ANTICANCER POTENTIAL OF PINK PEPPER FRUIT ESSENTIAL OIL: STUDY ON HUMAN CELL LINES OF LUNG CARCINOMA (H460), CERVICAL ADENOCARCINOMA (HeLa) AND COLORECTAL CARCINOMA (HCT116)

ORIGINAL SCIENTIFIC ARTICLE

Emir Horozić[1]✉, Lamija Kolarević[2], Suada Cipurković[3], Merima Ibišević[2], Lejla Mekić[2], Melisa Šehić[3], Ermina Cilović Kozarević[2], Darja Husejnagić[3], Edina Huseinović[3], Maja Pođanin[3], Enida Karić[2], Mirela Radin[4]

DOI: 10.51558/2232-7568.2024.17.2.43

RECEIVED 2024-10-28 **ACCEPTED** 2025-02-19

[1] Faculty of Technology, University of Tuzla, Urfeta Vejzagića 8, 75 000 Tuzla, Bosnia and Herzegovina
[2] Faculty of Pharmacy, University of Tuzla, Urfeta Vejzagića 8, 75 000 Tuzla, Bosnia and Herzegovina
[3] Faculty of Natural Sciences, University of Tuzla, Urfeta Vejzagića 4, 75 000 Tuzla, Bosnia and Herzegovina
[4] Faculty of Medicine, University of Sarajevo, Čekaluša 90, 71 000 Sarajevo, Bosnia and Herzegovina

✉ emir.horozic@untz.ba

ABSTRACT:
***Schinus terebinthifolius* Raddi is a plant species belonging to Anacardiaceae family, native to South America, with particular abundance in Brazil, Argentina and Paraguay. It is commonly known as Brazilian pepper tree. All plant parts have been used in traditional medicine for the treatment of several pathologies. In this paper, the cytotoxic effects of the essential oil of the commercial pink pepper fruit from the Tuzla market were investigated. To assess the cytotoxic potential, a tetrazolium salt reduction (MTT) viability assay was performed. The experiments were carried out on 3 human cell lines: lung carcinoma (H460), cervical adenocarcinoma (HeLa) and colorectal carcinoma (HCT116). Using GC/MS, 24 components of red pepper essential oil were identified, of which α-pinene, α-phellandrene, δ-3-carene and D-limonene dominate. The essential oil of the pink pepper fruit showed cytotoxic activity in the case of all tested cell lines under *in vitro* conditions.**

KEYWORDS: GC/MS analysis, cytotoxic activity, H460, HeLa, HCT116

INTRODUCTION

The most important role of secondary metabolites in plants is the resistance of plants to adverse external conditions such as climatic variations, mechanical damage, insects, etc. These metabolic end products are stored in leaves, flowers, roots and other plant parts, from which they can be isolated for other purposes, most importantly medicinal. Secondary metabolites are small organic molecules, interesting due to their structural diversity and biological effects. More than 30% of medicinal products derive from natural products [1,2]. Important group of plant-based secondary metabolites are essential oils, which are responsible for the characteristic fragrance and taste of the plant. Plants containing essential oils are known as aromatic. Aromatic plants and essential oils are very often used in medicinal purposes, due to their antiseptic, analgesic, sedative, anti-inflammatory, spasmolytic and locally anesthetic effects [3]. Essential oils generally consist of a variety of chemical compounds, mostly benzene and terpene derivatives. These derivatives contribute to the rich bioactivity of essential oils [4]. Essential oils can be synthesized in all plant organs, mostly buds, flowers, leaves, seeds, fruits, roots. There are several methods for extracting essential oils, and steam distillation is the most common. The isolation method depends on the localization of the essential oils, as they can be stored in secretory cells, cavities, canals, epidermic cells or glandular trichomes. Mostly, essential oils are plant derived but some of them are originate from microorganisms and animals [4].

Schinus terebinthifolius Raddi is a plant species belonging to Anacardiaceae family, native to South America, with particular abundance in Brazil, Argentina and Paraguay. It is commonly known as Brazilian pepper tree. All plant parts have been used

in traditional medicine for the treatment of several pathologies. It has been used for the treatment of ulcers, respiratory problems, wounds and arthritis. Antiseptic, antiinflammatory and haemostatic effects have also been noted. Many of these properties are associated with secondary metabolites of the plant, mainly polyphenols [5,6]. The resin obtained from the bark and stem is traditionally used in Brazil for cleaning the skin and the treatment of mycoses.

