Supporting Information

Daphnane Diterpenes from *Daphne genkwa* Activate Nurr1 and Have a Neuroprotective Effect in an Animal Model of Parkinson's Disease

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Materials and Methods

Stepping test (Adjusting steps)

At 1 week before 6-OHDA lesion and 2, 4, 5 and 6 weeks after 6-OHDA lesion, the rats were tested for hindlimb akinesia in stepping test. The rat was held in the same position with one paw touching the table and was then moved slowly sideways (5 sec for 0.9 m) by the experimenter. The number of adjusting steps was counted for both hind paws in the forehand directions of movement. The test was repeated fourth each day.[1]

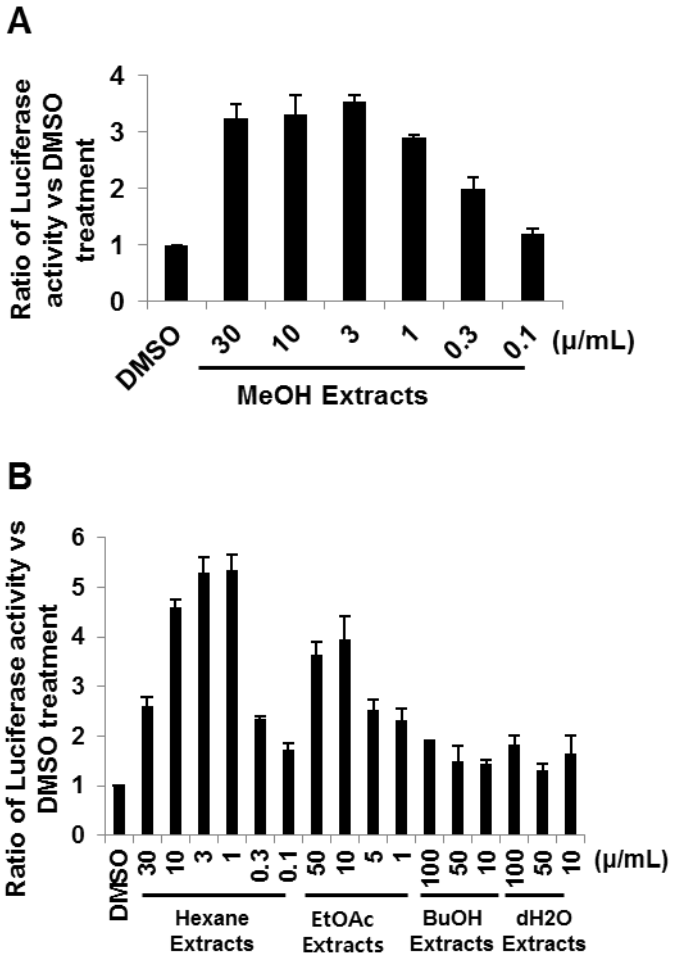

Figure S1. Activation of Nurr1 with extracts from *D. genkwa*. (A) Luciferase assay to measure Nurr1 activity with MeOH extract from *D. genkwa*, (B) and with hexane, EtOAc, BuOH, and dH2O extracts. Human neuroblastoma SK-N-BE(2)C cells were transfected with pTH2600LUC, pCMV Nurr1-myc, pZeoSV-Nurr1(LBD) and p8xGAL-Luc for the luciferase assay.

