

The 8th International Electronic Conference on Medicinal Chemistry (ECMC 2022) 01–30 NOVEMBER 2022 | ONLINE

Cytotoxic activity of *Schinus molle* L. berries and leaves

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Graphical Abstract





Abstract:

Perennial Schinus molle trees are called "Pirul" in Mexico. The bioactive essential oils of this aromatic plant, which is a member of the Anacardiaceae family, have been studied for their potential antibacterial, antifungal, insecticidal, and cytotoxic properties. The plant's principal traditional uses include painkiller, antiseptic, antibacterial, purgative, and diuretic. In the study, the plant, which is generally grown as an ornamental plant on the Mediterranean coasts of Turkey, was evaluated in terms of its cytotoxic properties based on its secondary metabolites. Raw and ripe fruits, together with the plant's leaves, were collected and extracted using different solvents. Both 70% methanol and water extracts of leaves, ripe fruits, and raw fruits were prepared. The 6 different extracts obtained were tested in cell lines of humans' most common cancer types (Du-145 prostate cancer, CaCo-2 colon cancer, and MCF-7 breast cancer). As a result, methanol extracts prepared from the ripe fruits of the plant decreased the viability of three different cancer cells, especially MCF-7 and Du-145 cell lines, at low concentrations below 50%. Especially in the MCF-7 cell line, the viability at 15 µg/mL was calculated as 46.03±1.19%. While the cell line with the most minor effect of the extracts was CaCo-2, the extracts with the most negligible antiproliferative effect were the water extracts of the leaves, raw, and ripe fruits.

Keywords: Anacardiaceae; cytotoxicity; Schinus molle;

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Schinus molle L.

- Schinus molle is a perennial tree
- A genus in the family Anacardiaceae
- They are native to parts of South America but have naturalized and become invasive weeds in many countries.
- It can grow to a height of 15 meters
- Common name:

Pink peppercorns, Pepper tree, California pepper tree, Peppercorn tree, Pepperina, Peruvian pepper tree, Peruvian mastic tree

Kasimala, M. B., & Kasimala, B. B. (2012). A review on Brazilian pepper plant: Schinus molle. *Journal of Atoms and Molecules*, *2*(2), 6. Bvenura, C., & Kambizi, L. (2022). Composition of Phenolic Compounds in South African Schinus molle L. Berries. *Foods*, *11*(10), 1376.



Schinus molle L.

There have been some documented beneficial culinary use for the berries;

- The berries are used whole to flavor syrups and beverages.
- They are often cooked with vegetables or used as a garnish.
- These berries can be used to make pastries and biscuits,

Bvenura, C., & Kambizi, L. (2022). Composition of Phenolic Compounds in South African *Schinus molle* L. Berries. *Foods*, *11*(10), 1376.



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Schinus molle L.

Besides the use of these fruits as food, their medicinal role is also impressive.

The whole berries can be used as antibacterial, antiviral, topical antiseptic, antifungal, antioxidant, anti-inflammatory, anti-tumoural, <u>antispasmodic</u>, analgesic properties, as well as a stimulant and an antidepressant. It has also been used in the treatment of toothache, <u>rheumatism</u>, <u>menstrual</u> <u>disorders</u>, and respiratory and urinary tract infection

do Rosário Martins, M., Arantes, S., Candeias, F., Tinoco, M. T., & Cruz-Morais, J. (2014). Antioxidant, antimicrobial and toxicological properties of Schinus molle L. Essential oils. *Journal of ethnopharmacology*, *151*(1), 485-492.



A wide variety of components have been isolated and identified from this plant, including tannins, triterpenoids, flavonoids, and saponins

S. *molle* fruits essential oils were rich in monoterpene hydrocarbons

The studies demonstrate the antioxidant, anti-inflammatory, and antimicrobial activity of berries. Perhaps these activities are strongly related to the polyphenolic compositions of the leaves' bark, as well as the leaves and berries of the *S. molle* tree.

