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Full Length Research Paper

Radix linderae essential oil improving the immunity activities and preventing the occurrence of decubitus in aged people

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To investigate the immune enhancement extract of radix linderae essential oil in aged people. One hundred and fifteen aged people over 70 years old were divided into two groups: vehicle-treated group (n=58) and radix linderae essential oil treatment group (n=57). Old peoples' hips and elbows in radix linderae essential oil treatment group were sprayed with radix linderae essential oil (dissolved in olive oil) for 6 months. Old peoples' hips and elbows in vehicle-treated group were sprayed with olive oil for 6 months. After 6 months treatment, people in essential oil-treated group have higher immunity function and lower incidence rate of decubitus than those in vehicle-treatment group. Radix linderae essential oil is useful to prevent occurrence of decubitus in aged people.

Key words: Radix linderae essential oil, decubitus, immunity.

INTRODUCTION

It is difficult for most people to understand the devastating consequences that can result from decubitus. For a person who normally uses a wheelchair, it can mean months of bed rest and hospitalization (Pueschel et al., 2005). In addition, after a decubitus ulcer has healed, the skin never fully recovers. Scarring, adhesions and tissue loss in the wake of a decubitus ulcer heighten future risk. Finally, as a person ages, tissue and circulation gradually become less resilient and viable. The prevention of decubitus becomes especially important (Sen et al., 2007).

Radix linderae, the root tubers of Lindera aggregata (Sims.) Kosterm. [L. strychnifolia (Sieb. et Zucc.) F.Vill.] (Lauraceae), is an important traditional herbal medicine in China (Wu-yao) and Japan (Uyaku) for treating several diseases, including chest and abdomen pain, indigestion, regurgitation, cold hernia and frequent urination (Jiangsu New Medical College, 1997; The Editorial Committee of the Administration Bureau of Traditional Chinese Medicine, 1999). Pharmacological studies on this plant have shown various bioactivities, such as antioxidation, protection against postischemic myocardial dysfunction, superoxide anion radical scavenging and slowing down the progression of diabetic nephropathy in db/db mice (Noda et al., 2007; Wang et al., 2004; Ohno et al., 2005), anti-inflammatory, analgestic and antimicrobial properties. The present study is an effort to investigate the role of radix linderae essential oil in improving the immunity activities and preventing the occurrence of decubitus in aged people.

Abbreviations: GC/MS, Gas chromatography/mass spectrometry; **IL-6,** interleukin 6; **IL-4,** interleukin 4; **IL-10,** interleukin 10; **TNF-α,** tumor necrosis factor-alpha.

MATERIALS AND METHODS

Radix linderae essential oil

GC-MS analysis

GC-MS analyses were performed on a QP2010 instrument equipped with an OV-1 capillary column (30 m × 0.25 mm, 0.25 μm). The oven temperature program initiated at 50°C, held for 3 min, then raised at 5°C/min to 250°C, held for 2 min. Other operation conditions were as follows: injector temperature, 250°C;

carrier gas, He (99.999 %), adjusted to a column velocity of flow 1.0 ml/min; splitting ratio 10:1; interface temperature, 250°C; standard electronic impact (EI) MS source temperature, 200°C; mass scan range, 35 to 500 amu; scan velocity, 5 scans/s.

Subjects

One hundred and fifteen aged people over 70 years old were recruited in this study. They were divided into two groups: vehicletreated group (n=58) and radix linderae essential oil treatment group (n=57). Old peoples' hips and elbows in radix linderae essential oil treatment group patients were sprayed with radix linderae essential oil (dissolved in camellia oil) for 6 months. Old peoples' hips and elbows in vehicle-treated group were sprayed with olive oil for 6 months. At the end of experiment, blood (10 to 15 ml) was drawn from patients for immunity indexs. Serum IL-6, IL-4, IL-10 and TNF-α levels were measured by ELISA kits.

