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Revisión / Review

Ecotoxicity assays in the evaluation of molluskicidal agents from natural products in freshwater mollusks of medical importance: Lack of information and the choice of tested organisms

[Ensayos de ecotoxicidad en la evaluación de agentes molusquicidas derivados de productos naturales en moluscos de agua dulce de importancia médica: falta de información y elección de organismos evaluados]

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Abstract: Several natural products have been tested on mollusks of medical importance aiming to control these animals. Diverse scientific groups have demonstrated interest in finding new molluskicides from natural origin. In the literature, many promising studies have examined the molluskicidal activity of natural products on freshwater mollusks with medical importance. We used the keywords "natural products" and "molluskicidal activity" in diverse scientific databanks. A total of 301 articles were found, 25 of which were used in this letter. Most of these articles did not present ecotoxicity test reports. Some studies have reported ecotoxicity assays using nontarget organisms that do not represent freshwater ecosystems. Few articles showed ecotoxicity test reports using appropriate nontarget organisms, and only 1 presented test with more than 1 representative organism. The present work demonstrates the need to realize ecotoxicity tests using representative organisms in studies with natural products on freshwater mollusks of medical importance.

Keywords: Environmental toxicity; Ecotoxicology; Ecotoxicity models; Plants; Molluscicide

Resumen: Varios productos naturales han sido evaluados en moluscos de importancia médica con el objetivo de controlar estos animales. Diversos grupos científicos han mostrado interés en encontrar nuevos molusquicidas de origen natural. En la literatura, muchos estudios prometedores han examinado la actividad molusquicida de productos naturales en moluscos de agua dulce con importancia médica. Se utilizaron las palabras clave "productos naturales" y "actividad molusquicida" en diversas bases de datos científicas. Se encontraron un total de 301 artículos, de los cuales 25 fueron utilizados en esta comunicación. La mayoría de estos artículos no presentaron informes de pruebas de ecotoxicidad. Algunos estudios reportaron ensayos de ecotoxicidad utilizando organismos no objetivo que no representan los ecosistemas de agua dulce. Pocos artículos mostraron informes de pruebas de ecotoxicidad utilizando organismos no objetivo apropiados, y solo uno presentó pruebas con más de un organismo representativo. El presente trabajo demuestra la necesidad de realizar pruebas de ecotoxicidad usando organismos representativos en estudios con productos naturales sobre moluscos de agua dulce de importancia médica.

Palabras clave: Toxicidad ambiental; Ecotoxicología; Modelos de ecotoxicidad; Plantas; Molusquicida

INTRODUCTION

Several natural products have been tested on mollusks of medical importance with the aim of controlling the populations of these animals. A large number of human and animal parasites have freshwater snails as intermediate hosts (Chontananarth *et al*., 2017; Lee *et al*., 2017). In this context, many methods have been used to control snail populations (Abd El-Ghany & Abd El Ghany 2017), with the use of chemical molluskicidal products being one of these methods (Abdel-Ghafar *et al*., 2016). However, these products have some problems reported in the literature, such as environmental toxicity and the need for repeated applications, among others (Rey 1987; Coura-Filho *et al*., 1992; Giovanelli *et al*., 2002; Dai *et al*., 2010; Oliveira-Filho *et al*., 2010; Lopes *et al*., 2011; Famakinde, 2018), which has raised interest in natural molluskicides (Elsareh *et al*., 2016). Several promising works in the literature have analyzed natural products with molluskicidal activity in freshwater mollusks of medical importance. The keywords "natural products" and "molluskicidal activity" were used. A total of 301 articles were found. Of these, 25 works were used in this letter.

