



Evaluation of antitumoral and antioxidant activities of the hydroalcoholic extract and fractions obtained from the fruit pericarp of *Sapindus saponaria* L.

José Rivaldo dos Santos Filho, Éverton da Silva Santos, Filipa Mandim, Adriana K. Molina, Lillian Barros, Regina Aparecida Correia Gonçalves, Arildo José Braz de Oliveira & Izabel Cristina Piloto Ferreira


To cite this article: José Rivaldo dos Santos Filho, Éverton da Silva Santos, Filipa Mandim, Adriana K. Molina, Lillian Barros, Regina Aparecida Correia Gonçalves, Arildo José Braz de Oliveira & Izabel Cristina Piloto Ferreira (17 May 2023): Evaluation of antitumoral and antioxidant activities of the hydroalcoholic extract and fractions obtained from the fruit pericarp of *Sapindus saponaria* L., Natural Product Research, DOI: [10.1080/14786419.2023.2211214](https://doi.org/10.1080/14786419.2023.2211214)



To link to this article: <https://doi.org/10.1080/14786419.2023.2211214>

 View supplementary material 

 Published online: 17 May 2023.

 Submit your article to this journal 

 Article views: 123

 View related articles 

 View Crossmark data 



Evaluation of antitumoral and antioxidant activities of the hydroalcoholic extract and fractions obtained from the fruit pericarp of *Sapindus saponaria* L.

José Rivaldo dos Santos Filho^a, Éverton da Silva Santos^a, Filipa Mandim^{b,c}, Adriana K. Molina^{b,c}, Lillian Barros^{b,c}, Regina Aparecida Correia Gonçalves^{a,d}, Arildo José Braz de Oliveira^{a,d} and Izabel Cristina Piloto Ferreira^{a,d}

^aPrograma de Pós-Graduação em Ciências Farmacêuticas, Universidade Estadual de Maringá, Maringá, Paraná, Brasil; ^bCentro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Bragança, Portugal; ^cLaboratório Associado para a Sustentabilidade e Tecnologia em Regiões de Montanha (SuTEC), Instituto Politécnico de Bragança, Bragança, Portugal; ^dDepartamento de Farmácia, Universidade Estadual de Maringá, Maringá, Paraná, Brasil

ABSTRACT

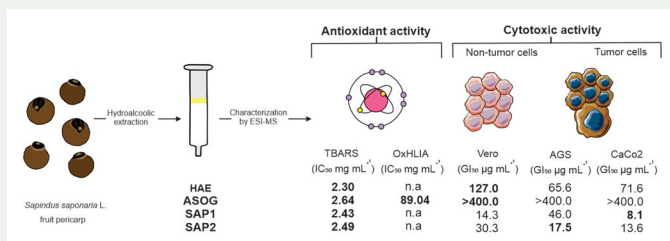
The fruits of *Sapindus saponaria* L., popularly known as 'saboieiro', have been used in medicine. This study evaluated the antioxidant and antitumor activities of the hydroethanolic extract (HAE) and fractions obtained from the fruit pericarp of *S. saponaria*. The HAE was obtained from the *S. saponaria* fruit pericarp by maceration; this was followed by fractionation using reversed-phase solid-phase extraction, resulting in fractions enriched with acyclic sesquiterpene oligoglycosides (ASOG) and saponins (SAP1, and SAP2), confirmed by mass spectrometry with electrospray ionization (ESI-QTOF-MS). The greatest cytotoxic activity was observed with the SAP1 fraction against the CaCo2 cell line with a GI_{50} of $8.1 \mu\text{g mL}^{-1}$, while the SAP2 fraction had a GI_{50} of $13.6 \mu\text{g mL}^{-1}$ against CaCo2. The HAE demonstrated the greatest antioxidant activity. *S. saponaria* has potential therapeutic use in the pharmaceutical industry as a natural anti-oxidant or antitumor product.

ARTICLE HISTORY

Received 26 December 2022
Accepted 3 May 2023

KEYWORDS

Acyclic sesquiterpene oligoglycosides; biological activity; saponins; *Sapindus saponaria*



CONTACT Arildo José Braz de Oliveira ✉ ajboliveira@uem.br 📠 Department of Pharmacy, State University of Maringá, Av. Colombo 5790, 87.020-900, Maringá, Parana, Brazil.

📄 Supplemental data for this article can be accessed online at <https://doi.org/10.1080/14786419.2023.2211214>.

