Role of Weak Molecular Interactions in the Mechanism of Action of a Series of Antihelmintics

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Abstract: Different physicochemical properties such as solute-solute and solute-solvent interactions, tautomerism, lipophilicity and solubility in water were determined for a serie of 6,7-diaryl-pteridines in order to relate those properties with their nematocide action.

Introduction

The pharmacological response of a drug can be the result of a complex formation between the drug and the receptor. This complex is generally the result of several types of interactions such as hydrophobic and electrostatic forces, hydrogen bonding and electron donor-acceptor complexes [1].

Previous works [2,3] have shown the nematocide activity for a serie of substituted 6,7-diaryl-pteridines (I) against different experimental models. Different structure-activity relationships (SARs) have been established for these compounds through neural networks [3].
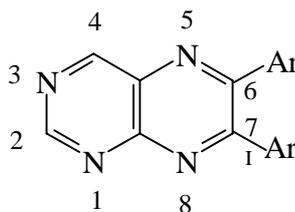
Experimental

Synthesis and nematocide accion for the studied compounds were previously described [2,3].

Results and Discussion

For 18 substituted 6,7-diaryl-pteridines the following physicochemical properties were determined: polar and hydrogen bonding interactions with the solvent, solute-solute interactions, tautomerism,

solubility in water and lipophilicity.

It was observed that only lipophilic interactions are related with the measured nematocide action (%R) for these drugs.

The logarithm of the chromatographic retention factor extrapolated to pure water, log k'$_w$, was used as a lipophilicity index. A typical ODS column and methanol-water as mobile phase were used. A linear regression between log k' and the Reichardt solvent parameter, $E_T(30)$, for binary methanol-water mixtures was used to obtain log k'$_w$ by extrapolation. This procedure is generally more appropriate than extrapolate from a log k' vs. % organic modifier plot since curvature is often observed [4].

The correlation matrix between % R (percentage of decrease in nematode concentration when 100 μg/ml of the drug in DMSO are used in *in vitro* assays) and log k'$_w$ is shown below.

	%R	log k'$_w$
% R	1.0000	0.6769
log k'$_w$	0.6769	1.0000

This results indicate that 67.69% of the variance in the biological activity produced by changes in drug concentration can be explained by lipophilic interactions.

References and Notes

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