

Supplementary

Article

Identification of Potential SARS-CoV-2 Main Protease and Spike Protein Inhibitors from the Genus *Aloe*: An *In silico* Study for Drug Development

Mohamed E. Abouelela ¹, Hamdy K. Assaf ¹, Reda A. Abdelhamid ¹, Ehab S. Elkhyat ¹, Ahmed M. Sayed ², Tomasz Oszako ³, Lassaad Belbahri ^{4,*}, Ahmed E. El Zowalaty ^{5,6,*} and Mohamed Salaheldin. A. Abdelkader ^{7,*}

- ¹ Department of Pharmacognosy, Faculty of Pharmacy, Al-Azhar University, Assiut-Branch, Assiut 71524, Egypt; m_abouelela@azhar.edu.eg (M.E.A.); hamdyss200@azhar.edu.eg (H.K.A.); reda.ahmed@azhar.edu.eg (R.A.A.); elkhyat@azhar.edu.eg (E.S.E.)
 - ² Department of Pharmacognosy, Faculty of Pharmacy, Nahda University, Beni-Suef 62513, Egypt; Ahmed.mohamed.sayed@nub.edu.eg
 - ³ Department of Forest Protection, Forest Research Institute, 05-090 Sekocin Stary, Poland; T.Oszako@ibles.waw.pl
 - ⁴ Laboratory of Soil Biology, University of Neuchatel, 2000 Neuchatel, Switzerland
 - ⁵ Sahlgrenska Center for Cancer Research, Department of Surgery, Institute of Clinical Sciences, University of Gothenburg, 405 30 Gothenburg, Sweden
 - ⁶ Wallenberg Centre for Molecular and Translational Medicine, University of Gothenburg, 405 30 Gothenburg, Sweden
 - ⁷ Department of Pharmacognosy, Faculty of Pharmacy, Sohag University, Nasr City, 82524, Sohag, Egypt
- * Correspondence: lassaad.belbahri@unine.ch (L.B.); ahmed.el.zowalaty@gu.se (A.E.E.Z.); m.salaheldin@pharm.sohag.edu.eg (M.S.A.A.)

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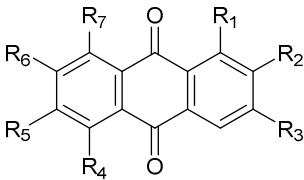
							
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1	OH	H	CH ₃	H	H	H	OH
2	OH	H	CH ₃	OH	H	H	OCH ₃
3	OH	H	CH ₂ (OH)	H	H	H	OH
4	OH	H	CH ₂ (OH)	H	H	OH	OH
5	OH	H	CH ₃	H	H	OH	OH
6	OH	H	CH ₃	H	H	OH	OCH ₃
7	OH	H	CH ₃	H	OH	H	OH
8	CH ₃	H	OH	H	H	H	OH
9	CH ₃	COOCH ₃	OH	H	H	H	OH
10	CH ₃	COOCH ₃	OH	H	H	H	OCH ₃
11	OH	H	CH ₃	OH	H	H	OH
12	OH	H	CH ₃	OCH ₃	H	H	H
13	OH	H	CH ₃	OH	H	OCH ₃	OH
14	CH ₃	H	OH	H	OH	H	OH
15	CH ₃	COOCH ₃	OH	H	OH	H	OH
16	OH	H	CH ₃	H	<i>O</i> -Prenyl	H	OH
17	OH	H	CH ₃	H	<i>O</i> -Prenyl- Prenyl	H	OH

Figure S1. Compounds isolated from genus Aloe (**1-17**).

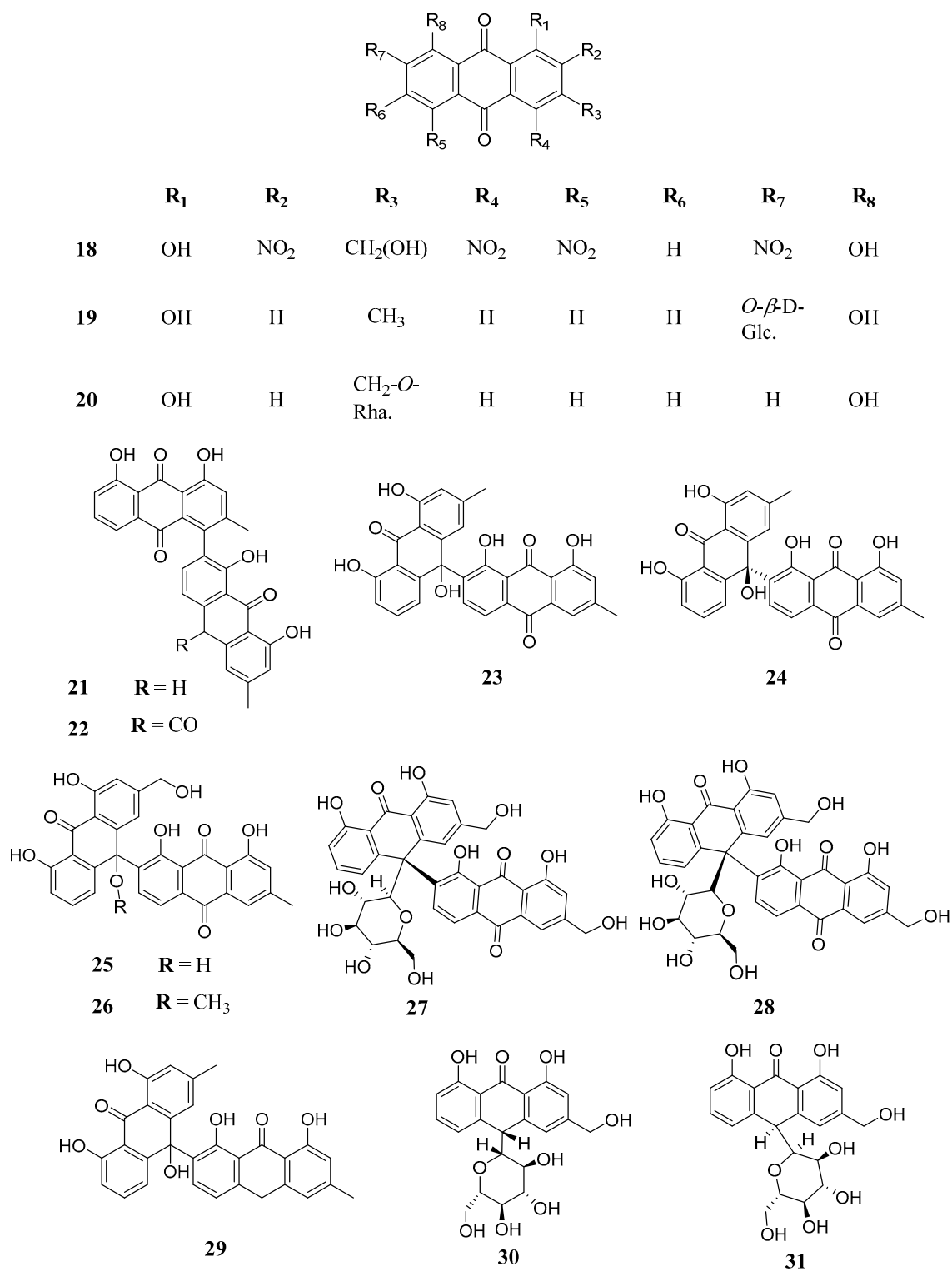


Figure S2: Compounds isolated from genus *Aloe* (18-31)

