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ANTIPROLIFERATIVE ACTIVITY AND CHEMICAL COMPOSITION OF AQUEOUS EXTRACTS AND ESSENTIAL OIL OF INFLORESCENCES OF *LAVANDULA DENTATA* L. AND *LAVANDULA ANGUSTIFOLIA* MILL

ATIVIDADE ANTIPROLIFERATIVA E COMPOSIÇÃO QUÍMICA DE EXTRATOS AQUOSOS E ÓLEO ESSENCIAL DE INFLORESCÊNCIAS DE LAVANDULA DENTATA E LAVANDULA ANGUSTIFÓLIA MILL

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ABSTRACT

The objective of this work was to determine and quantify the phenolic compounds present in extracts of *Lavandula angustifolia* Mill. and *Lavandula dentata* L. essential oils. Additionally, cytotoxicity of extracts and essential oils of these species was evaluated using the *Allium cepa* test. The inflorescences of 10 *L. dentata* and *L. angustifolia* plants were collected, of which aqueous extracts were prepared at concentrations of 5 and 20 g. L^{-1} and the essential oil was extracted. The essential oil was assessed for chemical composition through Gas Chromatography with a flame ionization detector coupled to mass spectrometry. The essential oil was diluted to obtain oil at a concentration of 0.3 %, which was used in the A. cepa test. Despite the variations between species with respect to the compounds found, there were no differences between their effects on the A. cepa test. Infusions in both concentrations and essential oil haven't genotoxicity.

Keywords: cytotoxicity; lavender; phenolic compound; plant extracts.

RESUMO

O objetivo deste trabalho foi determinar e quantificar os compostos fenólicos presentes em extratos de Lavandula angustifolia Mill. e Lavandula dentata L. e seus óleos essenciais. Além disso, a citotoxicidade dos extratos e óleos essenciais dessas espécies foi avaliada pelo teste de Allium cepa. Foram coletadas inflorescências de 10 plantas de L. dentata e L. angustifolia e preparados extratos aquosos nas concentrações de 5 e 20 g. L^{-1} e o óleo essencial foi extraído. O óleo essencial foi avaliado quanto à composição química através de Cromatografia Gasosa com detector de ionização de chama acoplado a espectrometria de massas.

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O óleo essencial foi diluído para concentração de 0,3 %, o qual foi utilizado no teste de A. cepa. Apesar das variações entre as espécies em relação aos compostos encontrados, não houve diferenças entre seus efeitos no teste de A. cepa. As infusões de óleo essencial não apresentam genotoxicidade.

Palavras-chave: *citotoxicidade; lavanda; compostos fenólicos; extratos vegetais.*

INTRODUÇÃO

The genus *Lavandula* includes more than 30 known species, subspecies and varieties (BIASI; DESCHAMPS 2009) belonging to the family Lamiaceae with Mediterranean origin and cultivated as ornamental and medicinal plants (SALEHI *et al.* 2018). Within the genus, the species *Lavandula angustifolia* Mill. and *Lavandula dentata* L. are highly used for their essential oils in perfumery, aromatherapy, cosmetology, physiotherapy, in addition to landscaping, conventional medicine and cooking (LORENZI; SOUZA 2008; BIASI; DESCHAMPS, 2009). The essential oil and extracts are used due to their therapeutic properties, cosmetic products, food manufacturing, insecticidal effects, veterinary products, repellent, allelopathy, acaricidal effect and aromatherapy (MARCHIDAN *et al.*, 2023).

The essential oil extracted from the flowers and branches of both species is clear with a sweet floral aroma (Mori *et al.* 2002). The oil is a sedative to the central nervous system and used to treat insomnia and for relaxation (LEE; LEE 2006), and neuroprotective properties of *Lavandula* species have been attributed to regulate oxidative stress markers (HANCIANU *et al.*, 2013; VAKILI *et al.*, 2014). However, the use of essential oils at high doses may lead to intoxication (LÁSZLÓ 2008), as many unknown chemical compounds may exist that have negative impacts.

Due to the presence of many unknown substances in medicinal plants, studies are required to assess the potential health risk to target organisms when ingested indiscriminately. The *Allium cepa* L. test is a low cost and effect method to evaluate possible toxicity towards cells (TEDESCO; LAUGHINGHOUSE 2012). The present study aimed to determine and quantify the phenolic compounds present in the extracts and essential oil of *L. angustifolia* and *L. dentata*, as well as assess the cytotoxicity of these components using the *A. cepa* test.

