Supplementary Material

Lotusin A, a novel pyrrole terpenoid hydrid from the Lotus roots (*Nelumbo nucifera* Gaertn.)

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ABSTRACT

Nelumbo nucifera Gaertn. has been used as traditional medicines and food. Up to the present, many unknown constituents are still being discovered. Most of the research about secondary metabolites and their pharmacological properties focus on alkaloid derivatives. In this study, one novel pyrrole terpenoid hydrid, lotusin A (**1**), and five reported substances, cholestanol (**2**), stigmast-4-en-3-one (**3**), quercetin (**4**), isohamnetin (**5**), and norartocarpetin (**6**) were isolated from methanol extract from the roots of *N. nucifera* Gaertn.. The structures (**1**–**6)** were identified *via* spectroscopic analyses of NMR (1D and 2D), HR-ESIMS, and comparisons with previous literatures. Compound **1**, a pyrrole terpenoid hydrid, is a unique isolation from plant natural products. **1** and **2** tested with inhibitory activity of NO production whereas all compounds absorbed growth inhibition assay of six bacterial strains. The results indicated that **1** moderately inhibited NO production with an IC_{50} value of 21.5 μM but no inhibition of microbial growth at concentration of 10 μM. Besides, compound of **1** also exhibited the good inhibition of *α*-glucosidase (IC_{50} = 18.2 μM), in contrast, the result did not satisfy to others. From molecular docking result, **1** has good interaction to with both of pro-inflammatory cytokines (iNOS, COX-2, TNF-α, IL-1β, and IL-6); transcription factors (Nrf2 and NF-κB), diabetes enzyme with binding energies of −6.4, −6.4, −5.0, −5.8, −6.1 kcal/mol; −6.1, −6.6 kcal/mol; and −6.4 kcal/mol, respectively, resulted that **1** is the promising candidate for anti-inflammatory and *α* -glucosidase inhibition. Moreover, *in silico* ADMET and toxicity predictions indicated that **1** had favourable safety and pharmacokinetic profiles.

Keywords: Lotus root, *Nelumbo nucifera* Gaertn., pyrrole, NO production, anti-inflammatory, *α*-glucosidase

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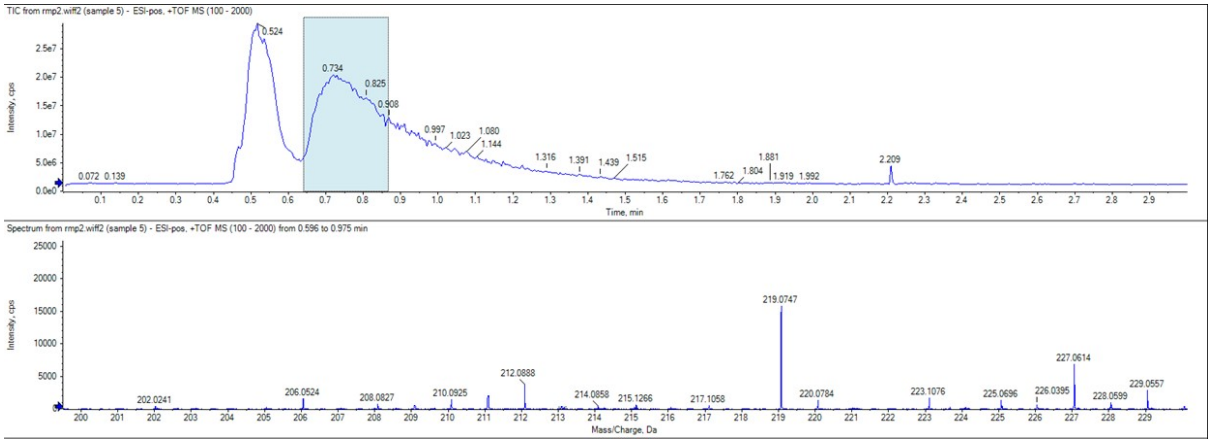