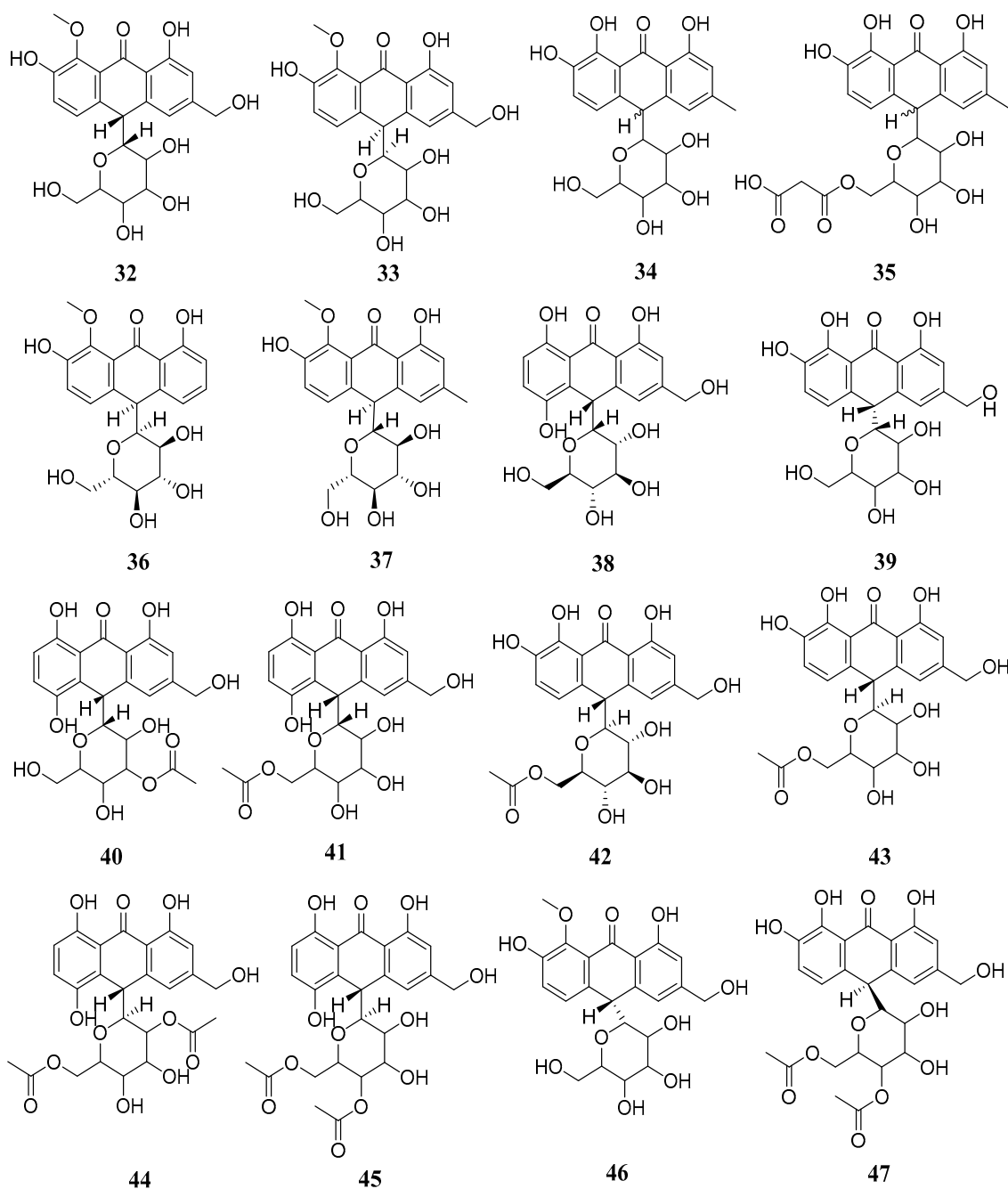


Figure S3: Compounds isolated from genus Aloe (32-47)

