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SHORT COMMUNICATION

Phytochemical compounds and antiradical, antimicrobial, and cytotoxic activities of the extracts from *Hypericum scabrum* L. Flowers

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ABSTRACT

Hypericum scabrum L. has been widely used in traditional medicine for the treatment of many diseases just as the other *Hypericum* species. In the present study, the antiradical, antimicrobial and cytotoxic activities of water and ethanol extracts of *H. scabrum* flowers were investigated. Their phytochemical contents and composition were also determined. The water and ethanol extracts are better scavenged ABTS (97.89 and 98.99%) and OH radicals (96.36 and 97.33%); the water extract is better scavenged DPPH radicals (91.66%) than the standard antioxidant BHA (94.33, 85.19, 90.16%, respectively). Flowers of *H. scabrum* contain flavonoids, phenolic acids, vitamins and phytosterols, dominated by catechin, vanillic acid, vitamin K and ergosterol. The extracts exhibit a strong cytotoxic activity against MCF-7, HCT-116, and LNCaP cancer cell lines. It is found that their antimicrobial activities are higher than the standard antibiotics. These results indicate that *H. scabrum* flowers have potent antiradical, antimicrobial and cytotoxic activities.

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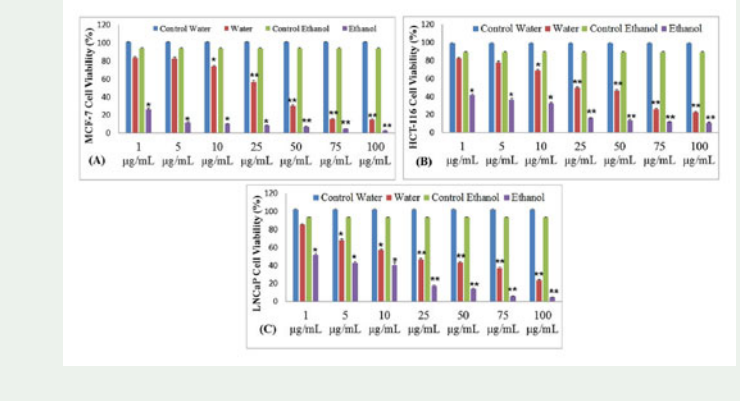

1. Introduction

There are 484 species of *Hypericum* worldwide, belonging to Hyperiaceae family, and 96 species (46 are endemic) grow in Turkey. In Turkish, these species are named as "kantaron, peygamber çiçeği, mayasıl otu, binbirdelik otu, kan otu, kılıç otu, yara otu and kuzukıran". *Hypericum* species have antimicrobial, antifungal, antioxidant, antiviral, antidepressant, anticonvulsant, antiseptic, antidiarrhea, antihemorrhoid and antieczema properties (Baytop, 1999; Crockett and Robson, 2011; Cirak and Kurt, 2014; Simonetti et al. 2016; Tahir et al. 2017).

Hypericum scabrum L. is a perennial herbaceous plant grown in dry rocky slopes in Turkey. This plant has been used in the treatment of hepatitis, cystitis, chronic gastritis, ulcer, wounds, hemorrhoids and constipation. It has been reported that it possesses antispasmodic, anti-inflammatory, sedative and antidepressant properties (Serbetci, 2002; Kizil et al. 2004; Ayan et al. 2009).

The determination of antiradical, antimicrobial and cytotoxic activity on plants has gained great demand. In recent years, because of the formation of antibiotic resistant bacteria or germs and unwanted side effects of the synthetic drugs, the researchers have preferred to investigate these natural drugs. Phytochemicals such as, vitamins, sterols, fatty acids, proanthocyanidins, carotenoids, flavonoids, phenolic compounds etc., which found in plants and known to have antioxidant properties, may help to reduce the cancer risk. The plant derived natural drugs including the phytochemical compounds have fewer side effects than synthetic antimicrobial and anticancer drugs. Therefore, the investigation of phytochemical and pharmacological properties of the plant-derived natural products gains very big importance (Pandey and Madhuri, 2009; Modi et al. 2012).

The aim of this study is to determine the phytochemical, antiradical, antimicrobial and cytotoxic properties of water and ethanol extracts of *H. scabrum* flowers.