© 2023 Informa UK Limited, trading as Taylor & Francis Group

1. Introduction

Sapindus saponaria L. belongs to the Sapindaceae family that occur in tropical and subtropical regions (Acevedo-Rodríguez et al. 2010; Somner et al. 2015). *S. saponaria* is popularly known as 'sabão-de-macaco, saboeiro, saboneteiro, fruta de sabão, or sabão-de-soldado', is a small tree occurring in the states of the North, Northeast and Center-West of Brazil, used in landscaping (Albiero et al. 2001).

Sapindus saponaria is known for the great presence of saponins, a natural surfactant found in its seeds and fruits (Albiero et al. 2001; Pelegrini et al. 2008), and acyclic sesquiterpenic oligoglycosides (Murgu and Rodrigues-Filho 2006). The plant has been widely used by the inhabitants of the north and northeast regions of Brazil for the treatment of inflammations, injuries and even cancer. The fruits, in particular, are used by the population to manufacture soap and as remedies against ulcers, skin lesions and inflammations (Albiero et al. 2001; Pelegrini et al. 2008). The bark, root, and fruits of *S. saponaria* specifically are used in folk medicine as a tranquilizer, astringent, diuretic, expectorant, tonic, blood purifier, and to fight coughs (Abreu Guirado 2005), in addition to cytotoxicity and genotoxicity (Albiero et al. 2001; Rashed et al. 2013a; Santos et al. 2020).

Considering the biological potential reported in the literature, the aim of the study was evaluate the antioxidant and antitumor activities of the hydroalcoholic extract and fractions from the fruit pericarp of *S. saponaria*.

2. Results and discussion

2.1. Characterization by mass spectrometry with electrospray ionization (ESI-QToF-MS)

As demonstrated by Murgu and Rodrigues-Filho (2006), the mass spectrum of the HAE revealed two main chemical families. This first region was called the acyclic sesquiterpene oligoglycoside (ASOG) region, which was formed by intense peaks of m/z from 1100 to 1550, with each peak in the cluster separated by 42Da. The other region, named the saponin (SAP) region, contained less intense peaks from m/z 700 to 1100, with some of the peaks also showing the pattern of 42Da mass differences.

In the ASOG fraction, a prevalent presence of peaks above m/z values of 1100 was observed, with each peak separated by 42Da (equivalent to repeated losses of COCH_2), confirming the enrichment of the ASOG fraction with acyclic sesquiterpene oligoglycosides (Figure S1). The putative identification by ESI-QTOF-MS showed four ASOG in negative mode (Table S1). In the SAP fractions, a prevalent presence of a extensive presence of peaks below the m/z of 1100 was observed, confirming the enrichment of the SAP fractions with saponins (Figure S2). The phytochemical profiling enable the putative identification of eleven saponins in negative mode (Table S2).

2.2. Antioxidant activity

The HAE, SAP1, SAP2 and ASOG fractions from the fruit **pericarp** of *S. saponaria* showed antioxidant activity (Table S3), preferentially by the TBARS assay, with the

best result with the HAE (IC_{50} of 2.30 mg mL^{-1}), followed by the SAP1 and SAP2 fractions (2.43 and 2.49 mg mL^{-1} , respectively) and ASOG fraction (2.64 mg mL^{-1}) all of which had better activity than the Trolox control (9.10 mg mL^{-1}). This TBARS assay is widely used to measure lipophilic compound oxidation and antioxidant activity of natural products (Ghani et al. 2017). The OxHLIA assay is based on the inhibition of free radical-induced membrane damage in erythrocytes by antioxidants (Takebayashi et al. 2010). In the OxHLIA assay only the ASOG fraction presented activity with an IC_{50} of $89.04 \mu\text{g mL}^{-1}$. The HAE and SAP fractions did not reveal any potential in protecting the erythrocyte population from haemolytic action

A number of species of the genus *Sapindus* have also shown pharmacological antioxidant activity, including *S. mukorossi* (Shah et al. 2017; Kora 2020), *S. trifoliatus* (Sahoo et al. 2010; Pradhan 2014), and *S. emarginatus* (Srikanth and Muralidharan 2010) and *S. Saponaria* (Niloufer and Lakshmi 2021).

2.3. Cytotoxic activity

The HAE, SAP1 and SAP2 fractions from *S. saponaria* showed activity against tumor cell lines (Table S4), which may be related to the saponins. Up to $400 \mu\text{g mL}^{-1}$ of the ASOG fraction, on the other hand, did not show capacity to inhibit the proliferation of any of the tumor cell lines tested. Moreover, up to $400 \mu\text{g mL}^{-1}$ of the ASOG fraction was not toxic for non-tumor cells (Vero, $GI_{50} > 400 \mu\text{g mL}^{-1}$).