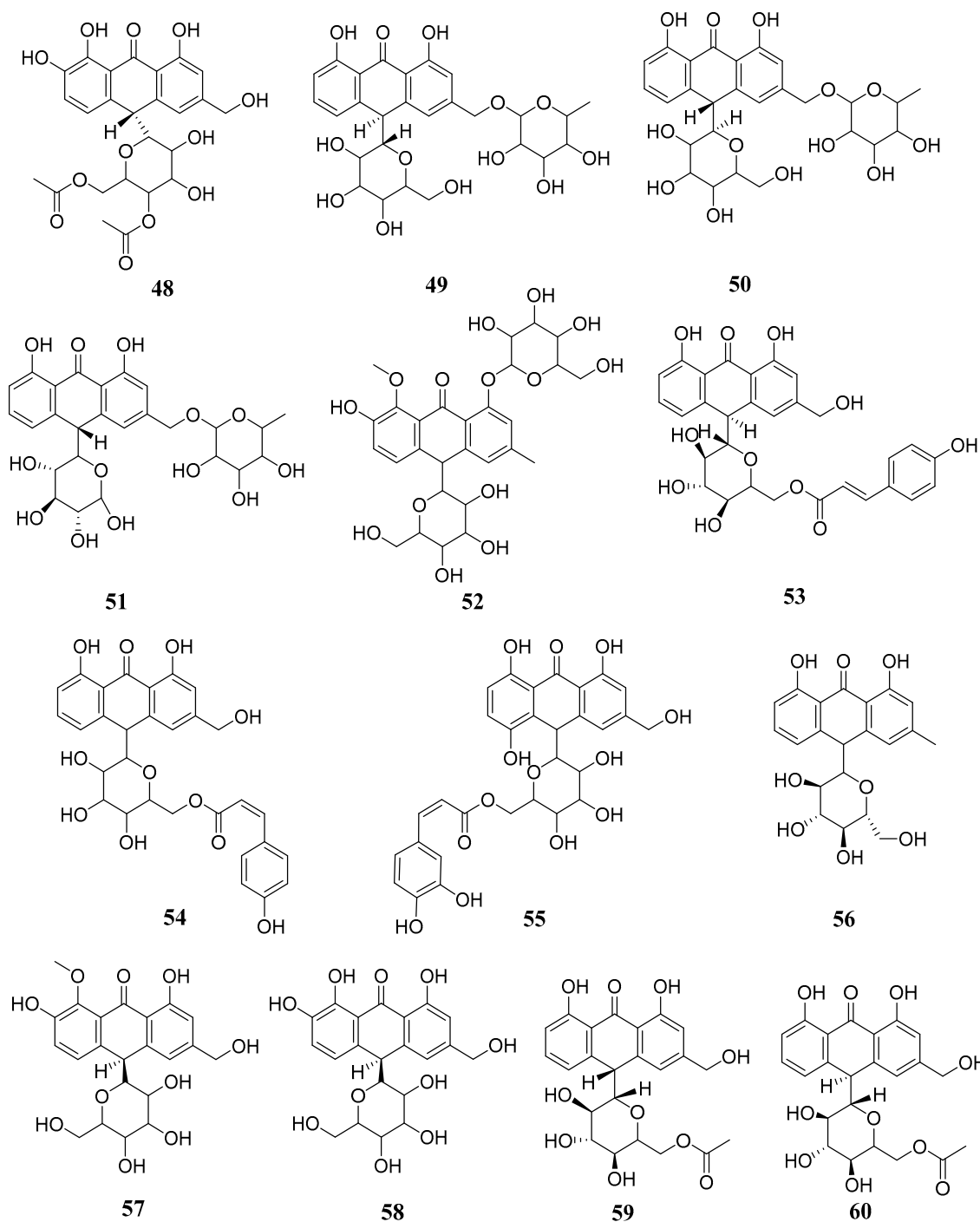
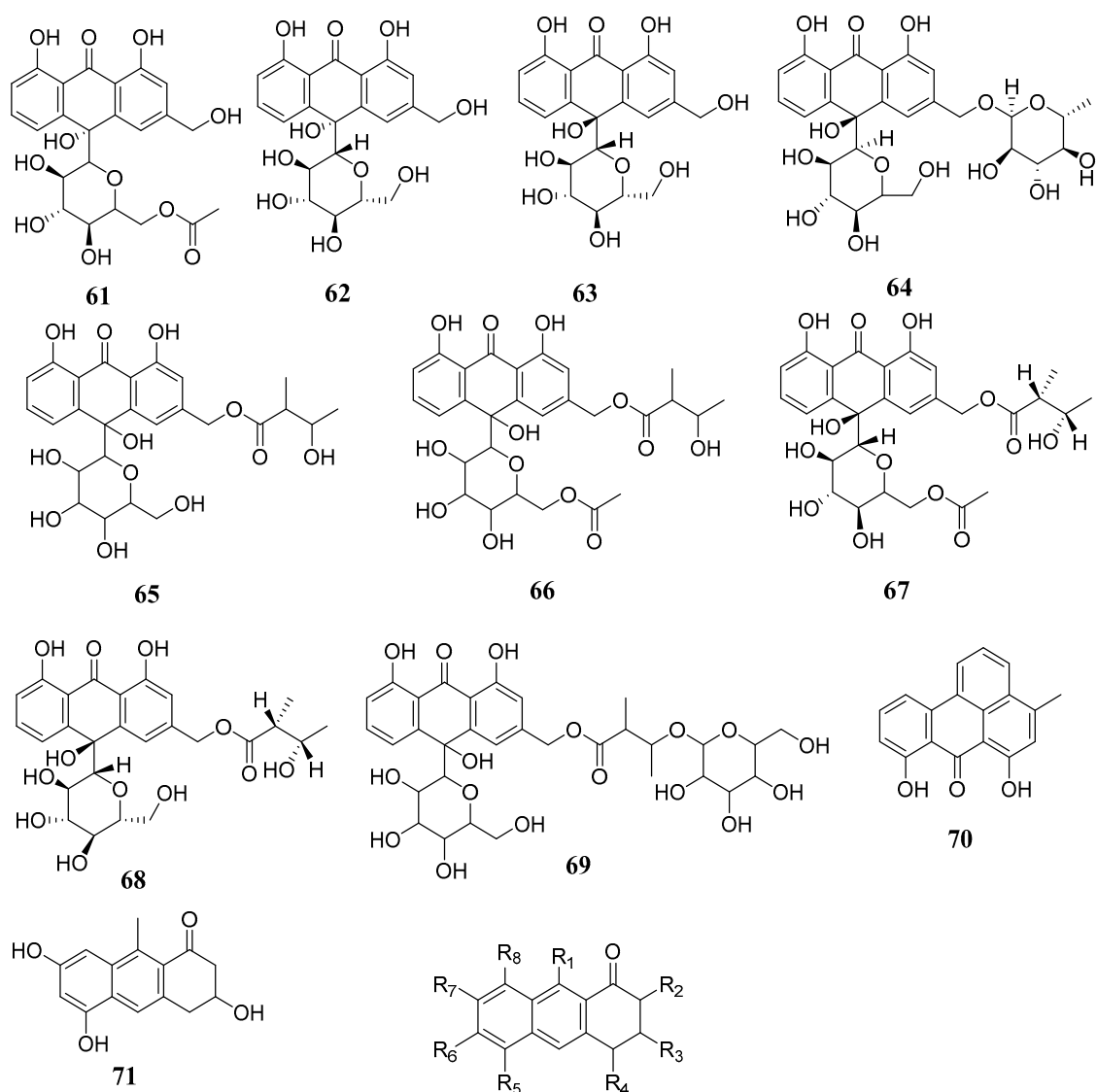


Figure S4: Com-

pounds isolated from genus Aloe (48-60)



	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈
72	CH ₃	H	OH	H	OH	H	OH	H
73	OH	H	OH	H	H	OH	H	CH ₃
74	OH	H	OH	H	H	OCH ₃	H	CH ₃
75	OH	OCH ₃	H	OH	H	CH ₃	H	OH

Figure S5: Compounds isolated from genus Aloe (61-75)

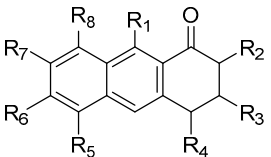
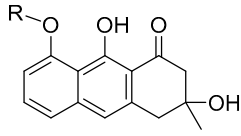
								
