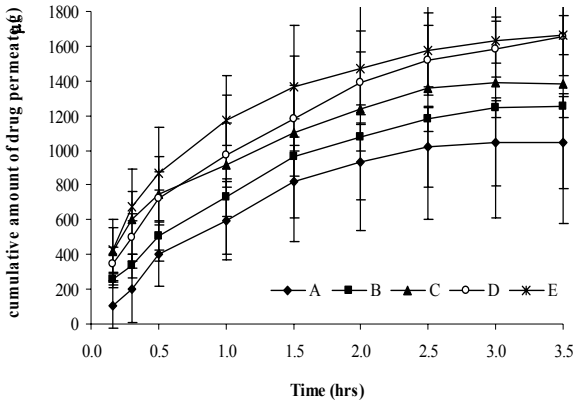

Figure 1. Cumulative amount of ketoprofen permeated *in vitro*

The results from the *in vivo* tests show that B and E gels (containing 0.5% w/w of cynaropicrin as extract and standard respectively) are characterized by significant differences in the amount of drug recovered in the stratum corneum, compared to the formulation A (without cynaropicrin). The drug permeated corresponds to less than 100 mg in case of A and about 125 and 122 mg in case of B and E respectively. This indicates that the amount of the drug able to penetrate the stratum corneum depends on the amount of cynaropicrin in the gel regardless how it has been added to the gel (as extract or as standard). However, the use of the extract results economically more advantageous than cynaropicrin as pure material: in fact due to the difficulties in the extraction and purification process, cynaropicrin is not easy to find as standard in the market and thus it is also very expensive.

In conclusion, the artichoke extract might be proposed as potential penetration enhancer for the percutaneous absorption of ketoprofen.

References

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[2]Williams AC and Barry BW. *Adv Drug Deliv Rev.* 2004; 56:603-618.
[3]Pedretti M. Erboristeria domani. Studio edizione S.a.s. Dic. 1986; 47-58.