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Antidiabetic Effects of Essential Oils of some Selected Medicinal Lamiaceae Plants from Yemen against α-Glucosidase Enzyme

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Abstract

Essential oils of four species used in traditional medicine in Bani Matar District in Yemen, family Lamiaceae were assessed chemically and biologically for their antidiabetic activity; *Leucas inflata*, *Marrubium vulgare*, *Salvia schimper* and *Origanum majorana*. The results indicated that *Salvia schimperi* essential oil exhibited the most dose-dependent inhibitory activity against α-gucosidase enzyme with IC_{50} of 14.26 µL (nearly similar to acarbose of IC_{50} 12.87 µL) followed by *Marrubium vulgare* oil with IC_{50} value at 35.47 µL. *Leucas inflata* essential oil exhibited weak dose-dependent inhibitory activity against α-glucosidase enzyme with IC_{50} of 159.66 µL and no effect was observed with *Origanum majorana*. The antidiabetic activities observed was due to the presence of compounds such as caryophyllene, bisabolol and farnesene. Our results obviously cleared that essential oils of *Salvia schimperi* and *Marrubium vulgare* exerted promising antidiabetic effects so; we recommended using such as oils as futural natural antidiabetic.

Keywords: Lamiaceae; GC/MS; α-Glucosidase; Antidiabetic effects

Introduction

Traditional medicines are used by about 60% of the world's population. These are not only used for primary health care in rural areas in developing countries, but also in developed countries as well where modern medicines are predominantly used [1].

The genera of *Leucas*, *Marrubium*, *Salvia* and *Origanum*, which belongs to the family Lamiaceae, play an important role in folk medicine, cosmetics, culinary, and for the commercial production of essential oils [2]. It is considered as a significant resource for traditional medicine in Yemen which is used to cure diseases related to kidney disease, diabetes, cough, wounds, stomachache, dysentery, diarrhea etc [3,4].

Diabetes mellitus is a major and emerging public health problem all over the world. It is growing at an alarming rate and is considered as the fifth leading cause of death in the world. The first WHO Global report on diabetes demonstrates that the number of adults living with diabetes has almost quadrupled since 1980 to 422 million adults. This dramatic rise is largely due to the rise in type 2 diabetes and factors driving it include overweight and obesity. In 2012, diabetes caused 1.5 million deaths. Its complications can lead to heart attack, stroke, blindness, kidney failure and lower limb amputation. WHO estimates that, globally, 422 million adults aged over 18 years were living with diabetes in 2014 [5]. According to the World Health Organization (2016), 2% of the mortality percentage in Yemen is due to diabetes [6].

Inhibition of α-glucosidase is an important factor to control postprandial hyperglycemia in type 2 diabetes mellitus [7] and the uses of medicinal plants are recommended by World health organization, particularly for patient in rural regions of poor countries who are unable to purchase the synthetic medication [8]. Therefore, extensive research has been directed toward the use of medicinal plants to control DM and its complications [9,10].

Recently there has been some research works on the chemical composition, antioxidant and antimicrobial activities of essential oils of the four mentioned plants [11-14]. However, to the best of our knowledge there is no information on the antidiabetic properties of these essential oils. So, this study was designed to investigate both the chemical constituents and the antidiabetic properties of the essential oils isolated from *Leucas*, *Marrubium*, *Salvia* and *Origanum* leaves.

Materials and Methods

Plant material

Four medicinal Lamiaceae taxa were collected during the rainy season in 22-2/8/2015 from different Location in Bani Matar District, Sana'a governorate, Yemen. The identification of the specimens was done by utilizing the available taxonomic and floristic literatures [15-18]. Voucher specimens have been deposited at the Herbarium of Faculty of Science, Ain Shams University and a duplicate of each herbarium specimen was kept at the Herbarium of Biology Department, Faculty of science Sana'a University.

Isolation of the essential oil

The fresh leaves and green branches of the four medicinal Lamiaceae taxa were chopped into small pieces. The essential oil was isolated from each part by hydrodistillation for 5 hr using a Clevenger-type all glass apparatus. Each oil was transferred to a screw-capped glass vial, dried (Na_2SO_4) and stored at 4°C in the dark until analysis.