	R₁	R₂	R₃	R₄	R₅	R₆	R₇	R₈
76	OH	H	OH	H	H	OH	COOCH ₃	CH ₃
77	OH	H	H	OH	H	CH ₃	H	OH
78	OH	H	H	OH	H	CH ₃	H	OCH ₃
79	OH	H	H	OH	H	CH ₃	H	<i>O</i> -β-D-Glc.
80	OH	OCH ₃	H	OH	H	CH ₃	H	<i>O</i> -β-D-Glc.
81	OH	OH	H	<i>O</i> -β-D-Glc.	H	CH ₃	H	OH
82	OH	OCH ₃	H	<i>O</i> -β-D-Glc.	H	CH ₃	H	OH
83	OH	H	OH	H	H	<i>O</i> -β-D-Glc.	H	CH ₃
84	OH	H	<i>O</i> -β-D-Glc.	H	H	OH	COOCH ₃	CH ₃
								
85	R = H							
86	R = CH₃							
	R₁	R₂	R₃	R₄				
87	CH ₃	OH	H	OH				
88	CH ₃	OH	H	CH ₃				
89	CH ₂ (OH)	OH	H	CH ₃				
90	CH ₂ (OH)	OCH ₃	H	CH ₃				
91	CH ₃	OH	H	CH ₂ COCH ₃				
92	CH ₃	OH	H	CH ₂ CH(OH)CH ₃				

Figure S6: Compounds isolated from genus *Aloe* (76-92)

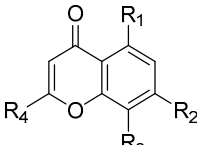


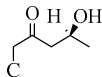



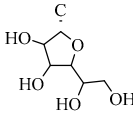
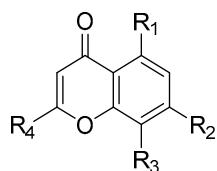
				
	R ₁	R ₂	R ₃	R ₄
93	OH	OCH ₃	H	CH ₂ (OH)
94	OH	OH	H	
95		H	H	CH ₂ (OH)
96	CH ₃	OH	CH ₂ COCH ₂ (OH)	CH ₂ COCH ₃
97		H	H	CH ₂ (OH)
98	CH ₃	OCH ₃	β -D-Glc.	
99	CH ₃	OCH ₃	β -D-Glc.	
100	CH ₃	OH	β -D-Glc.	CH ₂ CH(OH)CH ₃
101	CH ₃	OCH ₃	β -D-Glc.	CH ₂ (OH)CH(OH)CH ₃
102	CH ₃	OCH ₃	β -D-Glc.	
103	CH ₃	OH	β -D-Glc.	CH ₃
104	OH	OH	β -D-Glc.	CH ₃
105	OH	OH	α -D-Glc.	CH ₃
106	CH ₃	OH		CH ₂ COCH ₃
107	CH ₃	OH	β -D-Glc.	CH ₂ COCH ₃

Figure S7: Compounds isolated from genus Aloe (93-107)



	R₁	R₂	R₃	R₅
108	CH ₃	OCH ₃	β -D-Glc.	CH ₂ COCH ₃
109	CH ₃	OH		CH ₂ COCH ₃
110	CH ₃	OH	β -D-Glc.	
111	CH ₃	OH	β -D-Glc.	
112	CH ₃	OCH ₃	β -D-Glc.	
113	CH ₃	OCH ₃	β -D-Glc.	
114	CH ₃	OH		CH ₂ CH(OH)CH ₃
115	CH ₃	OH		CH ₂ CH(OH)CH ₃
116	CH ₃	OCH ₃		CH(OH)CH(OH)CH ₃
117	CH ₃	OCH ₃		CH ₂ CH(OH)CH ₃
118	CH ₃	OCH ₃		

Figure S8: Compounds isolated from genus Aloe (108-118)

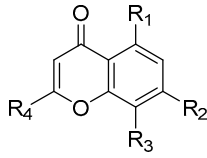
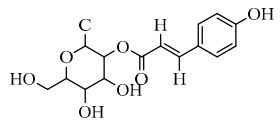

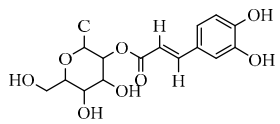

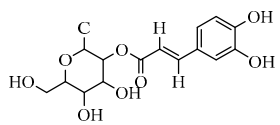

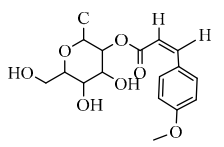

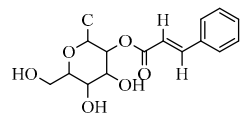

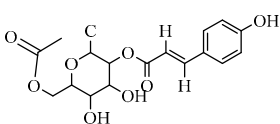

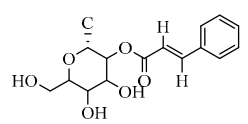
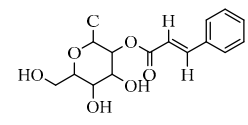
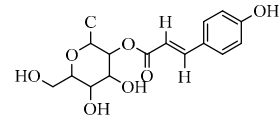
				
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120	CH ₃	OCH ₃		
121	CH ₃	OCH ₃		
122	CH ₃	OCH ₃		
123	CH ₃	OCH ₃		
124	CH ₃	OCH ₃		
125	CH ₃	OH		CH ₂ COCH ₃
126	CH ₃	OCH ₃		CH ₂ COCH ₃
127	CH ₃	OCH ₃		CH ₂ COCH ₃

Figure S9: Compounds isolated from genus Aloe (119-127)

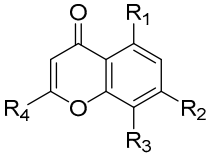
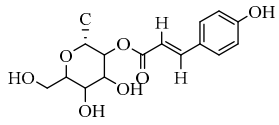
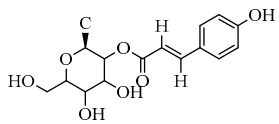
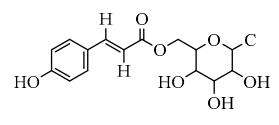
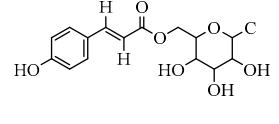
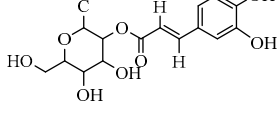
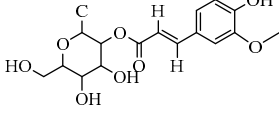
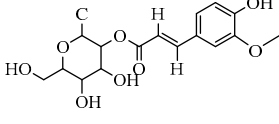
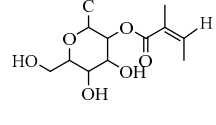
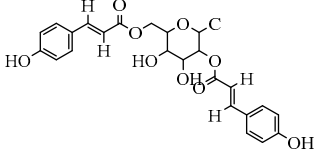
				