Fig.S.1. HR-ESIMS spectrum of compound **1**

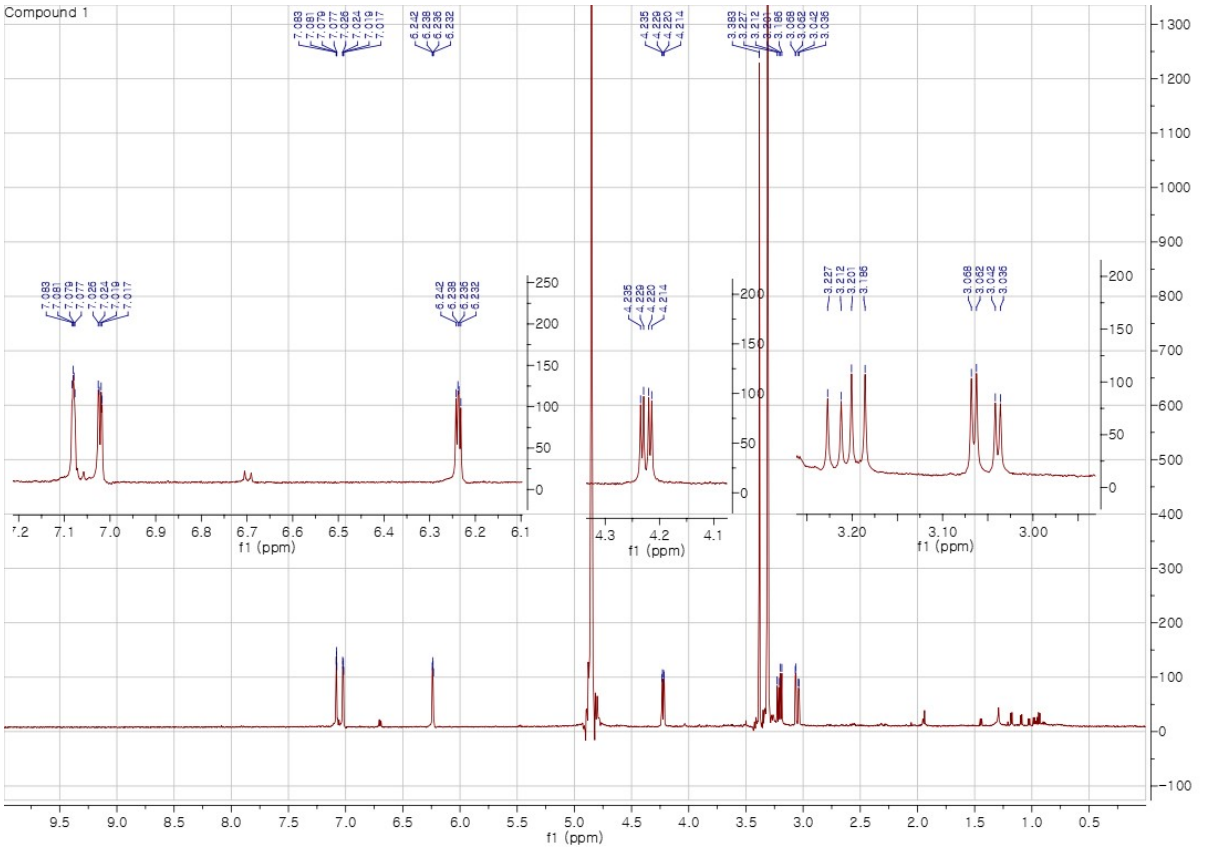


Fig.S.2. ^{1}H NMR spectrum of compound **1** in methanol-d_4 at 600 MHz

