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Exploring the Antiradical Potential of Lamiaceae Family Species: Implications for Functional Food Development in Neurodegenerative and Neuropsychiatric Diseases Context†

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Abstract: Neurodegenerative and neuropsychiatric diseases have become highly significant in Western societies. Unfortunately, these diseases currently lack a cure, and existing treatments merely manage the symptoms. Thus, it is imperative to explore new alternatives for either preventing these disorders or treating them effectively. One promising avenue for prevention lies in the development of neuroprotective and antioxidant functional foods. To this end, a study focused on ten species from the Lamiaceae Family, which have gained attention due to their well-known antioxidant, anti-inflammatory, anti-obesity, and anti-cancer properties, among others. The interest in their pharmacological applications has grown significantly in recent years. In order to uncover the biological potential of these species, the study involved performing decoctions and evaluating both the total phenolic content (TPC) and antiradical activity. The results revealed that TPC values ranged from 59.97±6.18 (*Ocimum basilicum* L. var *minimum*) to 374.0±16.9 (*Salvia officinalis* L.) mg gallic acid equivalents (GAE)/g of dry extract (dw). Additionally, the IC_{50} values for $DPPH^{\bullet}$ and $ABTS^{\bullet+}$ scavenging activities varied between 21.55±1.18 (*Origanum vulgare* L.) and 132.0±15.3 μg/mL (*O. basilicum* var *minimum*), and from 14.79±0.50 (*O. vulgare*) to 44.65±2.34 μg/mL (*O. basilicum*), respectively. The observed strong antiradical activity holds great promise for the future development of functional foods aimed at combating the oxidative stress implicated in these diseases and promoting overall brain health. By harnessing the potential of these Lamiaceae Family species, we may pave the way for innovative approaches to tackle neurodegenerative and neuropsychiatric conditions.

Keywords: Lamiaceae Family; Brain disorders; Functional foods; Oxidative stress

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1. Introduction

Oxidative stress is characterized by the imbalance between reactive oxygen species (ROS) and antioxidant defense mechanisms, and is a major contributor to the pathogenesis of several disorders [1] including cardiovascular diseases [2], diabetes [3], neurodegenerative and neuropsychiatric diseases [4,5], and cancer [6]. Consumption of

nutraceuticals and functional foods rich in antioxidants is a suitable strategy to delay the progression of these chronic disorders, since dietary supplementation will boost the antioxidant status of the body, enabling to reduce the production of oxidative stress biomarkers [7]. Antioxidants are, therefore, highly demanded for nutraceutical and functional food products development companies. Compared with synthetic antioxidants, such as butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA), natural antioxidants offer great advantages since they are considered safer and are also economically and easily available. They can be extracted from different natural matrices, such as edible vegetables, aromatic plants, fruits, seeds, agri-food by-products, algae, etc. [8,9].

Lamiaceae Family, commonly known as Mint Family, is composed by 236 genera and around 6900 to 7200 species with a worldwide distribution [10]. Several species are known for their pharmacological potential that results from a wide range of secondary metabolites produced, mainly flavonoids, phenolic acids, and terpenoids [10]. Amongst the bioactive properties reported, antioxidant, anti-inflammatory, antimicrobial and neuroprotective properties are the most studied ones [10,11].

The aim of this study was to valorize 10 Lamiaceae species belonging to *Lavandula*, *Mentha*, *Ocimum*, *Origanum*, *Rosmarinus, Salvia* and *Thymu*s genera, by assessing their antioxidant activity and possible utilization in the design of functional food products for neurodegeneration and neuropsychiatric prevention.