MATERIAL AND METHODS

Lavandula dentata and *L. angustifolia* seedlings were cultivated in test field plots in the Plant Science Department at the Federal University of Santa Maria – RS (53° 48’ 42” W and 29° 41’ S) between May 25, 2012 to May 27, 2013. The climate of this region is humid subtropical Cfa, with no defined dry season, and the soil is classified as dystrophic Red Argisol.

Before transplanting the seedlings of each species, a soil analysis was carried out by the UFSM Soil Department at a depth of 0.5 to 20 cm, where the following results were obtained:

pH SMP=5.2; Al^{3+}=2.2 $cmol_c/dm^{-3}$; $H^+ + Al^{3+}$= 10.9 $cmol_c/dm^{-3}$; Ca^{2+}=2.8 $cmol_c/dm^{-3}$ Mg^{2+}=0.9 $cmol_c/dm^{-3}$; P=53.1 mg/dm³; k= 120 mg/dm³ and M.O=1.9%. The acidity correction of the area was performed according to the fertilization and liming recommendation of the RS and SC Soil Chemistry and Fertility Commission (SBCS 2004).

Inflorescences of 10 plants of *L. dentata* and 10 plants of *L. angustifolia* were collected from which aqueous extracts were prepared and the essential oil was extracted. The aqueous extracts were prepared at concentrations of 5 g. L^{-1} (recommended concentration by Cunha, 2009) and 20 g. L^{-1} (higher than recommended concentration) for both species. The preparation was transferred into distilled water and infused for 10 minutes. The extracts were pooled and after reaching room temperature, assessed for the presence of phenolic compounds by HPLC. The eluted extracts were then used in the *Allium cepa* test. Essential oil diluted in ethanol was used to obtain oil at a concentration of 0.3 % for the *A. cepa* test.

Inflorescences were processed using hydrodistillation using the Clevenger apparatus to obtain the essential oil, which was evaluated for chemical composition by gas chromatography with a flame ionization detector (GC-FID) and gas chromatography coupled to mass spectrometry (GC-MS).

GC-FID analysis was carried out using an Agilent Technologies 6890N GC-FID system, equipped with a DB-5 capillary column (30m x 0.25 mm; film thickness 0.25 mm) and connected to a flame ionization detector (FID). The injector and detector temperatures were set to 280°C. The carrier gas was helium, at a flow rate of 1.3 mL/min. The thermal programmer was 50-300°C at a rate of 5°C/min. Samples were processed in duplicate in an identical manner. Component relative concentrations were calculated based on GC peak areas without using correction factors. The injection volume of the *Lavandula* sp. essential oil was 1 µL (BOLIGON *et al.* 2013a).

GC-MS analyses were conducted using an Agilent Technologies AutoSystem XL GC-MS system operating in the EI mode at 70 eV. The system was equipped with a split/splitless injector (250°C) and the transfer line temperature was set at 280°C. Helium served as the carrier gas at a flow rate of 1.5mL/min. Capillary columns utilized included an HP 5MS (30m x 0.25 mm; film thickness 0.25 mm) and an HP Innowax (30m x 0.32mm i.d., film thickness 0.50 mm). The temperature program mirrored that of the GC analyses, with an injected volume of 1 µL of the essential oil.

Identification of the compounds in the essential oil of *L. angustifolia* and *L. dentata* was based on retention index (RI), determined using references of the homologous series of *n*-alkanes, C_7-C_{30}, under identical experimental conditions, comparing with the mass spectra library search (NIST and Wiley) and mass spectra literature data (Adams, 1995). The relative amounts of individual components were calculated based on the GC peak area (FID response). All chemicals used were of analytical grade: methanol, acetic acid, gallic acid, chlorogenic acid, caffeic acid, rosmarinic acid and ellagic acid were purchased from Merck (Darmstadt, Germany). Quercetin, quercitrin, isoquercitrin, rutin, kaempferol, catechin and epicatechin were acquired from Sigma Chemical Co. (St. Louis, MO, USA).

