Quantitative structure–activity relationships in a series of endogenous and synthetic steroids exhibiting induction of CYP3A activity and hepatomegaly associated with increased DNA synthesis

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„...nucleus is a feature of CYP3-mediated **metabolism** [1,10] and this suggests that a specific...30] calculated via the Pallas System (**CompuDrug** Ltd., Budapest, Hungary). , and the...available experimental evidence from **metabolism** studies. Fig. 1 Fig. 1 Possible orientation..."

Abstract

The results of a quantitative structure–activity relationship (QSAR) study on a total of 14 steroids exhibiting induction of a CYP3A-associated activity and increase in liver weight/DNA synthesis is reported. It is found that different, but related, structural descriptors correlate with increase in ethylmorphine *N*-demethylase activity (r=0.92) and with the increase in liver weight (r=0.78) and DNA synthesis (r=0.78). Although there is a strong correlation between increase in liver weight and DNA content (r=0.999), neither of these correlated with ethylmorphine *N*-demethylase activity. These findings are discussed in the light of CYP3A induction, substrate specificity and inhibition; a proposed model of human CYP3A4 based on sequence homology with CYP102, a bacterial P450 of known crystal structure, demonstrates the possible mode of interaction between substrates and inhibitors within the putative active site.

Author Keywords: QSAR; CYP3A; Ethylmorphine *N*-demethylase

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