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Research Article

Phytochemical Composition of *Rosa foetida* Essential Oil and Evaluation of Antioxidant and Anti-oral Squamous Cancer Activities

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Abstract

Background: *Rosa foetida* is a popular plant in Iran due to its various medicinal applications.

Objectives: In the present study, the essential oil of *R. foetida* flowers was isolated to identify the chemical composition and evaluate the anti-oral cancer and antioxidant activity of the plant extract.

Methods: The essential oil was extracted using the hydro-distillation method. The GC-MS technique was employed to identify the essential oil composition. The anti-cancer activity of the essential oil against oral squamous cell carcinoma was evaluated using an MTT assay. The antioxidant activity of the hydroalcoholic extract of the plant was evaluated using a DPPH assay.

Results: The essential oil was dominated by heneicosane (27.72%), tricosane (24.30%), and nonadecane (14.75%). In the MTT assay, the essential oil exhibited dose-dependent activity against cell lines of HSC-2, HSC-3, HSC-4, and Ca9-22. The highest anticancer activity of *R. foetida* essential oil was observed against the Ca9-22 cell line with an IC_{50} of 218 µg/mL. The extract of *R. foetida* was rich in phenolics, with a total phenolic content of 164 ± 0.67 mg Gallic acid equivalents (GAE)/g. The extract scavenged the free radical of DPPH with an IC_{50} of 6.54 ± 0.2 µg/mL.

Conclusions: The obtained results revealed an acceptable anti-cancer activity against oral squamous cell lines and potent antioxidant activity for the flowers of *R. foetida*.

Keywords: Antioxidant Activity, Anti-cancer Activity, Heneicosane, Oral Squamous Cell Carcinoma, *Rosa foetida*

1. Background

The rose is one of the most common genera in the Rosaceae family (1). There are more than 120 species of roses distributed worldwide (2, 3). They are usually used as cut or garden flowers for their beauty. In addition, roses have been used in the food, perfume, and cosmetics industries (4, 5), as well as in the pharmaceutical industry for many years (6). So far, medicinal properties such as sedative, anti-stress, hematopoietic, and anti-fever effects have been reported for roses. The plants are useful remedies for stomach, liver, and intestine problems. Additionally, roses have suitable therapeutic functions on the skin, along with inflammatory diseases (4).

Rosa foetida is known as a common species in Iran, particularly distributed in the west, northwest, and center of the country (7). *Rosa foetida* has yellow petals due to the presence of carotenoids in the plant part (8). The *R. foetida* shrub is 80 to 120 centimeters in height and has strong branches that are upright or curved with a strong razor. In Iran, the plant is known by the local names of "Gol-e-Zard," "yellow rose," and "yellow Nastran" (7). In Europe, it is known as the Austrian briar (9). *Rosa foetida* grows wild in the mountains of Kurdistan in Iran. The decoction of plant petals is used

in Iranian traditional medicine to treat stomach aches and as an anti-diarrhea remedy (2, 5). *Rosa foetida* is an efficient drug to treat kidney stones, kidney diseases, and ducts (10, 11). It is also used in the treatment of heart and skin diseases (12).

2. Objectives

In the present study, we focus on the extraction of the essential oil of *R. foetida* and the identification of its chemical composition, as well as the evaluation of the anticancer activity of the plant's essential oil against oral malignancy cell lines using the MTT assay for the first time. Additionally, we evaluate the antioxidant activity of the extract of *R. foetida*.

3. Methods

3.1. Plant Material

The dried flowers of *R. foetida* were purchased from a reputable medicinal plants market in Mashhad. This plant originated from Mahallat, a city in Markazi province located in central Iran.

3.2. Essential Oil Extraction

A total of 150 g of dried flowers of *R. foetida* was extracted by the water distillation method using a Clevenger apparatus for 3 hours. The extraction was repeated four times. The essential oils were combined and kept in a vial. The obtained essential oil was dried over sodium sulfate and then stored in a small glass container in the refrigerator until analysis and biological evaluations (13).

