

Hemp (*Cannabis sativa* L.) seed phenylpropionamides composition and effects on memory dysfunction and biomarkers of neuroinflammation induced by lipopolysaccharide in mice

Yuefang Zhou[†], Shanshan Wang[†], Jianbo Ji[§], Hongxiang Lou[†], Peihong Fan^{†,*}

[†]Department of Natural Product Chemistry, Key Lab of Chemical Biology of Ministry of Education, School of

Pharmaceutical Sciences, Shandong University, Jinan 250012, China

[§]Department of Pharmacology, School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China

Corresponding author's e-mail address: fanpeihong@sdu.edu.cn (P.H. Fan)

1. Identification of standard compounds and TPA

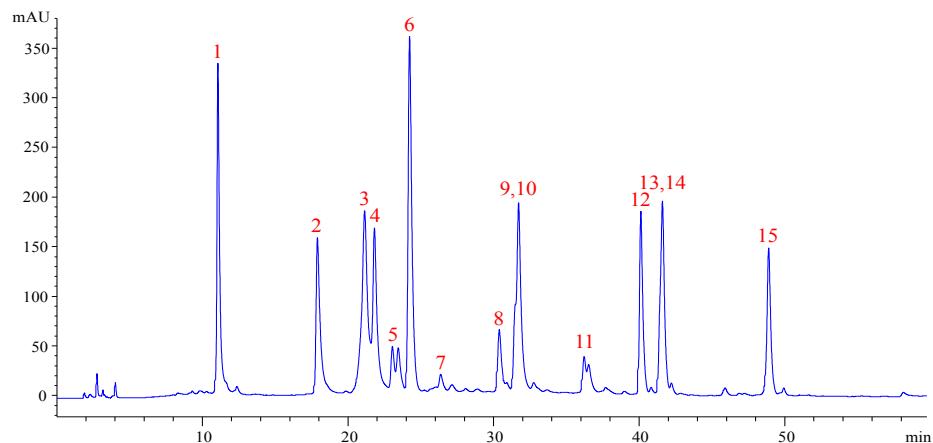


Figure S1. HPLC chromatogram of mixing standard compounds

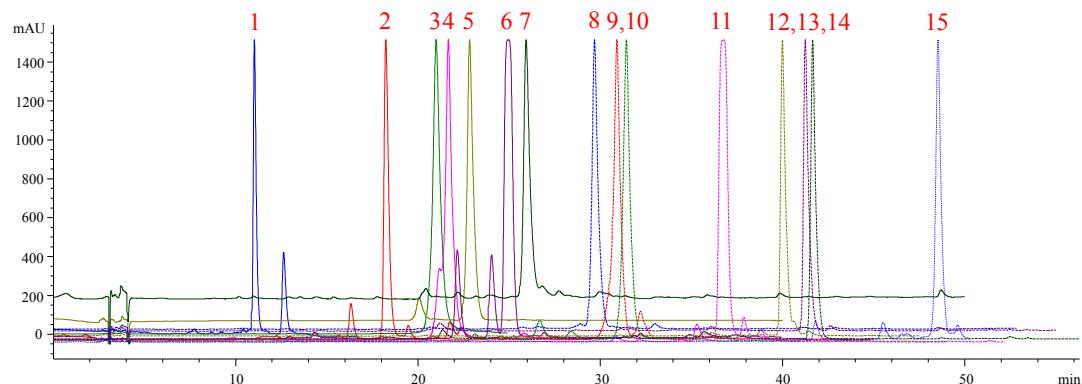


Figure S2. HPLC chromatogram of each standard compound

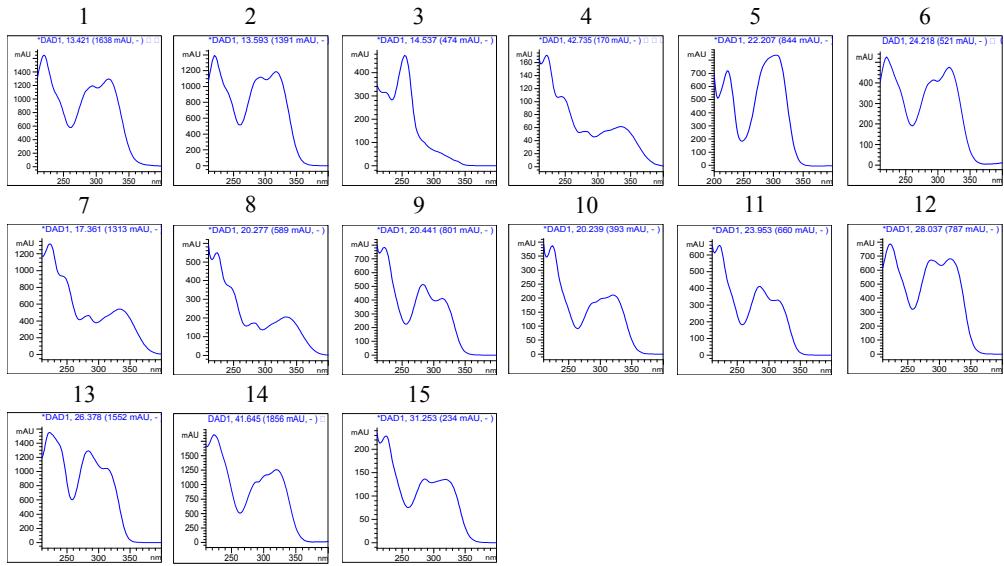
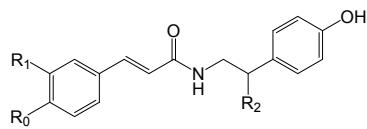


