

Discovery of anti-SARS-CoV-2 agents from commercially available flavor via docking screening

Jiao-Jiao Zhang^{1,†}, Xin Shen^{2,†}, Yong-Ming Yan¹, Yan Wang^{2,*}, Yong-Xian Cheng^{1,*}

¹ School of Pharmaceutical Sciences, Shenzhen University Health Science Center, Shenzhen 518060, P.R. China

² Center for Translation Medicine Research and Development, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen 518055, P.R. China

* To whom correspondence should be addressed: Tel: 86755-2690 2073; E-mail: yxcheng@szu.edu.cn (Y.-X. C.); 86755-2641 7985; E-mail: yan.wang@siat.ac.cn (Y. W.)

† These authors contributed equally to this paper.

Running Title: Flavor ingredients against 2019-nCoV by docking screening

Keywords: 2019-nCoV, novel coronavirus pneumonia, docking, ACE2, viral main protease, flavor

Abstract

Flavor and spice is largely consumed in food, cosmetics, and pharmaceutical industries. A novel coronavirus, recently named the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was first identified in humans in Wuhan China in 2019. This study is to examine whether the flavor components can prevent human from SARS-CoV-2 infection. Given that the druggable antiviral target ACE2 receptor and viral main protease were reported, 169 compounds were screened against these two targets by using autodock vina. According to our docking screening, 10 antiviral components, including glycyrrhizic acid, theaflavin 3,3'-digallate, agnuside, fenflumizole, angelicide, sageone, oleanic acid, benzyl (3-fluoro-4-morpholine-4-yl phenyl) carbamate, glycerol ester of rosin, and endere S can directly bind to both host cell target ACE2 receptor and viral target main protease, indicating their potential for SARS-CoV-2 treatment.

Introduction

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), previously named as 2019 novel coronavirus (2019-nCoV), is a positive-sense, single-strand RNA coronavirus. SARS-CoV-2 caused an ongoing outbreak of coronavirus disease 2019 (COVID-19), which started in December 2019 (1). Given that the emergence of SARS-CoV-2, drug repurposing study was immediately conducted by both virtual screening and cell-based screening, which provided several promising antiviral agents from approved drugs (2). Flavor and spice has been widely used in China and India since ancient time, some spice such as ginger and pepper is used to fight against dampness evil in the body according to the philosophy of traditional Chinese medicine, however, whether these components do prevent from virus infection is still questionable. Here we tried to use molecular docking screening to identify potential anti-SARS-CoV-2 agents from flavor ingredients.

Not surprisingly, spike protein of SARS-CoV-2 can directly bind to angiotensin converting enzyme 2 (ACE2) receptor of host cells (3). Inhibition of ACE2 catalytic pocket by small molecules could change the conformation of ACE2, indicating that ACE2 inhibitor could block SARS-CoV-2 entry (4,5). Therefore we selected ACE2 receptor as a protein model to quickly identify entry inhibitors of SARS-CoV-2.

Besides the blockade of viral entry, the inhibition of viral replication is another good strategy for antiviral drug discovery and development (6). Given that SARS-CoV-2 is a (+)SS RNA virus, its main protease could cut two replicase polyproteins, which is required to mediate viral replication and transcription. In this way, the inhibitor of main protease might block virus replication. The crystal structure of SARS-CoV-2 main protease (PDB: 6LU7) was reported (7). We consequently docked flavor components to main protease to look for antiviral replication agents.

Materials and Methods

The three dimensional structure of ligands (aroma oil components) were generated by CORINA online service (https://www.mn-am.com/online_demos/corina_demo). Then the PDB ligand was converted to PDBQT ligand using Autodock Tools. The protein model 1R4L was selected as ACE2 receptor docking model while 6LU7 was selected as M protease docking model. Both PDB files of protein models were fetched from Protein Data Bank. The docking screening were conducted by using AutoDock Vina v.1.0.2. The docking parameters for AutoDock Vina were kept at their default values. The grid box was 25 Å by 25 Å by 25Å, encompassing the catalytic pocket. The binding modes were clustered through the root mean square deviation (RMSD) among the Cartesian coordinates of the ligand atoms. The docking results were ranked by the binding free energy. The binding results were graphically presented by using PyMOL1.3 (Schrödinger, LLC).

Results

Totally we docked 169 flavor components to two drug targets. The top 10 hits are summarized in Tables 1 and 2. The top ten hits are glycyrrhizic acid, theaflavin 3,3'-digallate, agnuside, fenflumizole, angelicide, sageone, oleanic acid, benzyl (3-fluoro-4-morpholine-4-yl phenyl) carbamate, glycerol ester of rosin, and endere S. Interestingly, the majority of the components are also found in traditional Chinese medicine with the exception of fenflumizole and benzyl (3-fluoro-4-morpholine-4-yl phenyl) carbamate. As for ACE2 receptor, 11 out of 169 compounds exhibit good binding affinities (<-9 kcal/mol), they are glycyrrhizic acid, theaflavin 3,3'-digallate, agnuside, fenflumizole, angelicide, sageone, oleanic acid, benzyl (3-fluoro-4-morpholine-4-yl phenyl) carbamate, glycerol ester of rosin, endere S, and testosterone; Of which, glycyrrhizic acid and oleanic acid are triterpenoidal acids. Besides, 3 out of 169 compounds, glycyrrhizic acid, theaflavin 3,3'-digallate and agnuside, inhibit main protease with strong binding affinities (<-9 kcal/mol). Of note, the properties of glycyrrhizic acid against SARS-CoV-2 have been pointed out in our previous investigation (8). It is also interesting that theaflavin 3,3'-digallate, a phenolic compound present in ginger, was found to interact both with ACE2 receptor and M protease with considerable binding affinities. It is worth mentioning that the current mainstream view about SARS-CoV-2 is the observation of inflammation storm leading to the death. However, we believe that there should have typical “free