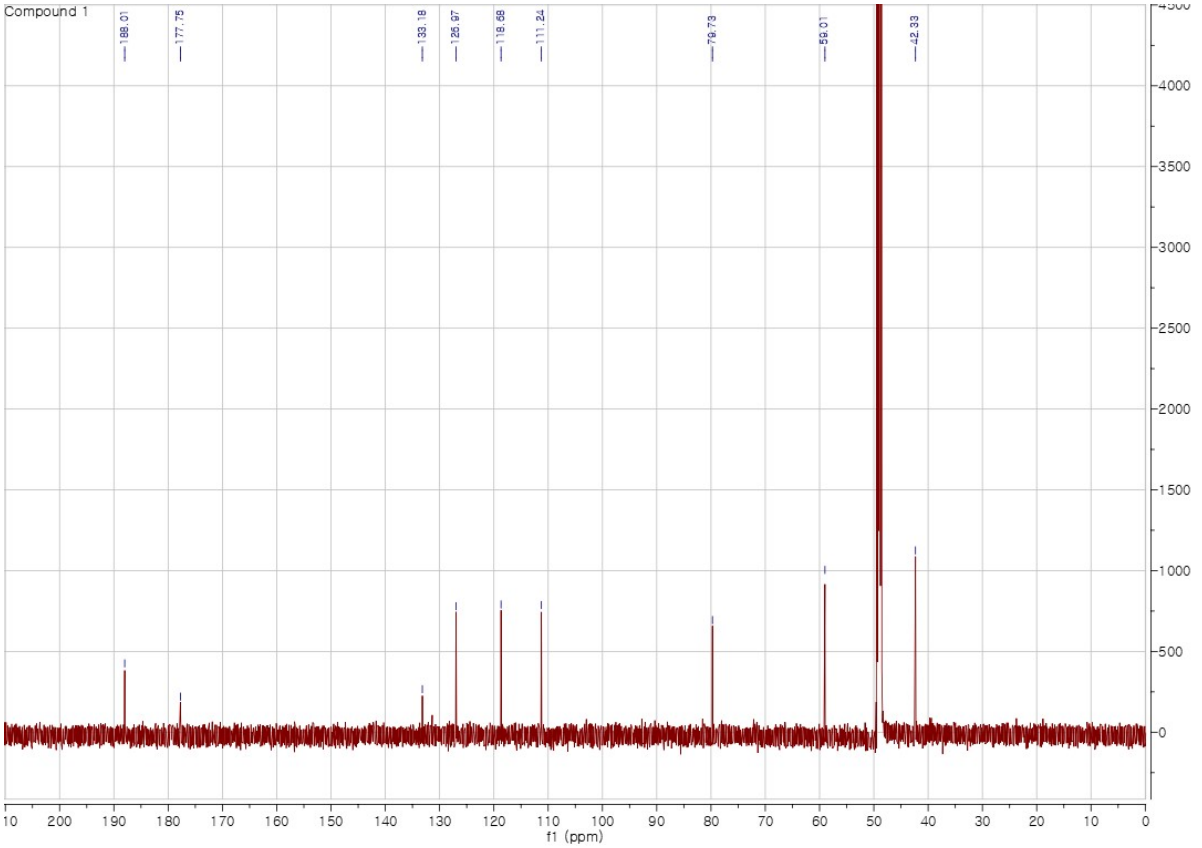


Fig.S.3. ^{13}C NMR spectrum of compound **1** in methanol-d_4 at 150 MHz

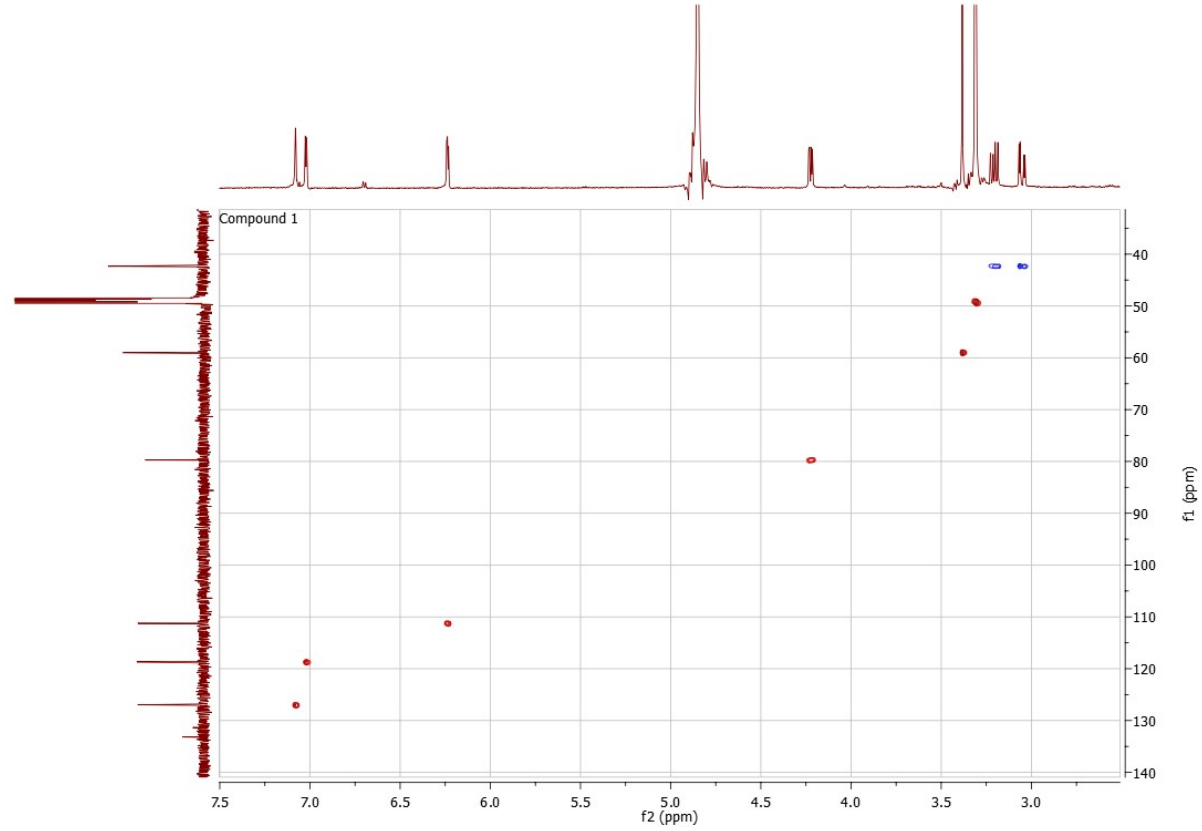