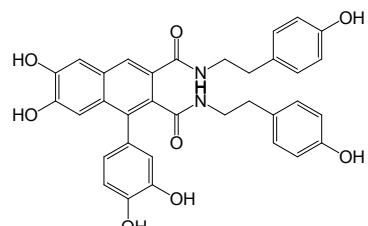
Figure S3. UV spectrum of each standard compound

Table S1 Compounds identified by HPLC, UV, and MS data of mixing standard compounds obtained from HPLC-DAD-MS

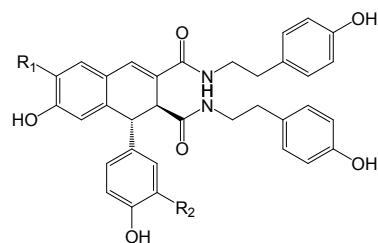
Peak NO.	Identity	HPLC RT (min)	Molecular weight	Molecular formula	UV λ_{\max} (nm)
1	N-trans-caffeoylectopamine	11.1	315	C ₁₇ H ₁₇ NO ₅	220,290,320
2	N-trans-caffeoyletyramine	17.9	299	C ₁₇ H ₁₇ NO ₄	220,290,320
3	Cannabisin A	21.1	594	C ₃₄ H ₃₀ N ₂ O ₈	255
4	Cannabisin B	21.8	596	C ₃₄ H ₃₂ N ₂ O ₈	220,245,280,340
5	N-trans-coumaroyltyramine	23.1	283	C ₁₇ H ₁₇ NO ₃	220,310
6	N-trans-feryroyltyramine	24.2	313	C ₁₈ H ₁₉ NO ₄	220,290,320
7	Cannabisin C	26.4	610	C ₃₅ H ₃₄ N ₂ O ₈	225,245,285,335
8	Cannabisin D	30.4	624	C ₃₆ H ₃₆ N ₂ O ₈	222,245,285,335
9	Cannabisin E	31.6	642	C ₃₆ H ₃₈ N ₂ O ₉	221,281,315
10	3,3'-demethyl-grossamide	31.7	596	C ₃₄ H ₃₂ N ₂ O ₈	225,285,300,320
11	Cannabisin M	36.2	596	C ₃₄ H ₃₂ N ₂ O ₈	220,285,315
12	(2,3-trans)-3-(3-hydroxy-5-me thoxyphenyl)-N-(4-hydroxyph enethyl)-7-{(E)-3-[{(4-hydroxy phenethyl)amino]-3-oxoprop- 1-enyl}-2,3-dihydro-benzo[b] [1,4]dioxine-2-carboxamide	40.1	610	C ₃₅ H ₃₄ N ₂ O ₈	225,281,311
13	Cannabisin F	41.5	624	C ₃₆ H ₃₆ N ₂ O ₈	221,285,320
14	Grossamide	41.6	624	C ₃₆ H ₃₆ N ₂ O ₈	221,285,300,320
15	Cannabisin O	48.9	935	C ₅₄ H ₅₃ N ₃ O ₁₂	222,285,320



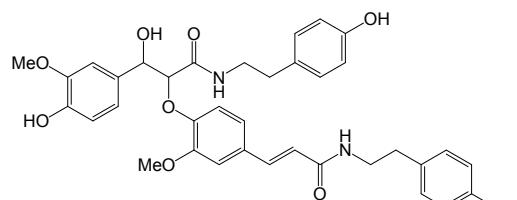
- 1** $R_0=OH$ $R_1=OH$ $R_2=OH$ ***N-trans-caffeoylectopamine***
2 $R_0=OH$ $R_1=OH$ $R_2=H$ ***N-trans-caffeoyletyramine***
5 $R_0=OH$ $R_1=H$ $R_2=H$ ***N-trans-coumaroyltyramine***
6 $R_0=OH$ $R_1=OMe$ $R_2=H$ ***N-trans-feryroyltyramine***