Schinus species are characterized by pungent-smell essential oils concentrated especially in fruits. Besides fruits, essential oils from leaves and flowers of *S. terebinthifolius* have been analyzed. Several variations in composition of essential oils from different regions were detected. Characterization of the chemical constituents of *S. terebinthifolius* fruit essential oil revealed the presence of monoterpene hydrocarbons, such as α-phellandrene, limonene, β-phellandrene, myrcene, and α-pinene as major components. Other reports suggested that the main components were sesquiterpenes, with germacrene-D, α-cadinol, and elemol as the main components. Composition of the leaf essential oil differs depending on a geographical position. Limonene, germacrene-D, β- caryophyllene, α-copaene, and α-pinene were reported as the main components of the Brazilian specimens. In Egypt specimen, β-caryophyllene, *cis*-β-terpineol, β-cedrene and citronellal were found as the major components [7,8]. Another research on the composition of essential oil isolated from leaves and twigs has revealed that major components were α-phellandrene, α-pinene, limonene, β-phellandrene and *p*-cymene. The most abundant compounds as second dominating chemical class were sesquiterpene hydrocarbons, precisely germacrene-D, bicyclogermacrene and β-cubebene [9].

*S. terebinthifolius*is promising medicinal plants for the treatment of inflammation, respiratory problems, rheumatism etc. Infusions and tinctures of bark and leaves are used traditionally to treat bacterial infections, to promote healing and for its anti-ulcerogenic effect. Chemical analysis of the bark showed the presence ofanthraquinones, xanthones and free steroids [10]. Some *in vitro* and *in vivo* studies reported antioxidant, antibacterial, and antifungal activities of *S. terebinthifolius* extracts [11]. Ethyl gallate, methyl gallate, quercitrin, myricitrin and myricetin with radical scavenging potential were isolated from leaves extract [12]. An aqueous extract of aerial part of *S. terebinthifolius* has been found effective against *Candida albicans*, but it was not determined which compounds were responsible for antifungal activity [13]. Acetate fraction of *S. terebinthifolius* leaves exhibited anti-inflammatory and anti-allergic effect when administered orally. It was also demonstrated that ethyl acetate extract from the leaves promotes a topical anti-inflammatory effect and antioxidant activity both *in vitro* and *in vivo* [14]. Among afore mentioned, some extracts of *S. terebinthifolius* showed promising antitumour effects. It was suggested that decoction of flowers, stalks and leaves of *S. terebinthifolius*, can be used for the treatment of tumour and leprosy [13]. Cytotoxic activity against four different human tumor cell lines was also detected for hexane and dichloromethane extracts of *S. terebinthifolius* leaves, but further investigations are needed in order to identify and isolate bioactive compounds with cytotoxic properties [15]. Antitumor activity of *S. molle* and *S. terebinthifolius* fruit essential oils was evaluated against the breast cancer cell line (MCF-7), and it was concluded that the investigated oils induced promising *in vitro* antioxidant activity and cytotoxicity on this cell line. *S. terebinthifolius* essential oil, rich in sesquiterpenes, has been found as the most active [11]. In a follow-up study, the crude oil of *S. terebinthifolius* leaves was subjected to chromatographic separation procedures toafford afraction composed of α- and β-pinenes. These compounds were tested *in vitro* against murine melanoma cell line, human melanoma, breast adenocarcinoma, leukemia and cervical carcinoma cell lines. The obtained results indicated that α-pinene, one of the major compounds of the investigated oil, might be responsible for its cytotoxic effect [16].

In this research, the chemical composition and cytotoxic activity of pink pepper essential oil were analyzed *in vitro* on three cell lines: H460 (lung carcinoma, large cell lung cancer), HeLa (cervical adenocarcinoma), and HCT116 (colorectal carcinoma). The aim is to examine the influence of the chemical composition on the cytotoxic activity of the essential oil and to compare the obtained results with previously published studies.

MATERIALS AND METHODS

The pepper sample was obtained commercially. Pink pepper originates from Vietnam. The sample was crushed using an electric mill and kept in a dark and dry place until subjected to distillation.

HYDRODISTILLATION

The crushed pink pepper fruit was subjected to hydrodistillation for four hours on a Clevenger apparatus. The obtained essential oil was separated, dried on anhydrous sodium sulfate and stored at -20°C until analysis.