2. Material and methods

2.1. Plant species

Ten different species from Lamiaceae Family were purchased from an herbal store (Ervanário Portuense, Portugal, https://www.ervanarioportuense.pt), namely, *Lavandula angustifolia* Miller (inflorescences; Lot 10.ALF.109.22.02), *Mentha piperita* L. (leaves and stems; Lot 07.HOR.51102.21.11S), *Mentha pulegium* L. (flowering aerial parts; Lot 02.POE.117J.22.2S), *Ocimum basilicum* L. (leaves; Lot 10.BAS.109.21.03), *Ocimum basilicum* var. *minimum* L. (leaves and stems; Lot 10.MNJ.660.14.1C), *Origanum majorana* L. (leaves; Lot 1402TR), *Origanum vulgaris* L. (leaves; Lot 11.ORE.1078.20.01), *Rosmarinus officinalis* L. (leaves; Lot 11.ALE.117.22.01), *Salvia officinalis* L. (leaves and stems; Lot 1922ALS), *Thymus vulgaris* L. (leaves and stems; Lot 12.TOM.117.22.01). All plant materials were powdered to a mean particle <1000 μm and stored at room temperature before use.

2.2. Extraction procedure

Decoctions were prepared by boiling 0.5 g of each powdered plant material into 125 mL of water, for 10 minutes, to simulate the traditional usage of these plant species. After this step, extracts were filtered and lyophilized.

2.3. Determination of Total Phenolic Compounds (TPC)

A spectrophotometric assay based on Folin-Ciocalteu reagent [12] was employed to determine TPC values of each extract, and calibration curves were performed using gallic acid. The formation of the blue complex was monitored at 760 nm in a microplate reader (Synergy HT, Biotek Instruments). Results were expressed as mg gallic acid equivalents (GAE) / g of extract dried weight (dw). Three independent assays were performed.

2.4. Antiradical acitvity

The antiradical capacity was assessed against two radicals, namely, $DPPH^{\bullet}$ and $ABTS^{\bullet+}$, according to well-established procedures [12]. Absorbances were monitored in a microplate reader (Synergy HT, Biotek Instruments) at 517 and 734 nm, respectively. Each sample was tested in triplicate and results are expressed as IC_{50} values.

2.5. Statistical Analysis

For both TPC values and antiradical activities, samples were compared using one-way analysis of variance (ANOVA) followed by the Tuckey's test. P-Values less than 0.05 were considered statistically significant. Pearson correlation between TPC and bio-activities was also performed. All statistical analyses were carried out with GraphPad Prism, version 8.0.1.

3. Results and Discussion

Table 1 displays the TPC values determined for the ten decoctions tested, ranging from 59.97 and 374.0 mg GAE/g extract dw. Among all samples, S. officinalis stout out for its highest content of phenolic compounds (374.0 mg GAE/g extract dw), followed by R. officinalis (195.1 mg GAE/g extract dw), Mentha species (188.9 and 140.4 mg GAE/g extract dw) and Origanum species (156.6 and 118.6 mg GAE/g extract dw). Brezoiu et al. [13] reported a TPC value for S. officinalis hydroethanolic (ethanol/water = 4/1 v/v) extract lower than the one shown in Table 1 (181.11 mg GAE/g extract dw) which may be related to the different solvent used for the extraction procedure. Indeed, Schnitzler et al. [14] compared different extraction solvents to extract phenolic compounds from S. officinalis and concluded that water achieved better results than all the tested ethanol-water mixtures. Concerning Mentha species, TPC values of 17.00 mg GAE/g dw (for M. pulegium) and 31.40 mg GAE/g dw (for M. piperita) were obtained for 80% aqueous methanolic extracts [15], while for an aqueous extract of M. piperita the value recorded was 230.8 mg GAE/g [16]. Yan et al. [17] determined the TPC values for 42 O. vulgare samples belonging to 5 subspecies from an oregano plant collection of the German National Genebank and obtained values between 79.5 mg GAE/g dw and 147.3 mg GAE/g dw for their 80% (v/v) hydromethanolic ultrasound-assisted extracts. Results obtained for O. majorana are better than those previously reported for an aqueous extract (9.2 mg GAE/g) [18], while the ones found for R. officinalis are in aggrement with those described before [19].

Table 1. Total Phenolic Content (TPC), DPPH$^{\bullet}$ and ABTS$^{\bullet+}$ scavenging activities of the ten decoctions.