2. Results and discussion

2.1. Antiradical activities

The antiradical activities of *H. scabrum* flower extracts are presented in Table S1. The water and ethanol extracts of *H. scabrum* (97.89, 98.99, 96.36 and 97.33%) are

exhibited higher ABTS and OH radical scavenging activities than the standard antioxidant BHA (94.33 and 85.19%), respectively. In the DPPH radical scavenging assay, BHA (90.16%) showed stronger activity than the ethanol extract (82.40%). The activity of the water extract (91.66%) was comparable to that of BHA. Ghasemi Pirbalouti et al. (2014) reported that the essential oils of *H. scabrum* flowers scavenged the DPPH radicals. The hydroalcoholic extract of *H. scabrum* seeds displayed 36.1% scavenging of DPPH radicals by Dadkhah et al. (2014). Our results (water: 91.66%; ethanol: 82.40%) are greater than that of the as-mentioned result. Leaves, seeds and flowers hexane extracts of *H. scabrum* had lower DPPH radical scavenging than standard antioxidants (Shafaghat, 2011; Shafaghat, 2012). Baris et al. (2011) reported that the scavenging activities of *H. scabrum* aerial parts (stems, leaves, flowers) ethanol extracts were found to be 90% for DPPH and 77% for OH. Our results are higher than the as-mentioned study because we have determined this value as 82.40% for DPPH and 97.33% for OH. Compared to findings of this study, the lower values reported in the previous studies might be due to the differences in plant parts studied and in solvents used for extraction.

2.2. Phytochemical study

The total contents of flavonoids, proanthocyanidins and phenolics of *H. scabrum* extracts are summarized in Table S1. Based on the results, significantly higher values were observed in the ethanol extract (5.913 mg CE/g extract, 1.916 mg CE/g extract and 137.53 mg GAE/g extract) than the water extract (5.063 mg CE/g extract, 1.610 mg CE/g extract and 117.57 mg GAE/g extract), respectively. It can be seen that *H. scabrum* flowers contain high amounts of flavonoids, proanthocyanidin and phenolics. Baris et al. (2011) determined that there was 262 μg GAE/mg extract of the total phenolic compounds in the ethanol extracts of *H. scabrum* aerial parts (stems, leaves, flowers). Dadkhah et al. (2014) reported that the hydroalcoholic extract of *H. scabrum* seeds contained 30.8 mg QE/g of total flavonoids.

Based on chromatographic analyses, the composition of flavonoids and phenolic acids in *H. scabrum* flowers is shown in Table S2. Morin, quercetin, kaempferol and catechin were detected as the flavonoids, and the catechin (28.65 μg/g) was the major component. As the phenolic acids, vanillic, hydroxycinnamic, caffeic, ferulic and rosmarinic acids were detected. Vanillic acid (134.25 μg/g) was the dominant component. Similar to our results, Ayan et al. (2009) showed that ethanol extracts of *H. scabrum* flowers contained rutin (0.749 mg/g), kaempferol (0.649 mg/g) and quercetin (0.672 mg/g).

The composition of vitamins, phytosterols and fatty acids in *H. scabrum* flowers is presented in Table S2. The detected vitamins were retinol (0.05×10^{-3} mg/g), δ-tocopherol (0.05×10^{-3} mg/g), vitamin D (0.75×10^{-3} mg/g) and vitamin K (3.55×10^{-3} mg/g). β-sitosterol (0.35×10^{-3} mg/g), ergosterol (95.1×10^{-3} mg/g) and stigmasterol (3.75×10^{-3} mg/g) were detected as the phytosterols. The fatty acids are found to 28.53% palmitic acid (16:0), 32.20% palmitoleic acid (16:1), 10.76% stearic acid (18:0), 9.12% oleic acid (18:1), 16.59% linoleic acid (18:2), 2.80% linolenic acid (18:3), 39.29% total saturated fatty acids, and 60.71% total unsaturated fatty acids. The saturated and unsaturated fatty acid contents of hexane extracts of *H. scabrum* flowers are found to be as 18.6 and 48.9%,

respectively (Shafaghat, 2011). Hexane extracts of *H. scabrum* leaves contained 21.3% of saturated and 53.3% of unsaturated fatty acids (Shafaghat, 2012). Ozen and Bashan (2003) showed that *H. scabrum* flowers were contained 5.06% palmitic acid (16:0), 2.36% stearic acid (18:0), 11.45% oleic acid (18:1), 32.53% linoleic acid (18:2) and 48.60% linolenic acid (18:3). In the light of these results, it is understood that *H. scabrum* is very rich in point of unsaturated fatty acids.