Analysis of essential oils by GC and GC-MS

GC analysis was carried out using a GC HP 5890 Hewlett Packard equipped with FID and HP-5 fused silica capillary column "30 m ×

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0.25 mm i.d., film thickness 0.25 μm", using a sample volume of 0.03 μL. Oven temperature was programmed from 60°C to 240°C at 3°C/min; injector temperature, 250°C; detector temperature, 280°C; carrier gas, helium (1.0 mL/min); automatic sample injection, 0.02 μL of the oil; split: 1/70. The relative proportions of the essential oil constituents were expressed as percentages obtained by peak area normalization. GC–MS analysis was performed on a Perkin-Elmer quadrupole MS system (Model 5) coupled with the GC HP 5972, equipped with a HP-5 capillary column. Oven temperature was programmed from 45°C to 240°C at 3°C/min; injector temperature, 250°C; carrier gas, helium (0.5 mL/min); automatic sample injection, 0.02 μL of the oil; split: 1/70. The MS operating parameters were: interface temperature: 300°C, ion source temperature: 200°C, EI mode: 70 eV, scan range: 41-400 amu.

Identification of the components

Mass spectra of the individual GC peaks were identified by a computer search of the commercial libraries (WILEY, NIST), as well as matching with published mass spectra [19]. The identification was further confirmed by the calculation of the retention indices (RI) relative to (C6–C22) *n*-alkanes [20].

α-Glucosidase inhibition assay

Fifty microliter from the essential oil and 100 μL of α-glucosidase solution (1.0 U/mL in 0.1 M phosphate buffer (pH 6.9) was incubated at 25°C for 10 min. Then, 50 μL of 5 mM p-nitrophenyl-α-D-glucopyranoside solution in 0.1 M phosphate buffer (pH 6.9) was added. The mixtures were incubated at 25°C for 5 min, before reading the absorbance at 405 nm in the spectrophotometer. The α-glucosidase inhibitory activity was expressed as percentage inhibition [21].

Results and Discussion

There are several essential oils which are screened for antidiabetic

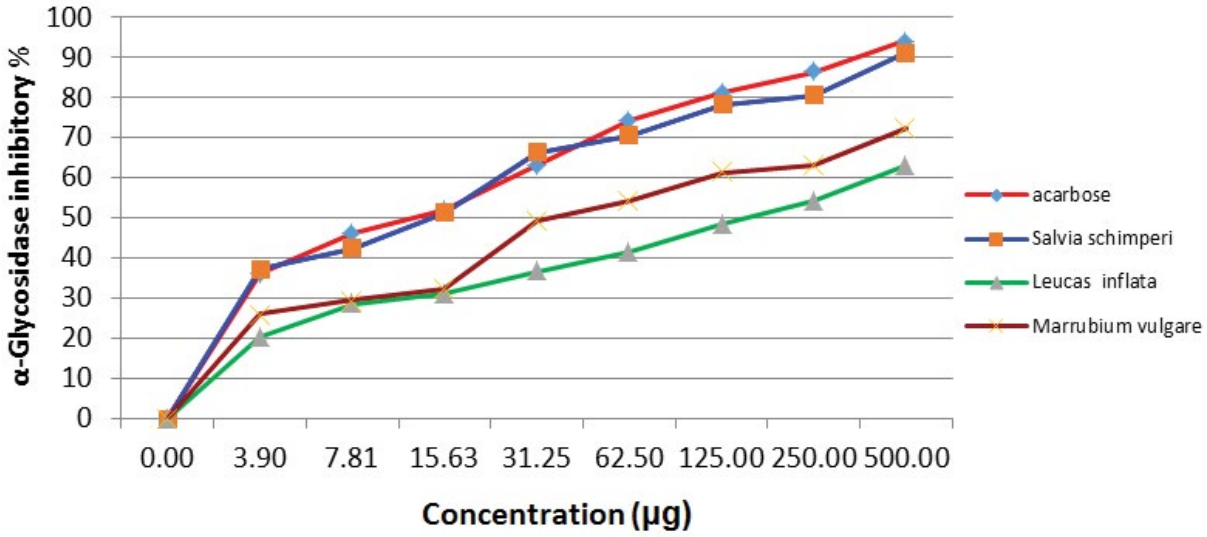

Figure 1: α-Glucosidase inhibition by acarbose and essential oil from of 4 selected medicinal Lamiaceae plants.

