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Research Article

Chemical Constituents and Anti-Inflammatory Effect of Incense Smoke from Agarwood Determined by GC-MS

De-Qian Peng,[1,2] **Zhang-Xin Yu**,[1] **Can-Hong Wang**,[1] **Bao Gong**,[1] **Yang-Yang Liu**,[1] **and Jian-He Wei**[1,3]

[1]*Key Laboratory of State Administration of Traditional Chinese Medicine for Agarwood Sustainable Utilization, Hainan Branch of the Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union Medical College, Haikou 570311, China*
[2]*School of Pharmacy, Hainan Medical University, Haikou 571199, China*
[3]*National Engineering Laboratory for Breeding of Endangered Medicinal Materials, Key Laboratory of Bioactive Substances and Resources Utilization of Chinese Herbal Medicine, Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100193, China*

Correspondence should be addressed to Jian-He Wei; wjianh@263.net

De-Qian Peng and Zhang-Xin Yu contributed equally to this work.

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Agarwood is generally used to make incense sticks in China and Southeast Asia. It emits smoke with a pleasant odor when burned. There are few reports on the chemical components of smoke generated by burning or heating agarwood. The agarwoods were produced by the whole-tree agarwood-inducing technique (AWIT), agarwood induced by axe wounds (AAW), burning-chisel-drilling agarwood (BCDA), wood of *Aquilaria sinensis* trees (AS), respectively. Herein, we used GC-MS to analyze the chemical constituents of incense smoke generated from AWIT, AAW, BCDA, AS, and the extracts of sticks from agarwood produced by the whole-tree agarwood-inducing technique (EAWIT), and 484 compounds were identified. A total of 61 chemical constituents were shared among AWIT, AAW, and BCDA. The experimental data showed that aromatic compounds were the main chemical constituents in agarwood smoke and that some chromone derivatives could be cracked into low-molecular-weight aromatic compounds (LACs) at high temperature. Furthermore, agarwood incense smoke showed anti-inflammatory activities by inhibiting lipopolysaccharide- (LPS-) induced TNF-α and IL-1α release in RAW264.7 cells.

1. Introduction

Agarwood, called chen-xiang in China, is a valuable resinous wood from *Aquilaria spp.* or *Gyrinops spp*. trees [1–3]. It has been applied in medicine and shown obvious medicinal effects, such as sedative, carminative, and antiemetic effects [4, 5]. Agarwood does not form until a tree has been affected by factors such as lightning strike, animal grazing, insect attack, and fungi [6, 7]. Moreover, it takes a long time (years or even decades) to form in the wild. Natural agarwood is considered to be the finest source of incense and has been applied in cultural, religious, and medicinal uses for centuries. The market demand for agarwood is increasing daily. As a result, the supply of wild agarwood is not enough to meet the market demand. Many *Aquilaria* plantations have been established in some Southeast Asian countries, such as Indonesia, Cambodia, Laos, Thailand, Vietnam, and Malaysia. *Aquilaria* trees have been planted in South China, for example, in Hainan, Guangdong, and Yunnan provinces [8]. Some artificial technologies designed to rapidly induce agarwood formation have been demonstrated to make *A. sinensis* (AS) trees produce agarwood [7, 9–11]. In 2009, Blanchette and Heuveling developed cultivated agarwood kits (CA-Kits) [12]. In 2013, Liu et al. developed a whole-tree agarwood-inducing technique (Agar-Wit) [11]. Recently, Peng et al. also developed a similar technology to induce

agarwood formation [13]. The above methods induce agarwood formation simply and effectively.

Presently, agarwood and its volatile components are seen as important and efficient natural substances that can be used to produce valuable products such as perfumes and incense because of their fragrance characteristics. Many teams have researched the chemical constituents of agarwood [1, 14–16]. The chemical constituents of agarwood essential oil or solvent extracts have been studied by column chromatography, spectroscopic techniques, gas chromatography (GC), and multidimensional GC analysis. Many studies have reported the use of GC-MS to analyze the volatile components in agarwood smoke obtained by heating. For example, in 1993, Ishihara et al. analyzed the volatile constituents in agarwood smoke and identified 53 chemical compounds from Vietnamese agarwood [17]. Nurlaila et al. identified 8 significant compounds from agarwood smoke by Z-score analysis [18]. Recently, Zhou et al. used glass fiber pads to absorb volatile constituents of agarwood smoke from different kinds of agarwood from different countries and extracted the samples with dichloromethane (CH_2Cl_2) for GC-MS analysis [19, 20]. Kao et al. analyzed agarwood smoke from Kynam agarwood by headspace (HS) preheating with gas chromatography-mass spectrometry (HS GC-MS) and identified 40 compounds [21]. However, there are no reports on agarwood smoke produced by Agar-Wit. Herein, we analyzed the chemical constituents of agarwood smoke produced by Agar-Wit and identified 484 compounds.

2. Experimental Setup

2.1. Chemicals and Reagents. All chemicals were purchased from J&K Scientific (Beijing, China), unless otherwise indicated.

The agarwood samples were identified by Prof. Jianhe Wei (Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union Medical College, China). Incense sticks of AWIT, AAW, BCDA, and AS were made by Bao Gong (Hainan Branch Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union Medical College, China).

2.2. Sample Preparation. Each stick was placed in a gas washing bottle (250 mL) fitted with an air inlet/outlet tube. The smoke components were collected by bubbling through a 30 mL amount dichloromethane during the 10 min burn time. In addition, sticks made from AWIT (3.0 g) were pulverized and extracted with CH_2Cl_2 (30 mL).

2.3. Sample Analysis. Chromatographic separation of the resulting mixture (1.0 μL) was undertaken on an Agilent 7890 A GC coupled to a 5975C quadrupole mass spectrometer and an automated 7683B sample injector system (Agilent Technologies, Santa Clara, California, USA). Chromatography was performed on a HP-5MS capillary column (30 m × 250 μm ID, 0.25 μm film thickness, 5% diphenyl methyl siloxane (Agilent Technologies, USA). Helium was used as carrier gas at a constant flow rate of 1.0 mL/min. The injections (1.0 μL) were performed in splitless injection mode (10 : 1) at 240°C. The operating parameters included the following temperature program: 40°C for 3 min, increase from 40°C to 140°C at a rate of 2.5°C/min, hold at 140°C for 5 min, increase from 140°C to 170°C at a rate of 1.5°C/min, hold at 170°C for 5 min, and increase to 280°C at a rate of 4°C/min. The total run time was 100.5 min as shown in Figure 1. The mass selective detector was operated with electron energy of 70 eV in electron ionization mode. The ion source and quadrupole temperatures were 230°C and 150°C, respectively. The scan range was 40–500 amu in full scan mode. Peak identification was completed by comparing mass spectra with those stored in the NIST 11 database and MSD ChemStation, or by comparing fragmentation patterns with those published by the Dai group [22]. Table 1 shows the representative data.

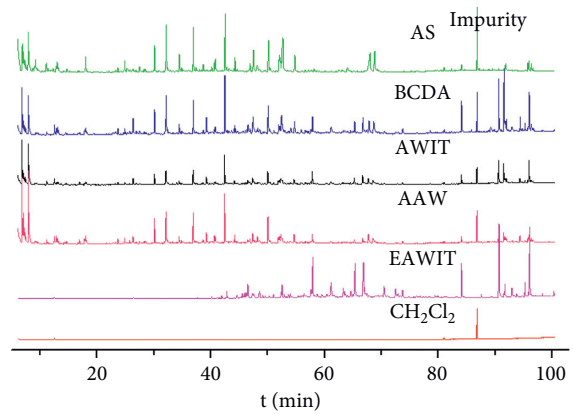


Figure 1: Gas chromatograph mass spectrometry (GC-MS) chromatograms of incense smoke (AWIT: whole-tree agarwood-inducing technique, AAW: agarwood produced by axe wounds, BCDA: burning-chisel-drilling agarwood, EAWIT: extract of stick from agarwood produced by whole-tree agarwood-inducing technique, AS: *A. sinensis*).

2.4. LPS-Stimulated TNF-α and IL-1α Release in RAW264.7 Cells

2.4.1. Isolation and Culture of RAW264.7 Cells. RAW264.7 cells in logarithmic growth phase were washed twice with phosphate-buffered saline (PBS) and inoculated in 96-well plates at a density of 1×10^4 cells per well, and 100 μL of cell suspension was added to each well. Three compound wells were set in each group and cultured at 37°C in 5% CO_2 for 24 h.

2.4.2. Measurement of TNF-α and IL-1α Production. The cells were incubated with 1 ng/mL LPS in the presence of indomethacin, AAW, BCDA, and AWIT (20, 40 and 80 μg/mL) and cultured at 37°C and 5% CO_2 for 24 h. Then, the levels of TNF-α and IL-1α in the cell-free culture supernatant were determined by ELISA kits.