3.3. Analysis of the Essential Oil

The gas chromatographic device Agilent 6890 was used to identify the chemical composition. A BPX5 type column was used. The essential oil was diluted with n-hexane at a ratio of 1 to 10. Then, 1 μL of the solution was injected into the instrument. The sample was injected with a split ratio of 1:35. The oven temperature program was set with an initial temperature of 50°C for 5 minutes, a thermal gradient of 3°C per minute to increase to 240°C, and 15°C per minute to reach 330°C, held for 3 minutes. The injection chamber temperature was 250°C. Helium was the carrier gas with a flow rate of 0.5 mL per minute. The Agilent 5973 was the mass spectrometer with an ionization voltage of 70 eV, using the EI ionization method, and an ionization source temperature of 220°C. The mass scan range was set from 40 to 500 amu. Chemstation software was used. To identify the chemical composition, a comparison of mass spectra fragmentation patterns with those of known compounds from reference books, articles, and information available in the computer library was applied (14, 15).

3.4. Anticancer Activities (MTT Test)

MTT is a colorimetric technique. Due to the ability of living cells to perform oxidative metabolism, the MTT dye is reduced, resulting in a color change from yellow to blue. This test determines the number of living cells (16, 17). In this research, the following cell lines were used to evaluate the anti-human oral squamous cell carcinoma and cytotoxicity effects of the essential oil of *R. foetida* using the MTT method:

(1) Normal cell line: HUVEC.

(2) Human oral squamous cell carcinoma cell lines: HSC-2, HSC-3, HSC-4, and Ca9-22.

Cell viability was calculated using the following equation:

$$Cell\ viability\ (\%) = \frac{Sample\ A.}{Control\ A.} \times 100$$

At least three independent replications were performed for each data set, and the results were presented as mean ± SD. Data statistical analysis was conducted using SPSS software version 19, employing one-way ANOVA and Duncan's test. Significance was considered at the level of $P \leq 0.05$.

3.5. Preparation of Rosa foetida Extract

A total of 40 g of dried flowers of *R. foetida* were immersed in 70% ethanol for 36 hours. After filtering, the extract was concentrated at 45°C under low pressure using a rotary evaporator (Buchi Rotavapor R-114). The concentrated crude extract was then dried on a glass plate at room temperature for 72 hours under a hood. The dried extract was kept in a refrigerator before the antioxidant evaluation.

3.6. Determination of the Amount of Total Phenolic Content

The total phenolic content (TPC) was determined by the Folin-Ciocalteu method with some modifications (16, 17). The TPC was calculated based on the standard curve of Gallic acid (5 - 250 μg/mL). The results were

Table 1. Chemical Composition of the Essential Oil of the Flowers of *Rosa foetida* from Iran [a]

Compound Name	RT Min.	RI [b]	RI [c]	Area (%)	Class of Compound
1. Octane	5.59	801	800	0.35	HC
2. Limonene	16.44	1035	1024	3.10	MH
3. l-Menthol	24.27	1190	1178	0.30	OM
4. Dodecane	24.85	1202	1200	0.31	HC
5. Cumaldehyde	27.64	1260	1238	0.60	OM
6. 3,5-dimethoxytoluene	28.63	1282	1282	0.64	OH
7. Thymol	29.83	1307	1289	1.77	OM
8. Carvacrol	30.21	1316	1296	2.05	OM
9. β-damascenone	33.49	1390	1386	0.35	OM
10. Tetradecane	33.98	1401	1400	0.32	HC
11. Geranyl acetone	36.33	1457	1453	0.49	OM
12. Curcumene-α	37.70	1490	1479	1.07	SH
13. β-bisabolene	38.72	1515	1505	0.45	SH
14. Trans-nerolidol	40.87	1569	1561	1.37	OS
15. Lauric acid	41.18	1577	1565	0.11	FA
16. Heptadecane	45.87	1701	1700	0.71	HC
17. Octadecane	49.43	1801	1800	0.41	HC
18. Nonadecane	52.84	1902	1900	14.75	HC
19. Eicosane	56.08	2001	2000	3.45	HC
20. Heneicosane	59.19	2052	2100	27.72	HC
21. Docosane	62.14	2201	2200	1.31	HC
22. Tricosane	65.00	2252	2300	24.30	HC
23. Tetracosane	67.72	2402	2400	1.85	HC

