Comment on "Serum albumin binding of structurally diverse neutral organic compounds: Data and models"

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In their article, Endo and Goss [1] indicate they measured the "bovine serum albumin (BSA) water partition coefficients ($K_{BSA/w}$) ... for 83 structurally diverse neutral organic chemicals in consistent experimental conditions" and correlate the resulting $K_{BSA/w}$ values against corresponding octanol-water partition coefficients (K_{ow}) and polyparameter linear free energy relationship models based on descriptors for the neutral forms of each compound. The authors further state that "[a]ll chemicals used were >99% neutral at pH 7.4." However, in their Supporting Information "Table S2. $K_{BSA/w}$ (L/kg) data measured in this study," the authors list the following compounds that - in contrast to their claims - would be <99% neutral (i.e., >1% ionized) at pH 7.4 (experimental pK_a values provided along with percent ionization at pH 7.4 in parentheses): N,N-diethylaniline, 6.16 [2] (5.4%); 3-chlorophenol, 9.12 [3] (1.9%); 4-bromophenol, 9.37 [3] (1.1%); and 4-iodophenol, 9.33 [3] (1.2%). For these compounds, significant ionization would occur at pH 7.4 which must be accounted for in any serum albumin binding modeling efforts.

References

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