Table 1: Chemical constituents and relative amounts of AAW, BCDA, AWIT, AS, and EAWIT.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
1	Ethylbenzene	6.774	6.215 (B)	3.296 (B)	6.384 (B)	1.313 (B)	—
2	Furfuryl alcohol	6.872	—	—	—	2.212	—
3	1,4-Xylene	7.080	3.709 (B)	—	—	1.765 (B)	—
4	1,3-Xylene	7.086	—	—	2.354 (B)	—	—
5	1,2-Xylene	7.098	—	1.326 (B)	—	0.778 (B)	—
6	Phenylacetylene	7.392	1.387 (B)	0.698 (B)	1.612 (B)	1.013 (B)	—
7	Phenyl carbamate	7.646	—	—	—	0.308 (B)	—
8	Phenylethylene	7.901	8.596 (B)	3.413 (B)	7.973 (B)	5.132 (B)	—
9	2-Methyl-2-cyclopenten-1-one	8.680	—	—	—	0.400	—
10	4,4-Dimethyl-2-cyclopenten-1-one	8.952	—	—	—	0.302	—
11	2,5-Dimethyl-2,4-hexadiene	9.056	—	—	—	0.408	—
12	Anisole	9.096	0.239 (B)	—	0.21 (B)	—	—
13	2(5*H*)-Furanone	9.200	0.202	0.132	0.299	0.981	—
14	3,4-Dihydro-*H*-pyran	9.356	0.202	0.202	—	0.381	—
15	Methyl-2-oxo-1-pyrrolidineacetate	9.605	—	0.222	—	—	—
16	Tetrahydro-22-desoxy-tomatillidine	9.610	—	—	—	0.211	—
17	1-Methylene-2-vinylcyclopentane	10.962	—	—	—	0.113	—
18	Benzaldehyde	11.118	0.671 (B)	0.28 (B)	1.008 (B)	1.146 (B)	—
19	5-Methyl-furfural	11.407	—	—	—	0.508	—
20	2,3-Dihydroxystearic acid	11.875	—	—	—	0.209	—
21	2-Chloro-2,2-difluoro-acetonitrile	11.950	—	—	—	0.157	—
22	2-Methyl-2-pentenal	12.192	—	—	—	0.104	—
23	Benzonitrile	12.308	—	—	—	0.359 (B)	—
24	2,2,4,6,6-Pentamethylheptane	12.510	0.902	0.753	1.152	—	0.126
25	Benzofuran	12.793	—	—	—	0.541 (B)	—
26	Phenol	12.839	1.225 (B)	0.558 (B)	0.592 (B)	0.852 (B)	—
27	2,2-Diethyl-3-methyl-oxazolidine	13.105	0.751	0.785	0.808	—	—
28	(2*S*, 3*S*)-2,3-Dimethoxy-N^1,N^1,N^1,N^4-tetramethyl-1,4-butanediamine	13.111	—	—	—	0.846	—
29	5-Norbornene-2-carboxaldehyde	13.654	0.169	—	0.189	—	—
30	4-Methylanisole	14.185	0.305 (B)	0.102 (B)	0.135 (B)	0.159 (B)	—
31	2-Azido-2,4,4,6,6-pentamethylheptane	14.445	0.255	0.187	0.220	—	—
32	2,3-Dioxabicyclo[2.2.2]oct-5-ene	14.671	0.424	0.189	0.175	—	—
33	3-Methyl-1,2-cyclopentanedione	14.717	—	—	—	0.369	—
34	2-Methyl-3-furanthiol	15.918	0.106	0.201	—	—	—
35	3-Methyl-phenol	16.635	0.219 (B)	0.176 (B)	0.12 (B)	—	—
36	2-Methyl-phenol	16.669	—	—	—	0.226 (B)	—
37	3-Methyl-bicyclo[3.3.0]oct-2-en-8-one	16.918	—	—	—	0.129	—
38	2,2,2-Bicyclo-2-octene	16.935	0.496	0.183 (B)	0.453 (B)	—	—
39	*p*-Cresol	17.801	0.73 (B)	0.473 (B)	0.321 (B)	0.205 (B)	—
40	Guaiacol	17.998	0.877 (B)	0.51 (B)	0.608 (B)	1.362 (B)	—
41	2-*t*-Butylamino-acrylonitrile	18.165	0.421	0.224	0.240	—	—

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
42	3,5-Dimethyl-4*H*-pyran-4-one	18.182	—	—	—	0.107	—
43	3-Hydroxy-2-methyl-4-pyrone	19.338	—	0.169	—	0.147	—
44	2,5-Dimethylphenol	21.677	0.223 (B)	0.129 (B)	—	0.165 (B)	—
45	2,3-Dihydroxybenzaldehyde	22.064	—	—	—	0.148 (B)	—
46	5-Ethyl-3-(3-methyl-5-phenylpyrazol-1-yl)-1,2,4-triazol-4-amine	22.215	0.152 (B)	—	—	—	—
47	Ethyl disulfide	22.220	—	—	0.094	—	—
48	1-Methylene-1*H*-indene,	22.740	0.166 (B)	—	—	—	—
49	2-Ethylphenol	22.913	0.129 (B)	—	—	—	—
50	Trehalose	22.914	—	0.324	—	—	—
51	2-Isopropyl-5-methyl-1-heptanol	23.197	—	—	0.059	—	—
52	3-Methyl-2-butene-1-thiol	23.208	0.120	—	—	—	—
53	2-Methylbutyl pentanoic acid ester	23.225	—	0.251	—	—	—
54	4-Methoxy-1,3-benzenediamine	23.300	—	—	—	0.216 (B)	—
55	2-Methoxy-3-methyl-phenol	23.306	0.236 (B)	—	—	—	—
56	2-Methoxy-4-methylphenol	23.676	0.444 (B)	0.283 (B)	0.271 (B)	0.309 (B)	—
57	2-Methoxy-5-methylphenol	23.688	—	0.327 (B)	—	—	—
58	3,6-Dimethyl-2,6-octadiene-4,5-diol	24.144	—	—	—	0.129	—
59	1,4 : 3,6-Dianhydro-α-d-glucopyranose	24.600	0.148	0.158	0.172	0.120	—
60	*trans*-Cinnamaldehyde	24.866	—	—	—	0.821 (B)	—
61	(1α, 2β, 5β, 6α)-Tricyclo[4.2.1.1(2,5)]deca-3,7-diene-9,10-dione	24.883	0.446	0.325	—	—	—
62	α-Methylene-benzeneacetaldehyde	24.895	—	—	0.247 (B)	—	—
63	2,4-Cyclopentadiene-1-ethanamine	25.045	0.128	—	0.230	—	—
64	1,11-Dibromo-undecane	25.062	—	0.101	—	—	—
65	Pyrocatechol	25.357	0.125 (B)	0.287	—	0.93 (B)	—
66	2,3-Anhydro-d-galactosan	25.357	—	—	0.204 (B)	—	—
67	2,3-Dihydrobenzofuran	25.727	0.369 (B)	0.382 (B)	0.299 (B)	0.255 (B)	—
68	1-Methyl-1*H*-pyrrole-2(5*H*)-one	26.131	—	—	0.203	—	—
69	2-Isopropoxyphenol	26.183	—	—	—	0.226 (B)	—
70	3-Methoxyphenol	26.206	0.263 (B)	—	—	—	—
71	5-Hydroxymethylfurfural	26.229	—	0.252	—	0.389	—
72	4-Phenyl-2-butanone	26.339	0.77 (B)	1.13 (B)	1.06 (B)	—	0.177 (B)
73	1-Methyl-4-amino-4,5(1*H*)-dihydro-1,2,4-triazole-5-one	26.847	—	—	—	0.259	—
74	Anisic aldehyde	26.905	0.306 (B)	0.301 (B)	0.389 (B)	—	—
75	2-Oxohexamethylenimine	27.032	—	0.185	—	—	—
76	3-Methoxy-2-benzenediol	27.454	0.401 (B)	0.365 (B)	0.251 (B)	0.582 (B)	—
77	3-Methoxybenzenethiol	27.731	0.131 (B)	—	—	—	—
78	1-Indanone	28.043	0.279 (B)	—	—	0.148 (B)	—
80	2-Isopropyl-3-methoxypyrazine	28.291	—	—	—	0.177	—

