[PE1-10] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

EXTERNAL GEL FORMULATIONS OF PROSTAGLANDIN E1 ETHYL ESTER,

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Purpose. External gel formulations of prostaglandin E1 ethyl ester (PGE1-EE), a prodrug of PGE1 as a therapeutic agent for erectile dysfunction, were tried and evaluated by in vitro skin penetration characteristics and in vivo pharmacodynamic effects in cat. Method. The in vitro skin penetration was performed with Franz diffusion cell and examined in aspects of alcohol/polyol ratios and various enhancers. The receptor compartment was filled with alcohol/water (30:70 v/v) solution. Pharmacodynamic effects were evaluated in mature male cats weighing 2.5-4.0 kg and 22-24 guage syringe was inserted into the right side and left side of corpus cavernosum to detect intra-cavernosal pressure (ICP). Results. In the skin penetration study, the flux of PGE1-EE was increased over 15-fold by the addition of alcohol and polyol (3:1 w/w) compared to that of control gel. In addition, employment of selective enhancers to the above gel system further increased the flux of PGE1-EE about 15-fold than enhancer-free gel. The gel system showed significant pharmacodynamic effect of about 120mmHg in ICP, even though there was a lag time of 20-30 min in average. Conclusion. PGE1-EE was formulated successfully to an external gel system with selective enhancers for the delivery of PGE1, manifesting the promising results of higher flux in skin penetration in vitro and enough pharmacodynamic effects in vivo.

[PE1-11] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Formulation and Biopharmaceutical Evaluation of Silymarin Using Self-MicroEmulsifying Drug Delivery Systems

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Carduus marianus extract (formally called silymarin) have been used mainly as a medicament for hepatobiliary diseases. The major component of silymarin is silybin, which constitutes between 50 and 70% of the drug and is the major active component. Many experiments show the efficacy of silybin parenterally administerated. But, its bioavailability is low after oral administration due to its low solubility in water. In order to improve its dissolution rate, silymarin was formulated in the form of self-microemulsifying drug delivery system (SMEDDS) which consists of Miglyol 812-Ethyl linoleate-GMO as a oil phase, HCO-50 containing 50% Tween 20 as surfactant (S) and Transcutol as cosurfactant (CoS), and the composition ratio of the oil phase was 15:60:25. Using the SMEDDS formulation of 10% oil phase in combination with the S/CoS mixing ratio of 1, the microemulsion existence range was found to be wider compared with the other SMEDDS formulation. The dissolution rate for silybin from SMEDDS was significantly higher than from conventional dosage form (capsule), irrespective of the pH of dissolution medium. Following oral administration in rats, SMEDDS provided also significant increase in the bioavailability compared with a conventional dosage form. Therefore, it may be concluded that a significant improvements in dissolution rate and bioavailability of silymarin are achieved with SMEDDS, and this developed SMEDDS formulation can be used as a possible alternative to conventional oral dosage form of silymarin to improve its bioavailability.