GC/MS ANALYSIS

The essential oil of the red pepper fruit was analyzed by the gas chromatography with mass detector (GC-MSD) technique. This technique enables the identification of individual organic volatile compounds in essential oils (monoterpene and sesquiterpene alcohols and phenols, esters, aldehydes, ketones, etc.) with the help of GC-MS software with integrated databases or libraries of compounds - Wiley7NIST05 and NIST14. A semi-quantitative method was used to determine the composition of EO, in which individual peaks of chemical components within the obtained chromatogram were identified by comparing their retention indices with the indices of compounds within the databases, and by matching the mass spectrum of the compounds in the sample with the mass spectrum within the databases.

GC/MS analysis of pink pepper fruit essential oil sample was performed on an Agilent Technologies, Inc. gas chromatograph (7820A) with capillary HP5-ms ultra inert column (-60 to 325 °C, 30 m × 250 μm, film thickness 0.25 μm). The gas chromatograph was equipped with an Agilent mass selective detector (MSD-5977E). Helium gas (purity 5.0) was used as carrier gas at a constant flow rate of 1.0 mL/min. The sample was injected in a volume of 1 μL. The oven temperature was programmed from 60 °C (hold 1 min) to 246 °C (hold 0 min) at a rate of 3 °C/min and then to 280 °C at a rate of 10 °C/min. Before and after each injection, three washes of the needle with solvent (n-hexane) were used. The program resulted in a total duration of 86.40 minutes. The mass detector (MSD) was operated in the 40-400 m/z range scan mode. The temperature of the MSD transfer line was 250 °C, and the temperature of the ion source was 230 °C. ChemStation software was used for instrument control and data analysis. The results are expressed as a percentage concentration (% (V/V)) of each component in relation to the entire area of the obtained chromatogram.

ANALYSIS OF ANTICANCER POTENTIAL

The experiments were carried out on 3 human cell lines. The following cell lines were used: H460 (lung carcinoma, large cell lung cancer (ATCC®HTB-177™), HeLa (cervical adenocarcinoma, ATCC® CCL-2™) and HCT116 (colorectal carcinoma ATCC® CCL-247™).

Cells were cultured as monolayers and maintained in Dulbecco's modified Eagle medium (DMEM), supplemented with 10% fetal bovine serum (FBS), 2mM L-glutamine, 100 U/mL penicillin and 100 μg/mL streptomycin in a humidified atmosphere with 5% CO_2 at 37˚C.

The panel cell lines were inoculated on to a series of standard 96-well microtiter plates on day 0, at 1.5×10^4 cells/mL. Essential oil were then added at 0.01 μL/mL, 0.05 μL/mL, 0.1 μL/mL, 0.5 μL/mL and 1 μL/mL concentration and incubated for a further 72 hours.

After 72 hours of incubation the cell growth rate was evaluated by performing the MTT assay, which detects dehydrogenase activity in viable cells. The MTT Cell Proliferation Assay is a colorimetric assay system, which measures the reduction of a tetrazolium component (MTT) into an insoluble formazan product by the mitochondria of viable cells. For this purpose the substance treated medium was discarded and 40 μL of MTT reagent was added to each well at a concentration of 0.5 μg/μL. After four hours of incubation the precipitates were dissolved in 160 μL of DMSO. The absorbance (A) was measured on a microplate reader at 570 nm. The absorbance is directly proportional to the cell viability. The percentage of growth (PG) of the cell lines was calculated according to one or the other of the following two expressions:

If $(A_{test} - A_{tzero}) \geq 0$ then: $PG = 100 \times (A_{test} - A_{tzero}) / (A_{cont} - A_{tzero})$
If $(A_{test} - A_{tzero}) < 0$ then: $PG = 100 \times (A_{test} - A_{tzero}) / A_{tzero}$

Where:
A_{tzero} = the average absorbance before exposure of cells to the test compound,
A_{test} = the average absorbance after the desired period of time (72 h),
A_{cont} = the average absorbance after 72 hours with no exposure of cells to the test compound.

Each test point was performed in quadruplicate in three individual experiments. The results are expressed as concentration-response graphs. A negative percentage indicates cytotoxicity following drug treatment where -100% shows no cells survived the treatment at the specific drug concentration. The results are also expressed as GI_{50}, a concentration necessary for 50% of inhibition.