Fig.S.4. HSQC spectrum of compound **1** in methanol-d_4

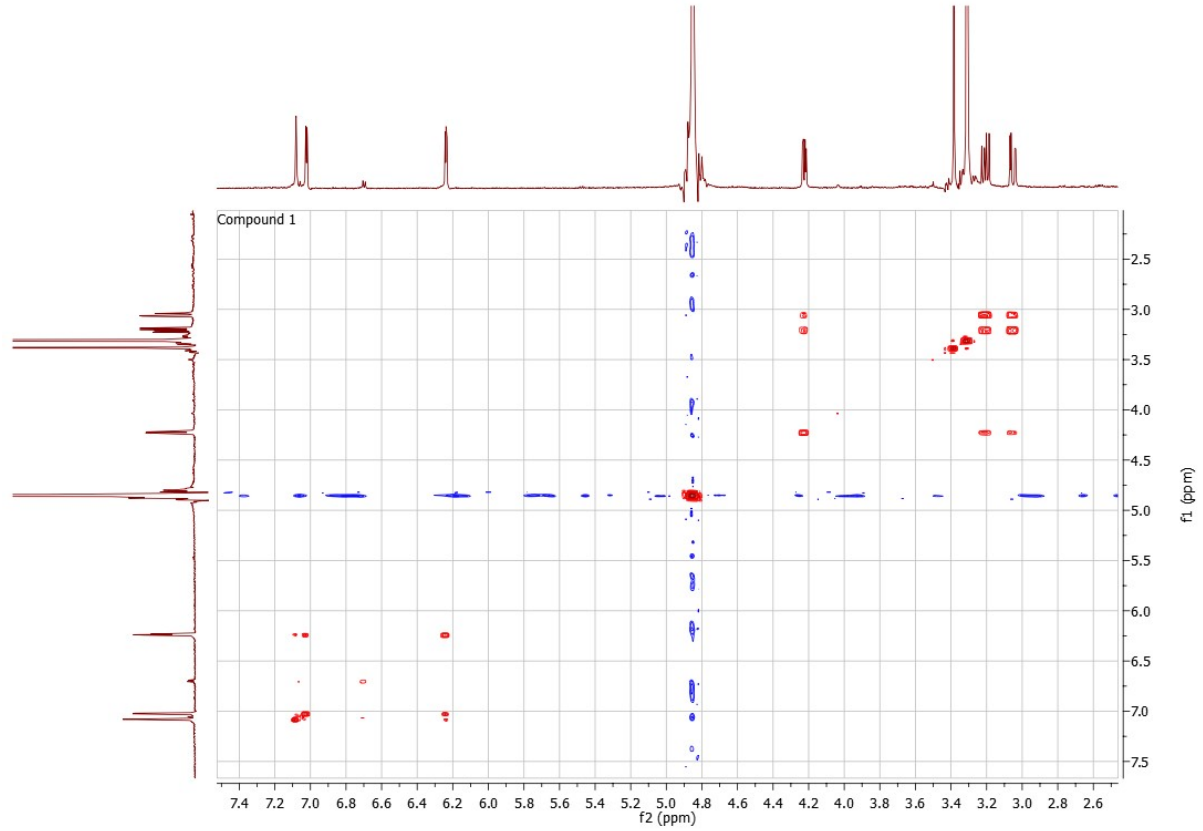


Fig.S.5. COSY spectrum of compound **1** in methanol-d_4

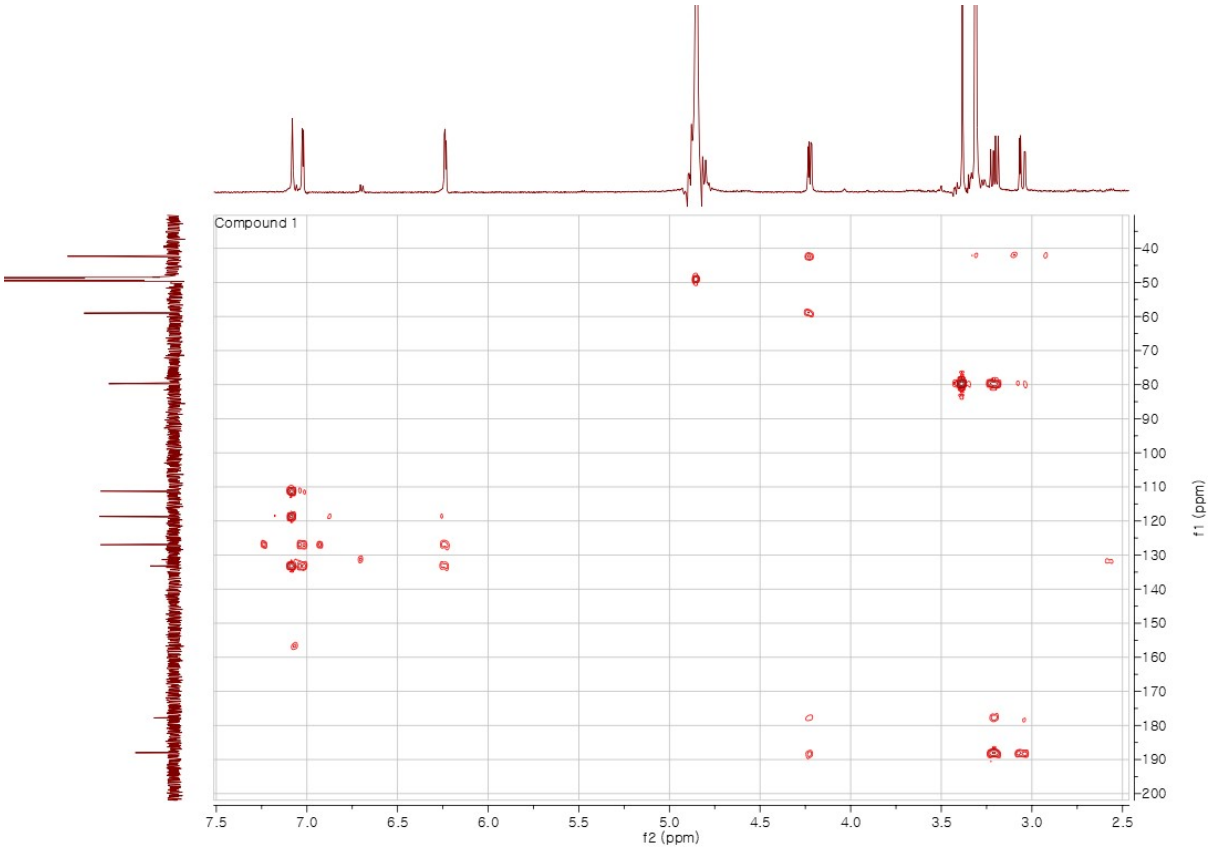