Sample conc.(μL)	Acarbose	*Salvia schimperi*	*Leucas inflata*	*Marrubium vulgare*	*Origanum majorana*
0	0	0	0	0	0
3.9	36.21 ± 1.2	37.35 ± 0.58	20.31 ± 1.2	25.9 ± 0.72	0
7.81	46.31 ± 0.63	42.32 ± 0.45	28.34 ± 1.5	29. 4 ± 1.2	0
15.63	52 ± 0.58	51.32 ± 0.63	30.93 ± 0.63	32.32 ± 0.72	0
31.25	63.25 ± 1.5	66.35 ± 0.58	36.58 ± 1.2	49.32 ± 0.63	0
62.5	74.15 ± 0.72	70.63 ± 1.5	41.63 ± 0.63	54.36 ± 0.58	0
125	81.32 ± 0.63	78.35 ± 1.5	48.32 ± 0.63	61.32 ± 1.2	0
250	86.47 ± 0.58	80.35 ± 0.63	54.38 ± 0.63	63.25 ± 1.5	0
500	94.35 ± 1.2	91.31 ± 1.2	63.25 ± 1.2	72.35 ± 0.63	0
All determinations were carried out in triplicate manner and values are expressed as the mean ± SD. IC_{50} value is defined as the concentration of inhibit 50% of its activity under the assayed conditions.					

Table 1: Anti-dibetic activity of the four selected lamiaceae plants.

Sample	Compounds	Area [%]ª				KI
		LI	MV	OM	SS	
1	*α*-Pinene	5.17	2.27	0.07	-	936
2	Sabinene	1.1	-	0.52	-	975
3	*β*-Pinene	-	-	0.08	-	981
4	*β*-Myrcene	1.12	-	0.21	-	990

5	*α*-Terpinene	1.64	-	1.4	-	1018
6	*p*-Cymene	2.13	-	0.87	-	1028
7	*d*-Limonene	0.72	-	0.4	-	1031
8	γ–Τερπινενε	4.49	-	5.07	-	1061
9	Terpinolene	1.24	-	-	-	1087
10	***l*-Linalool**	**25.38**	-	4.68	1.79	**1102**
11	*trans*-Pinene hydrate	-	-	4.21	-	1124
12	*trans*-Verbenol	-	-	2.21	-	1146
13	Camphor	-	-	0.04	-	1147
14	Pinocarvone	-	-	0.03	-	1167
15	Borneol	-	-	0.61	-	1175
16	Terpin-4-ol	5.96	-	-	0.54	1182
17	α-Terpineol	-	-	37.75	-	1186
18	Myrtenal	-	-	0.06	-	1198
19	–Τερπινεολ	5.9	-	8.02	-	1201
20	Dihydro carvone	-	-	0.05	-	1203
21	*trans*-Pipertiol	-	-	1.15	0.35	1209
22	Thymol methyl ether	-	-	0.38	-	1231
23	Geraniol	1.72	-	-	-	1248
24	Linalyl acetate	-	-	2.15	-	1254
25	Phenyl ethyl acetate	-	-	0.1	-	1255
26	Thujanol acetate	-	-	2.57	-	1277
27	Carvacrol	-	-	1.68	-	1296
28	Octandiol	-	-	0.05	-	1347
29	*α*-Copaene	-	2.71	-	-	1374
30	Geranyl acetate	0.72	-	0.05	-	1380
31	*E*-*β*-Damascenone	-	-	-	0.44	1381
32	*β*-Elemene	2.29	-	-	-	1389
33	***Z*-Caryophyllene**	**16.95**	**10.95**	**2.3**	**-**	**1404**
34	*α*-Gurjunene	-	-	-	2.59	1405
35	**4, 8-α-epoxy Caryophyllene**	**-**	**-**	**-**	**26.06**	**1418**
36	*β*-Humulene	1.11		0.1	1.7	1432
37	*β*-Farnesane	0.77	6.91	-	-	1444
38	*trans*-Muurola-3,5-diene	-	3.97	-	-	1457
39	*allo*-Aromadendendrene		-	-	1.85	1458
40	*α*-Isomethyl ionol	1.43	4.18	-	-	1466
41	Cumacrene	-	-	1.53	-	1469
42	Dauca-5,8-diene	0.64	-	-	-	1472
43	Cadina-1,4-diene	-	-	-	2.55	1498
44	Bicyclogermacrene	3.77	-	-	-	1505
45	***α*-Bisabolene**	-	**9.72**	-	-	**1507**
46	γ–Χαδινενε	-	4.35	-	-	1515
47	*Z*-Nerolidol	-	1.06	-	-	1534
48	*α*-Agarofuran	-	-	0.24	-	1547
49	*cis*-Muurolenol	-	-	0.04	-	1551
50	Cadinene ether	-	-	-	7.46	1557
51	**Caryophyllene oxide**	**1.69**	**3.72**	**-**	**20.7**	**1580**
52	Humulene oxide	-	-	-	1.03	1612
53	Cedrol	-	-	-	2.51	1617
54	*epi*-Eudesmol	-	-	-	0.44	1620
55	*epi*-Cubenol	-	-	-	5..35	1630
56	Isoborneol	-	1.76	-		1632
57	Selinadienol	-	-	-	1.13	1646
58	**Bisabolol**	**-**	**-**	**-**	**11.67**	**1666**
59	Cedranol	-	-	-	0.48	1680
60	Pentadecanone	-	1.46	-	-	1697
61	*E*-Ligustilide	-	1.82	-	-	1796
62	Bisoblol acetate	1.96	-	-	-	1799
63	Phytol	-	2.54	-	-	1943
64	*Z, Z*, Greanyl linool	-	5.86	-		1961
65	Pseudo phytol	-	1.95	-	0.44	1988