radical storm” or severe oxidative stress during SARS-CoV-2 in view of biomedical or chemical defense. Normally, inflammation and free radical including reactive oxygen species is a powerful weapon for human body against evils. Our present finding of theaflavin 3,3'-digallate and previous results regarding to phenolics as hits (8) prompted us to consider their effects against SARS-CoV-2 might be also associated with their antioxidant potency. With this rationale, we tentatively suggest that marketed antioxidants such as edaravone and intake of ginger with high content of phenolics might be beneficial for SARS-CoV-2 patients. Unfortunately, this hypothesis and therapeutic approach has been largely ignored during SARS-CoV-2 outbreak. Last but not the least, it is not surprising that the other flavor agents are not hits with super good binding energy (<-10 kcal/mol) (Table appendix) because their chemical structures are relative simple, so that it is difficult for them to occupy the whole catalytic pocket and provide high binding affinities.

Conclusion

Drug repurposing is a common strategy to fight novel coronavirus. However, most of drug repurposing study is about FDA approved drugs. Flavor ingredients were widely used to prevent plague in ancient China and India and are commercially available with good supply. We were curious that whether flavor ingredients can also prevent SARS-CoV-2 at this time. According to docking screening, we found that flavor ingredients including glycyrrhizic acid, theaflavin 3,3'-digallate, and agnuside are

most likely to directly bind to both viral M protease and ACE2 receptor, lending a hand for fighting against SARS-CoV-2.

Acknowledgments

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Competing interest statement

The authors declare no conflict of interest.

References

1. Huang CL, Wang YM, Li XW, Ren LL, Zhao JP, Hu Y, Zhang L, Fan GH, Xu, JY, Gu, XY, Cheng ZS, Yu, T, Xia JA, Wei A, Wu, WJ, Xie XL, Yin W, Li H, Liu, M, Xiao Y, Gao H, Guo L, Xie JG, Wang GF, Jiang RM, Gao ZC, Jin Q, Wang JW, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, 2020; doi: 10.1016/S0140-6736(20)30183-5.
2. Wang ML, Cao RY, Zhang LK, Yang XL, Liu J. Xu MY, Shi ZL, Hu ZH, Zhong W, Xiao GF. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res.*, 2020; doi: 10.1038/s41422-020-0282-0.
3. Wan YS, Shang J, Graham R, Baric RS, Li F. Receptor recognition by novel coronavirus from Wuhan: An analysis based on decade-long structural studies of

SARS. *J. Virol.*, 2020; doi: 10.1128/JVI.00127-20.

4. Du LY, He YX, Zhou YS, Liu SW, Zheng BJ, Jiang SB. The spike protein of SARS-CoV -a target for vaccine and therapeutic development. *Nat. Rev. Microbiol.*, 2009; 7(3): 226–236.

5. Towler P, Staker B, Prasad SG, Menon S, Tang J, Parsons T, Ryan D, Fisher M, Williams D, Dales NA, Patane MA, Pantoliano MW. ACE2 X-ray structures reveal a large hinge-bending motion important for inhibitor binding and catalysis. *J. Biol. Chem.*, 2004; 279(17):17996–8007.

6. Clercq ED. Strategies in the design of antiviral drugs. *Nat. Rev. Drug Discov.*, 2002; 1: 13–25.

7. Wit ED, van Doremalen NV, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. *Nat. Rev. Microbiol.*, 2016; 14: 523–534.

8. Yan YY, Shen X, Cao YK, Zhang JJ, Wang Y, Cheng YX. 2020, DOI: 10.20944/preprints202002.0254.v2.

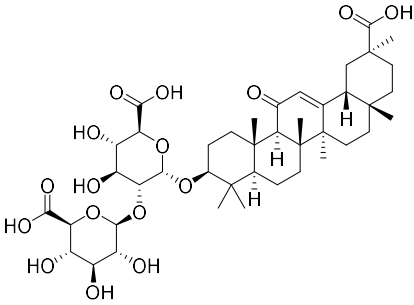
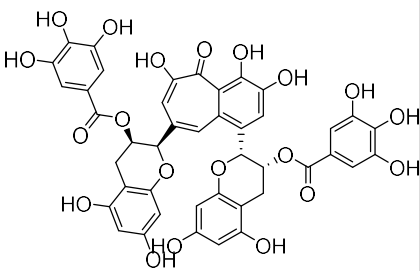
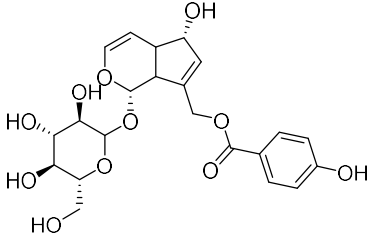
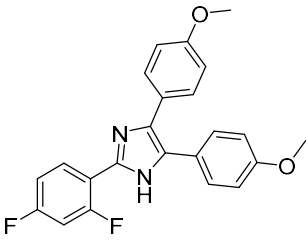
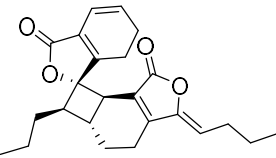
Table 1. Top 10 flavor agents docking results

