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Experiment and QSAR analysis for binding affinity of azole compounds with CYP2B and 3A

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Azole compounds were widely used as pesticides, fungicides and antifungal agents. These compounds have been known to bind with cytrochrome P450 (CYP) enzymes via coordination of the nucleophilic nitrogen of their heterocyclic ring to the heme iron in CYP. In this study, 18 azole compounds were measured for their binding to liver microsomal CYP2B and CYP3A with type Ⅱ spectral change. The measured binding affinities were discussed with their molecular properties. Typical type II difference spectra with a peak at 426-430 nm and a trough at 392-402 nm caused by the interaction between the CYP heme and each compound, were observed. With bilinear model of log *P*, a nice correlation was found between the binding constant and log *P*. From these results it is concluded that the molecular hydrophobicity of the azole compounds plays the major role in binding with CYP2B and CYP3A. The results here were also discussed in comparison with the 3D structure of several P450 proteins.