Antineutrophilic inflammatory secondary metabolites from *Solanum macaonense*

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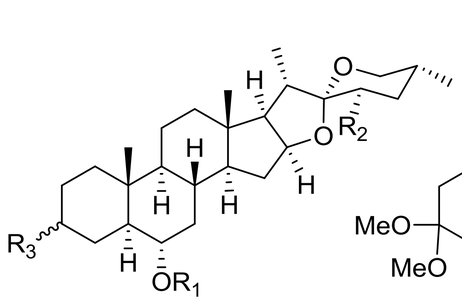
Introduction

Solanum macaonense Dunal (Solanaceae) that grows in the Taiwan southwestern plains. As a part of an ongoing on anti-inflammatory agents from Taiwanese *Solanum* species, it was found that the 95% MeOH-soluble and *n*-BuOH-soluble extracts of the aerial parts of *S. macaonense* showed activity against superoxide anion generation and elastase release induced by formyl-L-methionyl-L-leucyl-L-phenylalanine (FMLP)/ cytochalasin B (CB) in human neutrophils. However, neither phytochemical nor biological studies of *S. macaonense* have been reported to date.

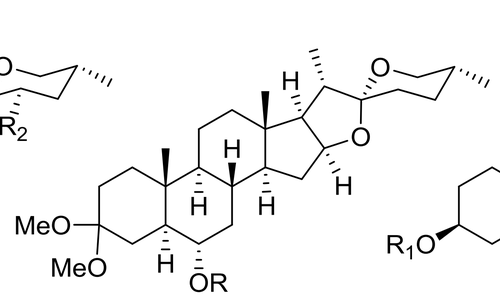
Solanum macaonense

Results and Discussion

Eight new spirostanol saponins (**1**–**8**) and ten new furostanol saponins (**9**–**18**), together with twenty-one known compounds including six spirostanols (**19**–**24**), four caffeic acid derivatives (**25**–**28**), two amides (**29**–**30**), seven flavonoids (**31**–**37**), one ligand (**38**), and benzaldehyde (**39**) were isolated from *S. macaonense*. All structures of compounds were determined from their spectroscopic data, and the compounds were tested for *in vitro* antineutrophilic inflammatory activity.

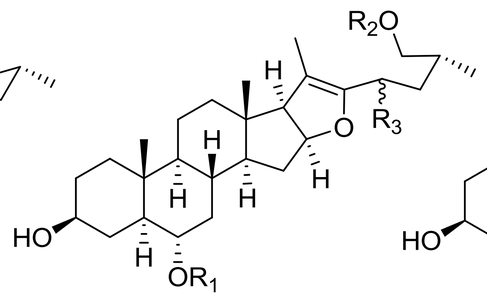


1 R_1 = S5, R_2 = H, R_3 = =O
3 R_1 = S5, R_2 = OH, R_3 = β-OH



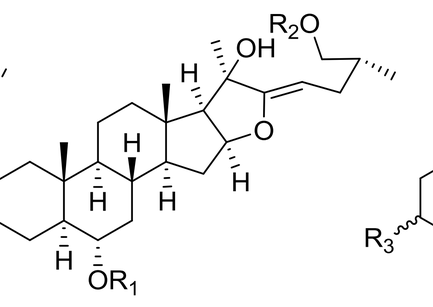
2 R = S5

4 R_1 = H, R_2 = S6
5 R_1 = S7, R_2 = H
6 R_1 = S8, R_2 = H
7 R_1 = S3, R_2 = S1
8 R_1 = S9, R_2 = H

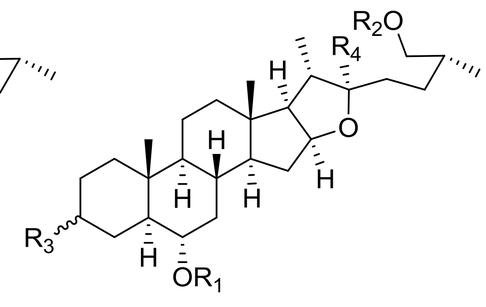


19 R_1 = H, R_2 = H
20 R_1 = H, R_2 = S1
21 R_1 = H, R_2 = S2
22 R_1 = H, R_2 = S3
23 R_1 = H, R_2 = S4
24 R_1 = H, R_2 = S5