	R₁	R₂	R₃	R₄
128	CH ₃	OH		CH ₂ COCH ₃
129	CH ₃	OH		CH ₂ COCH ₃
130	CH ₃	OH		CH ₂ COCH ₃
131	CH ₃	OCH ₃		CH ₂ COCH ₃
132	CH ₃	OCH ₃		CH ₂ COCH ₃
133	CH ₃	OH		CH ₂ COCH ₃
134	CH ₃	OCH ₃		CH ₂ COCH ₃
135	CH ₃	OH		CH ₂ COCH ₃
136	CH ₃	OH		CH ₂ COCH ₃

Figure S10: Compounds isolated from genus Aloe (128-136)

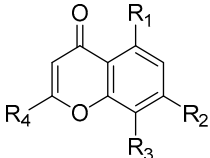
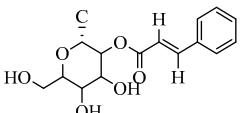
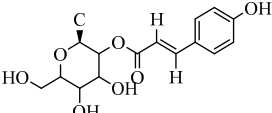
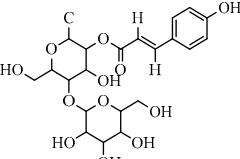
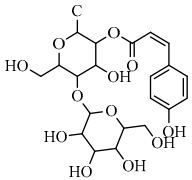
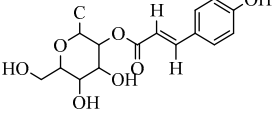
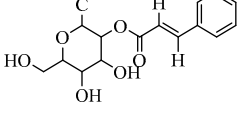

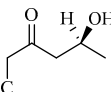
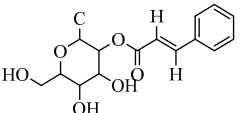

				
	R₁	R₂	R₃	R₄
137	CH ₃	<i>O</i> -β-D-Glc.		CH ₂ COCH ₃
138	CH ₃	<i>O</i> -β-D-Glc.		CH ₂ COCH ₃
139	CH ₃	OCH ₃		CH ₂ CH(OH)CH ₃
140	CH ₃	OCH ₃		CH ₂ CH(OH)CH ₃
141	CH ₃	OH		COOH
142	CH ₃	OCH ₃		
143		H	H	CH ₂ <i>O</i> -β-D-Glc.
144	CH ₃	OCH ₃		

Figure S11: Compounds isolated from genus *Aloe* (137-144)

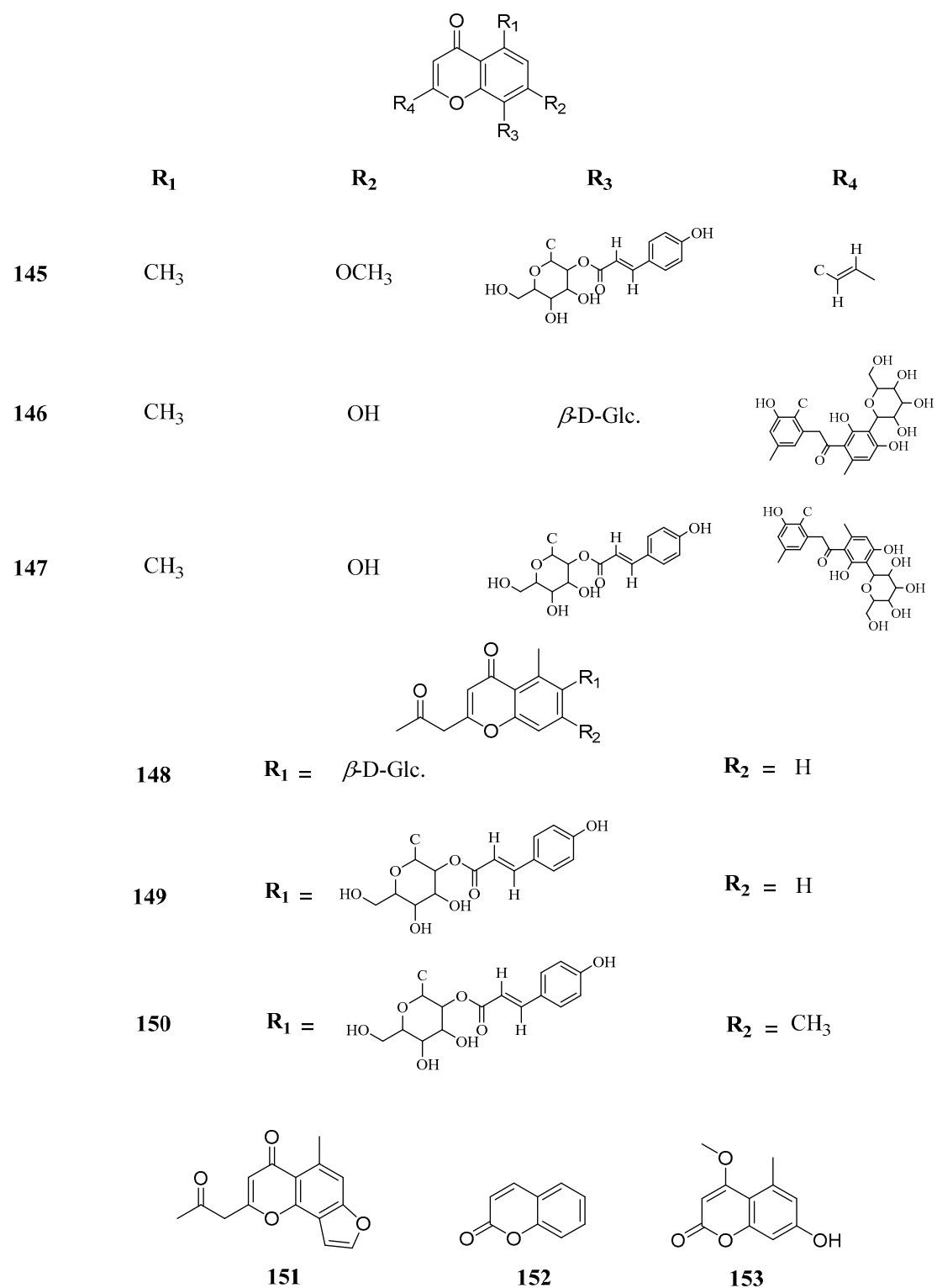
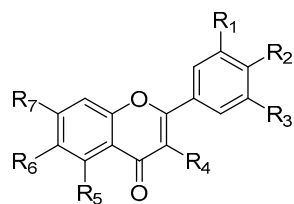
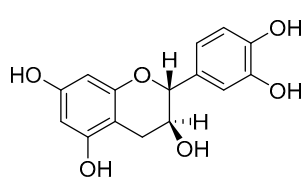


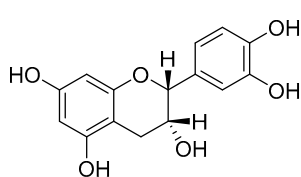
Figure S12: Compounds isolated from genus Aloe (145-153)