Fig.S.6. HMBC spectrum of compound **1** in methanol-d_4

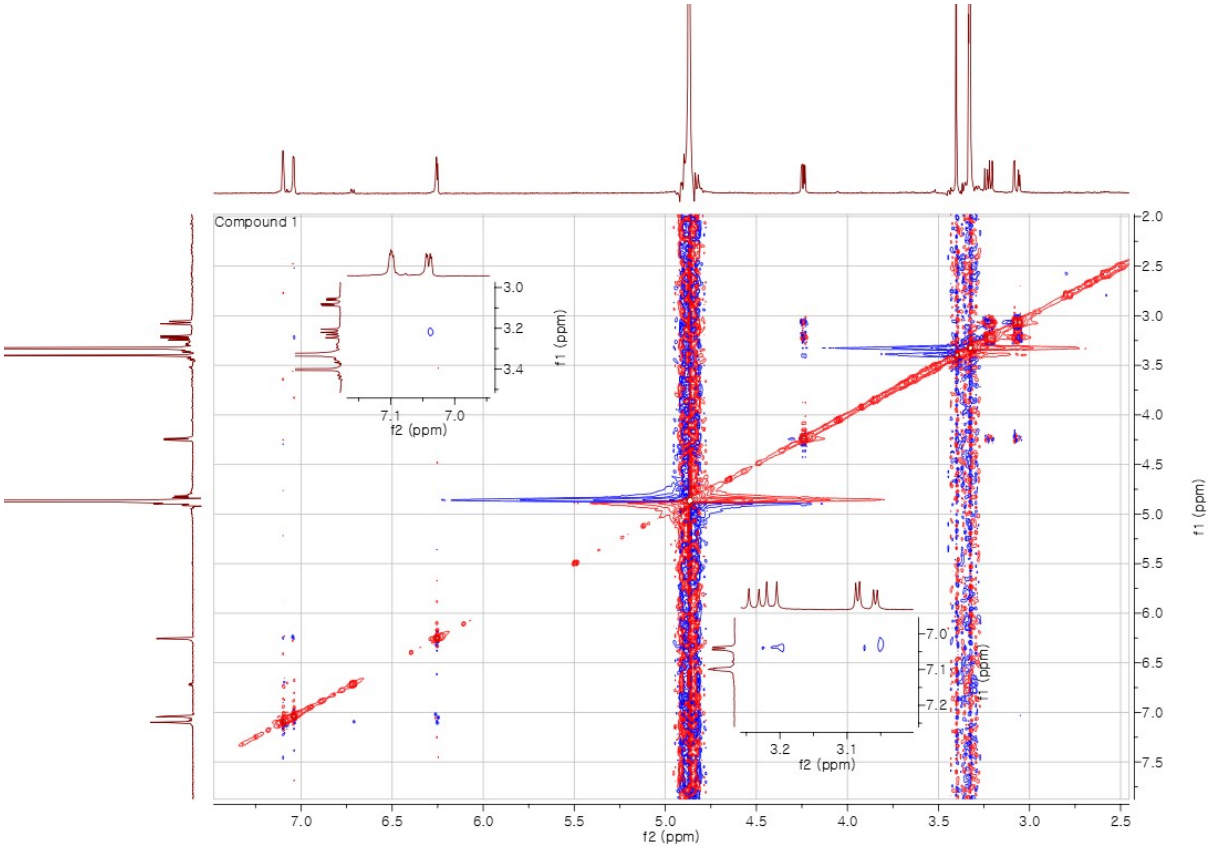
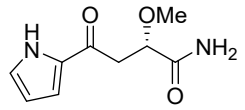
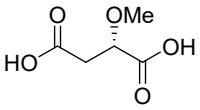


Fig.S.7. ROESY spectrum of compound **1** in methanol-d_4



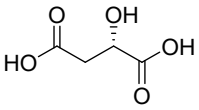
1 (*S*)

$[\alpha]^{26}_{D} = -16.6$ (*c* 5.0, acetone)



