GC-MS analysis Antioxidant, Anti-diabetic study of Volatile alkaloids extract of *Deverra scoparia* (Coss. & Dur.) (Apiaceae)

Amina Benras[*1], Roukia Hammoudi[2], Ibtissam Benyahia[1], Amina Chouh[3,4], Duygu Mısırlı[5], Elyas Kelai[6], Chawki Bensouici[3], Mahfoud Hadj Mahammed[1]

[1]Department of Chemistry, University of Kasdi Merbah, Ouargla, Algeria.

[2]Department of Biological Sciences, University of Kasdi Merbah, Ouargla, Algeria.

Biotechnology Research Center, Ali Mendjli New Town UV 03, B.P E73, Constantine, Algeria.

[4]Department of Biochemistry and Molecular and Cellular Biology, Faculty of Nature and Life Sciences, University of Mentouri Brothers Constantine, Algeria.

[5]Department of Biochemistry, University of Health Sciences, İstanbul, Türkiye.

[6]Technical Platform of Physico-Chemical Analysis (PTAPC – Ouargla). Scientific and Technical Research Center in Physico-Chemical Analyses (CRAPC), BP384, Bou-Ismail, Tipasa, RP 42004, Algeria.

[*]benras.amina@univ-ouargla.dz

Received: 02/2024, Published: 03/2024

Abstract

Background: *Deverra scoparia* Coss&Dur (Apiaceae) is an endemic Algerian plant known widely for its folk medicinal uses.

Objectives: The present research aimed to evaluate the pharmacological properties and chemical constituents of the volatile alkaloid (VA) extract of *D. scoparia*.

Methods: The aerial part of *D. scoparia* was hydro-distilled to obtain the VA extract, followed by fractionation based on different PH mediums, two fractions; diethylic ether (ETV) and dichloromethane (DV). Determination of the alkaloid amount (AA), the characterization analysis with GC-MS, and the in vitro pharmacological properties presented as an anti-oxidant and anti-diabetic assay for the ETV and DV fractions.

Results: The DV showed a high alkaloid amount (AA) concentration 62.89 ±0.05 µg EA/mg with nine (9) alkaloid compounds identified by Gas chromatography-mass spectroscopy GC-MS analysis, while the anti-oxidant potential was assessed via DPPH radical scavenging capacity and β-carotene linoleic acid bleaching assay, which revealed that ETV had a low IC50= 354.24± 2.20 and 67.60± 2.10 µg/ml respectively. Whereas, the anti-diabetic activity based on the inhibition of α-amylase enzyme the DV represented a remarkable inhibition IC50=163.69± 1.41µg/ml.

Conclusions: Due to the works' demonstration of the VA's significant pharmacological potential, future studies can concentrate on isolating alkaloid compounds and examining their pharmacological characteristics in vivo.

Keywords: Volatile alkaloid extract, GC-MS, anti-oxidant, anti-diabetic, alkaloid amount.

Tob Regul Sci.™ 2024;10(1): 1208 - 1221

DOI: doi.org/10.18001/TRS.10.1.76

1. Background

Medicinal plants or traditional medicine is a widely used expression that refers to the classic therapeutic method based on the uses of plants to treat several illnesses in folk ways such as urinary infection, fever, flu, diabetes, and eczema. the pharmacological potential of medicinal plants due to their bioactive compounds like flavonoids, polyphenols, coumarine, terpenes, sterols, and alkaloids[1 2]. Thus, these plants are required as future heed to treat chronic diseases ascribed to their potential such as anti-diabetic and anti-cancer [3,4].

Alkaloids are nitrogen compounds with various functions, and very powerful active ingredients at very small doses, with a very important place among secondary metabolites and form a large group[5,6]. More than 20% of plant species produce alkaloids, which are also one of the most important sources of our medicines because of their pharmacological properties[7–9]. Some of the isolated alkaloids such as morphine, quinine, ergonovine, aconitine, boldine, lobeline, and pilocarpine exhibited several pharmacological properties; analgesic, antimalarial, oxytocic, antiglaucoma facture[10].