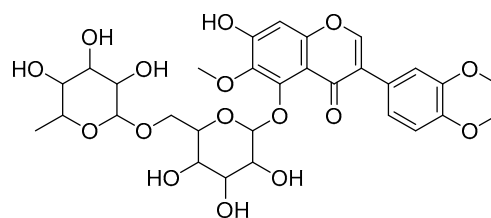
	R₁	R₂	R₃	R₄	R₅	R₆	R₇
154	H	OH	H	H	OH	H	OH
155	H	OH	H	OH	OH	H	OH
156	H	OH	OH	OH	OH	H	OH
157	OH	OH	OH	OH	OH	H	OH
158	OH	OH	H	<i>O</i> - α -L-Rha.	OH	H	OH
159	OH	OH	H	<i>O</i> - β -D-Glc.-6- <i>O</i> - α -L-Rha.	OH	H	OH
160	OCH ₃	OH	OCH ₃	<i>O</i> - β -D-Glc.-6- <i>O</i> - α -L-Rha.	OH	OCH ₃	OCH ₃



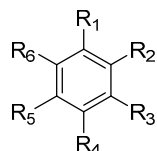
161



162

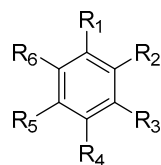


163



	R₁	R₂	R₃	R₄	R₅	R₆
164	OH	OH	H	H	H	H
165	OH	CHO	H	H	H	H
166	CH ₃	H	H	OH	H	H
167	COCH ₃	H	H	OH	H	H
168	CHO	H	H	OH	H	H

Figure S13: Compounds isolated from genus Aloe (**154-168**)



	R₁	R₂	R₃	R₄	R₅	R₆
169	CHO	H	H	OCH ₃	H	H
170	CH ₂ CH ₂ CO OH	H	H	OH	H	H
171	CH ₂ CH ₂ CO OCH ₃	H	H	OH	H	H
172		H	H	OH	H	H
173		H	H	OH	OH	H
174		H	H	OH	OCH ₃	H
175		H	OCH ₃	OH	OCH ₃	H
176	OH	H	CH ₃	H	OH	H
177	COOH	OH	H	H	OH	H
178	COOH	H	H	OH	OH	H
179	COOH	H	H	OH	OCH ₃	H
180	COOH	H	OH	OH	OH	H
181	COOH	H	OCH ₃	OH	OCH ₃	H
182	COCH ₃	CH ₃	H	OH	H	OH

Figure S14: Compounds isolated from genus Aloe (**169-182**)

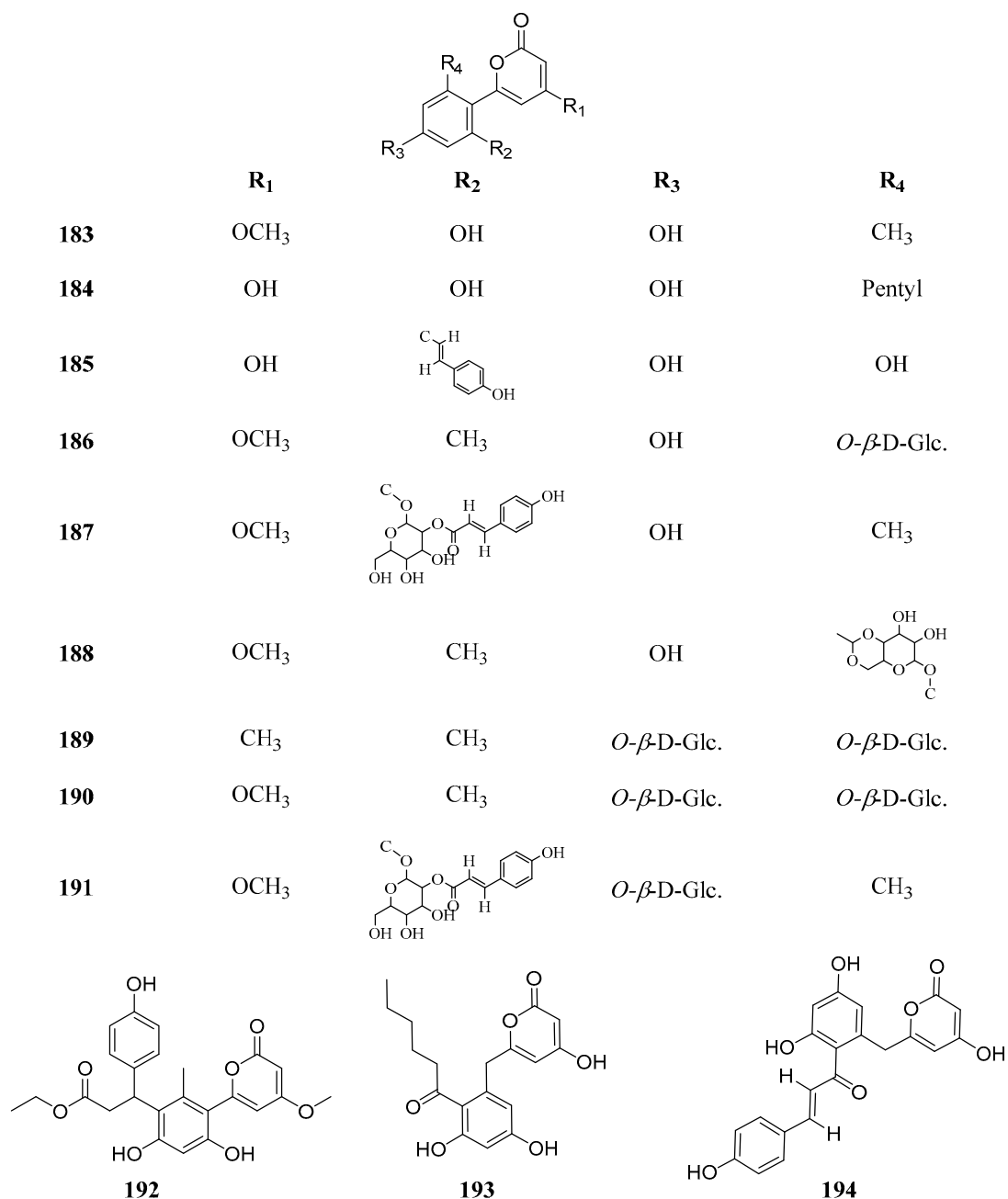


Figure S15: Compounds isolated from genus Aloe (183-194)