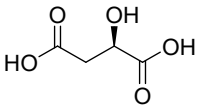
(*S*)-*α*-methoxysuccinic acid

$[\alpha]^{27}_{D} = -25.0$ (*c* 5.0, acetone)



(*S*)-malic acid

$[\alpha]_{D} = -25.8$ (*c* 5.5, pyridine)

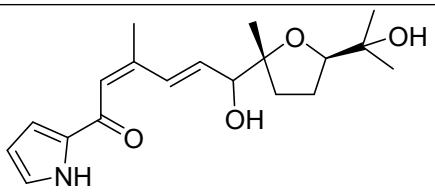
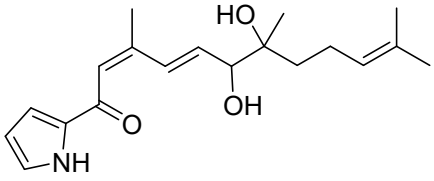
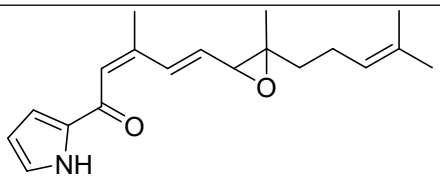
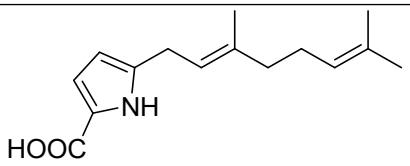
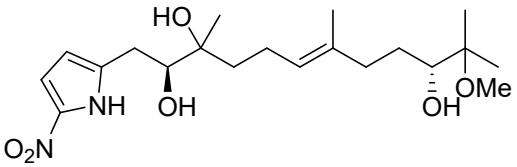
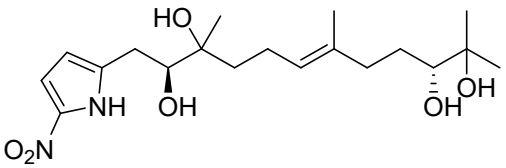
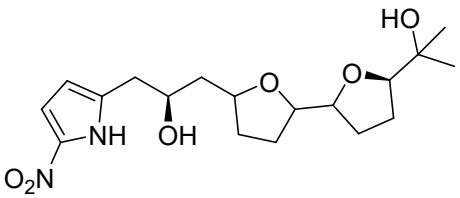
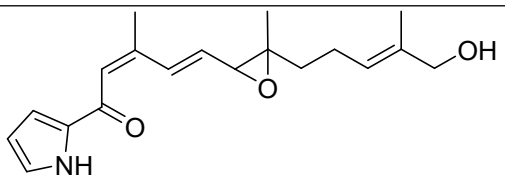


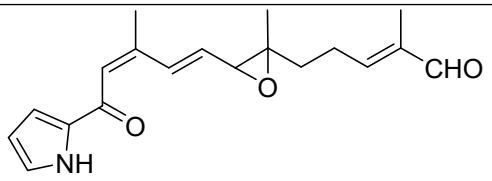
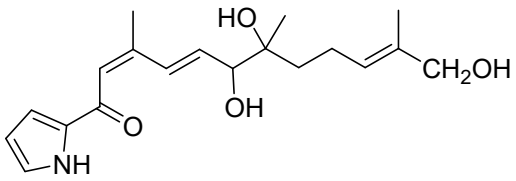
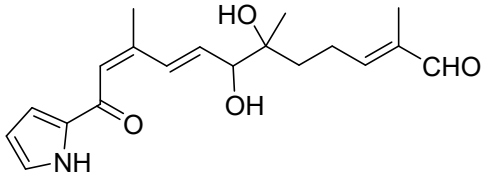
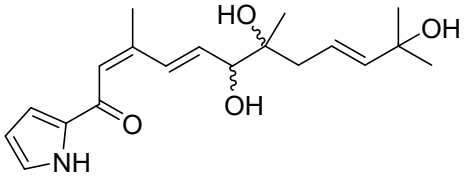
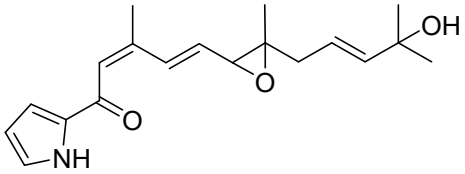
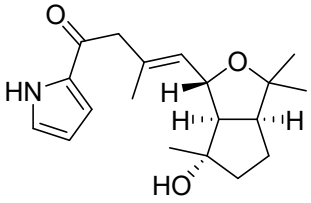
(*R*)-malic acid

