Influence of Caffeine on Pharmacokinetics of Micellar Drug Promethazine in rabbits

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Promethazine (PMZ) is an antihistamine drug. It also possesses sedative and neuroleptic properties and is characterized by significant pre-system metabolism. Molecules of PMZ have surface active nature and formation of micelles takes place in solution at CMC \((4.4\times10^{-2} \text{M})\). This affects strongly the interaction of PMZ with other drugs.

Caffeine (Caff) is a strong stimulator of central nervous system. Stimulation of metabolic processes in different organs and tissues, as well as secretory action of stomach proceed under the influence of Caff. It enters the human organism during consumption of beverages like tea, coffee, Coca-cola and so on. Therefore study of influence of Caff on pharmacokinetics of other drugs is important.

Plasma concentration-time curves of promethazine in the rabbit after oral administration of: 100 mg PMZ (×); 200 mg Caff + 100 mg PMZ (●); 100 mg PMZ + 200 mg Caff (▲).

Maximum concentration of PMZ is increased 2-4 fold, the additional third peaks are observed on pharmacokinetic curves, absorption rate of PMZ is sharply (2-3 times) increased, significant prolongation of its elimination and increasing of AUC value of PMZ occur in the presence of Caff (Fig.).

The obtained results indicate the enhancement of PMZ absorption under the influence of Caff, which may be conditioned by surface active nature of PMZ: the hydrophobic ring of phenothiazine in the molecule of PMZ interacts with methyl groups of Caff, which results in the suppression of association of PMZ molecules and hence their absorption in plasma is facilitated.

It should be taken into account, that consumption of Caff-containing beverages at the treatment by PMZ will cause increasing of maximum and current concentration of PMZ and its prolongation in organism. The revealed type of interaction may be typical of other surface active drugs.