Eryigit, T., Yildirim, B., Ekici, K., & Çirka, M. (2017). Chemical composition, antimicrobial and antioxidant properties of Schinus molle L. essential oil from Turkey. *Journal of Essential Oil Bearing Plants*, *20*(2), 570-577. Bvenura, C., & Kambizi, L. (2022). Composition of Phenolic Compounds in South African Schinus molle L. Berries. *Foods*, *11*(10), 1376.

Material and Metod

Schinus molle L. Aydın-Didim (August 2021)







Material and Metod



Chemical compositions

Total phenol Total flavonoid HPLC profiling



MTT assay for determination cytotoxic activity

MCF-7 Du-145 Caco-2

Zhishen J, Mengcheng T, Jianming W 1999. The Determination of Flavonoid Contents in Mulberry and Their Scavenging Effects on Superoxide Radicals. Food Chem 64(4): 555-559.

Results

Total Phenol, Total Flavonoid and HPLC profiling

Total phenol/flavonoid content and quantitative determination of chlorogenic acid, caffeic acid, and hyperoside in S. molle extracts (n=3),

Extracts	Total Phenol [mg _{GAE} /g _{extact}]	Total Flavonoid [mg _{CA} /g _{extract}]	Chlorogenic acid (%±SD*)	Caffeic acid (%±SD [*])	Hyperoside (%±SD [*])
S.m L MeOH	231.32±11.10	44.40±2.71	0.325±0.005	ND*	0.057±0.0006
S.m L water	172.00±5.84	40.32±2.37	0.396±0.024	0.006±0.0003	0.068±0.0002
S.m Ripe F MeOH	126.11±13.62	26.02±1.37	2.040±0.172	ND*	ND*
S.m Ripe F water	59.54±2.53	12.99±0.67	0.306±0.011	ND*	ND*
S.m Raw F MeOH	117.70±11.84	20.16±0.39	0.508±0.007	ND*	ND*
S.m Raw F water	63.48±1.57	15.18±3.66	0.209±0.014	ND*	ND*

*ND: Not Detected; *SD: Standard Deviation



HPLC chromatograms, **1**, Standards: (1)Chlorogenic acid, (2)Caffeic acid, (3)Coumaric acid, (4)Ferulic acid, (5)Rutin, (6)Hyperoside, and (7)Rosmarinic acid; 2, Methanol leaf extract; 3, Aqua leaf extract



Cytotoxic effects on MCF-7





Concentration (µg/mL)





Concentration (µg/mL)

RESULTS

	IC50(μg/mL)							
	S,m Ripe F MeOH	S,m Ripe F Water	S,m L MeOH	S,m L Water	S,m Raw F MeOH	S,m Raw F Water		
MCF-7	134,16±18,36	>1000	>500	>1000	7,90± 1,15	>1000		
Du-145	163,39±18,95	>500	113,61 ± 7,58	>500	67,63 ± 3,88	287,57 ± 8,22		
CaCo-2	437,68±5,57	>1000	>1000	>1000	116,58±10,05	>1000		



Conclusions

The leaves, ripe and raw fruits of *Schinus molle* L., were used. The parts of the plant were collected from the Didim. After the parts of the plant were extracted with 70% methanol and water, the total phenol and total flavonoid amounts were determined spectrophotometrically. Qualitative and quantitative analyzes of some phenolic compounds were performed by HPLC.

In addition, all extracts were evaluated for their cytotoxic effects on Du-145 prostate cancer, CaCo-2 colon cancer, and MCF-7 breast cancer cancer cell lines.

As a result, the extracts of the *S. molle* plant grown in Turkey were evaluated in terms of their cytotoxic effects, and preliminary studies were carried out. In the next stages, the possibility of the plant being a potential pharmaceutical product candidate will be evaluated in more detail and new studies will be guided according to the results obtained from the studies.

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Acknowledgments



I would like to thank Erciyes University and my colleagues for their contributions.