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
79	4-Ethyl-2-methoxyphenol	28.291	0.292 (B)	0.104 (B)	0.071 (B)	—	—
81	3-(4-Methylphenyl)-2-propenal	28.441	—	—	—	0.206 (B)	—
82	2,3-Dihydro-2-methyl-1*H*-inden-1-one	28.447	0.223	—	0.056 (B)	—	—
83	*α*-Methylcinnamaldehyde	28.557	—	—	—	0.127 (B)	—
84	2-Methylnaphthalene	28.621	0.285 (B)	—	—	—	—
85	1-Azabicyclo[2.2.2]octane-4-methanol	29.527	—	0.158	—	—	—
86	(*E*)-2,4,4,7-Tetramethyl-5,7-octadien-3-ol	29.666	—	—	—	0.179	—
87	4-Hydroxy-3-methoxystyrene	30.099	2.343 (B)	1.799 (B)	1.512 (B)	2.254 (B)	—
88	*o-tert*-Butyl phenol	30.417	—	—	—	0.131 (B)	—
89	3-Hydroxybenzaldehyde	30.844	—	—	—	0.252 (B)	—
90	2-Methoxybenzyl alcohol	31.081	—	—	—	0.106 (B)	—
91	*trans*-3-Hexenedioic acid-bis(trimethylsilyl) ester	31.411	0.127	—	—	—	—
92	2-*exo*-Chlorobicyclo[2.2.1]heptane-1-carbonyl chloride	31.942	0.282	—	0.285	—	—
93	2-Ethyl-1*H*-pyrrolo[2,3-b]pyridine	32.000	—	—	—	0.157	—
94	2,6-Dimethoxyphenol	32.115	3.013 (B)	2.939 (B)	2.178 (B)	—	—
95	*cis*-4,5-Diethyl-1,2-dimethyl-cyclohexene	32.190	—	—	—	4.085	—
96	Eugenol	32.358	0.517 (B)	0.303 (B)	0.262 (B)	—	—
97	3-Allyl-6-methoxyphenol	32.375	—	—	—	0.413 (B)	—
98	3,4-Dimethoxyphenol	32.566	—	0.112 (B)	—	0.219 (B)	—
99	3-Ethenyl-4-methyl-1*H*-pyrrole-2,5-dione	32.849	0.205	—	—	0.149	—
100	3-Cyclohexene-1-acetaldehyde	33.247	0.191	—	0.136	—	—
101	11-Methylene-tricyclo[4.3.1.1(2,5)]undecane	33.247	—	—	—	—	—
102	2-Propyl-phenol	33.848	—	—	—	0.1 (B)	—
103	4-Hydroxybenzaldehyde	33.975	—	—	—	0.225 (B)	—
104	Dichlorophenylsilane	34.010	—	—	0.321 (B)	—	—
105	Phenylboronic acid	34.016	0.406 (B)	0.143 (B)	—	—	—
106	Vanillin	34.408	0.8 (B)	0.83 (B)	0.708 (B)	1.842 (B)	—
107	4-(Methylthio)-benzaldehyde	34.593	0.254 (B)	—	—	—	—
108	(*E*)-isoeugenol	34.899	0.341 (B)	0.18 (B)	0.133 (B)	0.31 (B)	—
109	*o*-Methoxy-benzenethiol	35.084	0.125 (B)	—	—	0.197 (B)	—
110	2-Methoxy-1,4-benzenediol	35.217	—	—	—	0.209 (B)	—
111	2-Benzylidenemalonaldehyde	35.217	0.204 (B)	—	—	—	—
112	2-Vinylnaphthalene	35.442	0.115 (B)	—	—	—	—
113	3-Hydroxy-2-methyl-5-(1-methylethyl)-2,5-cyclohexadiene-1,4-dione	36.083	—	—	—	0.237	—
114	Biphenylene	36.234	0.105 (B)	—	—	—	—

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
115	2-Methoxy-4-(1-propen-1-yl)-phenol	36.892	2.962 (B)	2.126 (B)	2.379 (B)	3.254 (B)	—
116	4-Hydroxy-2-methoxybenzaldehyde	37.227	0.243	0.142	—	0.135 (B)	—
117	2-Methoxy-4-propyl-phenol	37.429	0.268 (B)	0.242 (B)	0.257 (B)	0.454 (B)	—
118	1,7-Dimethylpentacyclo[5.5.0(4,11).0(5,9).0(8,12)]dodecane-2,6-dione	37.689	—	—	0.126 (B)	—	—
119	2-Methoxy-6-[(4*H*-1,2,4-triazol-4-ylamino)methyl]-phenol	37.689	0.107	—	—	—	—
120	4-Hydroxybenzylidene acetone	37.707	—	0.101	—	—	—
121	*N*-Phenylthioformamide	37.712	—	—	—	0.126 (B)	—
122	7-Ethylbenzo[b]thiophene	38.053	—	—	—	0.153	—
123	5,6-Dimethyl-2-benzimidazolinone	38.382	—	—	—	0.164 (B)	—
124	Cyclohexylmethylbenzene	38.440	0.145 (B)	—	0.161 (B)	—	—
125	3,4-Dimethoxy-benzaldehyde	38.573	—	—	—	0.712 (B)	—
126	4′-(Methylthio)acetophenone	38.660	0.370	0.298 (B)	0.256 (B)	—	—
127	4-(4-Methoxyphenyl)-2-butanone	39.232	1.067 (B)	1.161 (B)	1.124 (B)	0.137	—
128	Pentadecane	39.434	—	—	0.168	—	—
129	Dibenzofuran	39.451	0.186 (B)	0.145 (B)	—	—	—
130	2′,6′-Dihydroxyacetophenone, bis(trimethylsilyl) ether	39.850	0.207 (B)	—	—	—	—
131	1-Methyl-1-phenylmethoxy-1-silacyclohexane	39.873	—	0.104 (B)	0.111 (B)	—	—
132	1,3,3-Trimethyl-2-(1-methylbut-1-en-3-on-1-yl)-1-cyclohexene	40.173	0.273	—	—	—	—
133	1,2-Dimethoxy-4-(methoxymethyl)benzene	40.196	—	0.178 (B)	—	—	—
134	2,4-Di-*tert*-butylphenol	40.202	—	—	—	0.287 (B)	—
135	2-(2-Hydroxyhex-1-enyl)-3-methyl-5,6-dihydropyrazine	40.260	0.138	—	—	—	—
136	5-(1,1-Dimethylethyl)-1,2,3-benzenetriol	40.653	0.578 (B)	0.34 (B)	0.212 (B)	0.684 (B)	—
137	Homovanillyl alcohol	40.780	0.594 (B)	0.507 (B)	0.417 (B)	1.119 (B)	—
138	[4-(1,1-Dimethylethyl)phenoxy]-acetate-methanol	41.912	—	—	—	—	0.159 (B)
139	(*S*)-4,5,6,7,8,8a-Hexahydro-8a*α*-methylazulen-2(1*H*)-one	42.137	0.109	—	—	—	—
140	Acetic acid-2-propylphenyl ester	42.160	—	0.114 (B)	—	—	—
141	3-Nitrobenzaldehyde-(*O*-methyl oxime)	42.420	—	—	—	—	—
142	2,3,5,6-Tetrafluoroanisole	42.443	4.532 (B)	3.741 (B)	4.13 (B)	—	—
143	3-*tert*-Butyl-4-hydroxyanisole	42.547	—	—	—	5.641 (B)	—
144	2,5-Dihydroxy-4-isopropyl-2,4,6-cycloheptatrien-1-one	42.819	—	—	—	0.329	—
145	*α*-Santalol	42.848	—	—	—	—	0.511 (S)
146	2,3-Dihydro-2,2-dimethyl-3,7-benzofurandiol	42.888	0.359 (B)	0.39 (B)	0.394 (B)	—	—
147	7-(1,1-Dimethylethyl)-3,4-dihydro-1(2*H*)-naphthalenone	43.119	—	—	—	—	0.105 (B)
148	3-Ethoxy-4-methoxybenzaldehyde	43.183	0.324 (B)	—	0.221 (B)	—	—

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
149	3-Hydroxy-4-methoxybenzoic acid-methyl ester	43.200	—	0.318 (B)	—	—	—
150	Ethyl vanillate	43.211	—	—	—	0.279 (B)	—
151	α-Amino-3′-hydroxy-4′-methoxyacetophenone	43.443	0.126 (B)	0.143 (B)	—	—	—
152	(3*S*, 4*R*, 5*R*, 6*R*)-4,5-Bis(hydroxymethyl)-3,6-dimethylcyclohexene	43.610	—	—	0.202	—	—
153	Carbonic acid-2,3-dimethylphenyl methyl ester	43.628	0.41 (B)	—	—	—	—
154	3-(4-Methoxyphenyl)propionic Acid	43.656	—	0.431 (B)	—	—	—
155	Hexadecane	44.078	0.329	0.351	0.321	0.127	—
156	2,6-Dimethoxy-4-(2-propen-1-yl)-phenol	44.274	0.785 (B)	0.619 (B)	0.521 (B)	1.029 (B)	—
157	2,6-Dimethyl-4-nitrophenol	44.586	0.256 (B)	—	—	—	—
158	[1*S*-(1α, 4α, 7α)]-1,2,3,4,5,6,7,8-Octahydro-1,4,9,9-tetramethyl-4,7-methanoazulene	44.592	—	—	—	—	0.406 (S)
159	2-Ethyl-4-methyl-4,6-bis(1-methylethyl)-4*H*-1,3,2-dioxaborin	44.592	—	—	—	0.139	—
160	8-*Epi*-γ-eudesmol	44.633	—	0.261 (S)	0.219 (S)	—	—
161	Methyl-2,6,6-trimethyl-3-oxo-1-cyclohexene-1-acrylate	44.737	—	—	0.155	—	—
162	2′,6′-Dimethylacetanilide	44.771	—	0.187	—	—	—
163	[1*S*-(1α, 4aβ, 8aα)]-1,2,4a,5,8,8a-Hexahydro-4,7-dimethyl-1-(1-methylethyl)-naphthalene	45.152	—	—	—	—	0.141 (S)
164	[1*R*-(1α, 3aα, 7aα)]-1,2,3,6,7,7a-Hexahydro-2,2,4,7a-tetramethyl-1,3a-ethano-3a*H*-indene	45.326	—	0.241 (B)	—	—	0.149 (S)
165	Agarospirol	45.551	—	0.238 (S)	0.195 (S)	—	0.413 (S)
166	Methyl 3-(bicyclo[2.2.1]hept-1-yl)-propenoate	45.586	—	—	—	0.116	—
167	Hinesol	45.719	0.126	—	—	—	0.251 (S)
168	(1α, 6α, 7α)-1,5,5-Trimethyl-2-methylene-bicyclo[4.1.0]heptane-7-methanol	45.736	0.121 (S)	—	—	—	—
169	(1*R*, 3a*R*, 4*R*, 7*R*)-1,2,3,3a,4,5,6,7-Octahydro-1,4-dimethyl-7-(1-methylethenyl)-azulene	45.748	—	—	0.191 (S)	—	—
170	[1*S*-(1α, 4α, 7α)]-1,2,3,4,5,6,7,8-Octahydro-1,4-dimethyl-7-(1-methylethenyl)-azule	45.776	—	0.222 (B)	—	—	—
171	Longifolene	45.990	—	—	—	—	0.565 (S)
172	10*S*,11*S*-Himachala-3(12),4-diene	46.007	0.155 (S)	—	—	—	—
173	Neoisolongifolene	46.042	—	0.262 (S)	0.248 (S)	—	—
174	Ledol	46.279	—	—	0.219 (S)	—	0.519 (S)
175	β-Eudesmol	46.325	0.150	0.343 (S)	—	—	—
176	Guaiol	46.498	—	—	0.939 (S)	—	—
177	γ-Selinene	46.504	0.589 (S)	1.164 (S)	—	—	1.868 (S)
178	1-Bromooctadecane	46.712	—	—	—	—	—
179	7,9-Dimethyl-hexadecane	46.729	0.169	—	0.219	—	—
180	(4-Methoxyphenyl)glycolic acid	46.752	—	—	—	0.212	—
181	3-(4-Hydroxy-3-methoxyphenyl)-2-propenoic acid	46.880	0.629 (B)	0.509 (B)	0.517 (B)	0.814 (B)	—
182	Dehydroaromadendrene	47.301	—	—	—	—	0.442 (S)
183	3,5-Dimethoxy-4-hydroxybenzaldehyde	47.353	1.599 (B)	1.78 (B)	1.891 (B)	2.92 (B)	—

