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In silico ecotoxicological evaluation of hydroxylated progesterone biotransformation products generated by the marine-derived fungus *Penicillium oxalicum* CBMAI 1996

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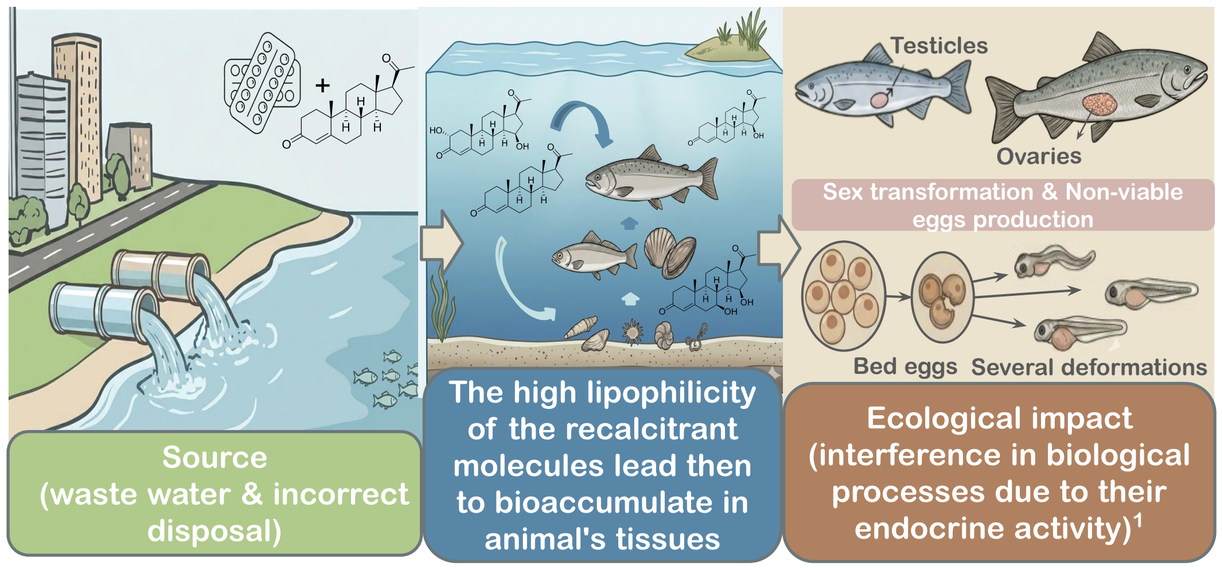
INTRODUCTION & AIM

Understanding the environmental behavior of recalcitrant molecules, particularly steroidal compounds, is crucial to assess their long-term ecological impact. The marine environment represents a major sink for substances widely consumed by modern societies, including pharmaceuticals and hormones, tending to bioaccumulate in aquatic organisms and interfere with biological processes due to their intrinsic endocrine activity. Progesterone is a widely used hormone and was therefore selected as the target compound in this study.



METHOD

Recent studies demonstrated that the marine-derived fungus *Penicillium oxalicum* CBMAI 1996, isolated from the sponge *Chelonaplysilla erecta*, promoted progesterone bio-oxidation, yielding three novel hydroxylated products— **15β-hydroxyprogesterone (1), 7β,15β-dihydroxyprogesterone (2),** and **2β,15β-dihydroxyprogesterone (3)** —whose structural elucidation has been previously reported in the literature[2].

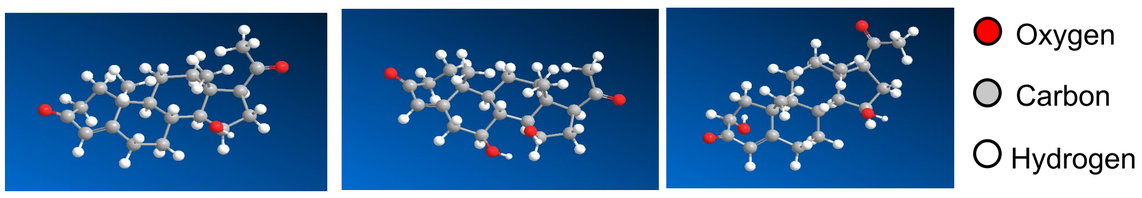
In the present work, the computational platforms ECOSAR 2.0 and SwissADME were employed to estimate lipophilicity (log K_{ow}) and predict acute and chronic ecotoxicological effects.

These validated in silico approaches enable rapid environmental hazard screening and support the interpretation of how enzymatic oxidation may influence the environmental persistence of steroidal contaminants.

Figure 1. Picture of *Chelonaplysilla erecta*[3].

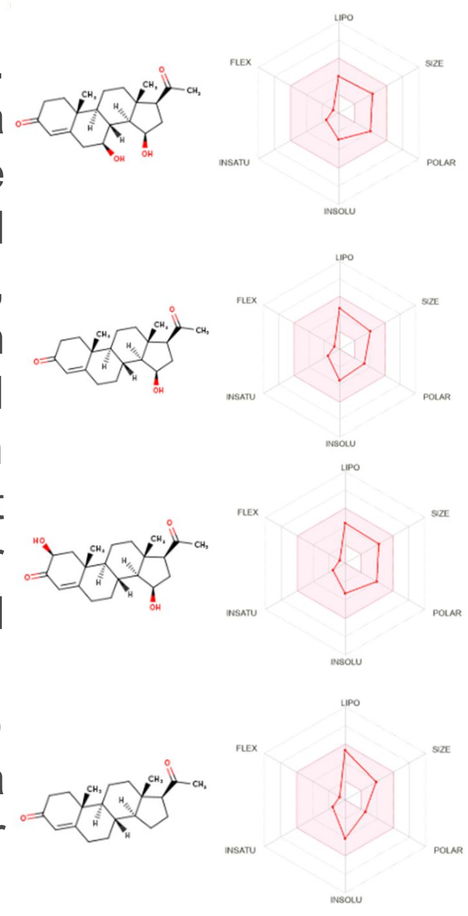
Figure 2. Plate culture of *Penicillium oxalicum* CBMAI 1996[4].

Ball-and-stick model of hydroxylated progesterone compounds



RESULTS & DISCUSSION

Regarding potential bioaccumulation and biomagnification processes, molecular simulations revealed a notable decrease in lipophilicity for the biotransformation derivatives, yielding log K_{ow} values of 3.20, 2.25, and 2.44 for compounds 1–3, respectively, compared to 4.02 for progesterone. These findings correlate with a significant reduction in both acute and chronic ecotoxicity toward representative aquatic organisms, including fish, daphnids, and green algae. The lethal dose of compound 2 reached 1050 mg/L for green algae, while its chronic effect threshold reached 1030 mg/L for fish — representing an 80-fold and 29-fold decrease in toxicity, respectively, relative to progesterone, indicating a progressive attenuation of their environmental risk.



CONCLUSION

Overall, these results demonstrate that microbial hydroxylation substantially alters the toxicological profiles of progesterone derivatives. Concurrently, ecotoxicological modeling highlights microbial oxidation as a key natural process and promising biotechnological pathway for the biodegradation and environmental attenuation of these persistent, recalcitrant steroids in marine ecosystems.

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