High performance liquid chromatography (HPLC-DAD) was performed with a Shimadzu Prominence Auto Sampler (SIL-20A) HPLC system (Shimadzu, Kyoto, Japan), equipped with Shimadzu LC-20AT reciprocating pumps connected to a DGU 20A5 degasser with a CBM 20A integrator, SPD-M20A diode array detector and LC solution 1.22 SP1 software.

Reverse phase chromatographic analyses were carried out under gradient conditions using a C_{18} column (4.6 mm x 250 mm) packed with 5 µm diameter particles; the mobile phase was water containing 2 % acetic acid (A) and methanol (B), and the composition gradient was: 5 % (B) for 2min; 25 % (B) until 10 min; 40, 50, 60, 70 and 80 % (B) every 10 min; following the method described by Boligon *et al.* (2012) with slight modifications. The aqueous extracts of *L. angustifolia* and *L. dentata* were filtered through a 0.45 µm membrane filter (Millipore) and then degassed by ultrasonic bath prior to use. The extracts were analyzed at a concentration of 5 g/m with a flow rate of 0.8 mL/min and the injection volume was 40 µl. Stock solutions of standards were prepared in the HPLC mobile phase at a concentration range of 0.025 – 0.4 mg/ml for catechin, epicatechin, quercetin, quercitrin, isoquercitrin, kaempferol and rutin, and 0.03 – 0.5 mg/ml for gallic, chlorogenic, caffeic, rosmarinic and ellagic acids. Quantification was carried out by integration of the peaks using the external standard method, at 257 nm for gallic acid, 280 nm for catechin and epicatechin, 325 nm for ellagic acid, rosmarinic acid, chlorogenic acid, caffeic acid and caffeic acid derivative, and 365 nm for quercetin, quercitrin, rutin and kaempferol. The chromatography peaks were confirmed by comparing their retention times with those of reference standards and by DAD spectra (200 to 600 nm). Calibration curves are as follows – gallic acid: $Y = 11894x + 1287.9$ ($r = 0.9997$); chlorogenic acid: $Y = 12571x + 1092.5$ ($r = 0.9993$); caffeic acid: $Y = 12748x + 1240.8$ ($r = 0.9991$); rosmarinic acid: $Y = 13593x + 1278.6$ ($r = 0.9998$); ellagic acid: $Y = 13367x + 1285.4$ ($r = 0.9998$); catechin: $Y = 13058x + 1387.6$ ($r = 0.9999$); epicatechin: $Y = 11678x + 1329.7$ ($r = 0.9990$); rutin: $Y = 12840x + 1197.1$ ($r = 0.9995$); quercetin: $Y = 13680x + 1241.5$ ($r = 0.9997$); isoquercitrin: $Y = 11985x + 1264.9$ ($r = 0.9998$); quercitrin: $Y = 13695x + 1357.4$ ($r = 0.9993$) and kaempferol: $Y = 14257x + 1348.8$ ($r = 0.9999$). All chromatography operations were carried out at room temperature (25°C) and in triplicate.

Limit of detection (LOD) and limit of quantification (LOQ) were calculated based on the standard deviation of the responses and the slope using three independent analytical curves, as defined by Boligon *et al.* (2013b). LOD and LOQ were calculated as 3.3 and 10 σ/S, respectively, where σ is the standard deviation of the response and S is the slope of the calibration curve.

In the *A. cepa* test, the meristematic cells of the rootlets are used to evaluate morphological and cellular structural alterations, as well as to determine the mitotic index. Eight groups of 4 bulbs were placed to root in distilled water, which constituted 8 treatments with 4 replicates each (50 ml per replicate). The treatments were: T1- Negative Control in distilled water; T2- Ethanol; T3- Aqueous extract of *L. angustifolia* by infusion at 5 g. L^{-1}; T4- Aqueous extract of *L. angustifolia* by infusion at 20 g. L^{-1}; T5- Essential oil of *L. angustifolia* 0.3 %; T6- Aqueous extract of *L. dentata* by infusion

at 5 g. L^{-1}; T7- Aqueous extract of *L. dentata* by infusion at 20 g. L^{-1}; T8- Essential oil of *L. dentata* 0.3 %. Of the 8 groups of bulbs, 7 were submitted to treatments for a period of 24 hours and one remained in distilled water to be used as a negative control.