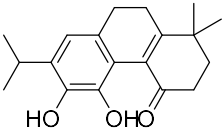
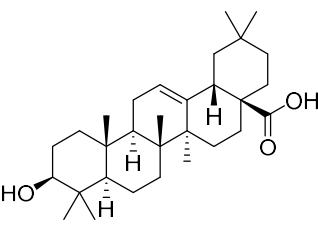
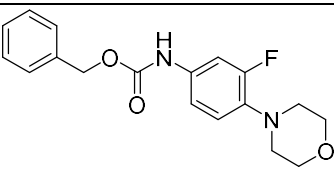
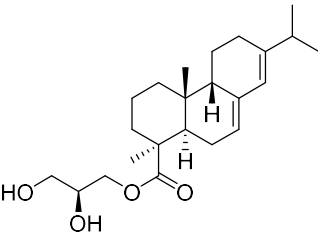
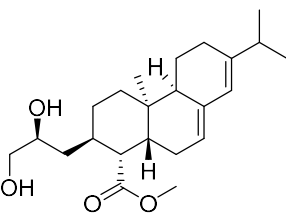
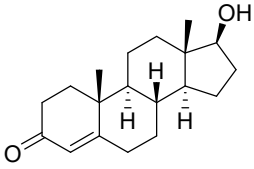
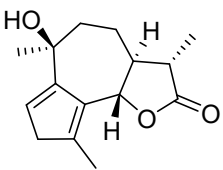
Ligand	Binding Energy		
	1R4L	6LU7	Sum
Glycyrrhizic acid	-9.6	-9.3	-18.9
Theaflavin 3,3'-digallate	-8.3	-10	-18.3
Agnuside	-9.6	-8	-17.6
Fenflumizole	-9.5	-7.7	-17.2
Angelicide	-9.7	-7.1	-16.8
Sageone	-9	-7.8	-16.8
Oleanic acid	-9.4	-7.3	-16.7
Benzyl (3-fluoro-4-morpholine-4-yl phenyl) carbamate	-9.4	-7.1	-16.5
Glycerol ester of rosin	-9.4	-6.9	-16.3
Endere S	-9.4	-6.8	-16.2

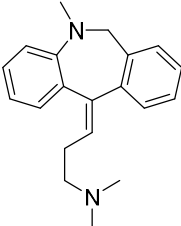
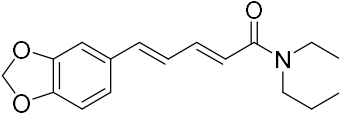
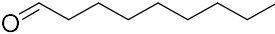
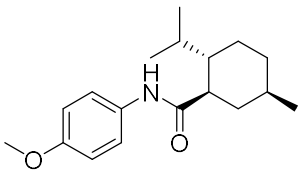
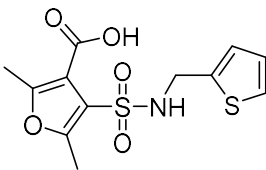
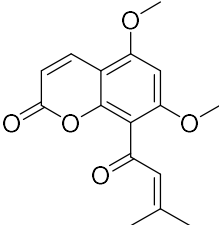
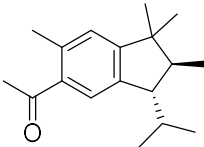
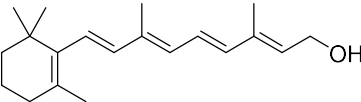
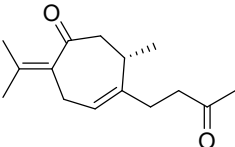
Table 2. Key residues for the inhibitor binding

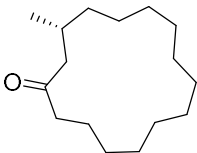
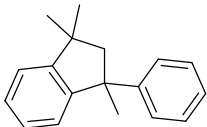
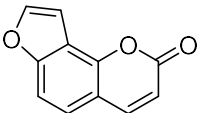
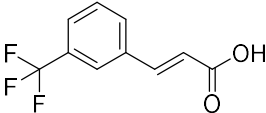
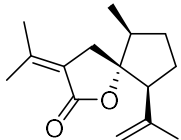
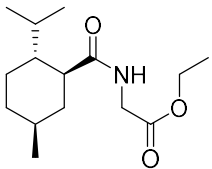
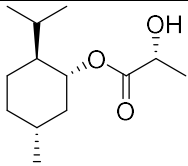
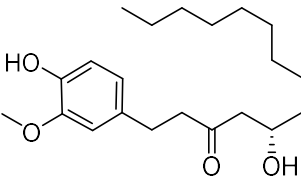
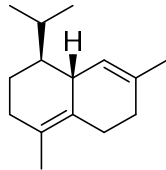
Ligand	Key residues	
	1R4L	6LU7
Glycyrrhizic acid	Arg273, His345, Ala348, Thr365, Arg518	Phe140, Gly143, His163, Gln189
Theaflavin 3,3'-digallate	Asn149, Asn154, Arg273, Asn277, His345, Lys363, Thr365, Arg518	Ser46, Tyr54, Phe140, Ser144, Cys145, Gly143, His163, Glu166, Gln189, Thr190
Agnuside	His345, Thr371, Glu406, Arg518	Thr24, Thr45, Leu141, Gly143, Ser144, Cys145, Glu166
Fenflumizole	His345	None
Angelicide	None	Gly143, Ser144, Cys145
Sageone	Arg273, His345	Gly143, Ser144, Cys145
Oleanic acid	Glu406	none
Benzyl (3-fluoro-4-morpholine-4-yl phenyl) carbamate	Arg273, His345, Thr445, Tyr515	Gly143, Ser144, Cys145, His163
Glycerol ester of rosin	Arg273, His374, Arg518	Gly143, His163
Endere S	Arg273, Arg518	Gly143, His163