Statistical analysis

All data were presented as mean ± SEM. The data were not normally distributed; Mann-Whitney non-parametric test and Kruskal – Wallis ANOVA were applied.

RESULTS AND DISCUSSION

Chemical composition of the radix linderae essential oil

The chemical composition of the radix linderae essential oil is presented in Table 1. A total of 73 components were identified by their retention indices RI, as well as by GC-MS and other spectroscopic techniques, accounting for 97% of the oil. Eight of the components accounted for the 60% of the oil (Table 1). The oil mainly comprised of Camphene (12.15%), Cyclohexene, 1-methyl-4-(1-methylethylidene)- (10.72%), p-menth-1-en-8-ol (6.11%), Bicyclo[2.2.1]heptan-2-ol, 1,7,7-trimethyl-, acetate, (1S-endo)- (12.89%), Naphthalene, 1,2,4a,5,8,8a-hexahydro-4,7-dimethyl-1-(1-methylethyl)-, (1à,4aá,8aà)-(ñ)- (8.58%), .tau.-Muurolol (4.50%), 1-(2,4-Dimethylphenyl)-2-(2-furyl)cyclopropane (3.52%) and α-Pinene (4.47%).

Effect of the radix linderae essential oil on immunity activities in aged people suffering from decubitus

Although TNF-α initially came to prominence because of its antitumor activity, most attention is now focused on its functions in the regulation of infectious, inflammatory, and immune phenomena. As a highly potent proinflammatory cytokine, TNF-α has activities ranging from activating macrophages and lymphocytes against bacterial, parasitic, and viral infections to inducing apoptosis (Chensue et al., 1995; Hernandez-Caselles and Stutman, 1993; Le and Vilcek, 1987; Vassalli, 1992; Momeni and Riahi, 2010; Nwachukwu and Peter, 2010). By comparison to the control values (before treatment), 6 months of the radix linderae essential oil treatment exhibited an decrease in the TNF-α level in aged people. There was a significant statistical ($p<0.05$) difference before and after essential oil treatment (Figure 1). In vehicle-treated group, no marked change in serum TNF-α level was observed. Serum TNF-α level in essential oil treatment group was significantly ($p<0.05$) lower than that in vehicle-treated group. Current evidence suggests that IL-6, which has been classified as both a pro- and anti-inflammatory cytokine, is rapidly induced during the initiation of inflammation when early TNF-α production is also induced and plays an important regulatory role in various immune responses and inflammatory conditions (Yimin et al., 2003; Tascon et al., 2000; Yrlid et al., 2000; Gordon et al., 1994; Cao et al., 1998). However, whether the balance between TNF-α and IL-6 production (TNF-α/IL-6 balance) affects the development of the immune response remains unclear. As shown in Figure 2, the level of serum IL-6 in aged people was decreased after 6 months of essential oil treatment. However, There was not a significant statistical ($p >0.05$) difference before and after essential oil treatment (Figure 2). In vehicle-treated group, no marked change in serum IL-6 level was observed. Serum IL-6 level in essential oil treatment group was significantly ($p<0.05$) lower than that in vehicle-treated group. We postulated that TNF-α and IL-6 production in an innate immune response may be negatively regulated by each other and that the TNF-α/IL-6 balance may be a key factor in regulating immune responses. IL-10, which is produced by a variety of cells including macrophages, B cells, subsets of CD41 and CD81 T cells, and resident brain cell populations including microglia, choroid plexus epithelial cells, and even neurons, has a strong immunosuppressive capacity (Deckert-Schlüter et al., 1997; Flesch and Kaufmann, 1994; Frei et al., 1993; Moore et al., 1993; Schlüter et al., 1997). Serum IL-10 level in essential oil treatment group was slightly reduced during the experiment (Figure 3). In vehicle-treated group, no marked change in serum IL-10 level was observed.