Deverra scoparia (Coss. & Dur.) (Apiaceae) is an endemic spontaneous plant used in folk Algerian medicine to treat a various illness such as pains, fevers, hepatitis, diabetes, and asthma[11,12]. This plant grows in most Sahara regions of Algeria[11]. This plant is also used as a spice by the Touareg people. Number research exhibits a variation of chemical compositions of the aerial part extract, and essential oil for *D. scoparia* plant like polyphenols, flavonoids, terpenes, and alkaloids, with various pharmacology activities[11]. To our knowledge, there is no research based on the study of volatile alkaloid extract of *D. scoparia* from the Tamenghest region.

2. Objectives

The present work's purpose was to determine the composition of the volatile alkaloid extract by GC-MS method and evaluate its anti-diabetic and ant-oxidant capacity.

3. Methods

3.1. Plant material

The *Deverra scoparia* Coss. & Dur plant, from Tamanrasset (23° 81' 756″ N, 05° 93' 888″ E) Algeria region, collected in autumn 2019. The Sahara flora [12] in comparison with the herbarium number PM/02 presented at the biogeochemistry of desert environments laboratory is used to identify the study plant. The aerial part of the plant is crushed into small parts after drying and conserved in a dark and dry place at ambient temperature for study.

3.2. Preparation of volatile extract

Radulović2012[13], methods used with some modification a Clevenger material was used to hydro-distill the crushed plant material 500g for four hours. The oil was collected, the hydrolat phase was acidified (0.5N HCl) and extracted with diethelic ether Et_2O. The organic phase was then concentrated and dried over anhydrous MgSO4 to yield a yellowish oily fraction (ETV), while the aquatic phase was treated with NH_4OH (25%) PH= 9 and exhausted with dichloromethane CH_2Cl_2 until negative dragendroff. This resulted in a brownish fraction (DV) after concentrated and dried.

3.3. Quantification of Alkaloids

The alkaloid amount AA in the fractions was measured using the methodology outlined by Shamsa (2008)[14], albeit with a few modifications. 1 ml of phosphate buffer solution (pH 4.7), 1 ml of bromocresol green solution (in a 1:1 (V/V) ratio, and 0.1 ml of each extract are added. The mixture is then vigorously agitated. Following decantation, 4 ml of chloroform is added to correct the volume to the yellow chloroform phase containing the alkaloid content. At 470 nm, the absorbance is measured. The atropine is used as a standard. The alkaloid concentration is reported in µg of atropine equivalent/mg of extract (µg EA/mg of extract).

3.4. GC-MS analysis

The fractions were analyzed with GC/MS analyses carried out by using Hewlett–Packard 6890N GC material, the DB-5MS capillary silica column (30 m, 0.25 mm, 0.25 µm), coupled with a selective mass detector. A 5°C/min heating rate was applied to raise the temperature from 70 to 290°C followed by isotherm for 20min[15]. A concentration of 1 mg/ml for each fraction in Et_2O solvent was prepared to inject 1µl of solution into a column. The identification of compounds was confirmed in comparison with the NIST17 database, mass spectrums, and literature.

3.5. Biological study

3.5.1. DPPH assay

The evaluation of the scavenging capacity of the free radical of VA extract was carried out according to Blois methods[16]. In the microplate (96-well) 160 µl of DPPH (2,2-diphenyl-1–picrylhydrazyl) methanol solution (0.1M) was added to 40 µl of various concentrations of each fraction; DV, and ETV. After 30 min incubation of the mixture on obsecrate at ambient temperature was read at 517 nm by using the microplate reader(Perkin Elmer EnSpire, Singapore). While the BHT, and BHA were used as antioxidant standard and the IC_{50} value was calculated according to the inhibition percentage determined at various fractions concentration (µg/ml).