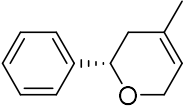
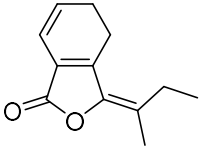
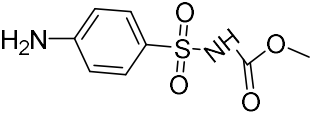
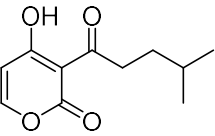
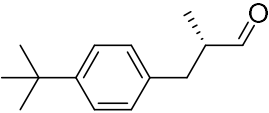
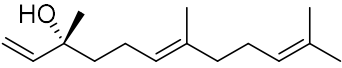
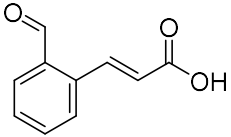
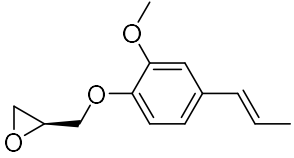
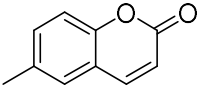
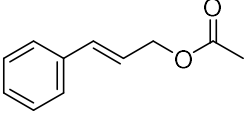
Appendix Table 1. Flavor agents docking results

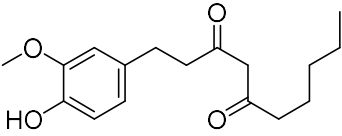
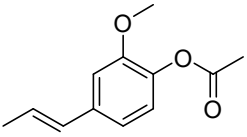
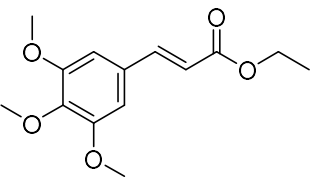
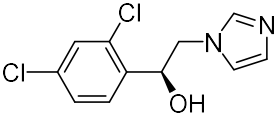
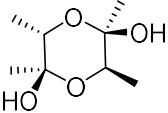
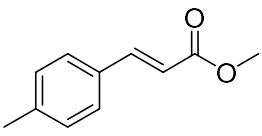
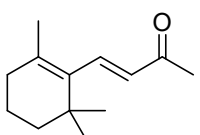
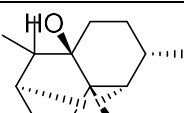
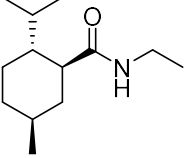
No.	Ligand	Structure	Binding Energy		
			1R4L	6LU7	Sum
1	Glycyrrhizic acid		-9.6	-9.3	-18.9
2	Theaflavin 3,3'-digallate		-8.3	-10	-18.3
3	Agnuside		-9.6	-8	-17.6
4	Fenflumizole		-9.5	-7.7	-17.2
5	Angelicide		-9.7	-7.1	-16.8

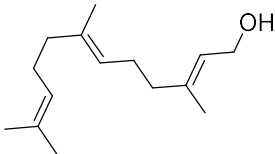
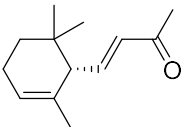
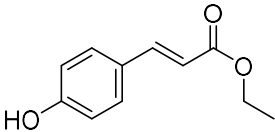
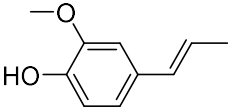
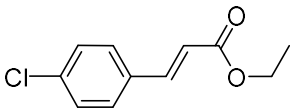
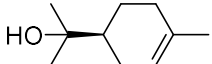
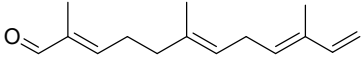
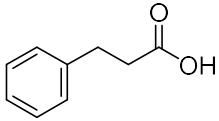
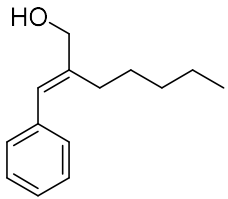
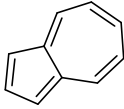
6	Sageone		-9	-7.8	-16.8
7	Oleanic acid		-9.4	-7.3	-16.7
8	Benzyl (3-fluoro-4-morpholine-4-yl phenyl) carbamate		-9.4	-7.1	-16.5
9	Glycerol ester of rosin		-9.4	-6.9	-16.3
10	Endere S		-9.4	-6.8	-16.2
11	Testosterone		-9	-6.8	-15.8
12	Artabsin		-8.7	-6.7	-15.4