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
184	2,4,6-Trimethyl-pyridine	47.428	—	—	—	—	0.383
185	Camphene	47.561	—	—	—	—	0.600
186	Ethyl (3-pyridyl)carbamate N-oxide	47.608	—	0.753	—	—	—
187	Hexamethyl-benzene	47.654	0.503	—	0.646 (B)	—	—
188	1-(1,3a,4,5,6,7-Hexahydro-4-hydroxy-3,8-dimethyl-5-azulenyl)-ethanone	47.896	—	—	—	—	0.142 (S)
189	2-Allyl-1,4-dimethoxy-3-methyl-benzene	48.029	0.249 (B)	—	0.33 (B)	—	—
190	2,5-Dibutyl-furan	48.150	—	—	—	1.392	—
191	Vanillylacetone	48.208	1.036 (B)	0.967 (B)	0.425 (B)	—	—
192	[1*S*-(1α, 7α, 8aβ)]-1,2,3,5,6,7,8,8a-Octahydro-1,4-dimethyl-7-(1-methylethenyl)-azulene	48.480	—	—	—	—	0.55 (S)
193	Dehydro-cyclolongifolene oxide	48.509	—	0.717 (S)	0.473 (B)	—	—
194	4-Methoxymethyl-6-methyl-1*H*-pyrazolo[3,4-b]pyridin-3-ylamine	48.572	—	—	—	0.283	—
195	1-Cyclohexyl-2-methoxy-benzene	48.601	—	—	0.384 (B)	—	0.72 (B)
196	*N*,*N*-Diethyl-2-benzoxazolamine	48.613	0.781 (B)	—	—	—	—
197	Octahydro-2-(1-methylethylidene)-4,7-methano-1*H*-indene	49.161	—	—	—	—	0.361 (B)
198	4,6,6-Trimethyl-2-(3-methylbuta-1,3-dienyl)-3-oxatricyclo[5.1.0.0(2,4)] octane	49.167	—	—	0.172	—	—
199	4-Methylene-1-methyl-2-(2-methyl-1-propen-1-yl)-1-vinyl-4-methylene-1-methyl-2-(2-methyl-1-propen-1-yl)-1-vinyl-cycloheptane	49.219	0.121	0.181	—	—	—
200	3-Phenoxy-phenol	49.467	0.325	0.154 (B)	0.134 (B)	0.248 (B)	—
201	(*Z*)-3,7-Dimethyl-1,3,6-octatriene	49.537	—	—	—	—	0.406
202	1,7-Dimethyl-7-(4-methyl-3-pentenyl)-tricyclo[2.2.1.0(2,6)]heptane	49.612	—	0.2 (S)	0.192 (S)	—	—
203	2-Acetate-1,3-dimethoxy-5-(1-propenyl)-benzene	50.057	3.206 (B)	2.309 (B)	—	—	—
204	2,5-Dimethoxyterephthalic acid	50.178	—	—	2.516 (B)	3.780	—
205	2-(2-Furanylmethylene)-6-methyl-cyclohexanone	50.270	—	—	—	—	0.255
206	4-Propylbiphenyl	50.380	0.704 (B)	0.711 (B)	—	—	—
207	1-Ethyl-3-(phenylmethyl)-benzene	50.386	—	—	0.745 (B)	—	—
208	*N*,*N*,*S*-Trimethyl-3-aminothiophenol	50.415	—	—	—	0.684 (B)	—
209	Neocurdione	50.438	—	—	—	—	0.161 (S)
210	*endo*-Borneol	51.056	—	—	—	—	0.611
211	9-Fluorenone	51.073	0.205 (B)	—	—	—	—
212	[1*S*-(1α, 3aβ, 4α, 8aβ, 9*R**)]-Decahydro-4,8,8-trimethyl-1,4-methanoazulene-9-methanol	51.108	—	0.488 (S)	0.295 (S)	—	—
213	Methyl α-hydroxy-4-methoxy-benzeneacetate	51.605	—	—	—	0.101 (B)	—
214	2,2′-Methylenebis[5-methyl-furan	51.743	—	—	—	—	0.136
215	4-Hydroxy-2-methoxycinnamaldehyde	51.882	0.937 (B)	0.897 (B)	0.78 (B)	—	—
216	3-(4-Hydroxy-3-methoxyphenyl)-2-propenal	52.072	—	—	—	2.664 (B)	—
217	Acetosyringone	52.096	0.967 (B)	0.829 (B)	0.88 (B)	1.499 (B)	—
218	*syn*-3,3,5,6,8,8-Hexamethyl-tricyclo[5.1.0.0(2,4)]oct-5-ene,	52.333	1.530	1.979	1.762	—	0.624

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
219	2-Phenylethyl-1,1,2,2-d4-amine	52.541	—	—	1.184 (B)	—	—
220	2-Methyl-5-(1-methylethyl)-phenol	52.552	—	—	—	—	1.377 (B)
221	2′-Hydroxy-3,3-dimethyl-3-phenylpropanal	52.558	0.762 (B)	—	—	—	—
222	2-[3-Methoxyphenyl]-propionic acid	52.581	—	1.048 (B)	—	—	—
223	3-(2-Pentenyl)-1,2,4-cyclopentanetrione	52.679	—	—	—	6.688 (B)	—
224	7-(1,3-Dimethylbuta-1,3-dienyl)-1,6,6-trimethyl-3,8-dioxatricyclo [5.1.0.0(2,4)]octane	52.951	0.340	0.621	0.732	—	0.491
225	*o*-Mentha-1(7),8-dien-3-ol	53.262	—	—	—	—	0.206
226	1,10b(2*H*)-Dihydropyrano[3,4,5-jk]fluorene	53.488	0.153 (B)	—	—	—	—
227	Anthracene	53.499	—	—	—	0.124 (B)	—
228	(1*S*, 6*R*, 9*S*)-5,5,9,10-Tetramethyltricyclo[7.3.0.0(1,6)]dodec-10(11)-ene	53.609	0.121	0.457	0.414	—	—
229	(*Z*)-3-Methyl-2-(2,4-pentadienyl)-2-cyclopenten-1-one	53.632	—	—	—	—	0.559
230	1-Methoxy-4-methyl-2-(1-methylethyl)-benzene	54.019	—	—	—	—	0.565 (B)
231	(1*Z*, 3a*α*, 7a*β*)-1*H*-1-Ethylideneoctahydro-7a-methyl-indene	54.089	0.466 (B)	0.773 (B)	0.531 (B)	—	—
232	3-(Phenylmethoxy)-1-propanol	54.233	—	—	—	—	0.238 (B)
233	*trans*-1,10-Dimethyl-2-methylene-decalin	54.510	—	—	—	—	0.113
234	3,5-Dimethoxy-4-hydroxyphenylacetic acid	54.649	1.383 (B)	1.359 (B)	1.391 (B)	2.15 (B)	—
235	(1a*R*, 4*S*, 4a*R*, 7*S*, 7a*R*, 7b*S*)-Decahydro-1,1,4,7-tetramethyl-1*H*-cycloprop [e]azulene	54.672	—	—	—	—	0.177 (S)
236	2,7-Dimethyl-5-(1-methylethenyl)-1,8-nonadiene	55.036	—	—	—	—	0.126
237	Longifolenaldehyde	55.261	—	0.12 (S)	—	—	—
238	(2*R*-*cis*)-1,2,3,4,4a,5,6,7-Octahydro-*α*,*α*,4a,8-tetramethyl-2-naphthalenemethanol	55.377	—	—	—	—	0.409 (B)
239	(4a*R*, 5*S*)-4,4a,5,6,7,8-Hexahydro-4a,5-dimethyl-3-(1-methylethylidene)-2(3*H*)-naphthalenone	55.850	0.459 (S)	0.535 (S)	0.609 (S)	—	0.611 (S)
240	1,2,4-Triethyl-benzene	56.130	—	—	—	—	0.301 (B)
241	Isoaromadendrene epoxide	56.145	0.114 (S)	—	0.143 (S)	—	—
242	2,3,4,5-Tetramethyl-tricyclo[3.2.1.02,7]oct-3-ene	56.405	—	—	—	—	0.659
243	Globulol	56.584	—	—	—	—	0.344 (S)
244	Octadecane	56.624	0.285	0.331	0.393	0.179	—
245	2,3-Dihydro-2,2-dimethyl-7-benzofuranol	56.803	—	—	—	—	0.258 (B)
246	1*β*, 2*α*-Dimethyl-3*α*, 5*β*-bis(1-methylethenyl)cyclohexane	56.844	—	—	0.285	—	—
247	4,6-Dimethoxy-1-naphthaldehyde	56.896	0.214 (B)	—	—	—	—
248	2-Bromo-1,3-dimethoxy-benzene	56.919	—	0.305 (B)	—	—	—
249	1,3,5-Triethyl-benzene	57.040	—	—	—	—	0.252 (B)
250	7-Methyl-pentadecane	57.144	—	—	0.189	—	—
251	2-Methyl-dodecane	57.150	0.154	—	—	—	—
252	Corymbolone	57.225	—	—	—	—	0.164 (S)
253	2,6,10,14-tetramethyl-Hexadecane	57.225	0.130	0.285	0.151	0.298	—
254	1-(2-Thienyl)-1-heptanone	57.520	—	—	0.500	—	—
255	1-(2-Thienyl)-1-hexanone	57.543	0.391	—	—	—	—