Rootlets with approximately 5 mm were collected and fixed in ethanol:acetic acid (3:1) for 24 hours. Once fixed, these were stored in 70 % ethanol under refrigeration until the slides were prepared. The slides were prepared using the squashing technique (GUERRA; SOUZA 2002) and observed and analyzed under light microscopy at 400X. One thousand cells were counted per bulb, totaling 4,000 cells per group of bulbs for each of the treatments. The mitotic index (MI) was calculated, and the presence of chromosomal alterations was scored. Data were subjected to comparisons using Tukey's test and an overall risk level of 5%.

RESULTS AND DISCUSSION

Determination and quantification of phenolic compounds

the concentration of compounds in the essential oils of both species varied, where α-pinene, camphene, sabinene, γ-terpinene, fenchone, fenchol, camphor and α-terpineol were found at concentrations at least 50 % higher in the essential oil of *L. dentata*. In a study conducted by Masetto *et al.* (2011), 20 components were identified in the essential oil of *L. dentata* inflorescences at different stages of inflorescence development (bud, pre-anthesis/anthesis and senescent flowers), where the major constituents were the hydrocarbonate monoterpenes (α-pinene, β-pinene and limonene) and the oxygenated monoterpenes (1.8-cineole, fenchone, linalor, alpha-fenchol and camphor). The authors attributed the differences to the stages of floral development and the harvest season.

In the essential oil of *L. angustifolia*, the compounds myrcene linalool, borneol, lacandulol, 4-terpineol, hexylbutyrate, verbonone, linalool acetate, lavandulol acetate, geranyl acetate, β-caryophyllene and α-bisabolol were identified. Xiaotian *et al.* (2020) found that the main compounds in the essential oil of *L. angustifolia* in their study were acetate, linalol, caryophyllene, (E)-3,7-dimethylocta-1,3,6-triene, 4-terpineol, lavandulyl acetate, borneol and eucalyptol.

In another study, Machado *et al.* (2013) identified 18 and 21 constituents in the essential oil of *L. angustifolia*, at two different harvest times, and in the two harvests the major compounds of the oil were linalool and linalyl acetate. The differences found in the composition and quantity of the constituents in the same species could stem from genetic and environmental factors.

Cytotoxicity of Lavender extracts and oils with A. cepa test

In this study, the *Allium cepa* test was used to evaluate the cytotoxicity of extracts and the essential oil of *L. angustifolia* and *L. dentata*. The analyzed variables were cell proliferation by the mitotic index and cell alterations in the different treatments analyzed.

The mitotic index of the infusion of *L. angustifolia* at 5 g. L^{-1} differed from the infusion of *L. dentata* 5 g. L^{-1} and from the negative control in distilled water. *L. dentata* at 5 g. L^{-1} also differed from the negative control. In both species, the infusion at a concentration of 20 g. L^{-1} reduced the mitotic index (MI) significantly (Tab. 1).

Table 1 - Means of the mitotic index and chromosomal alterations observed using the *Allium cepa* test in the different treatments with aqueous extracts and essential oils of *Lavandula angustifolia* Mill. and *Lavandula dentata* L., negative control in distilled water.

Treatments	Mitotic Index (%)	Chromosome alterations
T1- Negative control (distilled water)	4.42[a]	2.50 [a]
T2- Ethanol	4.95[a]	4.00 [a]
T3- *L. angustifolia* infusion at 5 g.L^{-1}	4.02[ab]	3.25 [a]
T4- *L. angustifolia* infusion at 20 g.L^{-1}	0.22[b]	2.00 [a]
T5- *L. angustifolia* essential oil at 0.3%	6.10[a]	4.25 [a]
T6- *L. dentata* infusion at 5 g.L^{-1}	0[b]	0 [a]
T7- *L. dentata* infusion at 20 g.L^{-1}	0[b]	0 [a]
T8- *L. dentata* essential oil at 0.3%	4.30[a]	1.25 [a]

Means followed by the same letter do not differ significantly by the Tukey test (p=0.05).

The infusions of *L. dentata* completely inhibited cell proliferation at concentrations of 5 and 20 g. L^{-1}, which may be related to the presence of the following phenolic compounds: gallic acid, catechin, chlorogenic acid, caffeic acid, caffeic acid derivatives, epicatechin, rosmarinic acid, ellagic acid, rutin, isoquercitrin, quercitrin, quercetin and kaempferol (Tab. 2 and Fig. 1). There could have been synergism and/or antagonism among the different phenolic compounds or between them and the remaining substances that were not analyzed.

