ACUTE TOXICITY OF BINARY MIXTURE BENZENE-ETHANOL AND PARTITION COEFFICIENT K_{OW} OF BENZENE AND ETHANOL

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SUMMARY

The study related to partition coefficients between n-octanol and water of compounds in binary mixture benzene-ethanol was carried out. Partition coefficients of benzene and ethanol for different values of molar ratio of benzene in the mixture were determined. Collected results show statistically significant deviations the K_{ow} of benzene for some molar ratios (0.2 to 0.6) from values for pure compound. For ethanol, there are no statistically significant deviations from values for pure compound, however there are some trends of changes of K_{ow}.

Key words: octanol/water, partition coefficient, binary mixture, mixture toxicity

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INTRODUCTION

The n-octanol/water partition coefficient (K_{ow}, also called P) is defined as the ratio of a concentration given compound in the octanol phase to its concentration in water phase of two-phase n-octanol/water system [Eq. 1].

$$K_{OW} = \frac{c\ (\text{octanol})}{c\ (\text{water})} \qquad [1]$$

It is known that K_{ow} is a function of a solute concentration for value higher then 0.01 mol/l. For its measurement very low concentrations of given compound (less then 10^{-2} mol/l) are used, when K_{ow} is very little depending on a concentration of measured compound.

Values of K_{ow} are usually measured at room temperature (20 °C or 25 °C). Effect of temperature is not high, usually in range 0.001 to 0.01 log K_{ow} units per degree, and may be positive or negative (1).

Partition coefficient n-octanol/water is not the same as the ratio of solubility of a compound in the n-octanol to solubility in the water because the organic and the water phase of the binary system octanol/water are not pure octanol and pure water. In the equilibrium organic phase contains 2.3 mol/l of the water and aqueous phase contains 0.0045 mol/l of the octanol (2).

Interest in the K_{ow} parameter was firstly mentioned in the study of quantitative structure-activity relationship (QSAR) (3), primarily with pesticides (4, 5) and followed with pharmaceuticals (6). Numerous studies showed, that K_{ow} was useful for correlating structural changes of drug chemicals with the change observed in some biological, biochemical, or toxic effect. The observed correlations could then be used to predict the effect of new, for example, drugs for which a value of K_{ow} could be measured or estimated. References (1) and (7) contain interesting discussion of the history of this parameter.

In recent years the n-octanol/water partition coefficient has become a key parameter in studies of the environmental fate of organic chemicals. It has been found to be related to water solubility, solid/sediment adsorption coefficients, and bioconcentration factors for aquatic life. Because of its increasing use in the estimation of these other properties, K_{ow} is required in the list of parameters for the chemical safety data sheet.

Because of an exposition of one chemical to environmental or occupational conditions is rather exception than rule, the study related to value of K_{ow} of a compound in the binary mixture was carried out. It should be prooved if particular compounds of mixture affect each other and determine K_{ow} of both compounds for different mixture ratios. The binary mixture benzene-ethanol was chosen because of availibility of biological data on its toxic effect (8). In case of a change of K_{ow} for ethanol or benzene in their binary mixture changes of corresponding biological effect should be compared and in the end it could help with the interpretation of biological effect of compound in mixtures (9).

CHEMICALS AND MEASUREMENT

Following chemicals were used for determination of K_{ow}: benzene (Aldrich, 99.9+%), ethanol according ČsL, n-octanol (Aldrich, 99 %), water (GORO AQUA 200, deionized, filtrated through 0,22 µm membrane).

References (1, 10, 11) describe various measurements techniques. Measured compound is added to a mixture of n-octanol and water whose volume ratio is adjusted according to the expected value of K_{ow}. Very pure n-octanol and water must be used, and concentration of the solute in the system should be less then 0.01 mol/l. The overall concentration of both compounds for determination of K_{ow} in binary mixture benzene-ethanol was 0.005 mol/l. There was prepared a line of solutions of benzene molar ratio 1.0, 0.9, 0.8, 0.6, 0.4, 0.2, 0.1, 0.05, and 0.0. The system was shaken gently until equilibrium was achieved (5 to 10 h). Centrifugation is required to separate the two phases, especially if an emulsion haw formed. Gas chromatography was used for determination of the ethanol, liquid chromatography with UV detection for determination of the benzene. Each compound was determined in both phases, i.e. in the n-octanol and in the aqueous phase.

RESULTS AND DISCUSSION

The Fig. 1 and Fig. 2 show values of K_{ow} for the benzene and the ethanol for different value of molar ratio of the benzene in the binary mixture benzene-ethanol. Values of K_{ow} for benzene and ethanol are expressed together with their confidence interval ($\alpha = 0.05$) and statistical analysis using t-test was carried out. Values of K_{ow} signed in plots ** are statistically significantly different ($\alpha = 0.05$) from values of K_{ow} for pure compound (not in mixture). The different values for benzene are mainly in the range 0.2 to 0.6 of the molar ratio of benzene. Ethanol shows positive deviations for range 0.6 to 1.0 and negative deviation for range 0.0 to 0.5 of the molar ratio of benzene.

