**MODELING ACUTE AQUATIC TOXICITY OF PHARMACEUTICAL COMPOUNDS USING IMMOBILIZED PLASMA PROTEIN CHROMATOGRAPHY**

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**ABSTRACT**

Pharmaceuticals have been recognized as contaminants of emerging concern. Unfortunately, little is known about their ecotoxicological effects on ecosystems and contamination needs to be further evaluated [1]. The evaluation of ecotoxicity is a necessity according to the REACH regulation “no data no market” [2]. In this work, the potential of immobilized plasma protein chromatography to predict ecotoxicological endpoints of pharmaceutical compounds was investigated. For this purpose, a data set of chromatographic retention data for 36 structurally diverse drugs was used. Standardized retention times were measured immobilized human serum albumin (HSA) and immobilized alpha-1-acid glycoprotein (AGP) stationary phases [3]. As ecotoxicological endpoints, half-maximal lethal concentration (LC50) values of fish and half-maximal effective concentration (EC50) (immobilization) values of water flea (daphnia magna spp.) determined with a two-day static method were considered. Ecotoxicity showed a dependence on lipophilicity and the positive charge of compounds. Therefore, AGP binding resulted in satisfactory models, owing to its function as a binder of neutral and basic lipophilic compounds. HSA binding however did not result in sound models, as it is influenced by the negative charge of compounds, contrary to the mechanism of toxicity. AGP models were superior statistically from those derived with octanol-water systems. From the two biomimetic properties investigated, AGP binding can be suggested as a promising indice to assess the ecotoxicological risk of drugs.

**KEYWORDS:** Pharmaceuticals; acute aquatic toxicity; biomimetic chromatography; human serum albumin binding (HSA); alpha-1-acid glycoprotein (AGP) binding.

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**REFERENCES**

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