The inhibition percentage was calculated by the formula:

$$\% \boldsymbol{Inhibition} = (\boldsymbol{A}0 - \boldsymbol{A}F)/\boldsymbol{A}0 \times \mathbf{100} \quad (1)$$

A0: control absorbance

AF: fraction absorbance

3.5.2. B-carotene- Linoleic Acid Bleaching assay

The β-carotene/linoleic acid model system was applied to determine the inhibition potential of β-carotene by D. scoparia VA fractions using the following method[17]. The β-carotene/linoleic acid emulsion was prepared by 0.5 mg of beta-carotene dissolved in 1 mL of chloroform. in a flask with 200 µl tween 40 and 20 µl linoleic acid the previous mixture was added. The vacuum evaporator was used to remove chloroform, and 50 µl of peroxide hydrogen was adjoined. The mixture absorbance was regulated between 0.8 and 0.9 at 470nm.

In the microplate (96 well) 160ul emulsion was added to 40ul of fractions / positive standard with a different concentration. the microplate was incubated for 120 min at 50°C, then the absorbance measured at t=0 and t=120 at 470 nm.

The percentage inhibition expressed by following equation:

$$I\% = 1 - [(AT0 - AHt)/(AC0 - ACt)] \times 100$$

I (%): percentage of inhibition

AF0: β-carotene Absorbance on fraction at t = 0.

AC0: β-carotene Absorbance on negative control at t = 0.

AFt: β-carotene Absorbance on fraction at 120 min.

ACt: β-carotene Absorbance on negative control at 120 min.

3.5.3. Enzymatic study

To examine the inhibition potential of alpha-amylase enzyme we used the iodine/potassium iodide technique[18], with a few adjustments. Using amylase solution in 1 U of sodium phosphate buffer SPB (6 Mm NaCl/ pH=6.9) and 25 µL of the sample fraction at different concentrations, the reaction mixture was produced in a 96-well microplate. 50µl of 1% starch solution was added to start the reaction after the final solution was incubated for 10 minutes at 37 °C. Simultaneously, an enzyme solution-free control was made. After a 20-minute re-incubation period at 37°C, the reaction was halted by adding 25 µL of 1 M HCl and 100 µL of iodine-potassium iodide solution. At 630 nm, the absorbance was measured. The a-amylase inhibition percentage was evaluated by the following equation:

$$I\% = 1 - [(Absc - Abse) - (Absf - Absb)/(Absc - Abse)].$$

Absf = Absorbance (fraction, Starch, Enzyme, IKI, HCl);

Absb = Absorbance (fraction, SPB, IKI);

Abse = Absorbance (fraction solvent "µl", Enzyme, Starch, HCl, IKI);

Absc = Absorbance (fraction solvent "µl", SPB, Starch, HCl, IKI).

4. Results

4.1. Alkaloids amount

The solvents used in this selective extraction aids us in separating the maximum component at different polarities, particularly the alkaloids. We observe that the DV contains the highest concentration of AA 62,89± 0.05 µg EA/mg (Table1).

4.2. GC-MS study

The GC-MS analysis results shows a variation in the chemical composition of DV and ETV; Forty-eight compounds were identified the oxygenated monoterpenes (11.77%, 17.88%), non-terpenes/ fatty acid (75.67%, 73.34%), and nitrogen compounds (NC) (2.02%, 0.6%) were similarly identified in DV and ETV in order, additionally of the sesterterpenes and sesquiterpenes in DV, while the monoterpenes was identified only in ETV(Figure1). Whereas the DV showed the high amount of NC 2.02% with nine compounds such as dimethylamino-3-phenylpropanoate**(1D),** 1H-Indole, 3-methyl-2-propanoyl **(2D),** Bicyclo[2.2.1]heptane-2-acetamide, N-(1,3-dihydro-5,6-dimethoxy-3-oxo-4-is**(3D),** 2H-Pyran-2-acetamide, tetrahydro-.alpha.-hydroxy-2-methoxy-5,6-dimethyl-4- **(4D),** Deacetylvindoline **(5D),** 2-amino-6-ethyl-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester **(6D),** 1H-Pyrazole, 1-(3-methylbutyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) **(7D),** 1,1,2-Ethenetriamine, N-[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]th **(8),** 2-(tetrahydrofuran-2-yl)piperidine **(9D).** Compared to ETV with 0.6% of NC with two compounds 1-Decyloxymethyl-3-methyl-1,3-dihydrobenzoimidazol-2-ylideneamine**(1E),** Triethanolamine **(2E)** (Table2).