RESULTS AND DISCUSSION

GC/MS ANALYSIS

By hydrodistillation, essential oil was isolated from red pepper with a yield of 1.77%. The chemical constitution of the essential oil obtained from the pink pepper are presented in Table 1. The identification of 24 components by GC/MS allowed for 97.1% of the

total pink pepper fruit oil to be identified. Monoterpenes constitute 80.1% of essential oil, whereas the identified sesquiterpenes corresponded to 17.1%. The most abundant components were four monoterpenes δ-3-carene (22.0%), D-limonene (16.5%), α-phellandrene (16.1%) and α-pinene (13.4%) followed by two sesquiterpenes germacrene D (4.9%) and caryophyllene (4.1%). GC/MS chromatogram of Pink pepper fruit essential is shown in Figure 1.

Table 1. Chemical composition of Pink pepper fruit essential oil

Test parameter / Component	Retention index	Retention time	Result v/v (%)
α-thujene	929	5.639	0.329
α-pinene	937	5.842	13.437
sabinene	974	6.971	1.580
β-pinene	979	7.077	2.649
β-myrcene	991	7.500	3.019
α-phellandrene	1005	7.973	16.134
δ-3-carene	1011	8.176	22.027
o-cymene	1022	8.650	2.949
D-limonene	1030	8.819	16.492
α-terpinolene	1088	11.043	1.442
5-isopropenyl-2-methyl-7-oxabicyclo[4.1.0]heptan-2-ol	1169	17.915	0.389
δ-elemene	1338	21.577	0.725
β-elemene	1391	23.877	0.315
caryophyllene	1419	24.968	4.058
trans-α-bergamotene	1435	25.658	0.249
humulene	1454	26.351	0.411
germacrene D	1481	27.484	4.906
bicyclogermacrene	1495	28.098	0.473
aciphyllene	1499	28.212	0.310
δ-cadinene	1524	29.184	0.764
elemol	1549	30.186	3.526
germacrene B	1557	30.444	0.288
caryophyllene oxide	1581	31.442	0.301
rosifoliol	1600	32.432	0.356

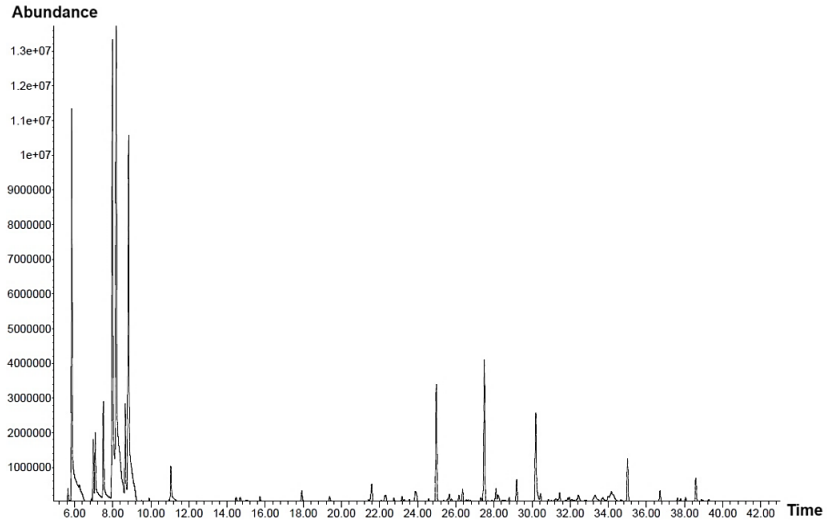

Figure 1. GC/MS chromatogram of Pink pepper fruit essential oil

ANTICANCER POTENTIAL

The treatment of HeLa, H460, and HCT116 cell lines with essential oil from pink pepper fruit demonstrated a dose-dependent decrease in cell growth. At the lowest concentrations of 0.01 µL/mL and 0.1 µL/mL, the essential oil had no effect on cell viability, with the growth percentage (PG) remaining at 100%. However, at a higher concentration of 1 µL/mL, a significant cytotoxic effect was observed, resulting in a 100% reduction in cell growth. This indicates that the essential oil of pink pepper exhibits potent anticancer activity at higher concentrations, effectively inhibiting the proliferation of these cancer cell lines. Dose-response profiles are shown in Figure 2. GI_{50} values for Pink pepper fruit essential oil are shown in Table 1.