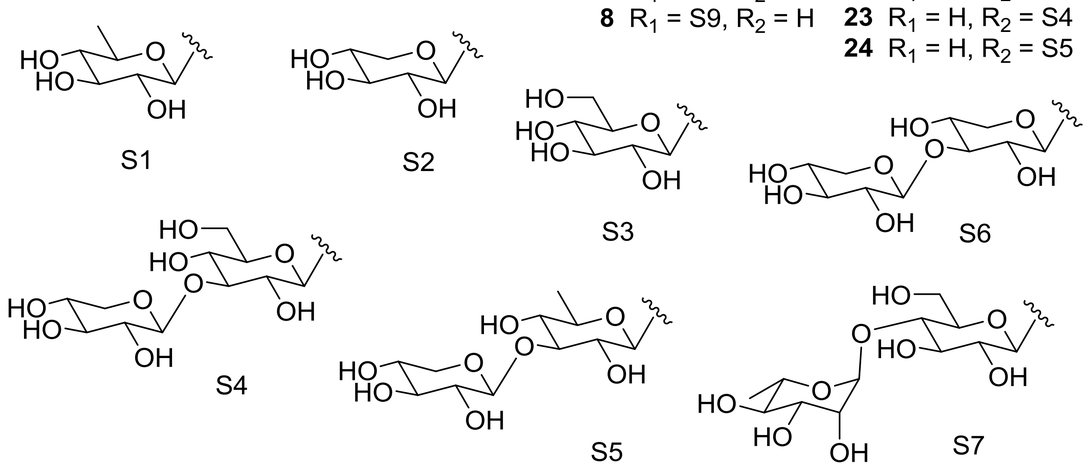
9 R_1 = S5, R_2 = S3, R_3 = H
11 R_1 = S5, R_2 = S3, R_3 = OH



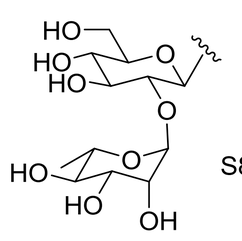
10 R_1 = S5, R_2 = S3



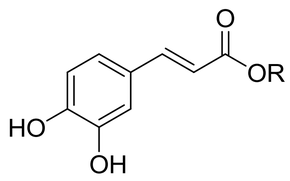
12 R_1 = S5, R_2 = S3, R_3 = β-OH, R_4 = OH
13 R_1 = H, R_2 = S3, R_3 = β-O-S3, R_4 = OH
14 R_1 = H, R_2 = S3, R_3 = β-O-S8, R_4 = OH
15 R_1 = S1, R_2 = S3, R_3 = β-O-S3, R_4 = OH
16 R_1 = S5, R_2 = S3, R_3 = β-OH, R_4 = OCH_3
17 R_1 = S5, R_2 = S3, R_3 = = O, R_4 = OCH_3
18 R_1 = S6, R_2 = S3, R_3 = = β-OH, R_4 = OCH_3



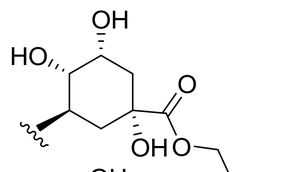
S1 S2 S3 S6 S4 S5 S7



S8



25 R = H



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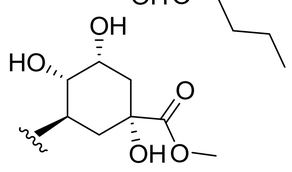
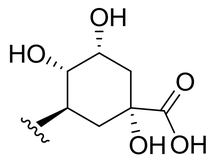
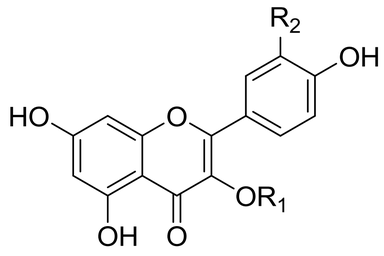


