TISSUE CONCENTRATIONS OF PORPHYRINS: EFFECTS OF REPEATED DOSAGE OF SELECTED POLYBROMOBENZENES IN RATS

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Introduction

The introduction of various new materials and technologies has become possible due to the usage of flame retardants. These compounds are added to a number of materials (eg. wood, textiles, electronical devices, plastics or hydraulic liquids) in order to reduce their flammability.[1] It is estimated that thanks to these substances, the number of deaths in fires has decreased by approx. 20% over the last 10 years. Such wide use of these substances (annual production is estimated for about 200000 tons) has resulted in noticeable contamination of the environment, and as a consequence, exposure of live organisms to these compounds.[2]

Interest of toxicologists in aromatic brominated compounds dates back to the Michigan accident (USA), where hexabromobiphenyl was (accidentally) by mistake added to cattle feed. In consequence, disturbances in heme synthesis in humans, described as porphyria, were observed.[3]

Available data on the influence of hexabromobenzenes (HBB) on heme synthesis are contradictory. Smith and Francis[4] basing on the changes in porphyrin concentration in the liver found that HBB exerts porphyrogenic effect. The data of other authors however, using similar approach do not confirm these findings.[5] Previous experiments described by Szymanska and Piotrowski[6] showed that repeated administration of HBB to rats resulted in the increase of porphyrins and ALA excretion in urine. HBB may undergo the process of debromination to tri-, tetra-, and pentabromobenzenes in rat tissues, soil or under the influence of light.[7-9]

The aim of the present study was to examine if and to what extent HBB and less brominated benzenes affect the concentration of porphyrins in livers and kidneys of rats.

Methods and Materials

The experiments were performed on female Wistar rats of body weight 180 - 200 g. The rats were divided into groups of 4 - 6 animals each and were given i.g. repeated (daily) doses:

Hexabromobenzene (HBB) - 15; 75; 375 mg/kg;

1,2,4,5 - tetrabromobenzenes (tetra-BB) - 8; 40; 200 mg/kg;

1,2,3 - tribromobenzenes (triBB) - 8; 40; 200 mg/kg;

1,3,5 - tribromobenzenes (triBB) - 12; 60; 300 mg/kg.

Groups of control animals (3 - 4 rats in each group) were run parallel with experimental groups, differing in exposure period. The animals were killed 24 h after the last dose (7^{th}, 14^{th}, 21^{st} and 28^{th} dose).

Porphyrins isolation from tissues was performed according to the method of Luo and Lim[10], and the determination of porphyrins in tissues was carried out by means of high performance liquid chromatography, according to Lim and Peters[11].

The following compounds were used as porphyrins standards – the mixture of octa-, hepta-, hexa-, penta- and tetracarboxyporphyrins (Porphyrin Acid Chromatographic Marker Kit obtained from Porphyrin Products, Logan USA).

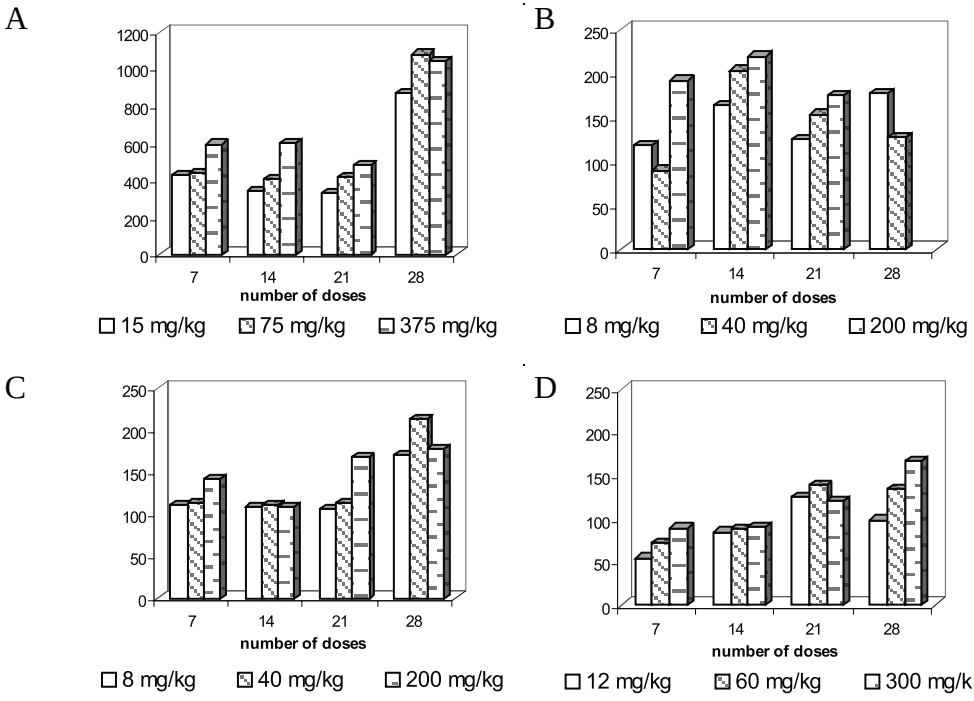

Figure 1. Concentration of octa- and heptacarboxyporphyrins in the liver of female rats after repeated exposure to different doses of HBB (A), tetraBB (B), 1,2,4-triBB (C), 1,3,5-triBB (D) (% of control).

The obtained results were analyzed statistically by means of Tukey test.

Results and Discussion

In the performed experiments concentration of octa- and heptacarboxyporphyrins in the liver and kidneys was estimated.