There was not marked ($p>0.05$) statistical difference between two groups. The cell surface receptor for IL-4 is composed of two polypeptide proteins that span the plasma membranes. One of these proteins chains, the IL-4Rα, binds to IL-4 with high affinity. Binding of IL-4 to the IL-4Rα on the cell surface results in its association with a second protein. The presence of IL-4 in extravascular tissues promotes alternative activation of macrophages into M2 cells and inhibits classical activation of macrophages into M1 cells. An increase in repair macrophages (M2) is coupled with secretion of IL-10 and TGF-β that result in a diminution of pathological inflammation. Release of arginase, proline, polyaminases and TGF-β by the activated M2 cell is tied with wound repair and fibrosis (Aster et al., 2009). In the present work, the level of serum IL-4 in aged people showed a

Table 1. The chemical composition of the radix linderae essential oil.

No	Component	RT	Percentage (%)
1	α-Pinene	4.59	4.47
2	Camphene	4.81	12.15
3	β-Pinene	5.15	0.90
4	Cyclohexene, 1-methyl-4-(1-methylethylidene)-	5.96	10.72
5	1,4-Cyclohexadiene, 1-methyl-4-(1-methylethyl)-	6.36	0.09
6	3-Cyclohexene-1-methanol, 2-hydroxy-à,à,4-trimethyl-	6.56	0.05
7	Cyclohexene, 1-methyl-4-(1-methylethylidene)-	6.80	0.52
8	Bicyclo[2.2.1]heptan-2-ol, 1,3,3-trimethyl-, (1R-endo)-	7.21	0.72
9	Cyclohexanol, 5-methyl-2-(1-methylethenyl)-	7.83	0.84
10	Borneol	7.97	0.93
11	3-Cyclohexen-1-ol, 4-methyl-1-(1-methylethyl)-	8.34	0.92
12	p-menth-1-en-8-ol	8.68	6.11
13	Bicyclo[3.1.0]hexan-3-ol, 4-methylene-1-(1-methylethyl)-, (1à,3à,5à)-	8.85	0.39
14	D-Verbenone	9.01	0.07
15	cis-Z-à-Bisabolene epoxide	9.13	0.05
16	Benzene, 2-methoxy-4-methyl-1-(1-methylethyl)-	9.37	0.32
17	2-Cyclohexen-1-one, 2-methyl-5-(1-methylethyl)-, (S)-	9.72	0.25
18	Bicyclo[2.2.1]heptan-2-ol, 1,7,7-trimethyl-, acetate, (1S-endo)-	10.58	12.89
19	Phenol, 2-methyl-5-(1-methylethyl)-	10.79	0.36
20	2-Cyclopenten-1-one, 3-methyl-2-(2,4-pentadienyl)-, (Z)-	10.90	0.15
21	Bicyclo(3.1.1)heptane-2,3-diol, 2,6,6-trimethyl-	11.21	0.21
22	(-)-Myrtenyl acetate	11.45	0.23
23	6-Isopropenyl-3-methoxymethoxy-3-methyl-cyclohexene	12.38	0.61
24	Nerolidyl acetate	12.66	0.03
25	Cyclohexane, 1-ethenyl-1-methyl-2,4-bis(1-methylethenyl)-, [1S-(1à,2á,4á)]-	12.85	1.41
26	6,8-Nonadien-2-one, 8-methyl-5-(1-methylethyl)-, (E)-	12.95	0.03
27	1H-3a,7-Methanoazulene, 2,3,4,7,8,8a-hexahydro-3,6,8,8-tetramethyl-, [3R-(3à,3aá,7á,8aà)]-	13.36	0.19
28	Bicyclo[7.2.0]undec-4-ene, 4,11,11-trimethyl-8-methylene-,[1R-(1R*,4Z,9S*)]-	13.49	0.07
29	ç-Elemene	13.71	0.05
30	3-[(3,4-Dimethoxy-benzylamino)-methyl]-8a-methyl-5-methylene-decahydro-naphtho[2,3-b]furan-2-one	13.95	0.06
31	Cubenol	14.11	0.05
32	Aromadendrene oxide-(1)	14.37	0.02
33	2-Isopropenyl-4a,8-dimethyl-1,2,3,4,4a,5,6,7-octahydronaphthalene	14.71	0.27
34	Naphthalene, 1,2,4a,5,6,8a-hexahydro-4,7-dimethyl-1-(1-methylethyl)-, (1à,4aà,8aà)-	14.81	0.14
35	Aromadendrene oxide-(1)	14.88	0.20
36	Eudesma-4(14),11-diene	15.01	0.59
37	Benzofuran, 6-ethenyl-4,5,6,7-tetrahydro-3,6-dimethyl-5-isopropenyl-, trans-	15.19	1.03
38	á-Guaiene	15.33	0.05
39	Epiglobulol	15.45	0.11
40	Naphthalene, 1,2,3,4,4a,5,6,8a-octahydro-7-methyl-4-methylene-1-(1-methylethyl)-, (1α,4aα,8aα)-	15.58	0.06
41	Naphthalene, 1,2,3,5,6,8a-hexahydro-4,7-dimethyl-1-(1-methylethyl)-, (1S-cis)-	15.76	0.32
42	á-Guaiene	16.07	0.18
43	Bicyclo[4.1.0]heptan-2-ol, 1á-(3-methyl-1,3-butadienyl)-2à,6á-dimethyl-3á-acetoxy-	16.22	0.28
44	3,7-Cyclodecadiene-1-methanol, à,à,4,8-tetramethyl-, [s-(Z,Z)]	16.38	1.20
45	Isoaromadendrene epoxide	17.04	0.03
46	ç-Gurjunenepoxide-(2)	17.24	0.33
47	Spiro[tricyclo[4.4.0.0(5,9)]decane-10,2'-oxirane], 1-methyl-4-isopropyl-7,8-dihydroxy-, (8S)-	17.32	0.24
48	Alloaromadendrene oxide-(1)	17.40	0.26
49	Cyclohexanone, 5-ethenyl-5-methyl-4-(1-methylethenyl)-2-(1-methylethylidene)-, cis-	17.64	2.35
50	Cubenol	17.87	0.79