N'Da and Smith (2014) classified the biological activities into 4 categories: inactive, $GI_{50} > 100 \mu\text{g mL}^{-1}$; weak activity, $GI_{50} < 100 \mu\text{g mL}^{-1}$; moderate activity, $GI_{50} < 30 \mu\text{g mL}^{-1}$; and potent activity, $GI_{50} < 10 \mu\text{g mL}^{-1}$. According to this classification, the HAE showed moderate activity against CaCo2 ($71.6 \mu\text{g mL}^{-1}$) and AGS ($71.6 \mu\text{g mL}^{-1}$), while being inactive against MCF-7 ($153.5 \mu\text{g mL}^{-1}$) and NCI-H460 ($241.4 \mu\text{g mL}^{-1}$). The most promising GI_{50} results were obtained with the SAP1 and SAP2 fractions. The SAP1 fraction having potent activity against CaCo2 ($8.1 \mu\text{g mL}^{-1}$), moderate activity against MCF-7 ($29.8 \mu\text{g mL}^{-1}$) and NCI-H460 ($16.4 \mu\text{g mL}^{-1}$), and weak activity against AGS ($46.0 \mu\text{g mL}^{-1}$). The SAP2 fraction demonstrated moderate activity against AGS ($17.5 \mu\text{g mL}^{-1}$) and CaCo2 ($13.6 \mu\text{g mL}^{-1}$), and weak activity against MCF-7 ($59.7 \mu\text{g mL}^{-1}$) and NCI-H460 ($61.4 \mu\text{g mL}^{-1}$). The tumor cell lines most susceptible to inhibition by the SAP fractions were CaCo2 and AGS (Table S4).

The HAE and fractions from *S. saponaria* also demonstrated activity against non-tumor cells (Vero, GI_{50} between 14.3 to $127.0 \mu\text{g mL}^{-1}$; Table S4). The SI is an excellent tool to assess the selective power of samples against tumor and non-tumor cells, and this number is expressive when near or ≥ 2.0 (Suffness and Pezzuto 1990). Given this aspect, the most promising results found for the SI were the HAE against AGS at 1.9 and against CaCo2 at 1.8; and with the SAP2 fraction against CaCo2 at 2.1 and AGS at 1.7; and with the SAP1 fraction against CaCo2 at 1.7 according to Table S4.

According to Albiero et al. (2001), the extracts and fractions of fruits from *S. saponaria* that demonstrated significant activity against an Ehrlich ascitic tumor. Saponins belong to a diverse group of compounds with high chemoprevention potential, and are characterized by a wide spectrum of anti-tumor activities (Koczurkiewicz et al. 2015). The action of saponins is related to their ability to interact with cell membranes,

resulting in short-term membrane rearrangements or complete destruction. This ability is responsible for both the cytotoxic and hemolytic activity of saponins (Lorent et al. 2014).

3. Conclusion

The results of this study showed that the SAP1 and SAP2 fractions (enriched with saponins) showed higher cytotoxic activity in relation to the HAE and the ASOG fraction (enriched with acyclic sesquiterpene oligoglycosides). The latter of which showed significant antioxidant activity. Therefore, *S. saponaria* has pharmacological potential for use in the pharmaceutical industry, such as in obtaining a natural antitumor or antioxidant product.

Acknowledgments

The authors would like to thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, 10.13039/501100002322), Complexo de Centrais de Apoio à Pesquisa (COMCAP, Universidade Estadual de Maringá, Brasil) and Fundação para a Ciência e a Tecnologia (FCT, Portugal) for financial support through national funds FCT/MCTES (PIDDAC), CIMO (UIDB/00690/2020 and UIDP/00690/2020) and SusTEC (LA/P/0007/2021). L. Barros thanks FCT, P.I., through institutional scientific employment program-contract, and for F. Mandim and A.K. Molina PhD grants (SFRH/BD/146614/2019; 2020.06231.BD).

Disclosure statement

The authors declare that they have no competing interests

Funding

The authors would like to thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, 10.13039/501100002322), Fundação para a Ciência e a Tecnologia (FCT, Portugal) for financial support through national funds FCT/MCTES (PIDDAC), CIMO (UIDB/00690/2020 and UIDP/00690/2020) and SusTEC (LA/P/0007/2021). L. Barros thanks FCT, P.I. through institutional scientific employment program-contract, and for F. Mandim and A.K. Molina PhD grants (SFRH/BD/146614/2019; 2020.06231.BD).

