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Influence of cimetidine and experimental diabetes mellitus on gabapentin pharmacokinetics in rats

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The organic cation transporter 2 (Oct2), which is expressed in the proximal kidney tubule, promotes elimination of endogenous compounds and drugs. Gabapentin (GAB), an anticonvulsant used to treat neuropathic pain, is eliminated by renal excretion partially dependent on the active secretion via Oct2. Experimental diabetes mellitus (EDM) induced by streptozotocin (STZ) in rats reduces significantly Oct2 activity. The aim of this study was to investigate the influence of EDM, glycemic control and cimetidine (Oct2 inhibitor) on the kinetic disposition of GAB in rats. Male Wistar rats ($n = 6$ per sampling time) were divided into four groups: control, cimetidine (single dose of 100 mg/kg cimetine i.p.), diabetes (40 mg/kg STZ, i.v.) and insulin-treated diabetes (40 mg/kg STZ i.v. and 2 IU insulin 2×/day, 14 days). All animals received oral single dose of 50 mg/kg GAB. There was no difference in apparent total clearance (CL_T/F; mL/h kg) [median (25th–75th percentiles)] between control [(358.1 (266.0–435.4)] × cimetidine [379.5 (223.6–411.5)] groups and between control × diabetes [352.0 (277.7–392.6)] groups, suggesting that Oct2 inhibition by cimetidine and EDM did not influence the kinetic disposition of GAB in rats. However, CL_T/F was increased in insulin-treated diabetes [530.3 (436.9–734.6)] when compared to diabetes group ($p = 0.0241$), which may be explained by glomerular hyperfiltration induced by insulin effects on renal blood flow. In conclusion, our data shows that cimetidine and EDM did not alter GAB pharmacokinetics in rats.

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Better understanding of bioavailability of cosmetic ingredients: Results from Cosmetics Europe Skin Bioavailability project

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Due to the animal testing ban for cosmetics, the Cosmetics Europe Skin Bioavailability and Metabolism Task Force was set up to improve existing methods and develop new tools to measure and predict skin bioavailability of cosmetic ingredients. Eight assays were conducted under standardised conditions (including skin penetration and metabolism, partition/diffusion coefficients in different skin layers and peptide binding) to allow comparison across chemicals and improvement of in silico skin penetration models. In a second step these assays were used to determine the fate of 50 chemicals after application to the skin. Results provide relevant and standardized information on the local skin and systemic concentrations of chemicals and can be used in combination with PBPK models, cheminformatics and AOPs to refine the assessment of local and systemic toxicity of chemicals applied to the skin. Results of up to 50 chemicals will be presented and discussed.

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