The essential oil at 0.3 % in both *L. dentata* and *L. angustifolia* did not affect cell proliferation, having no significant difference with the negative control in distilled water (Tab. 1).

The infusions at 5 g. L^{-1} and 20 g. L^{-1} and the essential oil of the two studied species at 0.3 % did not cause significant chromosomal alterations, compared to the negative control in distilled water (Tab. 1).

Many compounds were present in the essential oil of the studied species, but those considered major were 1,8-cineol, linalool and camphor, since the others were found in concentrations below 5 % (Tab. 3).

Even with the variations in the concentration of certain compounds in the essential oil of both species of *Lavandula*, there was no variation in the effect of the essential oil using the *A. cepa* test. However, there is a need for further studies using higher concentrations of essential oil, since our study only evaluated the concentration of 0.3 % of essential oil. In addition, the concentrations of compounds within the extracts used could be very low and not have an effect on the cell cycle and genetic material of *A. cepa.* An analysis of different times of exposure of *A. cepa* roots to treatments is also suggested.

Table 2 - Composition of *Lavandula angustifolia* Chaixex Vill. and *Lavandula dentata L.,* aqueous extract.

Compounds	***Lavandula angustifolia***		***Lavandula dentata***		***LOD***	***LOQ***
	mg.g^{-1}	**%**	**mg.g^{-1}**	**%**	**mg.mL^{-1}**	**mg.mL^{-1}**
Gallic acid	1.65 ± 0.03	0.16	4.93 ± 0.01	0.49	0.018	0.062
Catechin	4.52 ± 0.03	0.45	1.18 ± 0.01	0.11	0.043	0.141
Chlorogenic acid	3.18 ± 0.02	0.31	8.35 ± 0.02	0.83	0.007	0.023
Caffeic acid	15.83 ± 0.01	1.58	15.18 ± 0.03	1.51	0.015	0.049
Caffeic acid derivative*	11.72 ± 0.03	1.17	17.34 ± 0.01	1.73	-	-
Epicatechin	3.05 ± 0.02	0.30	1.69 ± 0.02	0.16	0.023	0.075
Rosmarinic acid	12.94 ± 0.02	1.29	10.58 ± 0.03	1.05	0.009	0.031
Ellagic acid	7.16 ± 0.01	0.71	10.13 ± 0.02	1.01	0.013	0.041
Rutin	1.85 ± 0.03	0.18	0.56 ± 0.01	0.05	0.029	0.095
Isoquercitrin	4.27 ± 0.01	0.42	7.93 ± 0.01	0.79	0.040	0.132
Quercitrin	0.98 ± 0.02	0.09	8.14 ± 0.02	0.81	0.037	0.125
Quercetin	5.36 ± 0.02	0.53	1.26 ± 0.02	0.12	0.008	0.029
Kaempferol	1.25 ± 0.02	0.12	4.59 ± 0.02	0.45	0.021	0.069

*Quantified was caffeic acid. Results are expressed as mean ± S.E. of three determinations.
LOD: limit of detection (µg/ml) and LOQ: limit of quantification (µg/ml).

Figure 1 - High performance liquid chromatography phenolics and flavonoids profile of *Lavandula angustifolia* Mill. (a) and *Lavandula dentata* L. (b) aqueous extracts. Gallic acid (peak 1), catechin (peak 2), chlorogenic acid (peak 3), caffeic acid (peak 4), caffeic acid derivative (peak 5), epicatechin (peak 6), rosmarinic acid (peak 7), ellagic acid (peak 8), rutin (peak 9), isoquercitrin (peak 10), quercitrin (peak 11), quercetin (peak 12) and kaempferol (peak 13).