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
256	2,4-Dimethylcyclopentane-1,3-dione	57.601	—	0.475	—	—	—
257	1-(2-Thienyl)-ethanone	57.612	—	—	—	—	1.207
258	1-(2,6-Dihydroxy-4-methoxyphenyl)-ethanone	57.716	—	—	—	0.162 (B)	—
259	5-(2-Thienyl)-4-pyrimidinamine	57.832	1.086	1.513	2.402	—	—
260	1,3-Benzenedicarboxylic acid-4-methyl-1,3-dimethyl ester	57.941	—	—	—	—	5.197 (B)
261	3,4-Dimethoxy-benzaldehyde oxime	58.051	—	—	0.196 (B)	—	—
262	1,2-Dimethoxy-4-(1,2-dimethoxyethyl)benzene	58.063	0.295 (B)	0.233 (B)	—	—	—
263	5-Methoxy-[1,2,4]triazolo[4,3-a]pyridine-3-thiol	58.149	—	—	—	0.335	—
264	Methyl-3-amino-4-methoxybenzoate	58.248	0.192 (B)	0.304 (B)	0.29 (B)	—	—
265	Isomaltol	58.271	—	—	—	—	0.623
266	9-Methyl-9-azabicyclo[4.2.1]nona-2,4-diene	58.721	0.103	—	—	—	0.970
267	Chlordimeform	58.791	—	0.309 (B)	—	—	—
268	Nootkatone	59.229	—	—	—	—	0.118 (S)
269	4-(3-Methyl-2-butenyl)-phenol	59.541	—	—	—	—	0.772 (B)
270	[2*R*-(2α, 4aα, 8aβ)]-1,2,3,4,4a,5,6,8a-Octahydro-4a,8-dimethyl-2-(1-methylethenyl)-naphthalene	59.663	—	0.125 (S)	—	—	—
271	[1*R*-(1R^*, 4*Z*, 9S^*)]-4,11,11-trimethyl-8-methylene-bicyclo[7.2.0]undec-4-ene	59.952	—	—	—	—	0.193 (S)
272	2,3,4,5,6-Pentamethyl-benzoic acid	60.200	0.221 (B)	0.151 (B)	—	—	—
273	[1a*R*-(1aα, 7α, 7aα, 7bα)]-1a,2,3,5,6,7,7a,7b-Octahydro-1,1,7,7a-tetramethyl-1H-cyclopropa[a]naphthalene	60.206	—	—	—	—	0.167 (S)
274	4,5-Dihydro-6-(4-fluorophenyl)-pyridazin-3(2*H*)-one	60.235	—	—	—	—	—
275	*N*(1)-[(3-Methoxyphenyl)methyl]-1*H*-1,2,3,4-tetrazole-1,5-diamine	60.367	—	—	0.17 (B)	—	—
276	1-Ethenyl-1-methyl-2-(1-methylethenyl)-4-(1-methylethylidene)-cyclohexane	60.396	—	—	—	—	0.601 (S)
277	(*E*,*E*)-1,5-Dimethyl-8-(1-methylethylidene)-1,5-cyclodecadiene	60.443	—	0.165 (S)	—	—	—
278	6,7-Dimethyl-8-(1-methylethyl)-2,4(1*H*,3*H*)-pteridinedione	60.708	—	0.105	—	—	—
279	*trans*-*Z*-α-Bisabolene epoxide	60.737	—	—	—	—	0.42 (S)
280	Aromadendrene oxide-(1)	61.066	—	—	0.814 (S)	—	—
281	Cedrol	61.072	0.376 (S)	—	—	—	—
282	1-Hydroxy-6-(3-isopropenyl-cycloprop-1-enyl)-6-methyl-heptan-2-one	61.153	—	1.008	—	—	—
283	(1*R*, 7*R*, 8a*S*)-1,2,3,5,6,7,8,8a-Octahydro-1,8a-dimethyl-7-(1-methylethenyl)-naphthalene	61.170	—	—	—	—	2.925 (S)
284	α-Farnesene	61.546	—	—	—	—	0.429
285	2-Methylene-6,8,8-trimethyl-tricyclo[5.2.2.0(1,6)]undecan-3-ol	61.592	—	0.156	—	—	—
286	Thiocyanic acid-4-(dimethylamino)phenyl ester	61.702	—	—	—	—	0.354
287	[4a*R*-(4aα, 7α, 8aβ)]-Decahydro-4a-methyl-1-methylene-7-(1-methylethenyl)-naphthalene	61.892	—	—	—	—	0.198 (S)
288	Decahydro-2,2,4,8-tetramethyl-4,8-methanoazulen-9-ol stereoisomer	62.060	—	—	—	—	0.306 (S)
289	Diphenylmethane	62.551	—	—	—	0.27 (B)	—
290	[1a*R*-(1aα, 4β, 4aβ, 7α, 7aβ, 7bα)]-Decahydro-1,1,4,7-tetramethyl-1*H*-cycloprop[e]azulen-4-ol	62.568	—	—	—	—	0.205 (S)
291	Spiro(tricyclo[6.2.1.0(2,7)]undeca-2,4,6,9-tetraene-11,1′-cyclopropane	62.568	0.198 (B)	—	—	—	—
292	4-Methyl-1-[2,6,6-trimethyl-2-cyclohexen-1-yl]-1-penten-3-one,	62.603	—	0.149	—	—	—
293	[1*S*-(1α, 7α, 8aα)]-1,2,3,5,6,7,8,8a-Octahydro-1,8a-dimethyl-7-(1-methylethenyl)-naphthalene	62.788	—	—	—	—	0.248 (S)