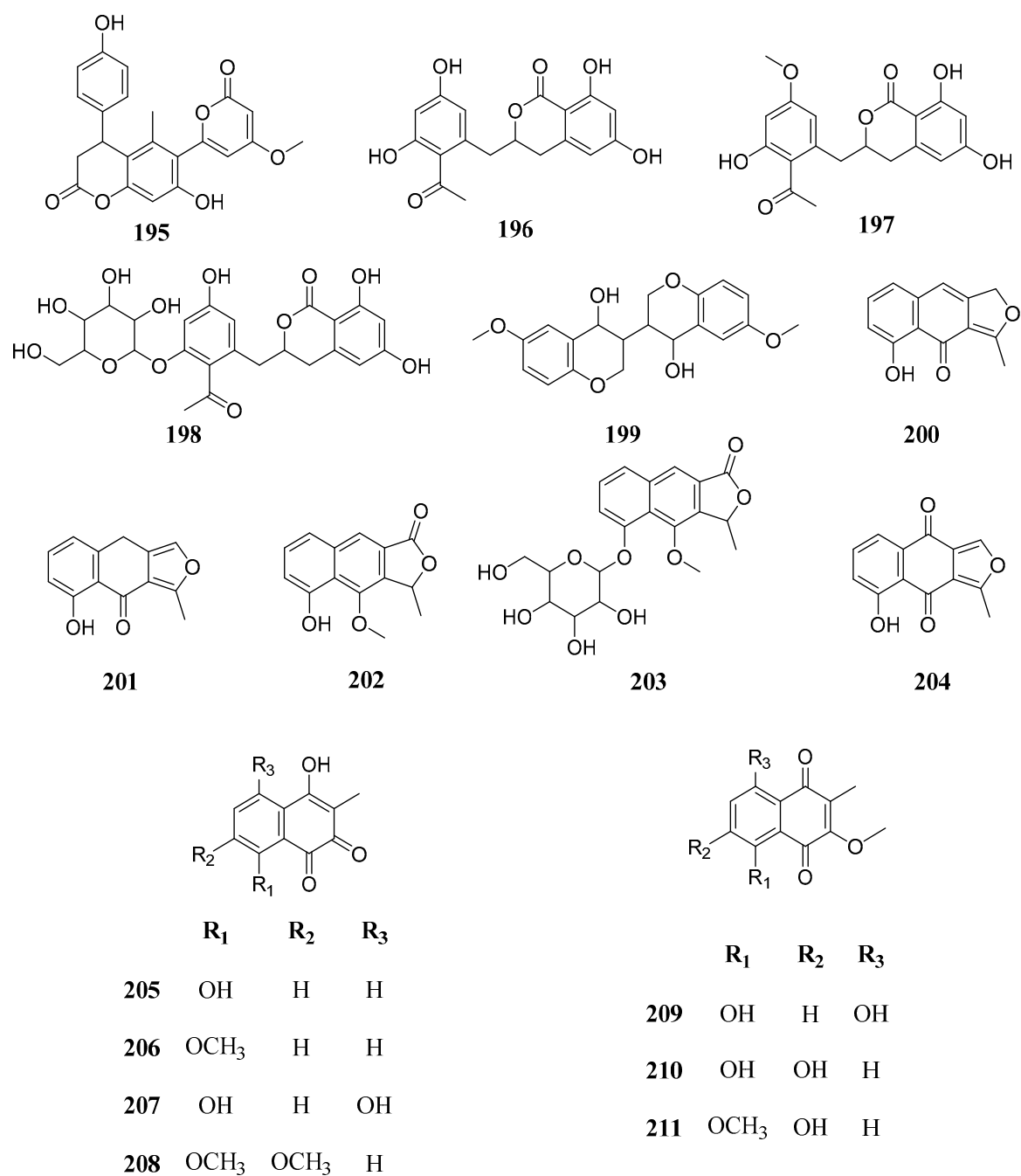


Figure S16: Compounds isolated from genus Aloe (195-211)

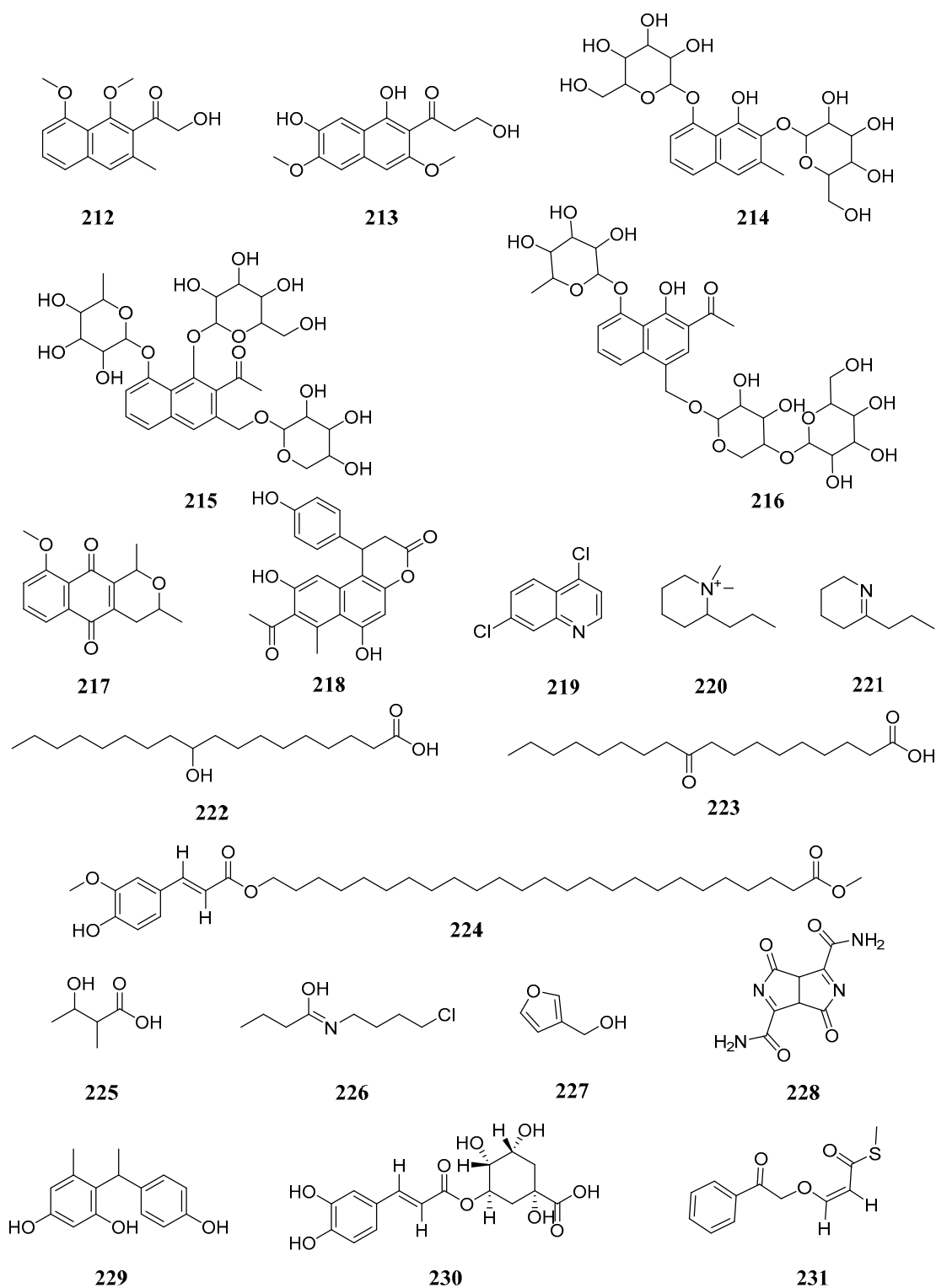


Figure S17: Compounds isolated from genus *Aloe* (212-231)