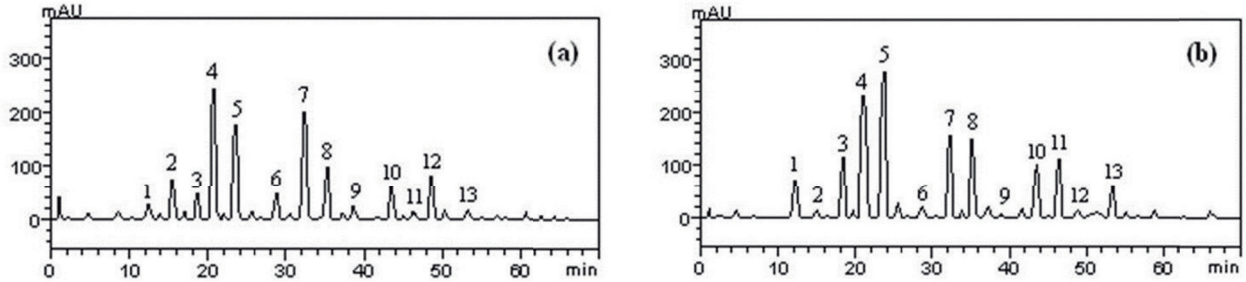

Table 3 - Composition of the essential oils isolated from the species of *Lavandula* (inflorescences of *Lavandula angustifolia* Mill. and *Lavandula dentata* L.).

Compounds	RI[a]	RI[b]	*Lavandula angustifolia*	*Lavandula dentata*
α-Thujene	930	931	0.19	0.12
α-Pinene	939	932	0.65	3.15
Camphene	953	954	0.37	1.10
Sabinene	976	976	0.01	4.17
β-Pinene	980	980	0.84	0.81
Myrcene	991	992	1.47	0.16
Limonene	1031	1030	1.00	1.73
1,8-Cineol	1033	1034	34.05	39.97
β-Ocimene	1040	1041	0.03	-
γ-Terpinene	1062	1062	0.41	1.16
cis-Sabinenehydrate	1068	1070	0.50	0.86
cis-Linalool oxide	1074	1074	0.13	0.32
Fenchone	1087	1085	-	5.63
Terpinolene	1088	1089	0.68	0.41
Linalool	1098	1100	18.07	5.08
Fenchol	1112	1109	0.93	3.64
Camphor	1143	1145	9.25	21.83
Borneol	1165	1166	4.19	0.81
Lavandulol	1167	1181	3.75	0.35
4-Terpineol	1177	1179	3.28	1.27
α-Terpineol	1189	1190	0.96	2.09
Hexylbutyrate	1191	1193	0.31	-
Verbenone	1204	1207	1.09	0.18
Neral	1228	1228	-	-
Linaloolacetate	1257	1253	4.67	0.07
Lavandulylacetate	1289	1289	1.82	0.93
Geranylacetate	1383	1384	3.04	-
β-Caryophyllene	1418	1418	1.43	0.26
Farnesene	1420	1421	0.56	0.45
Germacrene D	1480	1480	-	-
Lavandulylisovalerate	1510	1511	0.75	1.08
Caryophyllene oxide	1581	1581	0.04	0.19
Cadinol	1640	1641	1.26	1.67
α-Bisabolol	1683	1683	2.08	-
Total identified (%)	-	-	97.81	99,49

Relative proportions of the essential oil constituents were expressed as percentages.
[a]Retention indices from literature (Adams, 1995).
[b]Retention indices experimental (based on homologous series of *n*-alkane C_7-C_{30}).

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REFERENCES

ADAMS, R.P. **Identification of essential oil components by Gas Chromatography/Mass spectroscopy.** Allured Publishing Corporation: Illinois USA. 456 p., 1995.

BIASI, L. A., DESCHAMPS, C. **Plantas Aromáticas*:*** do cultivo à produção de óleo essencial. Curitiba: Layer Studio Gráfico e Editora Ltda. 160 p., 2009.

BOLIGON A.A., SAGRILLO M.R., MACHADO, L.F., FILHO, O.S., MACHADO, M.M., DA CRUZ, I.B.M., ATHAYDE, M.L. Protective effects of extracts and flavonoids isolated from *Scutia buxifolia* Reissekagainst chromosome damage in human lymphocytes exposed to hydrogen peroxide. **Molecules**, v. 17, p. 5757-5769, 2012.

BOLIGON, A.A., SCHWANZ, T.G., PIANA, M., BANDEIRA, R.V., FROHLICH, J.K., BRUM, T.F., ZADRA, M., ATHAYDE, M.L. Chemical composition and antioxidant activity of the essential oil of Taberna emontanacatharinensis A. DC. leaves. **Natural Product Research** v. 27, n. 1, p. 68-71, 2013a.