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
294	Caryophyllene	63.007	—	—	—	—	0.172 (S)
295	Nonadecane	63.059	0.129	0.134	0.125	0.145	—
296	7-Methoxy-3,4-dihydro-2[1*H*]-quinoxalinone	63.233	0.241 (B)	0.27 (B)	0.367 (B)	—	—
297	2-Allyl-1,4-dimethoxybenzene	63.296	—	—	—	—	1.347 (B)
298	Dehydroxy-isocalamendiol	63.493	—	—	0.241 (S)	—	—
299	3,4,5,6-Tetramethyl-2,5-octadiene	63.504	0.133 (S)	—	—	—	—
300	Megastigmatrienone	63.539	—	—	—	—	0.914
301	6-(1-Hydroxymethylvinyl)-4,8a-dimethyl-3,5,6,7,8,8a-hexahydro-1*H*-naphthalen-2-one	63.573	—	0.286 (B)	—	—	—
302	α-Ethyl-benzeneacetamide	63.729	—	—	—	—	0.442 (B)
303	8-Ethenyl-3,4,4a,5,6,7,8,8a-octahydro-5-methylene-2-naphthalenecarboxylic acid	63.747	—	0.175 (B)	—	—	—
304	[1*S*-(1α, 2β, 4β)]-1-Ethenyl-1-methyl-2,4-bis(1-methylethenyl)-cyclohexane	63.989	—	—	—	—	0.666 (S)
305	1-Methylphenazine 5-oxide	63.989	—	—	—	0.945 (B)	—
306	3-Phenylbicyclo(3.2.2)nona-3,6-dien-2-one	63.995	—	—	0.217 (B)	—	—
307	1-(1-Hydroxybutyl)-2,5-dimethoxybenzene	64.035	0.423 (B)	0.49 (B)	—	—	—
308	Methyleugenol	64.538	0.123 (B)	0.315 (B)	0.23 (B)	—	—
309	2-Ethyl-3,4-dihydro-2H-1-benzothiopyran	64.630	—	—	—	—	1.177 (B)
310	Acetic acid-cyano-hydroxyimino-methyl ester	65.006	—	—	—	—	0.484
311	*N*-Dimethylaminomethylene-anthranilic acid	65.012	0.252 (S)	0.26 (S)	0.165 (S)	—	—
312	2-Methyl-9-(prop-1-en-3-ol-2-yl)-bicyclo[4.4.0]dec-2-ene-4-ol	65.243	—	—	1.25 (S)	—	—
313	(1a*R*, 4a*R*, 7*R*, 7a*R*, 7b*S*)-Decahydro-1,1,7-trimethyl-4-methylene-1*H*-cycloprop[e]azulene	65.254	0.514 (B)	1.064 (B)	—	—	—
314	[4a*R*-(4aα, 5α, 8aα)]-4a,5,6,7,8,8a-Hexahydro-3,4a,5-trimethyl-naphtho[2,3-b]furan-9(4*H*)-one	65.381	—	—	—	—	4.963 (S)
315	7,7,8,8-Tetracyanoquinodimethane	65.716	0.137 (B)	—	—	—	—
316	4-(1,3,3-Trimethyl-bicyclo[4.1.0]hept-2-yl)-but-3-en-2-one	65.780	—	0.233	—	—	—
317	Alloaromadendrene oxide	65.820	—	—	—	—	0.543 (S)
318	γ-Elemene	66.207	—	—	—	—	0.835 (S)
319	1-(2,4,6-Trimethylphenyl)-3-(2-propynyl)-thiourea	66.698	0.68 (B)	1.52 (B)	1.68 (B)	—	5.466 (B)
320	3,4-Dimethylphenyl trifluoro-acetate	66.883	—	—	0.209 (B)	—	—
321	12-Azabicyclo[9.2.2]pentadeca-1(13),11,14-trien-13-ylamine	66.901	0.205	0.276	—	—	1.177
322	1-Butyl-1*H*-pyrrole	67.062	0.213	0.288	0.174	—	—
323	(3aα, 8β, 8aα)-5,6-1,2,3,3a,8,8a-Hexahydro-2,2,8-trimethyl-azulenedimethanol	67.259	—	—	—	—	0.631 (S)
324	(2*R*, 5*S*, 10*R*)-6,10-Dimethyl-2-(1-methylethenyl)-spiro[4.5]dec-6-en-8-one	67.386	0.326 (S)	—	—	—	—
325	*N*-Salicylidene-*N*′-salicyloylhydrazine	67.496	—	0.597 (B)	—	—	—
326	3,5-Dimethyl-benzenamine	67.507	—	—	—	—	0.633 (B)

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
327	2-Allyl-3-ethoxy-4-methoxyphenol	67.709	—	—	1.709 (B)	—	—
328	1,2-Dimethoxy-4-(3-methoxy-1-propenyl)benzene	67.732	1.572 (B)	—	—	—	—
329	Levomenol	67.778	—	—	—	—	0.305 (S)
330	*n*-Hexadecanoic acid	67.807	—	—	—	1.701	—
331	2,2,8,8-Tetramethyl-3,6-nonadien-5-one	67.958	—	—	—	—	0.428
332	3,5-Dimethoxy-4-hydroxycinnamaldehyde	68.119	0.123 (B)	1.723 (B)	—	3.472 (B)	—
333	1-Hydroxy-6-methylphenazine	68.529	1.19 (B)	1.897 (B)	1.555 (B)	—	—
334	Desaspidinol	68.847	—	—	—	3.559 (B)	—
335	2-Chloro-4-cyclohexyl-phenol	68.882	0.177 (B)	—	0.302 (B)	—	—
336	5-Ethyl-1,2,3,4-tetrahydro-naphthalene	68.899	—	—	—	—	0.779 (B)
337	Heptadecane	69.361	—	—	—	0.195	—
338	Humulane-1,6-dien-3-ol	69.384	—	—	—	—	0.784 (S)
339	8,8-Dimethyl-9-methylene-1,5-cycloundecadiene	69.777	—	—	—	—	0.465 (S)
340	2,4-Dichloro-1-nitrobenzene	70.083	—	—	—	—	0.429 (B)
341	1-(2-Benzyloxyethyl)cyclohexene	70.453	—	—	0.369 (B)	—	—
342	Caryophyllene oxide	70.476	—	—	—	—	2.082 (S)
343	Aromadendrene oxide-(2)	70.476	0.272 (S)	—	—	—	—
344	Diepicedrene-1-oxide	70.545	—	0.368 (S)	—	—	—
345	3,4-Dihydro-3,3,6,8-tetramethylnaphthalen-1(2*H*)-one	70.580	—	—	—	0.115 (B)	—
346	1-Methyl-2,4-bis(1-methylethenyl)-cyclohexane	71.031	—	—	—	—	0.248 (S)
347	[1a*R*-(1aα, 4aα, 7β, 7aβ, 7bα)]-Decahydro-1,1,7-trimethyl-4-methylene-1*H*-cycloprop[e]azulen-7-ol	71.140	—	—	—	—	0.512 (S)
348	3-Hydroxy-2-methyl-4-[4-*t*-butyl]-butanal	72.481	0.242	—	—	—	—
349	1-(1-Hydroxy-3-methoxy-2-naphthyl)ethanone	72.498	—	—	—	—	1.586 (B)
350	2-(Butenyl)-5-(1,1-dimethylethyl)-1,3-dimethyl-benzene	72.544	—	0.346 (B)	—	—	—
351	(1*R*, 2*R*, 6*S*, 7*S*, 8*S*) -1-Methyl-8-(1-methylethyl)-tricyclo[4.4.0.02,7]dec-3-ene-3-methanol	72.885	—	—	0.359 (S)	—	—
352	4-Hydroxy-4a,5-dimethyl-3-methylene-3a,4,4a,5,6,7,9,9a-octahydro-3*H*-naphtho[2,3-b]furan-2-one	72.896	0.194 (B)	—	—	—	—
353	1,2,3,4-Tetrahydro-6-nitronaphthalene	72.931	—	—	—	—	0.888 (B)
354	1-(3,3-Dimethyl-1-yl)-2,2-dimethylcyclopropane-3-carboxylic acid	72.960	—	0.324	—	—	—
355	*N*-(p-Methoxy-*trans*-styryl)-formamide	73.272	—	—	—	—	0.546 (B)
356	8,9-Dehydro-9-formyl-cycloisolongifolene	73.705	0.548 (S)	—	0.691 (S)	—	—
357	2-*tert*-Butyl-quinoxaline 4-oxide	73.745	—	—	—	—	1.237 (B)
358	β-Vatirenene	73.763	—	0.803 (S)	—	—	—

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
359	Octadecanal	73.919	—	—	—	0.144	—
360	[1*S*-(1*α*, 3a*β*, 4*α*, 7a*β*)]-Octahydro-1,7a-dimethyl-4-(1-methylethenyl)-1,4-methano-1*H*-indene	74.872	—	—	—	—	0.368 (S)
361	1-(1-Hydroxyethyl)-1-(diethylphosphonyl)-2-methylene-cyclopropane	74.878	—	0.109	—	—	—
362	1-Nonadecene	75.265	—	—	—	0.149	—
363	(*E*,*E*)-3,7-Dimethyl-10-(1-methylethylidene)-3,7-cyclodecadien-1-one	75.692	—	—	—	—	0.232 (S)
364	Alloaromadendrene	76.195	—	—	—	—	0.488 (S)
365	Heneicosane	76.235	—	0.148	0.177	0.127	—
366	2,3-Dihydro-7-hydroxy-2,2-dimethyl-4*H*-1-benzopyran-4-one	76.859	—	—	—	—	0.277 (B)
367	2-Butyl-5-hexyloctahydro-1*H*-indene	77.344	—	—	—	—	0.253
368	2,2’ : 5′,2″-Terthiophene	77.777	—	—	—	—	0.228
369	1-Methyl-4-(2-methyloxiranyl)-7-oxabicyclo[4.1.0]heptane	78.355	—	—	—	—	0.248 (B)
370	4,4-Dimethyl-1-phenyl-1-penten-3-one	78.563	—	—	—	—	0.199 (B)
371	1,5-Diphenyl-1-penten-3-one	78.603	0.16 (B)	0.354 (B)	0.139 (B)	—	—
372	(1-Methylbutyl)-benzene	79.424	—	—	—	—	0.266 (B)
373	Stearic acid	79.504	—	—	—	0.198	—
374	[1*S*-(1*α*, 2*α*, 3a*β*, 4*α*, 8a*β*, 9*R**)]-Decahydro-1,5,5,8a-tetramethyl-1,2,4-methenoazulene	79.666	—	—	—	—	0.186 (S)
375	*Z*-8-Methyl-9-tetradecenoic acid	79.799	—	0.105	—	—	—
376	1,2,3,4-Tetrahydro-1,5,7-trimethylnaphthalene	79.903	—	—	—	—	0.426 (B)
377	*N*-Phenyl-2-naphthylamine	80.746	0.121 (B)	—	0.186 (B)	—	—
378	*Z*-5-Nonadecene	81.024	0.196	—	0.181	0.230	—
379	Cyclopentadecane	81.047	—	0.188	—	—	—
380	Diaveridine	81.105	—	—	—	—	0.108 (B)
381	(*Z*)-3-Tridecen-1-yne	81.428	—	—	—	—	0.322
382	Ambrosin	82.277	—	—	—	—	0.102 (S)
383	2-Decanone *O*-methyl oxime	82.329	0.104	0.115	0.092	—	—
384	N,N-Dimethyldecanamide	82.352	—	—	—	0.140	—
385	[1a*R*-(1a*α*, 4a*β*, 8aS*)]-1,1a,5,6,7,8-Hexahydro-4a,8,8-trimethyl-cyclopropa[d]naphthalen-2(4a*H*)-one	82.710	—	—	—	—	0.124 (S)
386	Murolan-3,9(11)-diene-10-peroxy	83.248	—	—	—	—	0.267 (S)
387	Chromone derivative	85.396	0.109 (C)	—	0.08 (C)	—	—
388	Chromone derivative	85.818	0.132 (C)	0.217 (C)	0.151 (C)	—	—
389	Chromone derivative	86.783	2.245 (C)	1.812 (C)	1.697 (C)	3.633 (C)	—
390	Chromone derivative	87.187	0.104	—	—	0.112	—
391	Chromone derivative	87.539	—	—	—	—	0.331 (C)
392	Chromone derivative	88.724	0.159	—	—	—	—
393	Chromone derivative	88.880	0.118	—	0.123	—	—
394	Chromone derivative	88.891	—	—	—	—	—
395	Chromone derivative	88.897	—	0.152 (C)	—	0.175	—
396	Chromone derivative	89.209	0.14 (C)	0.662 (C)	0.345 (C)	—	0.334 (C)