[a] Area (%) of class of compound: [Hydrocarbons (HC): 75.48; monoterpene hydrocarbons (MH): 3.10; oxygenated monoterpene (OM): 5.56; oxygenated hydrocarbons (OH): 0.64; sesquiterpene hydrocarbons (SH): 1.52; oxygenated sesquiterpene (OS): 1.37; fatty acid (FA): 0.11].

[b] Kovats retention index.

[c] Kovats retention index from the literature.

expressed as mg of Gallic acid equivalents per gram of dried extract (GAE).

3.7. Determination of the Amount of Total Flavonoid Content

The total flavonoid content (TFC) was measured using the aluminum chloride method (18). The TFC was calculated based on the standard curve of rutin (5 - 250 µg/mL). The results were expressed as mg of rutin equivalents per gram of dried extract.

3.8. DPPH Radical Scavenging Activity

The antioxidant activity of the extract was measured based on the scavenging of DPPH, a stable free radical (16, 17). The mean values were calculated using the following equation. Butylated hydroxytoluene (BHT) was used as a positive control.

$$RSA\% = \frac{Ac - As}{Ac} \times 100$$

In this equation, Ac is the absorbance of the control (DPPH solution and solvent), and As is the absorbance of the sample (DPPH solution and extract solution).

4. Results

4.1. Chemical Composition of Essential Oil

Rosa foetida essential oil was pale yellow. A total of 24 components were identified, accounting for 87.78% of the *R. foetida* essential oil. The compounds are listed in Table 1. The major constituents of the oil were heneicosane (27.72%), tricosane (24.30%), and nonadecane (14.75%). *Rosa foetida* oil also contained two phenols, thymol (1.77%) and carvacrol (2.05%), and two alcohols, trans-nerolidol (1.37%) and L-menthol (0.3%).