BOLIGON, A.A., KUBIÇA, T.K., MARIO; D.B., BRUM, T.F., PIANA, M., WEIBLEN, R.; LOVATO, L., ALVES, S.H., SANTOS, R.C.V., ALVES, C.F.S., ATHAYDE, M.L. Antimicrobial and antiviral activity-guided fractionation from *Scutia buxifolia* Reissek extracts. **Acta Physiologiae Plantarum** v. 35, p. 2229-2239, 2013b.

CUNHA, A. P. **Plantas aromáticas em Portugal caracterizações e utilizações.** Lisboa: Fundação Calouste Gulbenkian, 328 p., 2009.

DALLA RIVA, A. **Caracterização morfológica e anatômica de *Lavandula dentata* L. e *L. angustifólia* Mill e estudos de viabilidade produtiva na região centro norte, RS.** 2011. 185 p. Dissertação (Mestrado em Agronomia) - Universidade de Passo Fundo, Passo Fundo-, 2011.

GUERRA, M., SOUZA, M. J. **Como observar cromossomos:** um guia de técnicas em citogenética vegetal, animal e humana. São Paulo: Funpec, 131 p., 2002.

HANCIANU, M., CIOANCA, O., MIHASAN, M., HRITCU. L. Neuroprotective effects of inhaled lavender oil on scopolamine-induced dementia via anti-oxidative activities in rats. **Phytomedicine**, v. 20, p. 446-452, 2013.

LEE, I. S., LEE, G. J. Effects of lavender aromatherapy on insomnia and depression in women college students. **Taehan Kanho Hakhoe Chi**, v. 36, n. 1, p. 136-143, 2006.

LORENZI, H., MATOS, E. J. A. **Plantas medicinais do Brasil:** nativas e exóticas. 2. ed. Nova Odessa: Instituto Plantarum de Estudos da Flora. 576 p., 2008.

LORENZI, H., SOUZA, V. C. **Botânica Sistemática:** guia ilustrado para identificação das familias de Fanerógamas nativas e exóticas no Brasil, baseado em APG II. 2. ed. Nova Odessa: Instituto Plantarum de Estudos da Flora. 640 p., 2008.

MACHADO, M. P., CIOTTA, M. N., DESCHAMPS, C., ZANETTE, F., CÔCCO, L. C., BIASI, L. A. Propagação *in vitro* e caracterização química do óleo essencial de *Lavandula angustifolia* cultivada no Sul do Brasil. **Ciência Rural**, v. 43, n. 2, p. 283-289, 2013.

MASETTO, M. A.M., DECHAMPS, C., MÓGOR, A. F., BIZZO, H. R. Teor e composição do óleo essencial de inflorescências e folhas de *Lavandula dentata* L. em diferentes estádios de desenvolvimento floral e épocas de colheita. **Revista Brasileira de Plantas Medicinais**, v. 13, n. 4, p. 413-421, 2011.

MORI, M., IKEDA, N., KATO, Y., MINAMINO, M., WATABE, K. Quality evaluation of essential oils. **Yakugaku Zasshi** , v. 122, n. 3, p. 253-265, 2002.

SALEHI, B., MNAYER, D., ÖZÇELIK, B., ALTIN, G., KASAPOĞLU, K. N., DASKAYA-DIKMEN, C., SHARIFI-RAD, M., SELAMOGLU, Z., ACHARYA, K., SEN, S., MATTHEWS, K.R., FOKOU, P. V. T., SHAROPOV, F., SETZER, W. N., MARTORELL, M., SHARIFI-RAD, J. Plants of the genus Lavandula: from farm to pharmacy. **Natural Product Communications**, v. 13, n. 10, 2018.

TEDESCO, S. B., LAUGHINGHOUSE IV, H. D. **Bioindicator of Genotoxicity:** The *Allium* cepa Test. In: SRIVASTAVA, J. K. Environmental Contamination. Rijeka: Intech Publisher p. 137-156, 2012.

VAKILI, A.; SHARIFAT, S., AKHAVAN, M.M., BANDEGI, A.R. Effect of lavender oil (*Lavandula angustifolia*) on cerebral edema and its possible mechanisms in na experimental model of stroke. **Brain Research**, v. 1548, p. 56-62, 2014.

XIAOTIAN, C., LANYUE, Z., CHENYU, Q., ZHIYUN, D., PENG, X., ZHANGMIN, X. Chemical compositions of essential oil extracted from *Lavandula angustifolia* and its prevention of TPA-induced inflammation. **Microchemical Journal**, v. 153, n. 104458, 2020.