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
397	Chromone derivative	89.515	—	—	0.064 (C)	0.14 (C)	—
398	Chromone derivative	89.769	—	—	0.221 (C)	—	—
399	Chromone derivative	89.787	—	0.125 (B)	—	—	—
400	Chromone derivative	89.844	0.286	—	—	—	—
401	Chromone derivative	89.867	—	0.108 (B)	—	—	—
402	Chromone derivative	90.595	—	—	3.447 (C)	—	—
403	Chromone derivative	90.601	1.127 (C)	—	—	—	—
404	Chromone derivative	90.630	—	—	—	0.179 (C)	—
405	Chromone derivative	90.641	—	3.239 (C)	—	—	—
406	Chromone derivative	90.676	—	—	—	—	7.398 (C)
407	Chromone derivative	91.000	—	—	0.197 (C)	—	—
408	Chromone derivative	91.000	0.121 (C)	—	—	—	—
409	Chromone derivative	91.017	—	0.148 (C)	—	—	—
410	Chromone derivative	91.485	—	—	3.502 (C)	—	—
411	Chromone derivative	91.485	1.32 (C)	—	—	—	—
412	Chromone derivative	91.571	—	—	—	—	0.542 (C)
413	Chromone derivative	91.571	—	4.593 (C)	—	—	—
414	Chromone derivative	91.629	—	—	—	0.105 (C)	—
415	Chromone derivative	91.710	—	—	0.649 (C)	—	—
416	Chromone derivative	91.716	0.132 (C)	—	—	—	—
417	Chromone derivative	91.727	—	—	—	—	1.405 (C)
418	Chromone derivative	91.745	—	0.561 (C)	—	—	—
419	Chromone derivative	91.803	—	—	0.592 (C)	—	—
420	Chromone derivative	91.808	0.481 (C)	—	—	—	—
421	Chromone derivative	91.837	—	—	—	0.411	—
423	Chromone derivative	91.837	—	0.539 (C)	—	—	—
422	Chromone derivative	91.953	—	—	0.88 (C)	—	—
424	Chromone derivative	91.953	0.434 (C)	—	—	—	—
425	Chromone derivative	91.987	—	0.796 (C)	—	—	—
426	Chromone derivative	92.571	—	—	—	—	0.143 (C)

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
427	Chromone derivative	92.894	—	0.254 (B)	—	—	—
428	Chromone derivative	92.935	—	—	—	—	1.293 (C)
429	Chromone derivative	92.958	—	—	0.221 (C)	—	—
430	Chromone derivative	92.969	—	0.485 (B)	—	—	—
431	Chromone derivative	93.339	—	—	—	—	0.388 (C)
432	Chromone derivative	93.784	—	—	—	—	0.6 (C)
433	Chromone derivative	94.136	—	—	—	—	0.14 (C)
434	Chromone derivative	94.356	—	—	0.731	—	—
435	Chromone derivative	94.361	—	—	—	—	0.125 (C)
436	Chromone derivative	94.361	0.596 (C)	—	—	—	—
437	Chromone derivative	94.390	—	0.832 (C)	—	—	—
438	Chromone derivative	94.795	—	—	0.323 (C)	—	—
439	Chromone derivative	94.800	0.187 (C)	—	—	—	—
440	Chromone derivative	94.812	—	0.371 (C)	—	—	—
441	Chromone derivative	95.228	—	—	—	—	1.254 (C)
442	Chromone derivative	95.228	—	—	0.596 (C)	—	—
443	Chromone derivative	95.257	—	0.614 (C)	—	—	—
444	Chromone derivative	95.268	0.165 (C)	—	—	—	—
445	Chromone derivative	95.609	—	—	—	—	0.217 (C)
446	Chromone derivative	95.748	0.243 (C)	—	—	—	—
447	Chromone derivative	95.754	—	—	0.237 (C)	—	—
448	Chromone derivative	95.765	—	—	—	0.478 (B)	—
449	Chromone derivative	95.771	—	0.206 (C)	—	—	—
450	Chromone derivative	95.834	—	—	—	—	0.414 (C)
451	Chromone derivative	95.904	0.291 (C)	—	—	—	—
452	Chromone derivative	95.921	—	—	—	0.678 (B)	—
453	Chromone derivative	95.967	0.713 (C)	—	—	—	—
454	Chromone derivative	95.973	—	—	3.243 (C)	—	—
455	Chromone derivative	96.019	—	2.703 (C)	—	—	—
456	Chromone derivative	96.088	—	—	—	—	7.2 (C)
457	Chromone derivative	96.308	—	—	0.178 (C)	—	—

Table 1: Continued.

No.	Name	RT (min)	Relative content (%)				
			AAW	BCDA	AWIT	AS	EAWIT
458	Chromone derivative	96.308	0.192 (C)	—	—	—	—
459	Chromone derivative	96.319	—	—	—	0.177 (B)	—
460	Chromone derivative	96.343	—	0.281 (C)	—	—	—
461	Chromone derivative	96.372	—	—	—	—	0.498 (C)
462	Chromone derivative	96.395	—	—	0.267 (C)	—	—
463	Chromone derivative	96.400	0.313 (C)	—	—	—	—
464	Chromone derivative	96.412	—	—	—	0.381	—
465	Chromone derivative	96.418	—	0.43 (B)	—	—	—
466	Chromone derivative	96.556	—	0.138 (B)	—	—	—
467	Chromone derivative	96.632	—	—	0.058 (C)	—	—
468	Chromone derivative	96.637	0.312 (C)	—	—	—	—
469	Chromone derivative	96.649	—	—	—	0.236 (B)	—
470	Chromone derivative	96.655	—	0.16 (B)	—	—	—
471	Chromone derivative	96.718	—	—	—	—	0.332 (C)
472	Chromone derivative	96.753	—	0.206	—	—	—
473	Chromone derivative	97.088	—	—	—	—	0.464 (C)
474	Chromone derivative	97.319	—	—	—	—	0.176 (C)
475	Chromone derivative	97.469	—	—	—	—	0.171 (C)
476	Chromone derivative	97.700	—	—	—	—	0.469 (C)
477	Chromone derivative	98.341	—	—	—	—	0.863 (C)
478	Chromone derivative	98.399	—	0.103	—	—	—
479	Chromone derivative	98.982	—	—	—	—	0.104 (C)
480	Chromone derivative	99.242	—	—	—	—	0.374 (C)
481	Chromone derivative	99.566	—	—	—	—	0.264 (C)
482	Chromone derivative	99.751	—	—	—	—	0.192 (C)
483	Chromone derivative	100.034	—	—	—	—	0.281 (C)
484	Chromone derivative	100.346	—	—	—	—	0.577 (C)
Total			97.620	97.164	99.859	97.040	96.079

B: aromatic compound; C: chromone derivative; S: sesquiterpenes; —: not detected.

Briefly, 10 μL of supernatant was mixed with an equal volume of reagents A and B [1 : 1 (v/v)] in a 96-well flat-bottom plate. The absorbance at 540 nm was measured after 10 min using an ELISA reader. The amounts of TNF-α and IL-1α were calculated from a standard curve created using known concentrations of standards.