Table 1. Contd.

51	à-Cadinol	18.04	1.38
52	Naphthalene, 1,2,4a,5,8,8a-hexahydro-4,7-dimethyl-1-(1-methylethyl)-, (1à,4aá,8aà)-(ñ)-	18.35	8.58
53	.tau.-Cadinol	18.48	0.72
54	á-Guaiene	18.59	0.59
55	.tau.-Muurolol	18.82	4.50
56	Aromadendrene oxide-(1)	18.92	0.48
57	ç-Himachalene	19.02	0.13
58	Vitamin A aldehyde	19.18	0.40
59	Isoaromadendrene epoxide	19.33	0.17
60	Ledene oxide-(II)	19.43	0.26
61	Globulol	19.66	0.59
62	2-(4a,8-Dimethyl-1,2,3,4,4a,5,6,7-octahydro-naphthalen-2-yl)-prop-2-en-1-ol	19.87	0.18
63	Isoaromadendrene epoxide	20.06	0.20
64	6-Isopropenyl-4,8a-dimethyl-1,2,3,5,6,7,8,8a-octahydro-naphthalen-2-ol	20.12	0.11
65	Longipinocarveol, trans-	20.19	0.20
66	Bicyclo[4.4.0]dec-2-ene-4-ol, 2-methyl-9-(prop-1-en-3-ol-2-yl)-	20.33	0.10
67	Alloaromadendrene oxide-(2)	21.20	0.15
68	Desacetylanguidine	21.66	0.20
69	4,4'-Dimethyl-2,2'-dimethylenebicyclohexyl-3,3'-diene	22.79	0.71
70	1-(2,4-Dimethylphenyl)-2-(2-furyl)cyclopropane	24.79	3.52
71	n-Hexadecanoic acid	25.41	0.21
72	Cyclohexanone, 2-(2-nitro-1-phenyl-2-propenyl)-, (R*,R*)-	25.86	0.29
73	Hexadecanoic acid, trimethylsilyl ester	26.39	0.80