MAIN TEXT

Shen *et al*. (2018), tested extracts of aerial parts of *Solidago canadensis* L. on the snail *Pomacea canaliculata* Lam, an intermediate host of the worm *Angiostrongylus cantonensis* (Song *et al*., 2016), which causes eosinophilic meningitis (Kliks & Palumbo, 1992). The petroleum ether extract of *S. canadensis* caused molluskicidal effect with an LC_{50} value of 180.0 mg/L in 48 h, showing greater activity compared to the positive control, the molluskicidal Mie Luo Yu Kang (Shen *et al*., 2018). In another study involving the snail *P. caniculata*, Yang *et al*. (2022), tested arecoline (1), a major biologically active compound of areca nut, on these snails (Coppola & Mondola, 2012; Yuan *et al*., 2012). Arecoline obtained LC_{50} values of 1.05, 2.12, and 3.54 mg/L in 72 h for snails with 15 ± 2, 25 ± 2 and 35 ± 2 mm shell diameters, respectively (Yang *et al*., 2022).

Despite the promising results, the work by Shen *et al*. (2018) and Yang *et al*. (2022), did not present ecotoxicity tests to assess the effects of their evaluated products on nontarget species. Other promising studies have investigated the molluskicidal activity of natural products on *P. caniculata*. However, they did not exhibit reports of ecotoxicity tests (Yang *et al*., 2017; Yang *et al*., 2019; Li & Zou, 2019; Chen *et al*., 2020; Zhang & Zou, 2020).

Ke *et al*. (2019), investigated the molluskicidal activity of benzo[c]phenanthridine quaternary alkaloids (QBAs) (2) from fruits of the *Macleaya cordata* species on *Oncomelania hupensis*. This snail is the only intermediate host of *Schistosoma japonica*, a helminth that transmits schistosomiasis (Ross *et al*., 2001; Ke *et al*., 2017). The authors used QBAs at concentrations of 2.5 mg/L and 10.0 mg/L and observed mortality of more than 90% of snails in 48 h, a result similar to that observed for niclosamide (Ke *et al*., 2019).

Ke *et al*. (2019), also did not report ecotoxicity tests after assays using *P. caniculata*, as well as other studies testing the molluskicidal activity of natural products such as *O. hupensis* (Ke *et al*., 2017; Xing *et al*., 2021).

Ibrahim & Ghoname (2018), evaluated the molluskicidal activity of the aqueous extract of leaves of *Anagallis arvensis* on the snail *Biomphalaria alexandrina*. Several species of the genus Biomphalaria act as intermediate hosts for helminths of the genus *Schistosoma*, which cause schistosomiasis (WHO, 2017a). The aqueous extract of *A. arvensis* showed LC_{50} and LC_{90} values of 37.9 and 48.3 mg/L, respectively (Ibrahim & Ghoname, 2018).

This study also did not present ecotoxicity tests or other studies reported in the literature involving *Biomphalaria* spp. snails (Mandefro *et al*., 2018; Mendes *et al*., 2018; de Carvalho Augusto *et al*., 2020; Matos *et al*., 2020; Silva *et al*., 2020).

Natural products are not exempt from risks to the environment. Therefore, the WHO Pesticide Evaluation Scheme (WHOPES), aiming to ensure the use of compounds in aquatic environments in tolerable and nontoxic concentrations, recommends checking the toxicity of these substances (Canesi *et al*., 2015; Schiavo *et al*., 2017; Schiffer & Liber 2017; WHO, 2017b).

Some works observed in the literature proposed testing the molluskicidal activity of natural products on freshwater snails of medical importance using the microcrustacean *Artemia salina* as a test organism (Rocha-Filho *et al*., 2015; Martins *et al*., 2017; Araújo *et al*., 2018; Silva *et al*., 2019; Aguiar *et al*., 2022; Batista *et al*., 2022). Although this organism is indicated as an experimental model because of its high sensitivity in ecotoxicological monitoring of new products (Lima *et al*., 2002; Albuquerque *et al*., 2014; Martins *et al*., 2014), the *A. salina* habitat is a saltwater environment. Therefore, this species does not live in the same habitat as the freshwater snails mentioned in this work.