2.3. Antimicrobial activities

The antimicrobial activities of *H. scabrum* flower extracts are summarized in Table S3. All the water and ethanol extracts inhibite the growth of *Escherichia coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Listeria monocytogenes*, *Klebsiella pneumonia*, *Bacillus subtilis*, *Bacillus megaterium*, *Staphylococcus aureus* and *Candida albicans*. All the extracts showed stronger antimicrobial activities than standard antibiotics (streptomycin sulfate and nystatin). *H. scabrum* extracts inhibit the growth of *B. cereus*, *L. monocytogenes*, *P. aeruginosa* and *Salmonella typhimurium* (Ghasemi Pirbalouti et al. 2014); *B. subtilis*, *Enterococcus faecalis*, *S. aureus*, *S. epidermidis*, *E. coli*, *P. aeruginosa*, *C. albicans*, *Saccharomyces cerevisiae* and *Aspergillus niger* (Shafaghat, 2012); *B. subtilis* and *S. epidermidis* (Shafaghat, 2011); *E. coli*, *S. aureus*, *P. aeruginosa* and *B. cereus* (Ghasemi Pirbalouti et al. 2011); *K. pneumonia*, *Enterobacter cloacae*, *Salmonella typhimurium*, S. *epidermidis*, *E. coli*, *Enterobacter aerogenes*, *S. aureus*, *K. oxytoca*, *Streptococcus pyogenes*, *P. aeruginosa*, *C. albicans* (Baris et al. 2011); *E. coli*, *B. cereus*, *B. brevis*, *Streptococcus pyogenes*, *P. aeruginosa*, *S. aureus* and *C. albicans* (Kizil et al. 2004); and *B. cereus*, *S. aureus*, *Clostridium perfringens* and *C. albicans* (Sokmen et al. 1999). It can be seen that *H. scabrum* has antimicrobial effect against many microorganisms.

2.4. Cytotoxic activities

The cytotoxic activities of *H. scabrum* flower extracts are shown in Figure S1. It was observed that the water extract at 10, 25, 50, 75 and 100 μg/mL concentrations significantly decreased the viability of MCF-7 and HCT-116 cancer cell lines after 24 hours; the same extract at 5, 10, 25, 50, 75 and 100 μg/mL concentrations significantly decreased the viability of LNCaP cancer cell lines after 24 hours. The ethanol extract at concentrations of 1, 5, 10, 25, 50, 75 and 100 μg/mL significantly decreased the viability of all three cancer cell lines. IC_{50} values of the extracts are presented in Table S4. Docetaxel, which is a semi synthetic toxoid compound produced from the needles of the European yew tree, and is the first chemotherapy agent, was used as positive control for these cancer cell lines. The cytotoxicity values of the ethanol extract (0.53, 1.79 and 3.32 μg/mL) against MCF-7, HCT-116 and LNCaP cancer cell lines are stronger than the water extract (23.03, 26.82 and 22.92 μg/mL). Naghibi et al. (2014) indicated that *H. scabrum* methanol extract showed the cytotoxic effect since its IC_{50} values against to the MCF-7 and HT-29 (colorectal carcinoma) cell lines were found to 54.6 μg/mL and 46.4 μg/mL, respectively. Hamzeloo-Moghdam et al. (2015) determined that the dichloromethane (DCM) and petroleum ether (PE) fractions of *H. scabrum* methanol extract were displayed cytotoxic activity because their IC_{50} values against

the MCF-7, A-549 (non-small-cell lung carcinoma), HT-29 and HepG-2 (hepatocellular carcinoma) cell lines were found to 43.89, 31.34, 25.72 and 24.73 μg/mL and PE fractions were determined to 11.87, 17.31, 22.6 and 18.31 μg/mL, respectively. It can be said that the *H. scabrum* flowers have significantly cytotoxic activities against these cancer cell lines.

3. Conclusions

The present study intended to assess the antiradical activities (ABTS, DPPH and OH radicals), phytochemical contents (total phenolic compounds, total flavonoids, total proanthocyanidin, flavonoids, phenolic acids, levels of lipid soluble vitamins, fatty acids and phytosterols), antimicrobial activities (*B. megaterium*, *B. subtilis*, *E. coli*, *P. aeruginosa*, *L. monocytogenes*, *K. pneumonia*, *P. vulgaris*, *S. aureus*, *C. albicans* microorganisms) and cytotoxic activities (MCF-7, HCT-116 and LNCaP cancer cell lines) of the *H. scabrum* flowers water and ethanol extracts. The as obtained results of this study indicate that *H. scabrum* flowers have great antiradical, antimicrobial and cytotoxic activities against to all the above-mentioned radicals, microorganisms and cancer cell lines. For this reason it can be said that this plant may be used for pharmacological purposes due to its high antiradical, antimicrobial and cytotoxic properties.

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