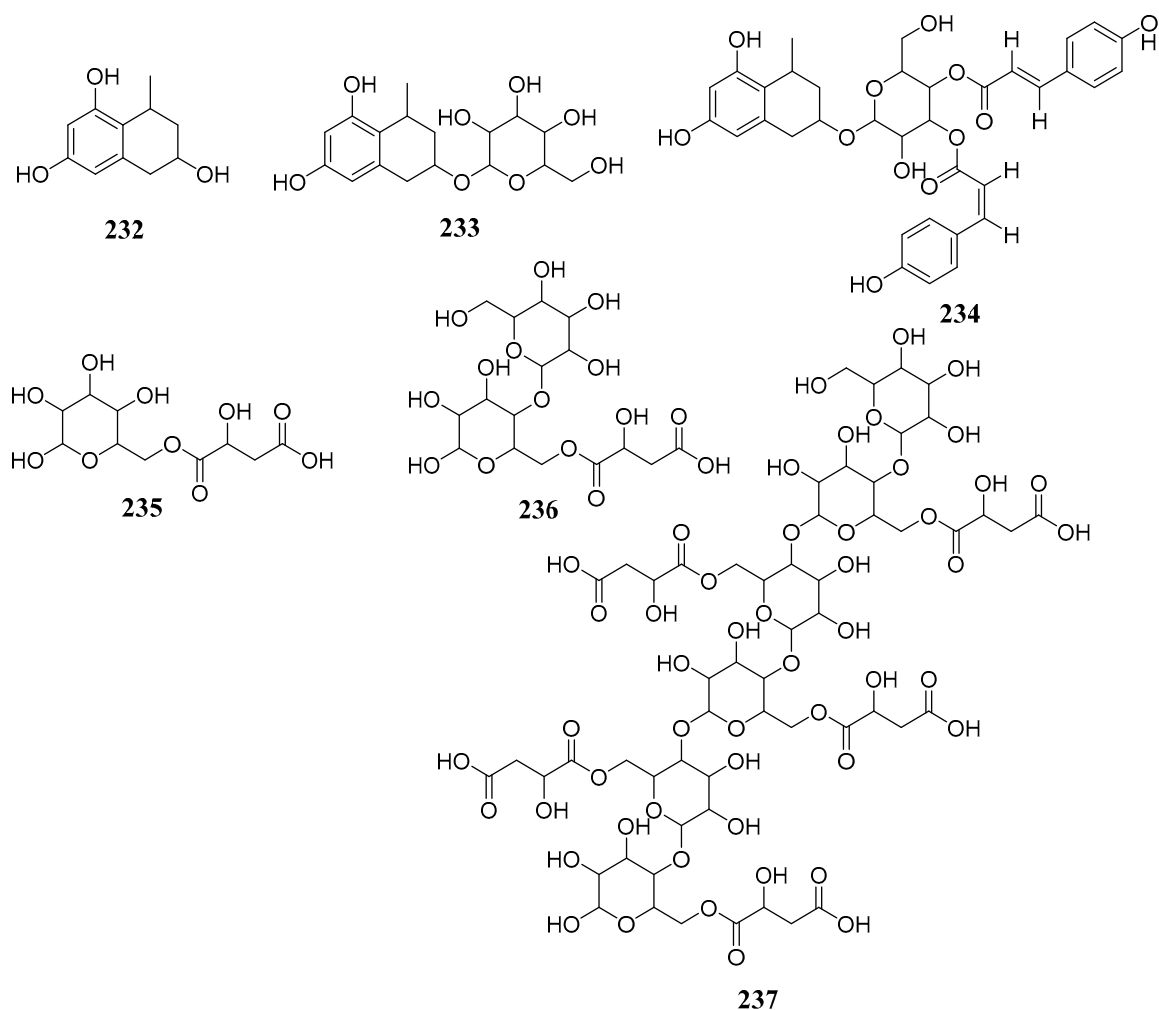


Figure S18: Compounds isolated from genus Aloe (232-237)

Table 1. Predicted pharmacokinetics of top scoring compounds.

Compound No.	115	120	131	132	134	159
BBB	0.044	0.041	0.0215873	0.03	0.02	0.02
Buffer_solubility_mg_L	12.77	18.077	4.84474	10.88	4.19	28.88
Caco2	12.86	10.71	11.4372	10.62	9.20	7.91
CYP_2C19_inhibition	Inhibitor	Inhibitor	Inhibitor	Inhibitor	Inhibitor	Inhibitor
CYP_2C9_inhibition	Inhibitor	Inhibitor	Inhibitor	Inhibitor	Inhibitor	Inhibitor
CYP_2D6_inhibition	Non	Non	Non	Non	Non	Non
CYP_2D6_substrate	Non	Non	Non	Non	Non	Non
CYP_3A4_inhibition	Inhibitor	Inhibitor	Inhibitor	Inhibitor	Inhibitor	Inhibitor
CYP_3A4_substrate	Substrate	Weakly	Weakly	Weakly	Weakly	Weakly
HIA	77.11	57.61	82.803611	66.18	79.98	2.86
MDCK	0.051	0.05	0.0511802	0.053	0.05	0.32
Pgp_inhibition	Inhibitor	Non	Non	Non	Non	Non
Plasma_Protein_Binding	77.20	73.52	74.833673	68.96	68.79	43.89
Pure_water_solubility_mg_L	3.29	4.86	3.74378	4.05	1.88	217.20
Skin_Permability	-3.73	-3.85	-3.65856	-3.80	-3.65	-4.66
SKlogD_value	1.72	1.58	1.44	1.49	1.63	-1.11
SKlogP_value	1.72	1.58	1.44	1.49	1.63	-1.11
SKlogS_buffer	-4.63	-4.50	-5.058	-4.72	-5.14	-4.32
SKlogS_pure	-5.22	-5.07	-5.17	-5.14	-5.49	-3.44