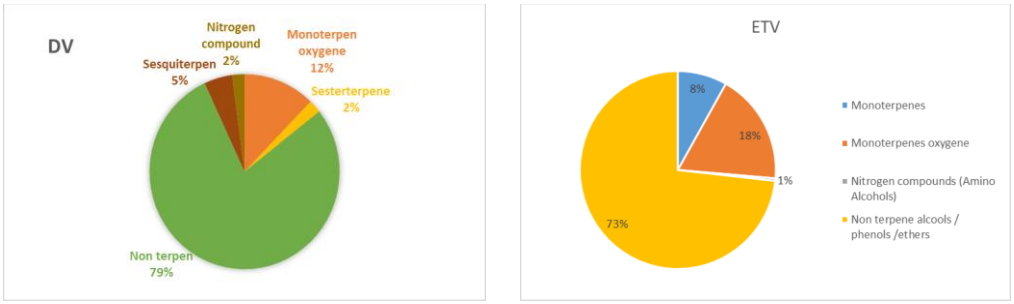

Figure 1. he identified volatile group compounds in DV & ETV fractions.

4.3. Pharmacological potential

4.3.1. Anti-oxidant assay

DPPH test (Figure2) represented the ability of the fractions in reducing the stable radical DPPH• purple to DPPH-H yellow, expressed with an (IC_{50}), the ETV fraction shows a low IC_{50} value 354,24± 2,20 µg/mL comparing to IC_{50}= 462,76± 2,38 µg/mL for DV fraction, however, the standards assessed, BHT (IC_{50} 12.99±0.41 µg/mL) and BHA (6.14±0.41 µg/mL) were more efficient than VA fractions' (Table1).

