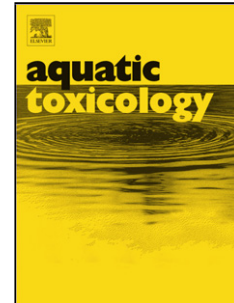


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STATINS: AN UNDESIRABLE CLASS OF AQUATIC CONTAMINANTS?

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Highlights

- Hypocholesterolaemic drugs are among the most prescribed human pharmaceuticals.
- Statins disrupts the cholesterol synthesis by inhibiting the enzyme HMGR
- We address the following question: is HMGR inhibited by statins across metazoans?
- We used comparative genomics, homology modelling and molecular docking
- The results indicates that statins are expected to inhibit metazoan's HMGRs

Abstract

Emerging pollutants, such as pharmaceuticals, may pose a considerable environment risk.

Hypocholesterolaemic drugs such as statins are among the most prescribed human pharmaceuticals in western European countries. In vertebrates, this therapeutic class disrupts the cholesterol synthesis by inhibiting the enzyme 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMGR), responsible for the limiting step in the mevalonate pathway. Recently, functional studies have shown that statins competitively inhibit HMGR in vertebrates and arthropods, two *taxa* that have diverged over 450 million years ago.

Importantly, chronic simvastatin exposure disrupts crustacean reproduction and development at environmentally relevant concentrations. Hence, a fundamental question emerges: what is the taxonomic scope of statins-induced HMGR inhibition across metazoans? Here, we address this central question in a large sampling of metazoans using comparative genomics, homology modelling and molecular docking. Sequence alignment of metazoan HMGRs allowed the annotation of highly conserved catalytic, co-factor

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