SUPPLEMENTARY MATERIAL

A new phenolic derivative with soluble epoxide hydrolase and nuclear factor-kappaB inhibitory activity from the aqueous extract of *Acacia catechu*

Ya Nan Sun^a, Wei Li^b, Seok Bean Song^c, Xi Tao Yan^d, Yan Zhao^a, A Reum Jo^a, Jong Seong Kang^a and Young Ho Kim^{a, *}

^aCollege of Pharmacy, Chungnam National University, Daejeon 305-764, Korea

^bSchool of Biotechnology, Yeungnam University, Gyeongsan, Gyeongbuk 712-749, Korea

^cGyeongbuk Institute for Bio-industry (GIB), Andong City, Gyeongbuk 760-380, Korea

^dShaanxi Key Laboratory of Natural Products & Chemical Biology, College of Science, Northwest A & F University, Yangling 712100, Shaanxi, China

Abstract

One novel phenolic compound, (4*S*,5*R*)-4-(3,4-dihydroxyphenyl)-5-(3-oxobutyl)dihydrofuran-2(3*H*)-one (**1**), as well as 12 known compounds (**2–13**) were obtained from the aqueous extract of *Acacia catechu* and their chemical structures were determined by spectroscopic analysis. Compounds **8** and **9** exhibited significant soluble epoxide hydrolase (sEH) inhibitory activities with IC₅₀ values of 26.6 ± 0.5 and 24.4 ± 5.6 μM, respectively. Compounds **7–10** showed significant inhibitory effects on TNFα-induced nuclear factor kappa B (NF-κB) transcriptional activity in a dose-dependent manner, with IC₅₀ values ranging from 11.15 to 19.45 μM.

Key words: *Acacia catechu*, Leguminosae, soluble epoxide hydrolase (sEH), NF-kappa B

Contents

Figure S1. HRESIMS Mass Spectrum of Compound **1**.

Figure S2. ^1H -NMR Spectrum of Compound **1** (pyridine- d_5 , 600 MHz).

Figure S3. ^{13}C -NMR Spectrum of Compound **1** (pyridine- d_5 , 150 MHz).

Figure S4. DEPT Spectrum of Compound **1** (pyridine- d_5).

Figure S5. COSY Spectrum of Compound **1** (pyridine- d_5).

Figure S6. HMQC Spectrum of Compound **1** (pyridine- d_5).

Figure S7. HMBC Spectrum of Compound **1** (pyridine- d_5).

Figure S8. ^1H - ^1H COSY and HMBC correlations of compound **1**.

Figure S9. The isolation scheme of compounds **1-13**.

Table S1. The sEH inhibitory activities of extract of *A. catechu*.

Table S2. Inhibitory effects of *A. catechu* on the TNF- α induced NF- κ B transcriptional activity.

Table S3. Cell toxicity activities of compounds **1-13**.

Figure S1. HR-ESIMS Mass Spectrum of Compound **1**.

Figure S2. ¹H-NMR Spectrum of Compound **1** (pyridine-*d*₅, 600 MHz)

Figure S4. DEPT Spectrum of Compound 1 (pyridine- d_5).

Figure S5. COSY Spectrum of Compound **1** (pyridine- d_5).

Figure S6. HMQC Spectrum of Compound **1** (pyridine- d_5).

Figure S7. HMBC Spectrum of Compound **1** (pyridine- d_5).

Figure S8. ^1H - ^1H COSY and HMBC correlations of compound **1**.

The isolation scheme of compounds **1-13**

Figure S9. The isolation scheme of compounds **1-13**

Table S1. The sEH inhibitory activities of extract of *A. catechu*

Inhibition of extracts on sEH ^b					
	100 μ M (%)	IC ₅₀ (μ M)		100 μ M (%)	IC ₅₀ (μ M)
MeOH Ext.	23.41 $\pm$ 2.42	N.T	EtOAc Fr.	47.12 $\pm$ 0.51	N.T
BuOH Fr.	56.84 $\pm$ 0.32	N.T	H ₂ O Fr.	5.62 $\pm$ 3.21	N.T
AUDA ^a		10.9 $\pm$ 1.2 nM			

N. T not tested.

^a AUDA: 12-(3-adamantan-1-yl-ureido)-dodecanoic acid butyl ester, positive control.

^b Tested compounds were examined in a set of experiments repeated three times.

Table S2. Inhibitory effects of *A. catechu* on the TNF- α induced NF- κ B transcriptional activity.

	IC ₅₀ (μ M)		IC ₅₀ (μ M)
MeOH Ext.	56.41 $\pm$ 4.32	EtOAc Fr.	31.42 $\pm$ 1.21
BuOH Fr.	71.12 $\pm$ 2.32	H ₂ O Fr.	>100
Apigenin ^b	1.64 $\pm$ 0.19		

^a Values are mean $\pm$ SD (n = 3);

^b Apigenin was used as positive control.

Table S3. Cell toxicity activities of compounds **1-13** on HepG2 cells.

Cytotoxicity assay on 10 μ M (%)			
1	94.60	10	95.65
2	90.19	11	97.33
3	101.96	12	111.32
4	105.69	13	99.15
5	100.54	MeOH Ext.	113.52
6	93.65	EtOAc Fr.	93.45
7	90.19	BuOH Fr.	92.39
8	89.54	H ₂ O Fr.	91.81
9	92.6		