4.2. Anticancer Activities

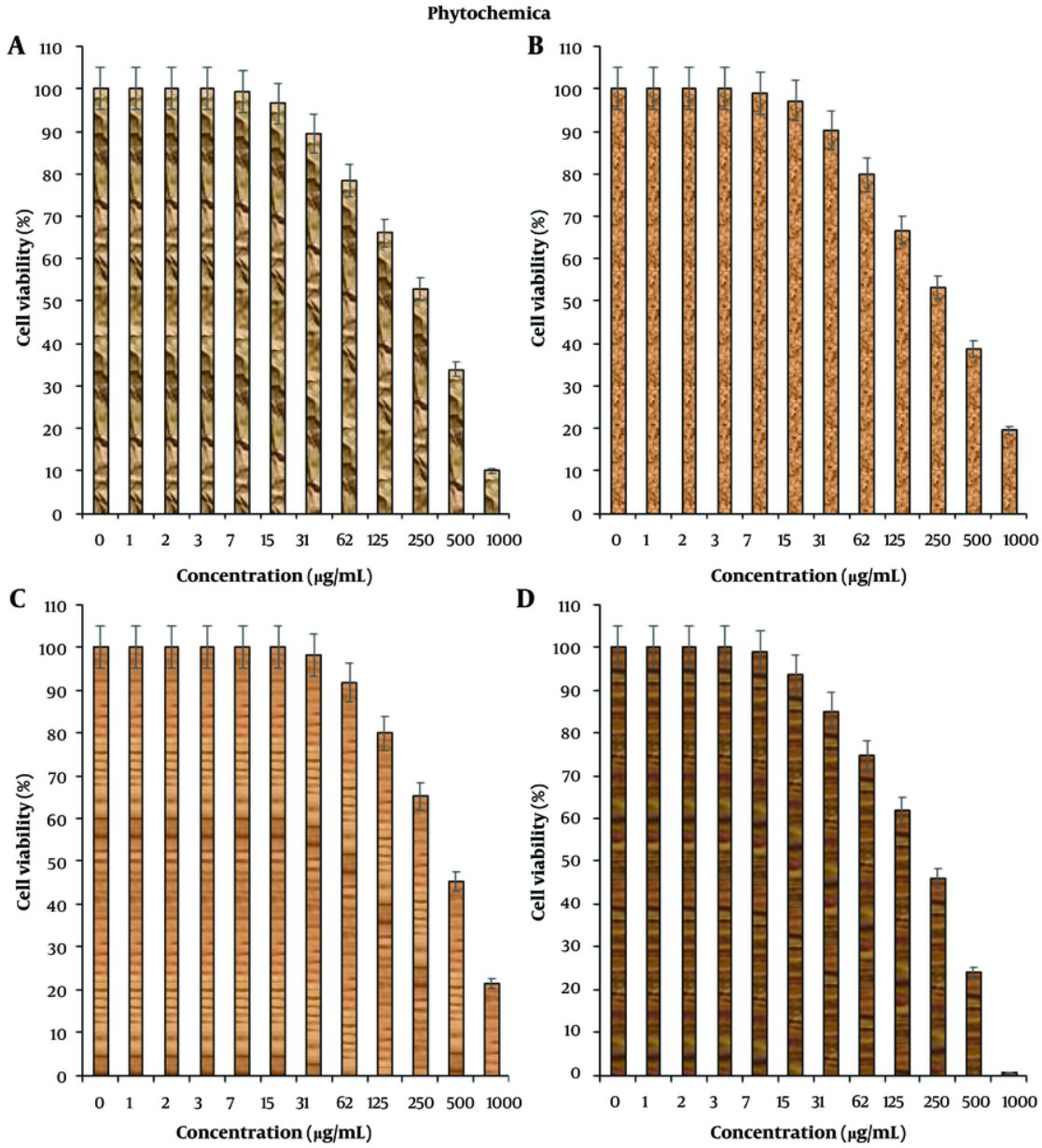

Figure 1. The anti-human oral squamous cell carcinoma properties of essential oil of *Rosa foetida* against HSC-2 (A); HSC-3 (B); HSC-4 (C); and Ca9-22 (D) cell lines

In this study, cells treated with different concentrations of *R. foetida* essential oil were assessed by MTT assay for 48 hours to evaluate the cytotoxicity properties on normal (HUVEC) and human oral malignancy cell lines, including HSC-2, HSC-3, HSC-4, and Ca9-22. The viability of the human oral malignancy cell lines was reduced dose-dependently in the presence of *R. foetida* essential oil. The IC_{50} of *R. foetida* essential oil was 288, 307, 440, and 218 µg/mL against HSC-2, HSC-3, HSC-4, and Ca9-22 cell lines, respectively (Figures 1, 2). The absorbance rate was evaluated at 570 nm, which