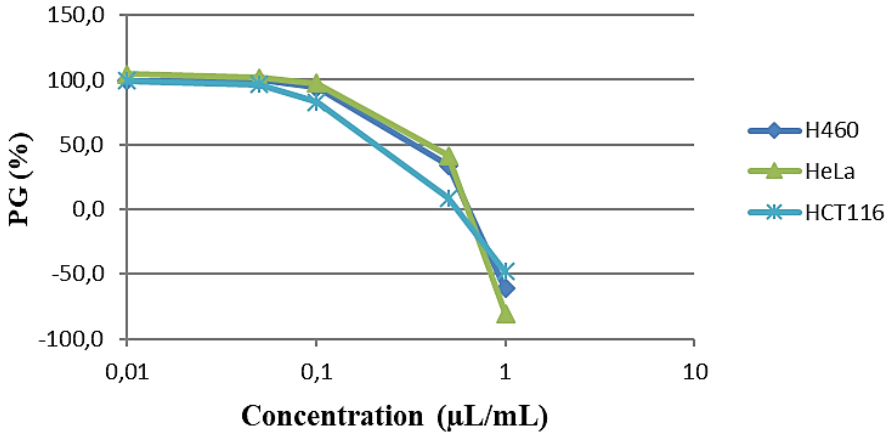

Figure 2. Dose-response profiles for Pink pepper fruit essential oil on H460, HeLa and HCT116 cell lines

Table 2. GI_{50} values for Pink pepper fruit essential oil

Cell lines	GI_{50} (nL/mL)
Lung carcinoma (H460)	423±121
Cervical adenocarcinoma (HeLa)	439±72
Colorectal carcinoma (HCT116)	271±42

Previous studies have shown that fruit essential oil is more cytotoxic on tumor cells than leaf oil, particularly effective in reducing cell viability in MCF-7 cell lines compared to A549 and HT-144 cells [17]. Santana et al. evaluated the activity of *S. terebinthifolius* leaves essential oil against five different tumor cell lines: B16F10-Nex2, A2058, HeLa, MCF-7, and HL-60, with HL-60 cells showing the most sensitivity. The crude oil was separated into a mixture of α- and β-pinenes, which exhibited moderate cytotoxicity. α-Pinene, a major compound (5.71%) isolated from the ripe fruits of *S. terebinthifolius*, was found to induce apoptosis and confer antimetastatic protection, suggesting it might be responsible for the observed cytotoxic effect of the crude oils [16]. The essential oil from *S. terebinthifolius* demonstrated greater anticancer effectiveness against the human breast cancer cells (MCF-7) compared to that from *S. molle* [11]. The ethanol extract of *S. terebinthifolius* fruit inhibited 50% of cell growth, indicating effective *in vitro* cytotoxic activity against the MCF-7 cell line. This cytotoxic activity is likely due to the polyphenolic content, as phenolic compounds are known to protect against cancer development and suppress cancer cell activity [18]. The methanolic extract (MEST) was also tested on ten human tumor cell lines from various tissues (U251, MCF-7, NCI-ADR/RES, 786-0, NCI-H460, PC-3, OVCAR-3, HT-29, K-562, and HaCaT). MEST showed selectivity for prostate, ovarian, breast, glioma, and non-tumoral cells, with the highest inhibitory activities observed in ovarian cancer cells [19]. A 2023 study investigated the chemical composition and cytotoxic activity of essential oils extracted from unripe and ripe pink pepper fruits. Chemical analysis revealed that the major components of unripe-EO were α-pinene (29.16%), dl-limonene (20.65%), and ρ-cymene (15.86%), while ripe-EO was characterized by l-phellandrene (38.91%), sylvestrene (23.02%), and α-pinene (21.62%). The cytotoxic activity of these essential oils was evaluated against HL-60 (acute promyelocytic leukemia) and SK-MEL-28 (malignant melanoma) cell lines, with significant cytotoxic effects, particularly from the unripe fruits

[20]. α-Pinene isolated from *S. terebinthifolius* leaves induces apoptosis and confers antimetastatic protection in a melanoma model. In a study where the viable B16F10-Nex2 murine melanoma cell line was injected into mice and treated with α-pinene intraperitoneally, a significant reduction in lung colonization was observed after 12 days, indicating a potent antimetastatic effect. These oils can also promote the depolarization of mitochondrial membranes, leading to apoptosis and necrosis [21]. Essential oils from the leaves, fruits, and bark of *Schinus terebinthifolius* of Egyptian origin exhibit significant cytotoxic activities against liver (HepG-2) and colon (Caco-2) carcinoma cells. Both cell lines displayed cytopathic effects, including cell distortion and degeneration. These structural changes are consistent with the observed reduction in cell viability, suggesting that the essential oils induce cell death through apoptosis or other cytotoxic pathways. These findings support the potential of these essential oils as sources of novel antitumor agents and underscore the need for further studies to isolate and characterize the bioactive compounds responsible for their cytotoxic effects [22].