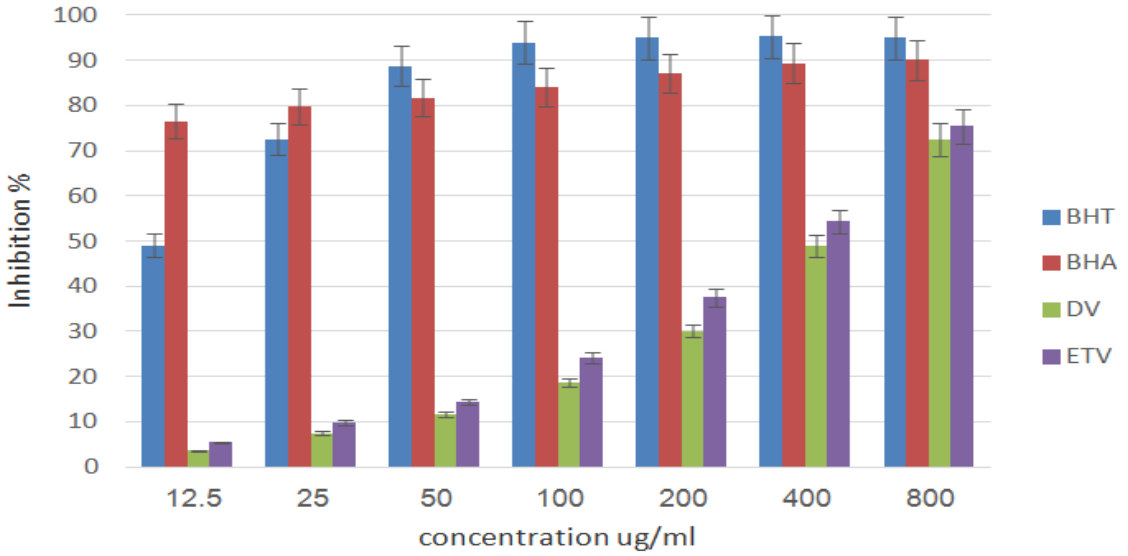

Figure 2. The DPPH inhibition potential rate with applied concentration µg/ml of fractions and standard.

β-carotene-linoleic acid potential was determined as an IC_{50} (Table1). The results showed that the VA fractions' of *D. scoparia* was partially able to effectively inhibit the linoleic acid oxidation, an IC_{50} = 67.60± 2.10 and 532.50± 2.34 µg/ml were registered for ETV and DV fractions respectively, with ETV exhibited the lowest (IC_{50} 67.60± 2.10 µg/ml). While the BHT and BHA used as a positive control with IC_{50}= 0.91±0.01 and 1.05±0.03 µg/ml in order are more effectual than the fractions tested. According of the results the ETV fraction have a good inhibiting of linoleic acid oxidation comparing to DV fraction (Figure3).

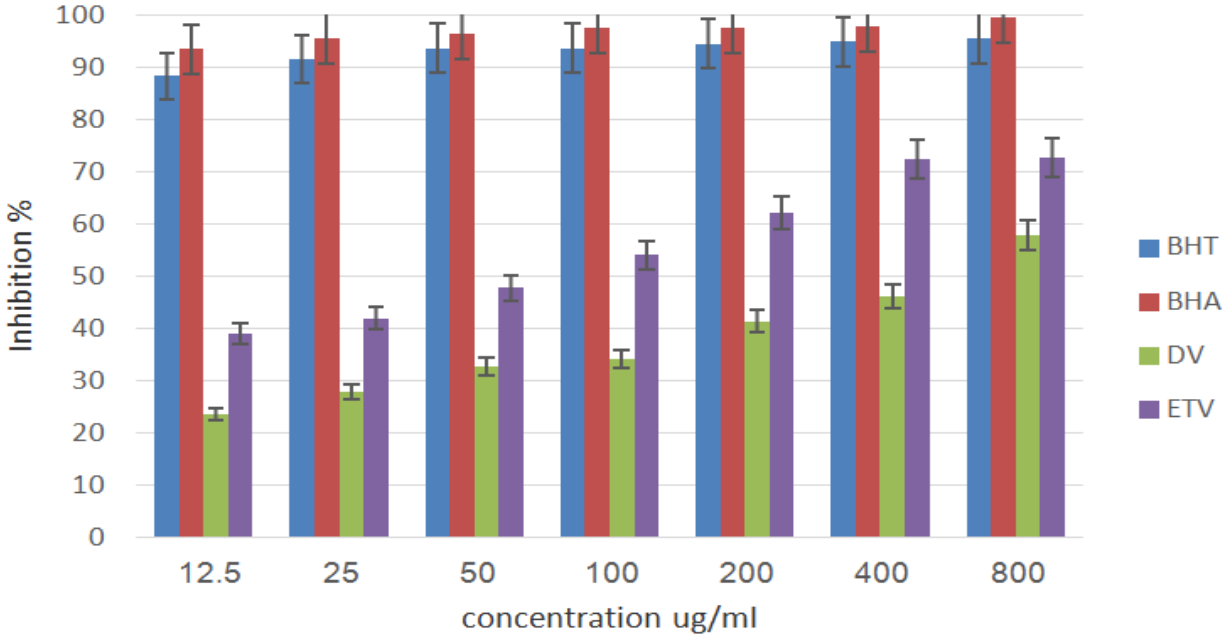

Figure 3. The β-carotene inhibition potential rate with applied concentration µg/ml of fractions and standard.

