Quantitative structure-activity relationship (QSAR) analysis for a series of rodent peroxisome proliferators: Interaction with the mouse liver peroxisome proliferator-activated receptor (mPPAR)

D. F. V. Lewis[*] and B. G. Lake[†]

[*] School of Biological Sciences, University of Surrey, Guildford, Surrey GU2 5XH, UK
[†] BIBRA International, Woodmansteme Road, Carshalton, Surrey SM5 4DS, UK

...namely, molecular weight, logP and pK, (**Compudrug** Ltd, Budapest, Hungary). HazardExpert...fomesafen would have to undergo hydrolytic **metabolism**, and this may also be the case for MEHP...acidic group, or one which is unmasked by **metabolism**, is a common feature of peroxisome proliferators...

Abstract

The results of quantitative structure-activity relationship (QSAR) analysis on a structurally diverse group of peroxisome proliferators are reported. The relative potencies of 11 peroxisome proliferators (with respect to clonbric acid) for induction of palmitoyl-CoA oxidation in rat hepatocyte cultures appear to be determined by a combination of lipophilicity (logP descriptor) and calculated binding affinity (logK) to a model of the mouse liver peroxisome proliferator-activated receptor (mPPAR) ligand-binding domain. It is possible that desolvation of the putative binding site and ligand ionization may also play a role in activation of the mPPAR.

Abbreviations: $\log D_{7.4}$, common logarithm of the distribution coefficient at pH 7.4; $\log K_{bind}$, calculated logarithm of the mPPAR binding affinity; logP, common logarithm of the octan-1-ol/water partition coefficient; MEHP, mono-(2-ethylhexyl)phthalate; mPPAR, mouse peroxisome proliferator-activated receptor ; MRA, multiple regression analysis; pK_a, negative common logarithm of the acid dissociation constant; PPAR, peroxisome proliferator-activated receptor; QSAR, quantitative structure-activity relationship; RXR, retinoid X receptor

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