

## Species differences in the metabolism of di(2-ethylhexyl)phthalate (DEHP) in several organs from mice, rats and marmosets

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In order to clarify species differences in kinetics of di(2-ethylhexyl)phthalate (DEHP), we measured the activities or expressions of five enzymes, lipase, UDP-glucuronyltransferase (UGT), cytochrome P450 4A (CYP4A), alcohol dehydrogenase (ADH), aldehyde dehydrogenase (ALDH) in several organs (liver, lungs, kidneys, and small intestine) from mice, rats, marmosets.

- 1) Lipase activity, measured by a forming rate of mono(2-ethylhexyl)phthalate (MEHP) from DEHP, was ranged from 22- to 148-times: the activity was highest in the small intestine from mice and the lowest in the lung from marmosets.
- 2) UGT activity for MEHP in the liver microsome was the highest in mice, followed by rats and marmosets. The differences, however, were only marginal when compared with those of lipase activity.
- 3) CYP4A was constitutively expressed in the liver from rats, but not in that from mice and marmosets at the same conditions.
- 4) ADH activity showed the highest in the liver from any animal either used 2-ethylhexanol (2-ET) or 2-phenoxyethanol (2-POET) as a substrate. ADH activity also represented species differences; the activity in the liver from marmosets was 1.6-3.9 times as high as those from rats or mice, which was quite different from the results of lipase or UGT activity.
- 5) ALDH activity was the highest in the liver from any animal, similar to ADH activity. In comparison among species, the activity was higher in rats or marmosets (2-14 times) than mice.

Thus, these results clearly show that species differences exist in the metabolism of DEHP, and lipase activity is the most prominent.