4.3.2. α-amylase inhibition potential

The evaluation of the anti-diabetic potent of *D. scoparia* VA fractions' based on the estimation of the capacity of ETV and DV fractions to inhibit the enzyme (α-amylase), the DV present a significant inhibition compared to the acarbose, and ETV, which is showed a no reaction response to the a-amylase enzyme. Indeed the DV exhibited a lowest IC_{50}= 163.69± 1.41 µg/ml, with a strong inhibition potential estimated 22 times higher than the positive standard (Table1).

Table1. The IC_{50} results of DPPH, β-carrotene, and α-amaylase with the AA of fractions and standard

	α-amylase IC_{50} (ug/ml)	Anti-oxydant IC_{50} (ug/ml)		Alkaloids amount AA (ugEA/mg)
		DPPH	β-carrotene	
DV	163.69± 1.41	462,76± 2,38	532.50± 2.34	62,89± 0.05
ETV	NA	354,24± 2,20	67.60± 2.10	28,72±0.03
Acarbose	3650,93±10,70	NT	NT	NT
BHT	NT	12.99±0.41	0.91±0.01	NT
BHA	NT	6.14±0.41	1.05±0.03	NT

NT: not tested. NA: no activity

5. Discussion

D. scoparia is a medicinal plant representing an interesting chemical composition and is used in folk medicine to treat several diseases. The plant has been reported for its pharmacological potential such as anti-microbial, anti-inflammatory, anti-oxidant, and anti-diabetic[19]. In the present study, we reported the effect of the VA fractions on the inhibition of alpha-amylase besides the antioxidant capacity, to identify the VA fractions' composition and determine their bioassay based on antioxidant and antidiabetic.

The alkaloid amount AA was quantified in the VA fractions (DV and ETV) as possible bioactive molecules. To extract the majority of alkaloid compounds a specific extraction was performed using a non-polar solvent as the best medium of these compounds[20].

A highest AA was recorded in the DV fraction (62,89± 0.05µgEA/mg) compared to the ETV fraction (28,72±0.03µgEA/mg), and atropine as standard (DV>ETV>standard). Our results are in agreement with[21] who showed that the alkaloids present remarkably in nonpolar solvents with an important amount compared to the polar solvents[22,23]. As confirmation of our findings, the VA fractions composition was identified according to the GC-MS analysis, which is a helpful and devoted method for the separation of volatile mixtures and identification effectively [24]. The extraction and separation method of VA fractions from the *D.scoparia* plant was effective, which

is validated by the identification of the major VA compounds in DV fraction with11 (Alkaloids/ NC), while just 2 NC were identified in the ETV fraction without similarity in fractions composition, these results corroborate the presence of VA compounds in the study plant additionally of other volatile compounds in agreement with Gonzalez (2021) [24] findings. In comparison with the previous works the AA concentration and the identification of VA compounds of *D. scoparia* in Volatile extract was studied for the first time in this work according to our knowledge.

Table 2. The identified compound results by GC-MS of DV and ETV fractions

R.time	Name	DV (A%)	ETV (A%)
5.73	Isocineole	-	1.40
5.77	α-Terpinene	-	1.21
5.94	o-Cymol	-	1.26
6.04	D-Limonene	-	0.92
6.72	δ.-Terpinene	-	1.03
7.46	p-Cymenene	-	2.29
9.77	L-4-terpineneol	-	5.03
9.97	p-cymenol	1.11	-
10.11	(+)-Fenchol	-	3.10
10.14	(1S)-1,3,3-trimethylnorbornan-2-ol	1.04	-
10.42	(+)-Sabinol	-	0.36
10.63	l-Verbenone	-	0.59
11.66	(+)-Carvotanacetone	-	1.68
11.69	p-Menth-4-en-3-one	0.97	-
12.99	(Z)-6-Methyl-2-(nonadec-10-en-1-yl)-2H-pyran-4(3H)-one	1.40	-
13.07	Carvacrol	-	2.53
13.11	o-Thymol	1.31	-
13.21	trans-β-Dihydroterpineol	1.35	-
13.55	2-hydroxy-1,8-cineol	2.61	-