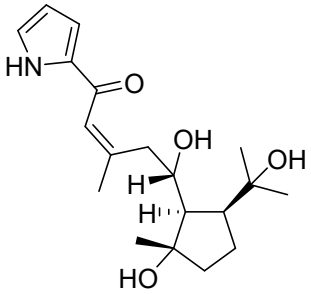
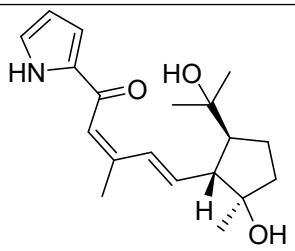
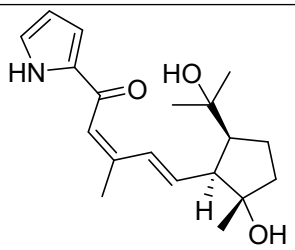
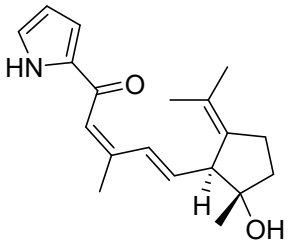
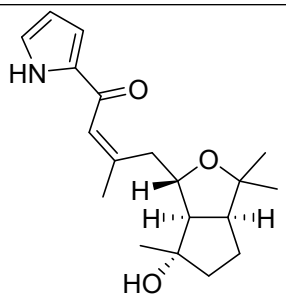
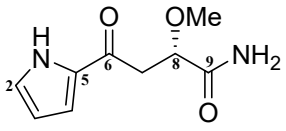
$[\alpha]_{D} = +25.5$ (*c* 5.5, pyridine)

Fig.S.8. Comparison of specific optical rotation of **1** and reported values

Table S1. Systematic comparison of isolated pyrrole terpenoids from natural source

No.	Name	Structure	Source	Reference [4-10]
1	glaciapyrrole A		*Streptomyces* sp. (NPS008187)	Journal of natural products 68.5 (2005): 780-783.
2	glaciapyrrole B			
3	glaciapyrrole C			
4	pyrrolostatin			
5	heronapyrrole A		*Streptomyces* sp. (CMB-M0423)	Organic letters 12.22 (2010): 5158-5161.
6	heronapyrrole B			
7	heronapyrrole C			
8	-		*Streptomyces* sp.	Magnetic Resonance in Chemistry 52.1-2 (2014): 57-59.

9	-			
10	-		*Streptomyces* sp.	Natural Product Communications 9.4 (2014): 1934578X1400900402
11	-		*Streptomyces* sp. Hd7–21	The Journal of Antibiotics 67.5 (2014): 415-417
12	(2*Z*,4*E*,9*E*)-6,7,11-trihydroxy-3,7,11-trimethyl-1-(1*H*-pyrrol-2-yl)dodeca-2,4,9-trien-1-one		*Streptomyces* sp. Hd7–21	Chemistry & Biodiversity 12.1 (2015): 153-156
13	(2*Z*,4*E*)-5-{3-[(2*E*)-4-hydroxy-4-methylpent-2-en-1-yl]-3-methyloxiran-2-yl}-3-methyl-1-(1*H*-pyrrol-2-yl)penta-2,4-dien-1-one			
14	strepyrrolin A		*Streptomyces* sp. KIB 015	Organic Chemistry Frontiers 10.4 (2023): 880-889.

15	strepyrrolin B			
16	strepyrrolin C			
17	strepyrrolin D			
18	strepyrrolin E			
19	-			
20	Compound 1		***Plant:*** *Nelumbo nucifera* Gaertn.	-

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10. L. Wang, Z. Zhou, J.-P. Huang, L. Zhang, X. Tuo, Z. Yu, S.-X. Huang, Y. Liu, J. Yang, *Org. Chem. Front.s*, 2023, **10**, 880-889.