A recommended organism for ecotoxicological testing is the fish *Danio rerio*. Thus, some scientific groups are using this model for evaluating ambient toxicity (Pereira *et al*., 2017; Jia *et al*., 2019). In another work, a species of water bug, *Diplonychus rusticus* Fabricius, was used to evaluate ecotoxicity (Hung *et al*., 2021).

The information analyzed above was included in Table No. 1 to enable a better analysis of the researched works.

Table No. 1
Mollusk species, ecotoxicity assays used, and animal model

Publications	Mollusk	Ecotoxicity Assays	Model
Shen *et al*., 2018	*P. canaliculata*	X	-
Yang *et al*., 2022	*P. canaliculata*	X	-
Chen *et al*., 2020	*P. canaliculata*	X	-
Zhang & Zou, 2020	*P. canaliculata*	X	-
Yang *et al*., 2017	*P. canaliculata*	X	-
Yang *et al*., 2019	*P. canaliculata*	X	-
Li & Zou, 2019	*P. canaliculata*	X	-
Ke *et al*., 2019	*O. hupensis*	X	-
Ke *et al*., 2017	*O. hupensis*	X	-
Xing *et al*., 2021	*O. hupensis*	X	-
Ibrahim & Ghoname, 2018	*B. alexandrina*	X	-
Mandefro *et al*., 2018	*B. pfeifferi*	X	-
Mendes *et al*., 2018	*B. glabrata*	X	-
de Carvalho Augusto *et al*., 2020	*B. glabrata*	X	-
Matos *et al*., 2020	*B. glabrata*	X	-
Silva *et al*., 2020	*B. glabrata*	X	-
Rocha-Filho *et al*., 2015	*B. glabrata*	✓	*A. salina*
Martins *et al*., 2017	*B. glabrata*	✓	*A. salina*
Araújo *et al*., 2018	*B. glabrata*	✓	*A. salina*
Silva *et al*., 2019	*B. glabrata*	✓	*A. salina*
Aguiar *et al*., 2022	*B. glabrata*	✓	*A. salina*
Batista *et al*., 2022	*B. glabrata*	✓	*A. salina*
Pereira *et al*., 2017	*B. glabrata*	✓	*D. rerio*
Jia *et al*., 2019	*O. hupensis* *B. alexandrina* *Bulinus truncatus*	✓	*D. rerio* *C. japonica* *M. nipponense*
Hung *et al*., 2021	*Pomacea canaliculata* *Gyraulus convexiusculus* *Tarebia granifera*	✓	*D. rusticus*

Jia *et al*. (2019), used more than one species to evaluate ecotoxicity. In addition to the already mentioned *D. rerio*, the authors also tested their product on the bird *Coturnix japonica* and on the freshwater shrimp *Macrobrachium nipponense*. Silva *et al*. (2015), indicated the use of more than one organism for ecotoxicological tests, providing greater reliability for the research. The authors realized tests with creatures of different trophic levels since different organisms may exhibit different sensitivities to substances. Therefore, Jia *et al*. (2019), is interesting since the authors evaluated more than one trophic level and representative organisms of the local fauna, which may live in the same habitat as the tested snail.

CONCLUSION

Among a quantity of 25 works used in this letter, 16 did not present reports of ecotoxicity tests, and 6 presented ecotoxicity tests. However, they did not use a freshwater ecosystem organism as a nontarget species. Only 3 publications presented reports of ecotoxicity tests with a representative model, and only 1 used more than one organism to assess ecotoxicity (Table No. 2). Therefore, the present work demonstrates the need to perform ecotoxicity tests in studies investigating the possible molluskicidal action of natural products on freshwater snails with medical importance. Furthermore, ecotoxicity tests using organisms of different trophic levels that are present in the natural habitat of studied snails are strongly recommended.

Table No. 2
Number of studies with ecotoxicity assays; representative models; and number of tested organisms

Number of Works	Works that presented ecotoxicity assays	Works that used a representative model	Works that used more than one organism
25	6	3	1

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