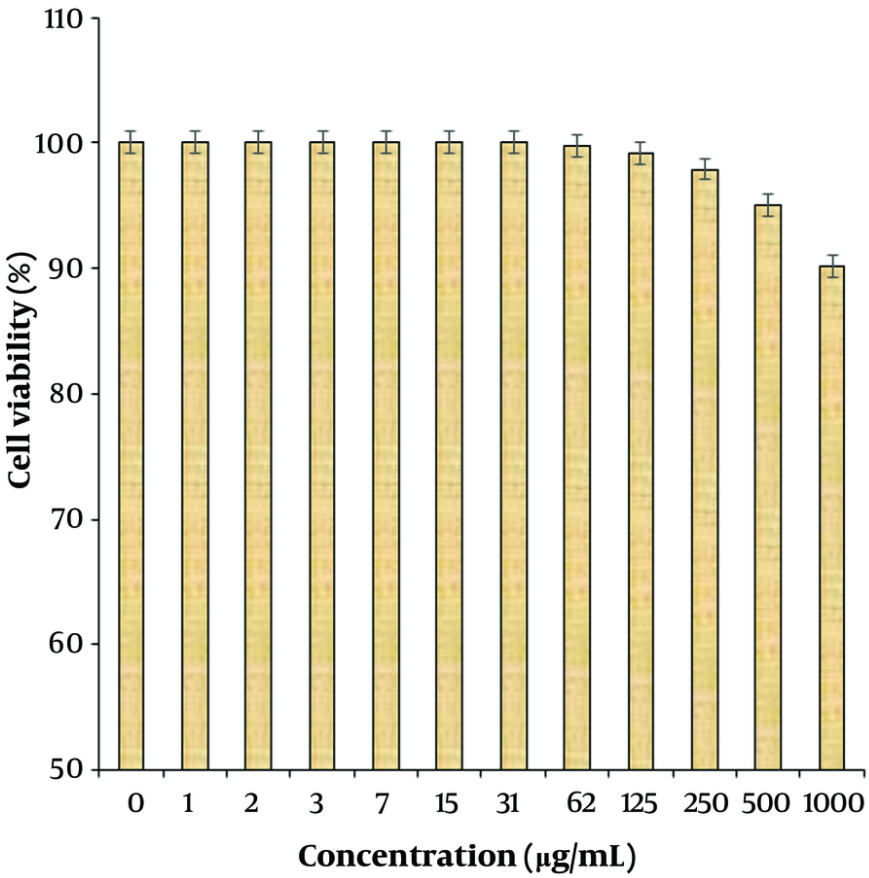

Figure 2. The cytotoxicity effects of essential oil of *Rosa foetida* against normal (HUVEC) cell line

indicated viability on the normal cell line (HUVEC) even up to 1000 µg/mL for *R. foetida* essential oil (Figures 1, 2).

4.3. Antioxidant Evaluation of Rosa foetida Extract

According to the obtained results, 164 ± 0.67 mg GAE/g and 75.5 ± 0.17 mg RU/g were calculated for the TPC and TFC of *R. foetida* extract, respectively. The plant extract scavenged DPPH with an IC_{50} of 6.54 ± 0.2 µg/mL, whereas the IC_{50} of BHT, as the selected standard, was 14.25 ± 1.18 µg/mL.

5. Discussion

5.1. Chemical Composition

So far, the chemical compositions of essential oils from various rose species have been reported. According to the reports, citronellol and geraniol have been identified as the main components of rose essential oils (19-21). These compounds are primarily responsible for the pleasant aroma of rose species. For *R. foetida*, previous research reveals that the major components differ because the flowers of *R. foetida* are odorless (2). Nonadecane, n-heptadecane, and n-dodecanoic acid have been reported as the main compounds of *R. foetida* essential oil from the west of Iran (2). In another study, n-nonadecane, n-heneicosane, 1-hexadecanol, n-tetradecane, and Z-octadecadienoic acid were identified as the main components of the plant's essential oil (22). These results are similar to the major compounds of *R. damascena*, which was dominated by nonadecane, heneicosane, and docosane (23).