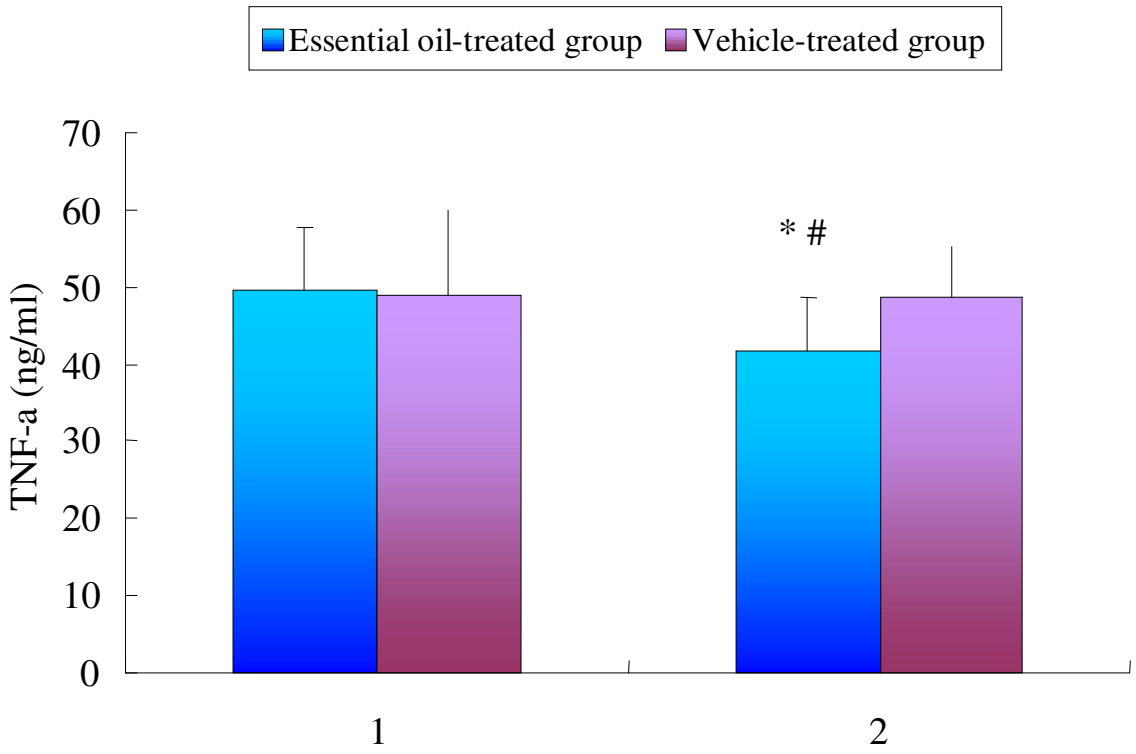

Figure 1. Effect of radix linderae essential oil treatment on serum TNF-α level in aged people.

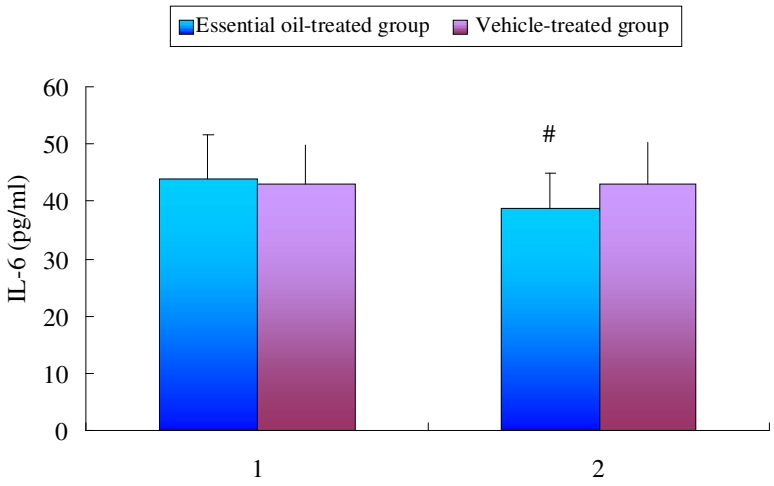

Figure 2. Effect of radix linderae essential oil treatment on serum IL-6 level in aged people.