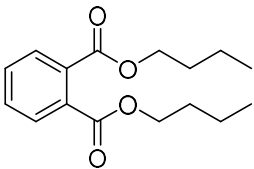
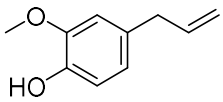
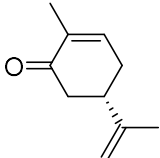
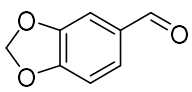
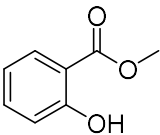
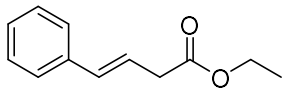
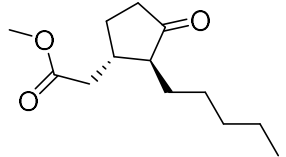
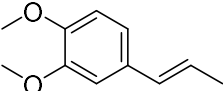
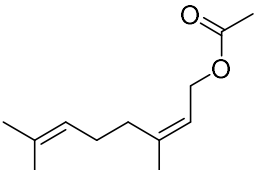
13	Elantrine		-8.6	-6.8	-15.4
14	Piperine		-8.3	-6.6	-14.9
15	Nonanal		-8.1	-6.6	-14.7
16	(1 <i>R</i> ,2 <i>S</i> ,5 <i>R</i>)-2-Isopropyl- <i>N</i> -(4-methoxyphenyl)-5-methylcyclohexane-1-carboxamide		-8.2	-6.2	-14.4
17	2,5-Dimethyl-4-(2-thienylaminosulphonyl)furan-3-carboxylic		-7.7	-6.6	-14.3
18	Angelicone		-7.9	-6.3	-14.2
19	Traseolide		-7.7	-6.3	-14
20	Vitamin A		-8.3	-5.6	-13.9
21	Curcumadione		-7.5	-6.1	-13.6

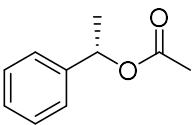
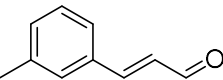
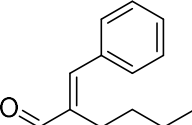
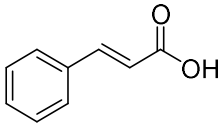
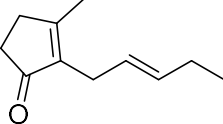
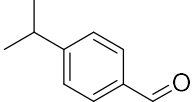
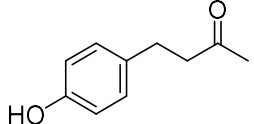
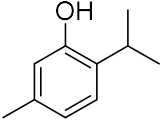
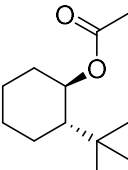
22	Muscone		-8	-5.6	-13.6
23	1-Phenyl-1,3,3-trimethylindan		-7.8	-5.7	-13.5
24	Angelicin		-7.5	-5.9	-13.4
25	3-(Trifluoromethyl)cinnamic acid		-7	-6	-13
26	Curcumanolide-A		-7.8	-5.2	-13
27	<i>N</i> -[(Ethoxycarbonyl)methyl]- <i>p</i> -menthane-3-carboxamide		-7.3	-5.4	-12.7
28	Menthyl lactate		-7.1	-5.5	-12.6
29	10-Gingerol		-7	-5.6	-12.6
30	(+)-Delta-Cadinene		-7	-5.4	-12.4

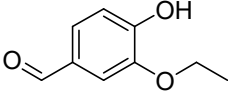
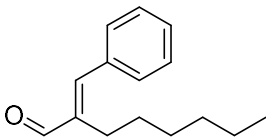
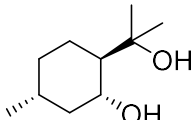
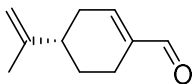
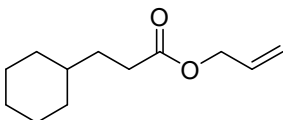
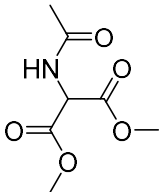
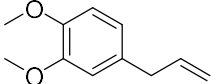
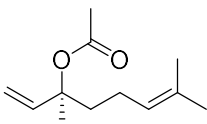
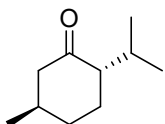
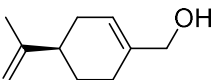
31	4-Methyl-2-phenyl-3,6-dihydro-2H-pyran		-7	-5.4	-12.4
32	Ligustilide		-7	-5.4	-12.4
33	Asulam		-6.9	-5.5	-12.4
34	Dhelwangin		-6.7	-5.7	-12.4
35	Lily aldehyde		-6.7	-5.5	-12.2
36	Nerolidol		-6.5	-5.6	-12.1
37	2-Formylcinnamic acid		-6.6	-5.4	-12
38	4-Epoxy isoeugenol		-6.4	-5.6	-12
39	6-Methylcoumarin		-6.7	-5.3	-12
40	Cinnamylacetate		-6.6	-5.4	-12

