Methyl deoxycholate monosulfate, a new antifouling compound with low bioaccumulative potential

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Fouling on ships represents serious economic and environmental problems due to accelerated fuel consumption, increased costs and time for cleaning and maintenance, emission of harmful gases, and transport of non-native species, causing a major human health and environmental impacts. The search for new antifouling products has become a fast-growing research field since the ban of the main antifouling paints in use, due to toxicological issues. Among the search for solutions for these issues, nearly fourteen sulfated steroids (thirteen of which were monosulfated), isolated from different marine species, were found to display antifouling activity [1]. Sulfation is used by Nature to avoid toxicity; therefore, the synthesis of sulfated derivatives could be an opportunity to develop new non-toxic antifouling compounds.

In this work, the synthesis of methyl deoxycholate 3-sulfate was achieved in two steps: Fischer esterification of the commercial deoxycholic acid under acidic conditions (HCl conc.), in methanol in excess at reflux (40% yield), followed by sulfation using triethylamine-sulfur trioxide adduct (3 equiv/OH) in dimethylacetamide at 100ºC (3% yield). Structure elucidation of this new compound was established by infrared (IR) and nuclear magnetic resonance (NMR). The sulfated derivative as well as the non-sulfated parent compound, methyl deoxycholate, were tested against the adhesive larvae of *Mytillus galloprovinciallis*. Following, KOWWIN™ v1.68 program developed by Syracuse Research Cooperation jointly with the Environmental Protection Agency (EPA) was used for *in silico* calculation of log Kow (octanol-water partition coefficient) in order to evaluate the bioaccumulation potential of both compounds and their predicted biomagnification through the food chain.

Both compounds were able to inhibit the settlement of mussels larvae with EC_{50} values around 8 μM but while sulfated derivative revealed a log Kow value of 1.49, the non-sulfated parent compound exhibited a log Kow value of 5.34. These results show the potential of sulfation to obtain new antifouling derivatives with low bioaccumulative potential (log Kow <3).

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