Gene Expression of Major Cytochrome P450 Drug Metabolizing Isoforms in Bovine Nasal Olfactory and Respiratory Mucosa

Presystemic elimination by local enzymatic degradation can play a key role in limiting the bioavailability of intranasally administered drug compounds. The aim of the present study was to evaluate the expression of cytochrome P450 (CYP450) enzymes in the bovine nasal mucosa as an in vitro model for human mucosal metabolism. The tissue specific localization of four CYP450 isoforms: 1A2, 2A6, 2C19, and 3A4 in bovine olfactory and respiratory explants was investigated using immunohistochemistry. The amplification of the specific genes obtained with RNA-polymerase chain reaction (RT-PCR) confirmed the expression of CYP450 isoforms in bovine liver tissues and the nasal mucosa. The relative expression levels of the selected isoforms in the nasal mucosa were quantified by real time RT-PCR, and compared with that in those hepatic tissues, for relative comparison of the metabolic barrier properties of the liver and nasal mucosa. The nasal olfactory and respiratory mucosa showed abundant expression of 3A4 while there was a greater difference between the two mucosal tissues in expression levels of 1A2, 2A6 and 2C19. Higher variability was obtained in the olfactory and respiratory expression levels of 1A2 and 2C19 between different cow samples studied than those of 3A4. Our results provide a basis for further explorations of the xenobiotic metabolizing capacity of the bovine nasal mucosa.