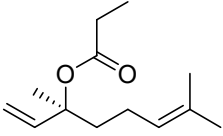
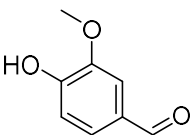
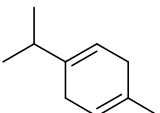
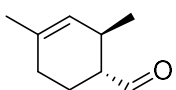
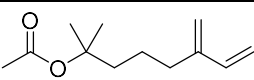
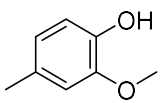
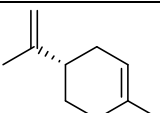
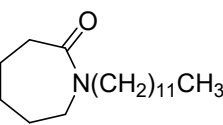
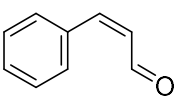
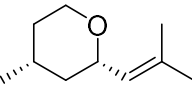
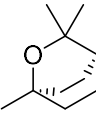
41	Gingerdione		-6.7	-5.3	-12
42	2-Methoxy-4-[(1 <i>E</i>)-1-propenyl]phenyl acetate		-6.5	-5.5	-12
43	3-(3,4,5-Trimethoxyphenyl)propenoic acid ethyl ester		-6.7	-5.2	-11.9
44	α -(2,4-Dichlorophenyl)-1 <i>H</i> -imidazole-1-ethanol		-6.5	-5.4	-11.9
45	3-Hydroxy-2-butanone dimer		-6.7	-5	-11.7
46	4-Methylcinnamic acid methyl ester		-6.6	-5.1	-11.7
47	β -Lonone		-6.8	-4.9	-11.7
48	Patchouli alcohol		-6.6	-5	-11.6
49	<i>N</i> -Ethyl- <i>p</i> -menthane-3-carboxamide		-6.7	-4.9	-11.6

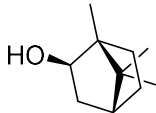
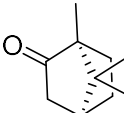
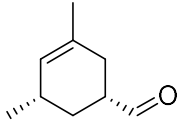
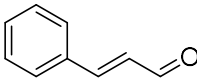
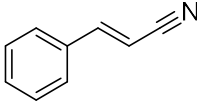
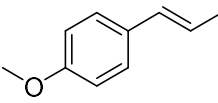
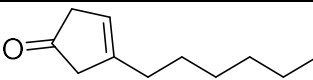
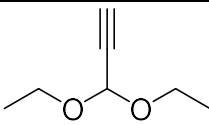
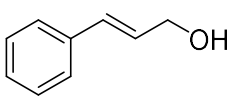
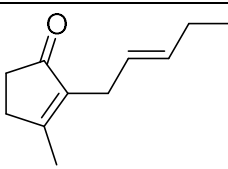
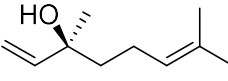
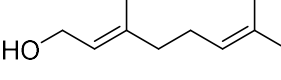
50	(<i>E,E</i>)-Farnesol		-6.3	-5.1	-11.4
51	α -Ionone		-6.4	-5	-11.4
52	Ethyl (<i>2E</i>)-3-(4-hydroxyphenyl)acrylate		-6.5	-4.9	-11.4
53	Isoeugenol		-6.2	-5.2	-11.4
54	Ethyl 4-chlorocinnamate		-6.2	-5	-11.2
55	Terpineol		-6.4	-4.8	-11.2
56	(<i>E,E,E</i>)-2,6,10-Tri methyl-dodeca-2,6,9,11-tetraen-1-al		-6.2	-5	-11.2
57	3-Phenylpropionic acid		-6.3	-4.8	-11.1
58	2-Benzylidene-1-heptanol		-6.3	-4.8	-11.1
59	Azulene		-6.1	-4.9	-11

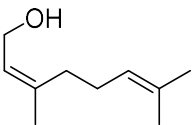
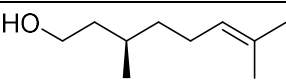
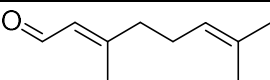
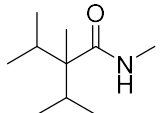
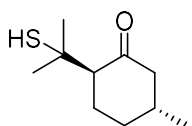
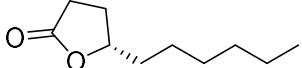
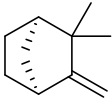
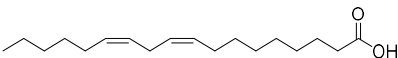
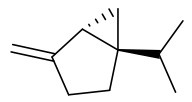
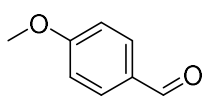
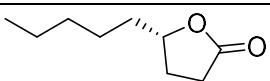
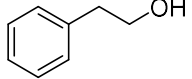
60	Dibutyl phthalate		-5.9	-5.1	-11
61	Eugenol		-6.1	-4.9	-11
62	<i>L</i> -(-)-Carvone (Spearmint oil)		-6	-5	-11
63	Piperonyl aldehyde		-6	-5	-11
64	Methyl salicylate (Wintergreen oil)		-6.1	-4.9	-11
65	Ethyl cinnamate		-6.2	-4.8	-11
66	Methyl dihydrojasmonate		-6.2	-4.7	-10.9
67	Methyl isoeugenol		-6.1	-4.8	-10.9
68	Neryl acetate		-5.9	-5	-10.9