Species	TPC (mg GAE/g dw)	DPPH$^{\bullet}$ scavenging activity (IC_{50}, μg/mL)	ABTS$^{\bullet+}$ scavenging activity (IC_{50}, μg/mL)
Lavandula angustifolia Miller	94.97±11.82^{e}	42.66±0.98^{c,d}	36.36±1.71^{b}
Mentha piperita L.	188.9±6.5^{b}	34.52±3.76^{c,d}	28.17±2.52^{c}
Mentha pulegium L.	140.4±4.1^{c,d}	43.31±1.90^{c}	25.15±2.74^{c}
Ocimum basilicum L.	68.32±8.92^{e,f}	40.41±1.57^{c,d}	44.65±2.34^{a}
Ocimum basilicum var *minimum* L.	59.97±6.18^{f}	132.0±15.3^{a}	37.45±1.12^{b}
Origanum majorana L.	118.6±14.4^{d,e}	54.71±17.13^{b}	24.83±0.80^{c}
Origanum vulgare L.	156.6±9.2^{c}	21.55±1.18^{d}	14.79±0.50^{d}
Rosmarinus officinalis L.	195.1±18.3^{b}	25.78±1.13^{c,d}	19.06±0.57^{d}
Salvia officinalis L.	374.0±16.9^{a}	29.64±1.71^{c,d}	28.04±0.39^{c}
Thymus vulgaris L.	70.96±4.24^{e,f}	43.77±0.36^{c}	28.50±0.91^{c}

Results are expressed as mean ± standard deviation of three assays (n=3). In each column, different superscript letters mean statistically significant differences at $p< 0.05$.

Concerning DPPH$^{\bullet}$ scavenging activity, all plant extracts were active, displaying IC_{50} values in the range of 21.55 μg/mL (*O. vulgare*) and 132.0 μg/mL (*O. basilicum* var. *minimum*), with the order of potency being: *O. vulgare* ≈ *R. officinalis* ≈ *S. officinalis* ≈ *M. piperita* ≈ *O. basilicum* ≈ *L. angustifolia* ≈ *M. pulegium* ≈ *T. vulgaris* > *O. majorana* > *O. basilicum* var *minimum*. Except for the study published by Dorman et al. [16] in which the reported IC_{50} values of the aqueous extracts against DPPH$^{\bullet}$ were higher (e.g., 335.0 μg/mL for *O. vulgare*, 236.5 μg/mL for *R. officinalis*, 265.8 μg/mL for *S. officinalis*, 382.4 μg/mL for *T. vulgaris*, and c.a. 150 μg/mL for *M. piperita*), all the values reported by other authors for

aqueous and hydroethanolic extracts are in the same range as those presented in Table 1 [15,18,20–24].

The strongest $ABTS^{\bullet+}$ scavenging activity was observed for O. vulgare and R. officinalis, followed by O. majorana ≈ M. pulegium ≈ S. officinalis ≈ M. piperita ≈ T. vulgaris > L. angustifolia ≈ O. basilicum var minimum > O. basilicum (Table 1) and the obtained IC_{50} values are in the same range of those determined by other authors. Mapeka et al. [25] tested different extracts of Lamiaceae species, and the IC_{50} values were as follows: O. majorana (IC_{50} = 5.79 μg/mL), R. officinalis (IC_{50} = 10.56 μg/mL), S. officinalis (IC_{50} = 17.18 μg/mL), M. piperita (IC_{50} = 19.96 μg/mL), T. vulgaris (IC_{50} = 27.48 μg/mL), O. basilicum (IC_{50} = 53.54 μg/mL).

Correlation analysis between TPC and antiradical activity data showed that there is not a strong correlation between chemical composition and bioactivities (r = -0.454 between TPC and $DPPH^{\bullet}$ scavenging activity, r = 0.451 between TPC and $ABTS^{\bullet+}$ scavenging activity, and r = -0.400 between both $DPPH^{\bullet}$ and $ABTS^{\bullet+}$ scavenging activities), meaning that other classes of coumpounds may also contribute to the overall activity.

4. Conclusions

In this study, 10 decoctions prepared from Lamiaceae species were evaluated for their potential antiradical activity. All extracts displayed strong activity, holding great promise for the future development of functional foods designed to combat the oxidative stress implicated in chronic disorders, such as, neurodegenerative and/or neuropsychiatric diseases.

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