15.09	2-(tetrahydrofuran-2-yl)piperidine	**0.30**	-
15.53	Triethanolamine	-	**0.34**
15.58	(+)-Pinanediol	1.09	-
15.83	Benzene, 1,2-dimethoxy-4-(2-propenyl)	-	0.67
18.70	Butylated Hydroxytoluene	-	0.97
18.95	Myristicin	**14.35**	**13.58**
21.54	Apiole	**45.01**	-
21.58	Cyclopenta[1,3]cyclopropa[1,2]cyclohepten-3(3aH)-one, 1,2,3b,6,7,8-hexahydro-6,6-dimethyl	**23.51**	-
21.61	1,3-Benzodioxole, 4,7-dimethoxy-5-(2-propenyl)	**12.88**	-
22.24	(+)-Rosifoliol	2.67	-
22.60	1,1,2-Ethenetriamine, N-[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-N-methyl	**0.08**	-
24.12	(E)-3-Butylidene-4,5-dihydroisobenzofuran-1(3H)-one	0.60	-
24.20	Alloaromadendrane-4beta,10alpha-diol	0.46	-
26.51	dimethylamino-3-phenylpropanoate	**0.56**	-
27.15	1H-Indole, 3-methyl-2-propanoyl	**0.12**	-
30.35	Bicyclo[2.2.1]heptane-2-acetamide, N-(1,3-dihydro-5,6-dimethoxy-3-oxo-4-isobenzofuranyl)	**0.08**	-
36.92	1-Decyloxymethyl-3-methyl-1,3-dihydrobenzoimidazol-2-ylideneamine	-	**0.15**
43.10	2H-Pyran-2-acetamide, tetrahydro-.alpha.-hydroxy-2-methoxy-5,6-dimethyl-4-methylene	**0.04**	-
44.55	Deacetylvindoline	**0.07**	-
46.86	2-amino-6-ethyl-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester	**0.06**	-
47.35	1H-Pyrazole, 1-(3-methylbutyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)	**0.06**	-
Total		111,73	37,11

R. time: retention time, A%: area percentage.

The antioxidant assay has been assessed using two different methods. It is important to use many assays to take into consideration the composition of fractions that act through various mechanisms such as the prevention of peroxides decomposition, inhibition of continued hydrogen abstraction, reductive capacity, and radical scavenging[11]. The VA fractions exhibited antioxidant activity partially by scavenging free radicals and preventing the β-carotene bleaching. Thus, the ETV fraction with a weak AA concentration exhibited the strongest antioxidant effect, which can be related to the presence of monoterpene compounds such as limonene[11]. The results illustrate that DPPH radical scavenging potential of ETV is related positively to the concentration of some compound in fraction such us monoterpenes. Although this fraction show a remarkable DPPH radical scavenging potential. This observation agrees with other studies where the antioxidant was found to correlate well with the essential oil containing a remarkable monoterpene content[25].