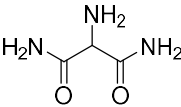
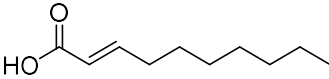
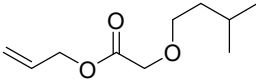
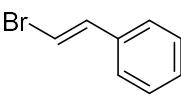
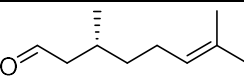
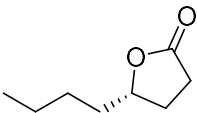
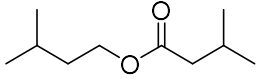
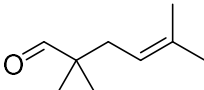
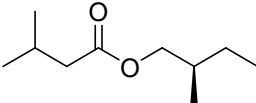
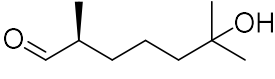
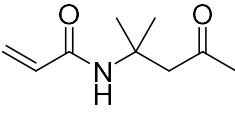
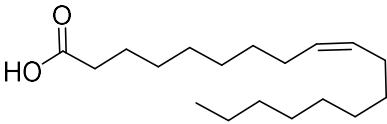
69	1-Phenylethyl acetate		-6.1	-4.8	-10.9
70	3-Methyl cinnamaldehyde		-6.1	-4.7	-10.8
71	Butyl cinnamic aldehyde		-6.1	-4.7	-10.8
72	Cinnamic acid		-5.9	-4.9	-10.8
73	<i>cis</i> -Jasmone		-5.9	-4.9	-10.8
74	Cuminaldehyde		-6.1	-4.7	-10.8
75	Raspberry ketone		-5.9	-4.9	-10.8
76	Thymol		-6.1	-4.7	-10.8
77	2-Tert-Butylcyclohexyl acetate		-6.2	-4.5	-10.7

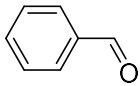
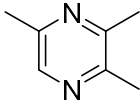
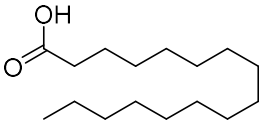
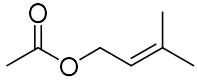
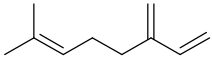
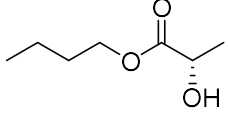
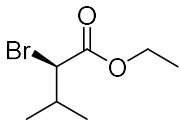
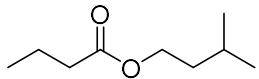
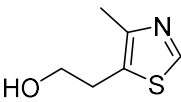
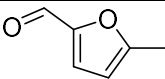
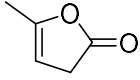
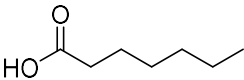
78	Ethyl vanillin		-5.7	-5	-10.7
79	α -Hexylcinnamaldehyde		-5.8	-4.8	-10.6
80	<i>p</i> -Menthane-3,8-diol		-6.1	-4.5	-10.6
81	(-)-Perillaldehyde		-5.9	-4.6	-10.5
82	Allyl cyclohexanepropionate		-5.9	-4.6	-10.5
83	Dimethyl 2-acetamidopropionate		-5.9	-4.6	-10.5
84	1,2-Dimethoxy-4-(2-propenyl)-benzene		-6.1	-4.4	-10.5
85	Linalyl acetate		-5.9	-4.6	-10.5
86	Menthone		-5.9	-4.6	-10.5
87	Dihydro cuminyl alcohol		-5.8	-4.6	-10.4

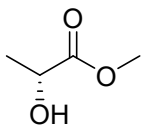
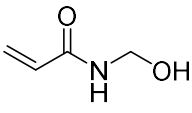
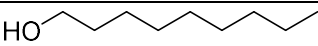
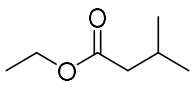
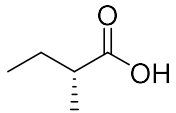
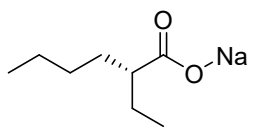
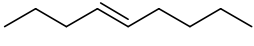
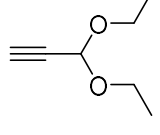
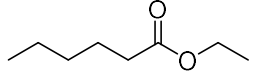
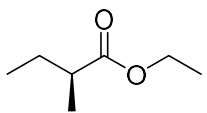
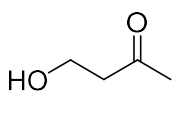
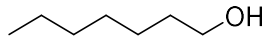
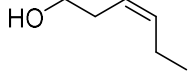
88	Linalyl propionate		-5.9	-4.5	-10.4
89	Vanillin		-5.5	-4.9	-10.4
90	γ -Terpinene		-5.8	-4.6	-10.4
91	2,4-Dimethyl-3-cyclohexene formaldehyde		-5.7	-4.7	-10.4
92	2-Acetoxy-2-methyl-6-methylene-7-octene		-5.8	-4.5	-10.3
93	2-Methoxy-4-methylphenol		-5.6	-4.7	-10.3
94	Limonene		-5.8	-4.5	-10.3
95	Azone		-6.1	-4.1	-10.2
96	<i>cis</i> -Cinnamaldehyde		-5.6	-4.6	-10.2
97	Fema 3236		-5.8	-4.4	-10.2
98	1,8-Cineole		-5.9	-4.3	-10.2