5.2. Anticancer Activities

The study of the biological activity of essential oils is one of the intriguing aspects of the field of medicinal plants. Many research groups have evaluated the anticancer and anti-inflammatory activities of essential oils. Essential oils may have antioxidant effects due to their capacity to interfere with mitochondrial function, making them potentially effective anti-tumor agents. Many radical-producing agents are used in the treatment of cancer tumors. In this context, the production of radicals and the toxic or mutagenic side effects that damage healthy tissues can be well controlled (24). Plant extracts as pharmaceutical carriers can address some of the current drug delivery limitations in cancer treatment. It seems that the anti-human oral squamous cell carcinoma effect of recent essential oils is due to their antioxidant effects (25, 26). Recent studies have confirmed that some components play a significant role in anticancer, antioxidant, and anti-inflammatory activities. These components mostly include aromatic ones such as eugenol, thymol, carvacrol, and limonene, suggesting that plants containing these components can exhibit anticancer, antioxidant, and anti-inflammatory activities. Based on the results of the MTT assay and identified components, the anticancer activity of *R. foetida* is likely related to the presence of these components in the essential oil (27-29).

5.3. Antioxidant Activities

Phenolic compounds are known as one of the most important groups of natural compounds found in plants. These compounds have several health-promoting effects, such as anti-platelet aggregation, anti-tumor activity, protection against pathogens, and inhibition of certain processes (18, 30). Shameh et al. evaluated the TPC of six different species of rose in Iran, including *R. canina*, *R. moscata*, *R. damascena*, *R. webbiana*, and *R. hemisphaerica* (31). According to the reported results, the TPC of *R. foetida* was higher than that of *R. damascena* and *R. webbiana* (32, 33). However, *R. canina* and *R. pimpinellifolia* were rich in TPC (1).

Flavonoids are widely distributed in the plant kingdom worldwide and are perhaps the most important natural phenols (18). Previous studies have reported the presence of flavonoids in rose species. According to reported results, the TFC from *R. moscata* was higher than that of *R. foetida* based on the quercetin standard curve (31). On the other hand, *R. damascena* was poorer than *R. foetida* in TFC (33). Zheng et al. reported the TFC of five edible rose flowers in China, namely *R. centifolia*, *R. chinensis*, *R. gallica*, *R. rugosa*, and *R. rugosa*, with less TFC in comparison to *R. foetida* (30).

The evaluation of radical scavenging activity (RSA) is one of the most common methods to measure the antioxidant properties of plant extracts. By oxidizing, antioxidants eliminate free radical mediators and prevent other radical reactions. Plants with richer antioxidant compounds can protect cells from oxidative damage (34, 35). Previous studies have reported the RSA of different rose species. *R. canina*, *R. pimpinellifolia*, and *R. damascena* were more potent than *R. foetida* (1, 35). However, *R. damascena*, *R. rugosa*, *R. centifolia*, *R. chinensis*, *R. gallica*, and *R. rugosa* were weaker in comparison to *R. foetida* (32, 36).

5.4. Conclusion

In recent years, herbal medicine as an effective remedy to treat various diseases has gained more attention worldwide. The high side effects of chemical drugs may be the most important reason for this increased interest in medicinal plants. In the present research, we have reported the chemical compositions of *R. foetida*, a popular plant in the Middle East. The essential oil of the plant flowers was rich in heneicosane, tricosane, and nonadecane. The viability of oral squamous cancer cell lines was reduced dose-dependently in the presence of *R. foetida* essential oil. Conversely, the essential oil did not show any toxicity against the normal cell line of HUVEC. The plant extract demonstrated high antioxidant activity by scavenging the free radical DPPH. The results revealed that *R. foetida* can be considered a potent antioxidant and anticancer agent for treating oral squamous cancer; however, more experiments, including in vivo assays, should be conducted.

Footnotes

Authors' Contribution: Study concept and design: M. R. and A. Z.; Analysis and interpretation of data: B. M. and M. Z.; Drafting of the manuscript: M. R. and B. M.; Critical revision of the manuscript for important intellectual content: B. M., A. H., and M. Z.; Statistical analysis: M. R. and A. Z.

Conflict of Interests Statement: The authors declare that they have no conflict of interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

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