Tipo	Periódico
Título	Effects of Myristicin in Association with Chemotherapies on the Reversal of the Multidrug Resistance (MDR) Mechanism in Cancer
Autores	Elisa Frederico Seneme, Daiane Carla dos Santos, Carolina Afonso de Lima, Ícaro Augusto Maccari Zelioli, Juliana Mozer Sciani, Giovanna Barbarini Longato
Autor (es) USF	Elisa Frederico Seneme, Daiane Carla dos Santos, Carolina Afonso de Lima, Juliana Mozer Sciani, Giovanna Barbarini Longato
Autores Internacionais	-
Programa/Curso (s)	Programa de Pós-Graduação Stricto Sensu em Ciências da Saúde
DOI	https://doi.org/10.3390/ph15101233
Assunto (palavras chaves)	multidrug resistance; glycoprotein-P; myristicin; cisplatin; docetaxel
Idioma	inglês
Fonte	Título do periódico: Pharmaceuticals ISSN: 1424-8247 Volume/Número/Paginação/Ano: 15/10/1233/2022
Data da publicação	07 de outubro de 2022
Formato da produção	digital
Resumo	A range of drugs used in cancer treatment comes from natural sources. However, chemotherapy has been facing a major challenge related to multidrug resistance (MDR), a mechanism that results in a decrease in the intracellular concentration of chemotherapeutic agents, resulting in reduced treatment efficacy. The protein most frequently related to this effect is P-glycoprotein (P-gp), which is responsible for promoting drug efflux into the extracellular environment. Myristicin is a natural compound isolated from nutmeg and has antiproliferative activity, which has been reported in the literature. The present study aimed to evaluate the effect of the association between myristicin and chemotherapeutic agents on the NCI/ADR-RES ovarian tumor lineage that presents a phenotype of multidrug resistance by overexpression of P-gp. It was observed that myristicin showed no cytotoxic activity for this cell line, since its IC50 was >1 mM. When myristicin was associated with the chemotherapeutic agents cisplatin and docetaxel, it potentiated their cytotoxic effects, a result evidenced by the decrease in their IC50 of 32.88% and 75.46%, respectively. Studies conducted in silico indicated that myristicin is able to bind and block the main protein responsible for MDR, P-glycoprotein. In addition, the molecule fits five of the pharmacokinetic parameters established by Lipinski, indicating good membrane permeability and bioavailability. Our hypothesis is that, by blocking the extrusion of chemotherapeutic agents, it allows these agents to freely enter cells and perform their

	functions, stopping the cell cycle. Considering the great impasse in the chemotherapeutic treatment of cancer that is the MDR acquired by tumor cells, investigating effective targets to circumvent this resistance remains a major challenge that needs to be addressed. Therefore, this study encourages further investigation of myristicin as a potential reverser of MDR.
Fomento	Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP 2016/06137-6). Universidade São Francisco.