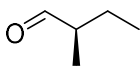
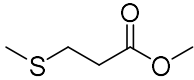
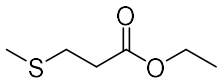
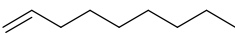
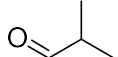
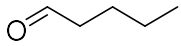
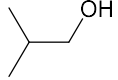
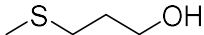
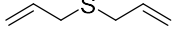
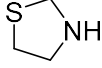
99	(±)-2-Bornanol		-5.7	-4.4	-10.1
100	(-)-Camphor		-5.8	-4.3	-10.1
101	3,5-Dimethyl-4-cyclohexene formaldehyde		-5.4	-4.7	-10.1
102	Cinnamic aldehyde		-5.7	-4.4	-10.1
103	Cinnamonnitrile		-5.7	-4.4	-10.1
104	Anethol		-5.8	-4.3	-10.1
105	2-Hexyl-2-cyclopenten-1-one		-5.5	-4.5	-10
106	3,3-Diethyloxy-1-propargyne		-5.5	-4.5	-10
107	Cinnamyl alcohol		-5.6	-4.4	-10
108	Jasmone		-5.9	-4.1	-10
109	Linalool		-5.5	-4.5	-10
110	Geraniol		-5.3	-4.6	-9.9

111	Nerol		-5.4	-4.5	-9.9
112	(R)-(+)- β -Citronel lol		-5.3	-4.6	-9.9
113	Citral		-5.4	-4.4	-9.8
114	N,2,3-Trimethyl-2- isopropylbutamid e		-5.7	-4.1	-9.8
115	Para-Mentha-8-th iolone		-5.6	-4.2	-9.8
116	γ -Decalactone		-5.3	-4.5	-9.8
117	Comphene		-5.5	-4.2	-9.7
118	Linoleic acid (Grape seed oil)		-5.1	-4.6	-9.7
119	Sabinene		-5.4	-4.3	-9.7
120	Anisaldehyde		-5.3	-4.3	-9.6
121	Apricolin		-5.4	-4.2	-9.6
122	Phenylethyl alcohol		-5.3	-4.3	-9.6

123	2-Aminomalonamide		-5.1	-4.4	-9.5
124	(2E)-Decenoic acid		-5	-4.5	-9.5
125	Allyl (3-methylbutoxy) acetate		-5.4	-4.1	-9.5
126	β -Bromostyrene		-5.3	-4.2	-9.5
127	Citronellal		-5.3	-4.2	-9.5
128	γ -Octanoic lactone		-5.3	-4.2	-9.5
129	Isoamyl isovalerate		-5.7	-3.8	-9.5
130	2,2,5-Trimethyl-4-hexenal		-5.5	-3.9	-9.4
131	2-Methylbutyl isovalerate		-5.3	-4.1	-9.4
132	7-Hydroxy-3,7-dimethyloctanal		-5.2	-4.2	-9.4
133	DAAM (Diacetone acrylamide)		-5.1	-4.3	-9.4
134	Oleic acid		-5.3	-4	-9.3

135	Benzaldehyde		-5	-4.2	-9.2
136	2,3,5-Trimethylpyrazine		-5	-4.1	-9.1
137	Palmitic acid		-4.9	-4.2	-9.1
138	Prenyl acetate		-5.1	-4	-9.1
139	7-Methyl-3-methylenecycloocta-1,6-diene		-5.2	-3.8	-9
140	Butyl lactate		-4.9	-4	-8.9
141	Ethyl 2-bromo-3-methylbutyrate		-5	-3.9	-8.9
142	Isoamyl butyrate		-5.2	-3.7	-8.9
143	5-(2-Hydroxyethyl)-4-methylthiazole		-4.7	-4.1	-8.8
144	5-Methylfurfural		-4.8	-4	-8.8
145	α -Angelic lactone		-4.9	-3.9	-8.8
146	Heptanoic acid		-4.8	-4	-8.8

147	Methyl lactate		-4.5	-4.1	-8.6
148	<i>N</i> -Methylol acrylamide		-4.3	-4.2	-8.5
149	<i>n</i> -Nonanol		-4.5	-4	-8.5
150	Ethyl isovalerate		-4.8	-3.6	-8.4
151	2-Methyl butyric acid		-4.6	-3.8	-8.4
152	Sodium-2-ethylca proate		-4.8	-3.6	-8.4
153	4-Nonene		-4.4	-3.9	-8.3
154	Propargylaldehyd e diethyl acetal		-4.6	-3.7	-8.3
155	Ethyl hexanoate		-4.7	-3.5	-8.2
156	Ethyl 2-methylbutyrate		-4.5	-3.6	-8.1
157	Butanone alcohol		-4.1	-3.7	-7.8
158	Heptanol		-4.2	-3.5	-7.7
159	Leaf alcohol		-4.2	-3.5	-7.7

160	2-Methylbutyraldehyde		-4.1	-3.5	-7.6
161	Pineapple methyl ester		-4.4	-3.2	-7.6
162	Ethyl 3-methylthiopropionate		-4.1	-3.4	-7.5
163	1-Nonene		-4.2	-3.2	-7.4
164	Isobutyraldehyde		-3.8	-3.2	-7
165	Valeraldehyde		-3.8	-3.2	-7
166	Isobutanol		-3.6	-3.2	-6.8
167	3-Methylthio-1-propanol		-3.4	-3.3	-6.7
168	Allyl Sulfide		-3.6	-3	-6.6
169	Thiazolidine		-3	-2.9	-5.9