3. Results and Discussion

3.1. GC-MS Analysis. *n*-Hexane, methanol, DMSO, and CH_2Cl_2 were used to collect the chemical constituents of incense smoke from agarwood. The GC-MS peaks of incense smoke samples collected using CH_2Cl_2 were the most

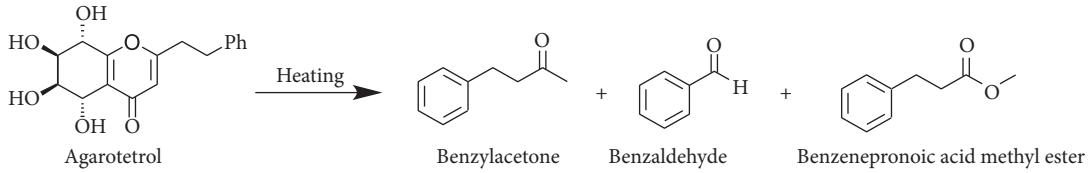
intense among the peaks obtained using the above solvents. Therefore, CH_2Cl_2 was selected to dissolve the chemical constituents of smoke samples (agarwood and AS). Finally, 484 compounds in total (Table 1 and Figure 1) were identified from the incense smoke samples (AAW, BCDA, AWIT, and AS) and the samples obtained by CH_2Cl_2 extraction of sticks from AWIT. The numbers of compounds identified in incense smoke from AAW, BCDA, AWIT, AS, and EAWIT were 167, 158, 141, 127, and 131, respectively. Aromatics and chromone derivatives were the main chemical constituents in AAW, BCDA, and AWIT; among all chemical constituents, aromatics represented 69.617, 55.038, and 60.483%, and chromone derivatives represented 9.252, 17.725, and 16.946%, respectively.

The chemical constituents of incense smoke may be quantifiable. Therefore, the chemical constituents of incense smoke from agarwood produced by AWIT were compared with the corresponding constituents from agarwood produced by AAW and BCDA. A total of 61 compounds in the AWIT sample, representing 54.837%, were also found in the AAW and BCDA samples. The major compounds (relative content >1%) were phenylethylene (7.973%); ethylbenzene (6.384%); 2,3,5,6-tetrafluoroanisole (4.130%); 5-(2-thienyl)-4-pyrimidinamine (2.402%); 2-methoxy-4-(1-propen-1-yl)-phenol (2.379%); 2,6-dimethoxyphenol (2.178%); syn-3,3,5,6,8,8-hexamethyltricyclo[5.1.0.0(2,4)]oct-5-ene (1.762%); 1-(2,4,6-trimethylphenyl)-3-(2-propynyl)-thiourea (1.680%); phenylacetylene (1.612%); 1-hydroxy-6-methylphenazine (1.555%); 4-hydroxy-3-methoxystyrene(1.512%) 3,5-dimethoxy-4-hydroxyphenylacetic acid (1.391%); 2,2,4,6,6-pentamethylheptane (1.152%); 4-(4-methoxyphenyl)-2-butanone (1.124%); 4-phenyl-2-butanone (1.060%); and benzaldehyde (1.008%). Moreover, chromone derivatives and sesquiterpenes are the main components responsible for pharmacodynamic effects [23–25]. In this experiment, 21 compounds, representing 16.946%, were identified as chromone derivatives according to the peaks at m/z 91, 121, 137, 107, 160, 176, 190, 220, 250, 266, 280, 282, 296, 310, 312, 326, 328, and 342 [22], and 16 compounds were identified as sesquiterpenes, representing 6.768%. In short, aromatic compounds were the main chemical constituents of incense smoke from agarwood, including AWIT, AAW, and BCDA samples.

To identify whether agarwood (AAW, AWIT, and BCDA) contained chemical constituents of AS, incense smoke produced from AS was tested by the same method. No sesquiterpenes were detected among the chemical constituents of the smoke, and chromones only represented 4.569%, which was less than the contents in AWIT (16.946%), AAW (9.252%), and BCDA (17.725%). Finally, 29 compounds, representing 32.627%, were also found in AWIT, AAW, and BCDA. The main compounds (relative amount >1%) were phenylethylene (5.132%); 2-methoxy-4-(1-propen-1-yl)-phenol (3.254%); 3,5-dimethoxy-4-hydroxybenzaldehyde (2.920%); 4-hydroxy-3-methoxystyrene (2.254%); 3,5-dimethoxy-4-hydroxyphenylacetic acid (2.150%); vanillin (1.842%); acetosyringone (1.499%); guaiacol (1.362%); ethylbenzene (1.313%); benzaldehyde (1.146%); homovanillyl alcohol (1.119%); 2,6-dimethoxy-4-(2-propen-1-yl)-phenol (1.029%); and phenylacetylene (1.013%). These components may be from the residue of *A. sinensis*, a sticky powder, making agarwood powder bind, used in the preparation of sticks of AS (making sticks from pure AS alone is difficult, so the addition of a sticky powder is necessary) or agarwood in *A. sinensis* (AS can form agarwood in the process of storage).

The data for incense smoke from agarwood (AAW, AWIT, and BCDA) showed that low-molecular-weight aromatic compounds (LACs) represented more than 55% of the total constituents. Michiho Ito et al. reported that chromone derivatives could be converted and produce the pleasant smell of agarwood through the generation of LACs in the process of heating [26,27] (Scheme 1). Chromone derivatives are among the main chemical constituents of agarwood. They can generate unique and different LACs at high temperature (when burned). As a result, many LACs were detected in the agarwood smoke. To verify the results, an extraction experiment of sticks from AWIT was carried out at room temperature (to avoid high temperature). The results showed that chromone derivatives, sesquiterpenes, and aromatics were the main chemical constituents, representing 26.547, 26.767, and 26.941% of the total constituents, respectively. Few chemical constituents of EAWIT were observed before 40 min (t_R), as shown in Figure 1, while there was far higher number of peaks after 58 min (t_R), which is indicative of chromone derivatives and sesquiterpenes. Interestingly, the chemical constituents of incense smoke showed the opposite trend in Figure 1. The results indicated that high-molecular-weight compounds might be cracked into low-molecular-weight compounds at high temperature. In other words, some chromone derivatives and sesquiterpenes might be converted into low-molecular-weight compounds, which is consistent with the reported literature [26, 27]. Therefore, low-molecular-weight compounds accounted for a high percentage of the incense smoke obtained from agarwood during burning. Moreover, some studies suggested that the inhalation of some LACs had a sedative or hypnotic effect on mice and that benzylacetone in particular reduces mouse locomotor activity [28–30]. Hence, inhalation of the pleasant aroma generated by agarwood during heating could lead to pharmacological effects.

3.2. Effect of Chemical Constituents on TNF-α and IL-1α Release in LPS-Stimulated RAW264.7 Cells. As shown in Tables 2 and 3, normal inactivated RAW264.7 cells produced low amounts of TNF-α and IL-1α after 24 h of incubation at 37°C, and exposure to LPS induced higher amounts of TNF-α and IL-1α. In contrast, under indomethacin treatment, AAW, BCDA, and AWIT produced a concentration-dependent decrease at concentrations of 20, 40, and 80 μg/mL. The TNF-α and IL-1α levels of model group were significantly higher than those of the normal



Scheme 1: LACs generated from agaroterol on heating.

Table 2: LPS-induced release of TNF-α in RAW264.7 cells.

Drug/dose		80 μg/mL	40 μg/mL	20 μg/mL
Normal	189.09 ± 15.25			
Model	236.09 ± 18.79**			
Indomethacin		152.39 ± 16.67###	169.14 ± 18.23###	200.19 ± 19.42#
AAW		157.69 ± 15.98###	181.79 ± 19.45##	209.19 ± 21.03#
BCDA		165.09 ± 16.12###	194.84 ± 17.67##	213.04 ± 22.43#
AWIT		154.89 ± 17.13###	187.84 ± 18.37##	212.84 ± 19.35#

Note. This result is the average of three parallel experiments. $^{**}P < 0.01$ vs normal; $^{###}P < 0.001$, $^{##}P < 0.01$, $^{#}P < 0.05$ vs model.

Table 3: LPS-induced release of IL-1α in RAW264.7 cells.

Durg/dose		80 μg/mL	40 μg/mL	20 μg/mL
Normal	15.00 ± 1.78			
Model	20.43 ± 2.32*			
Indomethacin		10.38 ± 2.12##	12.52 ± 2.65##	17.87 ± 1.85#
AAW		10.78 ± 2.56##	15.72 ± 2.57#	19.10 ± 2.58
BCDA		15.05 ± 1.74#	18.99 ± 2.97	22.19 ± 2.94
AWIT		10.88 ± 1.97##	12.15 ± 2.72##	22.52 ± 2.93

Note. This result is the average of three parallel experiments. $^{*}P < 0.05$ vs normal; $^{##}P < 0.01$, $^{#}P < 0.05$ vs model.

group ($P < 0.05$ or $P < 0.01$). The incense components of AAW, BCDA, AWIT, and indomethacin significantly reduced TNF-α and IL-1α levels ($P < 0.05$, $P < 0.01$, or $P < 0.001$), showing better anti-inflammatory effects. These results showed that the anti-inflammatory activities of AAW, AWIT, and indomethacin were comparable and superior to that of BCDA.

4. Conclusions

The chemical constituents of incense smoke from AAW, BCDA, AWIT, AS, and EAWIT were analyzed by GC-MS, and 484 compounds were identified. Aromatic compounds were the main chemical constituents of incense smoke from AAW, BCDA, and AWIT. A total of 61 aromatic compounds from AWIT, representing 54.837%, were also found in AAW and BCDA. All experimental data suggested that aromatic compounds were the main chemical constituents in agarwood smoke and that some chromone derivatives could be cracked into LACs at high temperature. Furthermore, agarwood incense smoke showed anti-inflammatory activities by inhibiting lipopolysaccharide- (LPS-) induced TNF-α and IL-1α release in RAW264.7 cells.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest in any form.

Authors' Contributions

De-Qian Peng, Zhang-Xin Yu contributed equally to this work.

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