CONCLUSION

The treatment of HeLa, H460, and HCT116 cell lines with essential oil from pink pepper fruit demonstrated a dose-dependent decrease in cell growth. At the lowest concentrations of 0.01 μL/mL and 0.1 μL/mL, the essential oil had no effect on cell viability, with the growth percentage (PG) remaining at 100%. However, at a higher concentration of 1 μL/mL, a significant cytotoxic effect was observed, resulting in a 100% reduction in cell growth.

REFERENCES

[1] Hoffmann, K.H. "Essential oils", Z. Naturforsch. C: J Biosciences, vol. 75, no. 7-8, pp. 177, 2020.

[2] Twaij, B.M., Hasan, M.N. "Bioactive Secondary Metabolites from Plant Sources: Types, Synthesis, and Their Therapeutic Uses", *Int J Plant Bio*, vol. 13, pp. 4-14, 2022.

[3] Bakkali, F., Averbeck, S., Averbeck, D., Idaomar, M. "Biological effects of essential oils - A revie",. *Food Chem Toxicol*, vol. 46, no. 2, pp. 446-75, 2008.

[4] Wani, A.R., Yadav, K., Khursheed, A., Rather, M.A. "An updated and comprehensive review of the antiviral potential of essential oils and their chemical constituents with special focus on their mechanism of action against various influenza and coronaviruses", *Microb Pathog*, vol. 152, 104620, 2021.

[5] Sereniki, A., Linard-Medeiros, C.F.B., Silva, S.N., Silva, J.B.R., Peixoto Sobrinho, T.J.S., da Silva JR, et al. "*Schinus terebinthifolius* administration prevented behavioral and biochemical alterations in a rotenone model of Parkinson's disease", *Rev Bras Farmacogn*, vol. 26, no. 2, pp. 240-245, 2016.

[6] da Rocha, P.D.S., Paula, V.M.B., Olinto, S.C.F., Dos Santos, E.L., Souza, K.P., Estevinho, L.M. "Diversity, Chemical Constituents and Biological Activities of Endophytic Fungi Isolated from *Schinus terebinthifolius* Raddi", *Microorganisms*, vol. 8, no. 6, pp. 1-13, 2020.

[7] Santos, A.C., Rossato, M., Agostini, F., Serafini, L.A., Santos, P.L., Molon, R., Dellacassa, E., Moyna, P. "Chemical composition of the essential oils from leaves and fruits of *Schinus molle* L. and *Schinus terebinthifolius* Raddi from Southern Brazil", *J Essent Oil-Bear Plants*, vol. 12, no. 1, pp. 16-25, 2009.

[8] Barbosa, L.C., Demuner, A.J., Clemente, A.D., Paula, V.F., Ismail, F. "Seasonal variation in the composition of volatile oils from *Schinus terebinthifolius* Raddi", *Química Nova*, vol. 30, pp. 1959-1965, 2007.

[9] Ennigrou, A., Casabianca, H., Vulliet, E., Hanchi, B., Hosni, K. "Assessing the fatty acid, essential oil composition, their radical scavenging and antibacterial activities of *Schinus terebinthifolius* Raddi leaves and twigs", *J Food Sci Tech*, vol. 55, pp. 1582-1590, 2018.

[10] de Lima, M.R., de Souza Luna, J., dos Santos, A.F., de Andrade, M.C., Sant'Ana, A.E., Genet, J.P., Marquez, B., Neuville, L., Moreau, N. "Anti-bacterial activity of some Brazilian medicinal plants", *J Ethnopharmacol*, vol. 105, no. 1-2, pp. 137-147, 2006.

[11] Bendaoud, H., Romdhane, M., Souchard, J.P., Cazaux, S., Bouajila, J. "Chemical composition and anticancer and antioxidant activities of *Schinus molle* L. and *Schinus terebinthifolius* Raddi berries essential oils", *J Food Sci*, vol. 75, no. 6, pp. 466-472, 2010.