Many studies reported the antioxidant potential of *D. scoparia* carried out on its essential oils. A significant correlation between the monoterpenes amount and the antioxidant potent of *D.scoparia* essential oils' was found using DPPH, reducing power, and phosphomolebdenum assays. While there is no report related to the antioxidant activity assessed by β- carotene bleaching in our knowledge. The IC_{50} values of DPPH radical scavenging ranged from 0.91+0.02 to 11210+0.26ug/ml in several studies based on the essential oil and solvent extract of *D. scoparia* [11,23,26,27], in the other hand the essential oil of D.scoparia exhibit an inhibition potential of b-carotene evaluated with 37% [11] in contrast, there is no research related to the evaluation of inhibition capacity of b-carotene by D.scoparia solvent extract in our knowledge. This literature was in agreement with our findings where ETV is richer in monoterpenes (8.17%) as volatile compounds with IC_{50} of DPPH (354,24± 2,20µg/ml) compared to DV IC_{50} (462,76± 2,38 µg/ml) which had a strong AA concentration with (0%) monoterpenes indeed, this was remarkably shown in b-carotene inhibition where the ETV fraction presented an inhibition percentage stronger 7 times (67.60± 2.10 µg/ml) than the DV fraction 532.50± 2.34 µg/ml, thus, this result explains the variation of the antioxidant capacity of fractions, by the presence of a synergistic effect between the ETV compounds which showed the strong inhibition, while the DV compounds exhibited antagonism effect caused a weak inhibition, it can be related to the presence of alkaloid compounds in this fraction where they composition influence their antiradical potential.

Diabetes, commonly referred to as diabetes mellitus, is a chronic illness brought on by a collection of metabolic problems that are typified by hyperglycemia, or elevated blood sugar levels, which are brought on by either insufficient or ineffectual insulin production[28]. To treat diabetes two treatments are available insulin injections or intake drugs of anti-diabetic for long-term[29]. To decrease the level of glucose after eating, the inhibitors of alpha-amylase enzyme are used to delay the carbohydrates complex' digestion[30]. According to that the important agent in this reaction is the alpha-amylase enzyme[31], based on that we investigated in this paper by looking for its bio inhibitors.

One of the tested fractions; DV exhibited an intensive inhibitory action against alpha-amylase stronger than synthetic standard (acarbose), which explains the powerful anti-diabetic effect of this fraction. The examination of *D.scoparia*, VA extract capacity to inhibit alpha-amylase enzyme based on the alkaloid compounds potential on the inhibition of the enzymes[10,32], which illustrates that alkaloid compounds showed important pharmacological properties such as phenyl ethyl amine alkaloid, piperidine, and indole which are identified by GC-MS analysis in DV fraction. Furthermore, the anti-diabetic effect that was more powerful than acarbose an interesting inhibitory effect against alpha-amylase explaining its constitution presents bioactive compounds[33] that assure this inhibition compared to ETV, which is not active against this enzyme despite its high antioxidant activity. These results suggest the imputation of bioactive compounds present in the fraction like sesterterpenes, sesquiterpenes, and even alkaloids that can react positively in a very low concentration[32]. According to that, DV fraction exhibited a powerful inhibiting to the study enzyme, with a higher potent result compared to the acarbose. Moreover, some literature on the *Pituranthos chloranthus* recorded the anti-diabetic potent of this genus[34] as well as the *D. tortuosa* [35], in addition to Gupta(2022)[36] represented that alkaloid compounds were able to control diabetes. All these findings extremely agreed with our results. As well as related to the composition of the fractions where it is observed by GC-MS analysis that there is no similarity between fractions composition, which can explain that the variation in chemical composition is strongly related to the pharmacological potential of fractions. Regarding that, it should be evaluated the anti-diabetic potential of isolated alkaloids which be highlighted in this plant in future research.

6. Conclusion

The present work results assure that *D. scoparia* contains volatile alkaloid compounds with antioxidant and anti-diabetic potential, indeed allowing it an alternative bio-ant diabetic agent and other therapeutic uses. Thus, future research will be based on isolating and identifying these active compounds and evaluating their pharmacological capacities in vivo.

Acknowledgements

We are grateful to the advice and support of Mr. Baelhadj HAMDI AISSA, The director of the Biogeochemistry of Desert Environments laboratory, Mr. EDDOUD Amar, a professor from the Department of Natural and Life Sciences SNV, Kasdi-Merbah University for his helping in the identification of plant material and the valorization of our work, and also Mrs LAKHDARI Wassima a doctor from the National Institute of Agronomic Research of Algeria (INRAA), Touggourt Station, Touggourt, and Dr. ZAOUI Oussama for helping us.

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