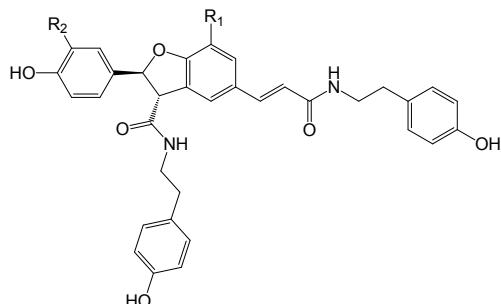
3 Cannabisin A



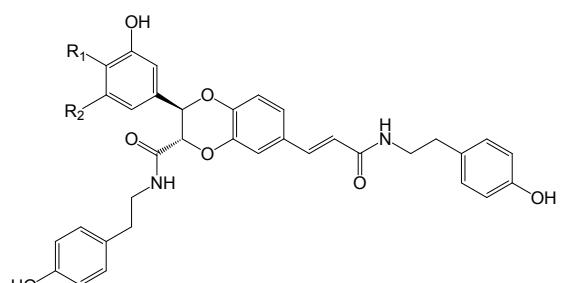
- 4** $R_1=OH$, $R_2=OH$ **Cannabisin B**
7 $R_1=OMe$, $R_2=OH$ **Cannabisin C**
8 $R_1=OMe$, $R_2=OMe$ **Cannabisin D**



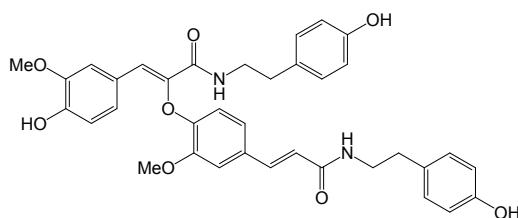
9 Cannabisin E



- 10** $R_1=OH$, $R_2=OH$ **3,3'-demethyl-grossamide**
14 $R_1=OMe$, $R_2=OMe$ **Grossamide**



- 11** $R_1=OH$, $R_2=H$ **Cannabisin M**
12 $R_1=H$, $R_2=OMe$ **Isocannabisin N**



13 Cannabisin F

Figure S4. Chemical Structures of the identified compounds in Table 1.

2. The quantification of TPA

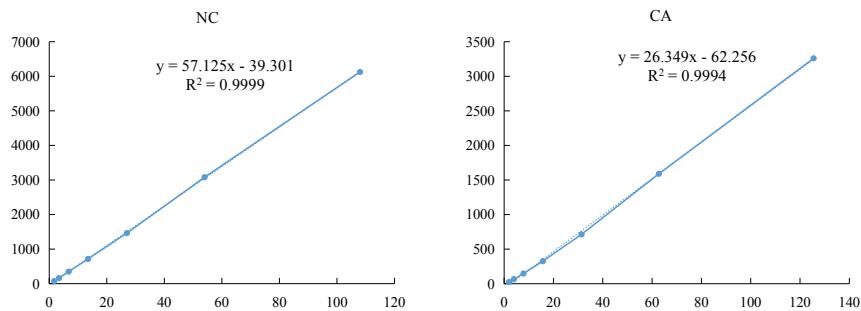


Figure S5. The standard curves of NC and CA.

Table S2 The concentration and peak area of NC and CA

NO.	NC(μg/mL)	Peak area of NC	CA(μg/mL)	Peak area of CA
1	108.00	6123.9	125.50	3259.6
2	54.00	3080.8	62.75	1589.8
3	27.00	1463.1	31.38	713.6
4	13.50	716.1	15.69	325.8
5	6.75	349.1	7.84	147.3
6	3.38	159.7	3.92	64.9
7	1.69	75.3	1.96	25.1

3. Time-line of drug treatment and experimental schedule

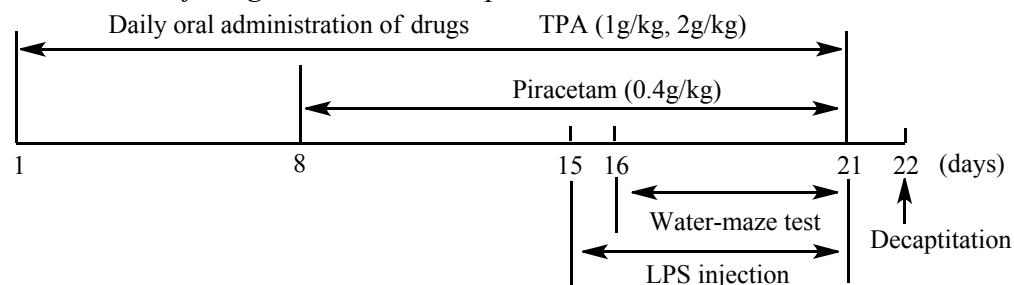


Figure S6. Time-line of drug treatment and experimental schedule