References

- Abreu Guirado OA. 2005. Potencial medicinal del género *Sapindus* L. (Sapindaceae) y de la especie *Sapindus saponaria* L. Rev Cubana Plant Med. 10:3–4.
- Acedo-Rodríguez P, Van Welzen P, Adema F, Van der Ham R. 2010. Sapindaceae. In: Kubitzki K, editor. Flowering plants eudicots. Berlin: Springer; p. 357–407.
- Albiero ALM, Bacchi EM, Mourão KSM. 2001. Caracterização anatômica das folhas, frutos e sementes de *Sapindus saponaria* L. (Sapindaceae). Acta Sci Biol Sci. 23:549–560.
- Ghani MA, Barril C, Bedgood DR, Jr, Prenzler PD. 2017. Measurement of antioxidant activity with the thiobarbituric acid reactive substances assay. Food Chem. 230:195–207.

- Koczurkiewicz P, Czyż J, Podolak I, Wójcik K, Galanty A, Janeczko Z, Michalik M. 2015. Multidirectional effects of triterpene saponins on cancer cells-mini-review of in vitro studies. *Acta Biochim Pol.* 62(3):383–393.
- Kora AJ. 2020. Antibacterial and antioxidant activities of aqueous extract of soapnuts (*Sapindus mukorossi*). *CTBP.* 14(4):388–395.
- Lorent JH, Quetin-Leclercq J, Mingeot-Leclercq M-P. 2014. The amphiphilic nature of saponins and their effects on artificial and biological membranes and potential consequences for red blood and cancer cells. *Org Biomol Chem.* 12(44):8803–8822.
- Murgu M, Rodrigues-Filho E. 2006. Dereplication of glycosides from *Sapindus saponaria* using liquid chromatography-mass spectrometry. *J Braz Chem Soc.* 17(7):1281–1290.
- N'Da DD, Smith PJ. 2014. Synthesis, in vitro antiparasitic and antiproliferative activities of a series of quinoline-ferrocene hybrids. *Med Chem Res.* 23(3):1214–1224.
- Niloufer S, Lakshmi LB. 2021. In-vitro analysis of phytochemical, anti-oxidant capacity of seed ethanolic extracts of *Sapindus saponaria* Vahl and anti-bacterial activity on common dental pathogens. *Res J Pharm Technol.* 14(1):351–355.
- Pelegri DD, Tsuzuki JK, Amado CA, Cortez DA, Ferreira ICJ. 2008. Biological activity and isolated compounds in *Sapindus saponaria* L. and other plants of the genus *Sapindus*. *Lat Am J Pharm.* 27(6):922–927.
- Pradhan D. 2014. Pharmacological effect of some fractions obtained from *Sapindus trifoliatus* acting as an antioxidant and against mammary cell proliferation. *Afr J Pharm Pharmacol.* 8(1):455–463.
- Rashed K, Ćirić A, Glamočlija J, Calhelha RC, Ferreira IC, Soković M. 2013. Antimicrobial activity, growth inhibition of human tumour cell lines, and phytochemical characterization of the hydromethanolic extract obtained from *Sapindus saponaria* L. aerial parts. *Biomed Res Int.* 2013:659183.
- Sahoo P, Padhy K, Pradhan D, Tripathy G, Bhoi R, Pattanayak S, Sahoo S. 2010. Antidiabetic and antioxidant activity of ethanolic extract of *Sapindus trifoliatus* Linn. *Int J Pharma Biol Sci.* 1(2):PS45.
- Santos BT, Valdés LM, Vélez LEP, Rodríguez YG, Argüelles BMO, González VGS. 2020. Saponin contents and antiproliferative in vitro effects on PC3 human prostate cancer *saponaria* L. extracts cell line of *Sapindus*. *Rev CENIC Cienc Biol.* 51(2):100–108.
- Shah M, Parveen Z, Khan MR. 2017. Evaluation of antioxidant, anti-inflammatory, analgesic and antipyretic activities of the stem bark of *Sapindus mukorossi*. *BMC Complement Altern Med.* 17(1):1–16.
- Somner G, Ferrucci M, Acevedo-Rodríguez P, Perdiz R, Coelho R, Medeiros H. 2015. Sapindaceae in Lista de Espécies da Flora do Brasil. Jardim Botânico Do Rio De Janeiro, <http://floradobrasil.jbrj.gov.br/jabot/floradobrasil/FB216>, Accessed 10 November 2022.
- Srikanth J, Muralidharan P. 2010. Evaluation of antioxidant properties of *Sapindus emarginatus* vahl. *Asian J Exp Biol Sci.* 1(3):693–699.
- Suffness M, Pezzuto JM. 1990. Assays related to cancer drug discovery. *Methods Plant Biochem: Assays Bioactivity.* 6:71–133.
- Takebayashi J, Chen J, Tai A. 2010. A method for evaluation of antioxidant activity based on inhibition of free radical-induced erythrocyte hemolysis. *Methods Mol Biol.* 594:287–296.