66	7-Hydroxy-4,8-dimethyl Coumarin	-	1.35	-	-	2013
67	Manool	-	1.98	-	-	2060
68	**Octadecenol**	**-**	**10.44**	**-**	**-**	**2077**
69	Olic acid	-	1.21	-	-	2142
70	Labdl 4-ene-8,13-diol	-	-	-	1.51	2207
71	**Octadecenol acetate**	-	**5.36**	-	-	**2209**
Total Peak [%] No. of Identified Compounds						
Compound Class		**LI**	**MV**	**OM**	**SS**	
		Area [%]a	**Area [%]a**	**Area [%]a**	**Area [%]a**	
Monoterpene Hydrocarbons		17.61	2.27	10.94	-	
Sesquiterpene Hydrocarbons		25.53	38.61	3.93	16.57	
Monoterpene oxygenated		41.12	3.34	83.98	**3.12**	
Sesquiterpene oxygenated		5.08	14	0.28	69.37	
Diterpene oxygenated		-	30.69	-	1.95	
Total hydrocarbon compounds		**43.14**	**40.88**	**14.76**	**16.57**	
Total oxygenated compounds		**46. 2**	**48.03**	**84.26**	**74.44**	
Total		89.34	88.91	99.02	92.65	
a) Percentage of a component to the total identified components						
b) Components identified according to computer search of the commercial libraries (WILEY, NIST).						
c) KI: Kovats Retention Index.						
Plant abbreviations :(LI) *Leucas inflata* ,(MV) *Marrubium vulgare* , (OM) *Origanum majorana* , (SS) *Salvia schimperi*						

Table 2: Essential oil composition of 4 medicinal plants of Lamiaceae in Yemen.

potential that inhibit α-glucosidase enzyme [7,22,23]. The inhibition of α-glucosidase by the essential oils of *Leucas inflata*, *Marrubium vulgare*, *Salvia schimperi* and *Origanum majorana* are shown in Figure 1 and Table 1. The results indicated that *Salvia schimperi* and *Marrubium vulgare* essential oils exhibited dose-dependent inhibitory activities against α-glucosidase with IC_{50} of 14.26 µL and 35.47 µL respectively, compared to acarbose (IC_{50} value at 12.87 µL). *Leucas inflata* essential oil exhibited weak dose-dependent inhibitory activity against α-glucosidase with IC50 of 159.66 µL and *Origanum majorana* leaves essential oil had no effect.

The higher inhibitory effects observed in *Salvia schimperi* could be attributed to the presence of major components; 4,8-α-epoxy caryophyllene (26.06%), caryophyllene oxide (20.7%), bisabolol (11.67%), cadinene ether (7.46%) and cubenol (5.35%). The inhibitory effects observed in *Marrubium vulgare* could be attributed to the presence of major components as caryophyllene (10.95%), octadecanol (10.44%), α-bisabolene (9.72%), β-farnesane (6.91%), geranyl linalool (5.86%) and octadecenol acetate (5.36%) (Table 2).

The inhibition of α-glucosidase by both plants could be attributed to the presence of previously mentioned compounds which reported with their activity against this enzyme. B-caryophyllene has been proved to have high inhibitory effects against α-glucosidase enzyme [22]. α-Bisabolol along with α-farnesene isolated from *Matricaria chamomilla* L., showed also significant α-glucosidase inhibitory activity [24].

So the amount and the synergistic effect of these compounds in both oils are responsible for that activity. However, further test could be carried out to characterize the active principles responsible for these activities.

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