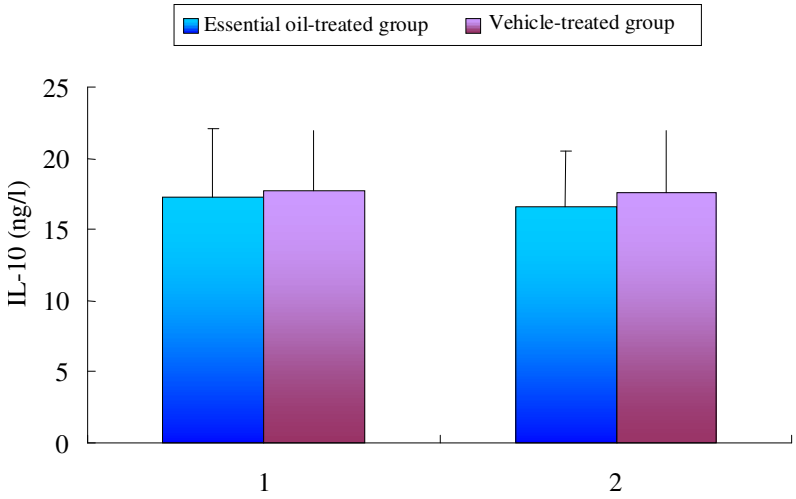

Figure 3. Effect of radix linderae essential oil treatment on serum IL-10 level in aged people.

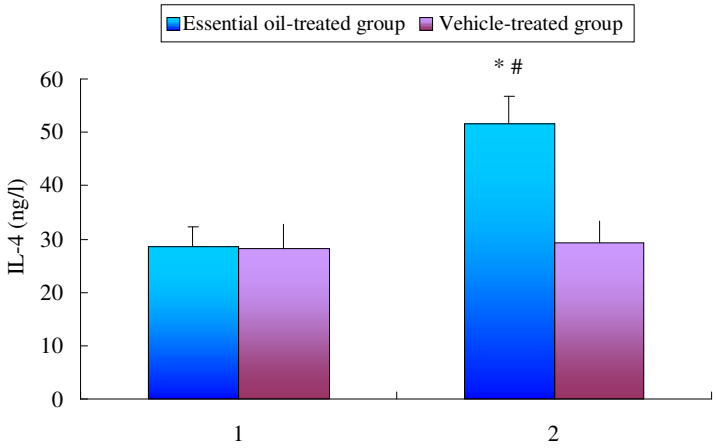

Figure 4. Effect of radix linderae essential oil treatment on serum IL-4 level in aged people.

Table 2. Effect of the radix linderae essential oil treatment on incidence rates of decubitus.

Group	Patients suffering from decubitus	Incidence rates (%)
essential oil treatment (57)	1	1.8
vehicle-treatment (58)	9	15.6

large increase ($p<0.01$) with the radix linderae essential oil treatment (Figure 4). In vehicle-treated group, no marked change in serum IL-4 level was observed. Serum IL-4 level in essential oil treatment group was significantly ($p<0.01$) higher than that in vehicle-treated group.

In the present study, only 1 patient (1.8%) in essential oil treatment group suffered from decubitus. However, 9 patients (15.6%) in vehicle-treated group suffered from decubitus. Comparing vehicle-treated group, incidence rates (%) in essential oil treatment group was markedly decreased (Table 2).

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