Calculating the Aqueous pK_a of Phenols: Predictions for Antioxidants and Cannabinoids

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Accurate acid dissociation constants (K_a, $pK_a = -\log K_a$) are essential physico-chemical quantities that impact chemical, environmental and biochemical research. Phenolic compounds can play important roles as antioxidants; however, limited experimental aqueous pK_a exist, especially for complex phenols. Twenty phenols with pK_a values from 4.06 to 11.92 were used to explore the predictive capabilities of several methodologies. The correlations between calculated $G°(A^-)$-$G°(HA)$ values (where HA and A^- are the acid and its corresponding conjugate base, respectively) and experimental pK_a values led to the best results with mean absolute errors between 0.22 and 0.40 pK_a units. Correlations were tested with 9 phenols of varying complexities and pK_a predictions were made for 12 phenolic antioxidants and 9 cannabinoids whose pK_a values are needed for further biochemical studies.