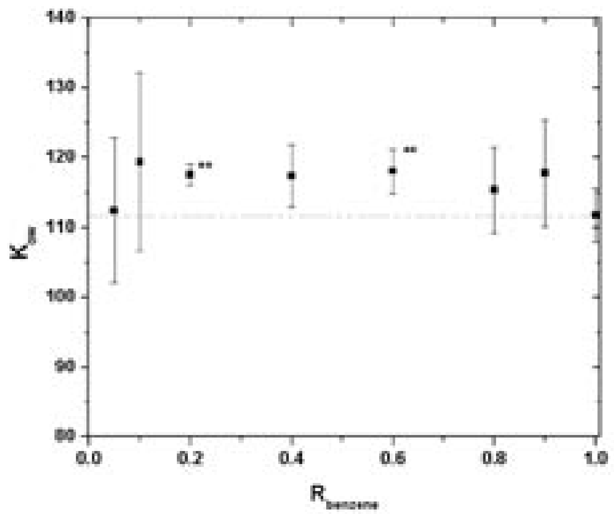

*Fig. 1. Partition coefficient K_{ow} for benzene in binary mixture benzene-ethanol. The dashed line shows value of K_{ow} for pure benzene. Values of K_{ow} signed in Fig. ** are statistically significantly different ($\alpha = 0.05$) from values of K_{ow} for pure compound (not in mixture).*

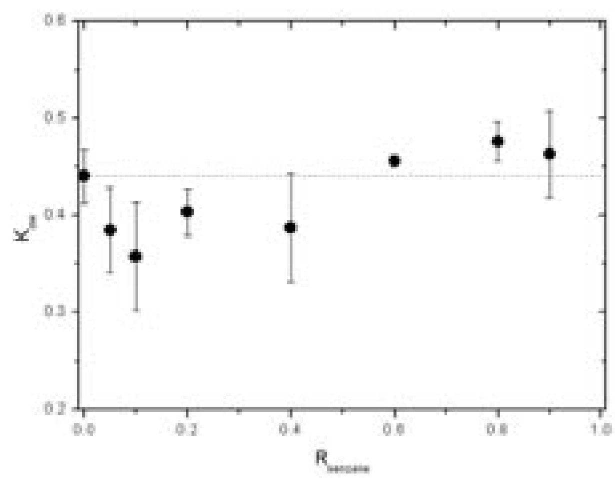

Fig. 2. Partition coefficient K_{ow} for ethanol in binary mixture benzene-ethanol. The dashed line shows value of K_{ow} for pure ethanol (not in mixture).

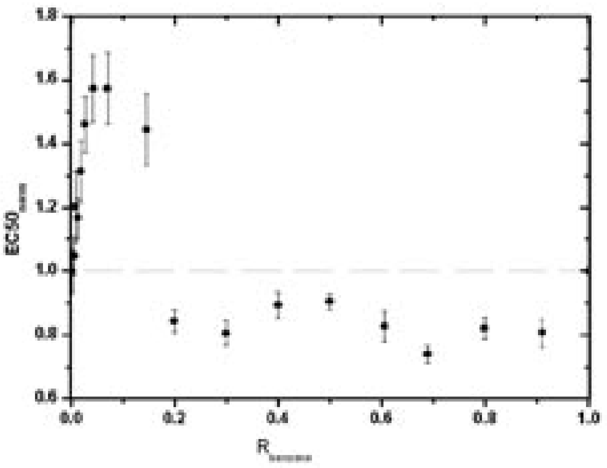

Fig. 3. Acute toxicity EC_{50} (normalized value) of binary mixture benzene-ethanol, determined as the inhibition of movement of Oligochaeta Tubifex tubifex. The dashed line shows EC_{50} in case of additivity (normalized value 1). The normalization was used for purpose of better explanation of toxic effect of mixture and for mathematical modeling. Values of normalized EC_{50} above dashed line indicate inhibition of the toxic effect and values below dashed line indicate potentiation of the toxic effect.

Fig. 3 shows normalized acute toxicity indexes (normalized EC_{50}, *Tubifex tubifex*) for binary mixture benzene-ethanol (8, 12).

The inhibition of the movement of worms *Tubifex* was measured as the effective concentration that causes 50% maximal response (13).

CONCLUSION

The study related to influence of binary mixture benzene-ethanol to partition coefficient of particular compound of the mixture was carried out. Partition coefficients of benzene and ethanol for different values of molar ratio of benzene were determined. Collected results show statistically significant deviations of the K_{ow} of benzene for some ratios (0.2 to 0.6) from values for pure compound. For ethanol, there are no statistically significant deviations from values for pure compound. But also there are some trends of changes of K_{ow}. These changes should be used for explanation of toxic effect of benzene-ethanol mixture and could be useful for estimation of acute toxicity above-mentioned mixture using QSAR analysis.

Acknowledgements

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