[12] Ceruks, M., Romoff, P., Fávero, O.A., Lago, J.H. "Constituintes fenólicos polares de *Schinus terebinthifolius* Raddi (Anacardiaceae)", *Química Nova*, vol. 30, pp. 597-599, 2007.

[13] Schmourlo, G., Mendonça-Filho, R.R., Alviano, C.S., Costa, S.S. "Screening of antifungal agents using ethanol precipitation and bioautography of medicinal and food plants", *J Ethnopharmacol*, vol. 96, no. 3, pp. 563-568, 2005.

[14] da Silva Nascimento, M., dos Santos, P.H., de Abreu, F.F., Shan, A.Y., Amaral, R.G., Andrade, L.N., Souto, E.B., Santos, M.I., de Souza Graça, A., Souza, J.B., Raimundo e Silva, J.P. "*Schinus terebinthifolius* Raddi (Brazilian pepper) leaves extract: *in vitro* and *in vivo* evidence of anti-inflammatory and antioxidant properties", *Inflammopharmacology*, vol. 31, no. 5, pp. 2505-2519, 2023.

[15] de Mesquita, M.L., de Paula, J.E., Pessoa, C., de Moraes, M.O., Costa-Lotufo, L.V., Grougnet, R., Michel, S., Tillequin, F., Espindola, L.S. "Cytotoxic activity of Brazilian Cerrado plants used in traditional medicine against cancer cell lines", *J Ethnopharmacol*, vol. 123, no. 3, pp. 439-445, 2009.

[16] Santana, J.S., Sartorelli, P., Guadagnin, R.C., Matsuo, A.L., Figueiredo, C.R., Soares, M.G., da Silva, A.M., Lago, J.H. "Essential oils from *Schinus terebinthifolius* leaves–chemical composition and *in vitro* cytotoxicity evaluation", *Pharm Bio*, vol. 50, no. 10, pp. 1248-1253, 2012.

[17] Magalhaes, M.L., Ionta, M., Ferreira, G.A., Campidelli, M.L.L., Caetano, A.R.S., Brandao, R.M., Nelson, D.L., Cardoso, M. "Genotoxic, cytotoxic and fungicidal activity of the essential oil extracted from the leaves and fruits of the pink pepper ("*Schinus terebinthifolius*" Raddi)", *Aust J Crop Sci*, vol. 15, no. 7, pp. 997-1004, 2021.

[18] Alqathama, A., Abdelhady, M.I.S., Al-Omar, M.S., Barghash, M.F., Shallan, A.I. "Antioxidant, Anti-inflammatory and Cytotoxic Activity of Schinus terebinthifolia Fruit and Isolation of a New Immunomodulatory Polyphenolic Compound", *Pharmacogn Mag*, vol. 19, no. 1, pp. 13-22, 2023.

[19] da Silva, M.M., Iriguchi, E.K.K., Kassuya, C.A.L. *et al.* "*Schinus terebinthifolius*: Phenolic constituents and *in vitro* antioxidant, antiproliferative and *in vivo* anti-inflammatory activities", *Rev Bras Farmacogn*, vol. 27, pp. 445-452, 2017.

[20] Reis, M.Y.F.A., Xavier, L.M.A., de Souza, R.M., Ramalho, Í.M.M, Nascimento, Y.M.D., Ferreira, M.D.L., Damasceno, B.P.G.L., Sobral, M.V., Sampaio, F.C. "Pink pepper (*Schinus terebinthifolius* Raddi) essential oil: Phytochemical composition and cytotoxic activity", *Nat Prod Res*, vol. 22, pp. 1-7, 2023.

[21] Matsuo, A.L., Figueiredo, C.R., Arruda, D.C., Pereira, F.V., Scutti, J.A., Massaoka, M.H., Travassos, L.R., Sartorelli, P., Lago, J.H. "α-Pinene isolated from *Schinus terebinthifolius* Raddi (Anacardiaceae) induces apoptosis and confers antimetastatic protection in a melanoma model", *Biochem Biophys Res Commun*, vol. 411, no. 2, pp. 449-454, 2011.

1. El-Nashar, H., Mostafa, N., Hafez, M., Eldahshan, O., Singab, A.N., Singab, B. "Chemical composition, antimicrobial and cytotoxic activities of essential oils from *Schinus terebinthifolius* Raddi growing in Egypt", *Int J Pharmacogn Phytochem Res*, vol. 11, pp. 235-239, 2019.

THIS PAGE OF
TECHNOLOGICA ACTA
INTENTIONALLY LEFT BLANK