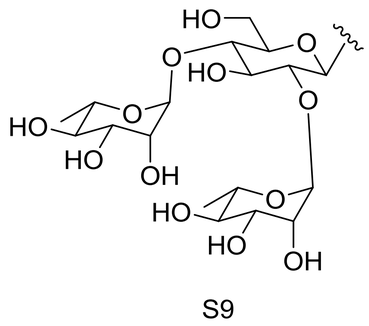
27 R =



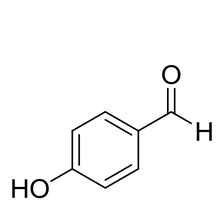
28 R =



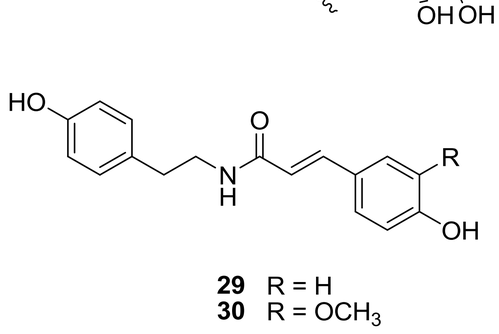
31 R_1 = H, R_2 = H
32 R_1 = gal, R_2 = H
33 R_1 = glc, R_2 = H
34 R_1 = gal$^{6}\!-\!^{1}$rha, R_2 = H
35 R_1 = glc$^{6}\!-\!^{1}$rha, R_2 = H
36 R_1 = glc, R_2 = OH
37 R_1 = glc$^{6}\!-\!^{1}$rha, R_2 = OH



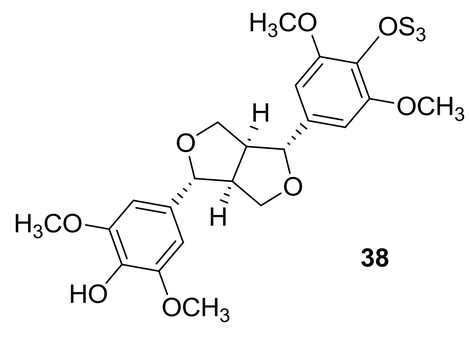
S9



39



29 R = H
30 R = OCH_3



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Effects of All Compounds on Superoxide Anion Generation and Elastase Release in FMLP/CB-induced Human Neutrophils[a]

compound	superoxide anion	elastase release
	IC_{50} (μM)[b]	IC_{50} (μM)[b]
1	> 10	3.2 ± 0.2*
4	> 10	4.2 ± 0.4*
19	6.1 ± 0.5*	> 10
20	7.0 ± 0.8*	3.7 ± 0.3*
21	7.6 ± 0.4*	4.4 ± 0.6*
24	4.0 ± 0.1*	1.0 ± 0.2*
25	3.3 ± 0.8*	>10
26	4.6 ± 1.1*	4.0 ± 0.3*
27	4.8 ± 0.3*	>10
28	4.2 ± 0.7*	>10
31	> 10	4.0 ± 0.5*
DPI[c]	0.7 ± 0.4*	
Sivelestat[c] (nM)		50.2 ± 0.2

[a]Results are presented as means ± S.E.M. (n = 3 or 4) (* p < 0.001 compared with the control value). Compounds **2**, **5**, **6**, and **23** were not tested. Compounds **3**, **7**–**18**, **22**, **29**–**30**, and **32**–**39** were inactive in both assays (IC_{50} > 10 μM). [b]Concentration necessary for 50 % inhibition (IC_{50}). [c]Diphenyleneiodonium (DPI) and sivelestat were used as positive controls for superoxide anion generation and elastase release, respectively.

It was found that both immediate inflammation responses including superoxide anion generation and elastase release were significantly inhibited by treatment with spirostanols **20**, **21**, **24**, and caffeic acid derivative **26** (superoxide anion generation: IC_{50} 7.0, 7.6, 4.0, 4.6 μM; elastase release: IC_{50} 3.7, 4.4, 1.0, 4.0 μM, respectively). However, compounds **1**, **4**, and **31** exhibited effects on the inhibition of elastase release only, with IC_{50} values of 3.2, 4.2, and 4.0 μM, respectively, while **19**, **25**, **27**, and **28** was active against superoxide anion generation only, with an IC_{50} value of 6.1, 3.3, 4.8, and 4.2 μM. Accordingly, spirostanols and caffeic acid derivatives may be promising lead compounds for further neutrophilic inflammatory disease studies, such as asthma, chronic obstructive pulmonary disease and acute respiratory distress syndrome.

Acknowledgements

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