Repeated administration of HBB caused significant increase in these porphyrins concentration in the rat liver. The obtained values were from 3 to 10 times higher than in control group. This elevation, caused by all doses of the investigated compound, was detected in all performed measurements (Fig. 1A).

Exposure to tetraBB also resulted in the increase of high carboxylated porphyrins in the liver; but much less pronounced. The concentrations of the examined porphyrins reached 100 - 200 % of the control values. During the 2nd and 3rd week of the exposure, these concentrations depended on the dose of the administered tetraBB (Fig. 1B).

Tribromobenzenes, however, only slightly affected the concentrations of the investigated porphyrins in the liver, which is illustrated in Fig. 1C and 1D. The highest dose (200 mg/kg) of 1,2,4-triBB proved to be the most effective. We observed approx. 1.5 fold increase in the examined parameter. The second isomer 1,3,5-triBB, however, administered 7 and 14 times caused a decrease in

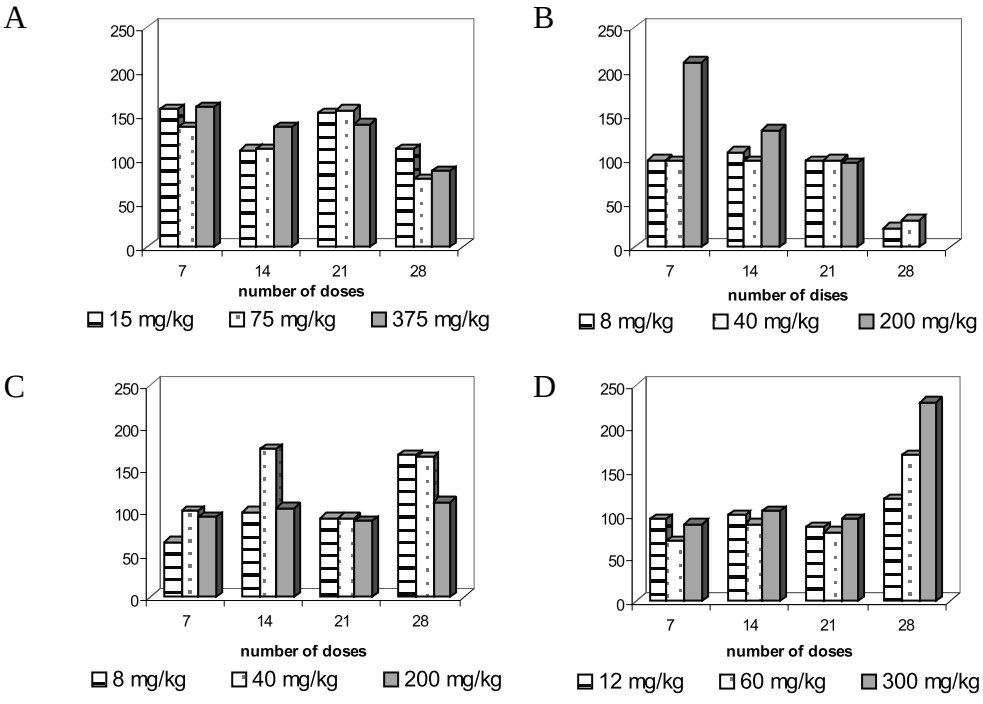

Figure 2. Concentration of octa- and heptacarboxyporphyrins in the kidney of female rats after repeated exposure to different doses of HBB (A), tetraBB (B), 1,2,4-triBB (C), 1,3,5-triBB (D) (% of control).

concentration of okta- and heptacarboxyporphyrins by about 10 - 40 % in comparison with control animals. Prolonging the time of exposure to this compound resulted in the increase of porphyrins concentration, reaching 120 - 160 % of the control values.

The observed changes in okta- and heptacarboxyporphyrins concentrations in the kidneys following the administration of the examined compounds are presented in Fig. 2. The most significant increase in these porphyrins concentration was observed in 1st and 3rd week of HBB administration. The obtained values during this time were 40 - 60 % higher than the values obtained in control group (Fig. 2A). Repeated administration of brominated benzenes practically did not affect the levels of the investigated porphyrins in the rat kidneys.

Repeated administration of HBB and less brominated benzenes proved that porphyrogenic effect of HBB considerably surpasses the effect of the remaining examined compound. HBB turned out to be the most effective compound. It caused significant accumulation of porphyrins in tissues. TetraBB exemplified much weaker porphyrogenic effect, while the activity of two triBB was the weakest.

Acknowledgements

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References

1. IPCS (1997) Environmental Health Criteria 192, Flame Retardants: A General Introduction. WHO, Genewa ISBN 92 4 157192 6.
2. Bromine Science and Environmental Forum (2000): An introduction to Brominated Fire Retardants, Brussels, Belgium.
3. IPCS (1994) Environmental Health Criteria 152, Polybrominated Biphenyls. WHO, Genewa ISBN 92 4 157152 7.
4. Smith A.G., Fransis J.E. (1980) Res Comm Chem Pathol Pharmacol 28, 377.
5. Carlson G.P. (1979) Experientia 35, 513.
6. Szymañska J.A., Piotrowski J.K. (2000) Chemosphere 43, 1689.
7. Yamaguchi Y., Kawano M., Tatsukawa R. (1988) Chemosphere 17, 703.
8. Koss G., Döring H., Würminghausen B., Koransky A. (1982) Toxicol Lett 14, 69.
9. Szymañska J.A., Piotrowski J.K. (2000) Chemosphere 41, 1689.
10. Luo J., Lim C.K. (1995) Biomedical Chromatography 9, 113.
11. Lim C.K., Peters T. (1984) Clin Chim Acta 139. 55.