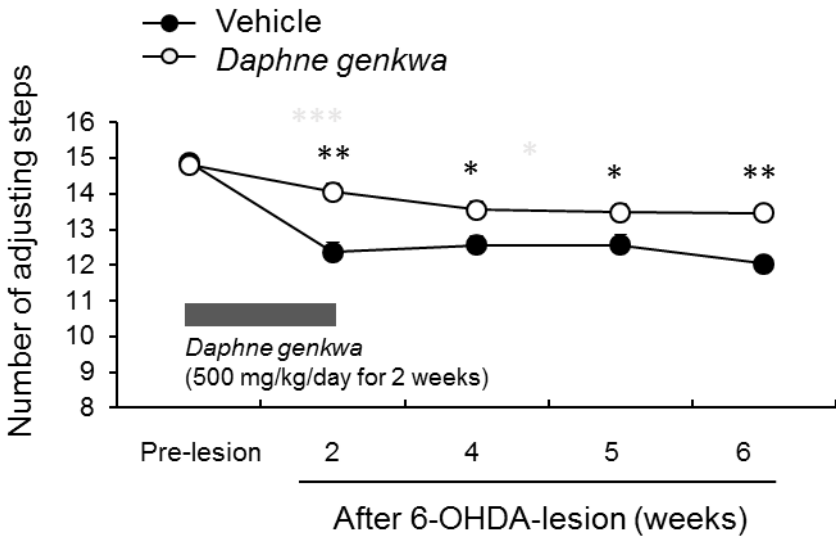

Figure S2. Protective effects of the methanol extract of *Daphne genkwa* in vivo 6-OHDA model. Adjusting steps in the contralateral hindlimb in the rats. The performance of the right paw was severely impaired by the 6-OHDA lesion. Adjusting steps of the contralateral hindlimb was significantly improved by administration of *Daphne genkwa* (500 mg/kg/day for 2 weeks) in all time points (n = 9-11, Student's t-test, *$p < 0.05$ and **$p< 0.01$).

Table S1. NMR Spectroscopic data (300 MHz, CD_3OD) of **1**.

No.	δ_C, type	δ_H (J in Hz)
1	37.2 CH_2	1.89, 2.28 m
2	35.2 CH	2.27, m
3	83.1 CH	5.20, d (3.9)
4	83.0 C	-
5	73.8 CH	4.00, s
6	63.1 C	-
7	65.1 CH	3.41, s
8	37.9 CH	3.09, d (3.0)
9	82.1 C	-
10	49.4 CH	2.95, m
11	36.6 CH	2.60, m
12	37.3 CH_2	1.70, d (14.1), 2.28, d (14.1)
13	86.1 C	-
14	84.0 CH	4.56, d (2.7)
15	148.5 C	-
16	111.4 CH_2	5.05, br s, 4.89, t (1.5)
17	19.5 CH_3	1.81, s
18	21.6 CH_3	1.35, d (6.9)
19	14.0 CH_3	1.08, d (5.7)
20	66.2 CH_2	3.99, d (12.3), 3.61, d (12.0)
1′	118.7 C	-
2′	138.2 C	-
3′, 7′	127.4 CH	7.70, m
4′, 6′	128.9 CH	7.37, m
5′	130.3 CH	7.36, m
1″	168.5 C	-
2″	131.8 C	-
3″, 7″	130.7 CH	8.06, d (7.5)
4″, 6″	129.8 CH	7.51, t (7.5)
5″	134.5 CH	7.62, d (7.5)

The assignments were aided by ^1H, ^{13}C, NOESY, HMQC, and HMBC.

Table S2. NMR Spectroscopic data (300 MHz, CD_3OD) of **2**.

No.	δ_C, type		δ_H (J in Hz)
1	160.2	CH	7.58, brs
2	138.3	C	-
3	209.9	C	-
4	74.6	C	-
5	71.6	CH	4.10, s
6	63.4	C	-
7	64.9	CH	3.61, s
8	37.1	CH	3.66, s
9	80.0	C	-
10	48.9	CH	3.89, m
11	45.3	CH	2.61, d (7.2)
12	80.4	CH	5.17, s
13	85.4	C	-
14	81.8	CH	5.05, d (2.4)
15	145.2	C	-
16	114.0	CH_2	4.99, s, 5.07, s
17	19.1	CH_3	1.86, s
18	18.9	CH_3	1.35, d (7.5)
19	10.1	CH_3	1.75, m
20	65.3	CH_2	4.03, d (12.3) , 3.65, d (12.0)
1′	118.4	C	-
2′	124.4	CH	5.64, d (15.6)
3′	136.0	CH	6.66, dd (15.3, 10.8)
4′	130.2	CH	6.11, dd (15.3, 11.1)
5′	140.0	CH	5.89, m
6′	33.8	CH_2	2.14, d (7.2)
7′	30.0	CH_2	1.44, m
8′	32.7	CH_2	1.33, m
9′	23.7	CH_2	1.31, m
10′	14.5	CH_3	0.91, t (6.9)
1′′	167.1	C	-
2′′	131.3	C	-
3′′, 7′′	130.8	CH_2	7.95, d (7.2)
4′′, 6′′	129.9	CH_2	7.47, t (7.2)
5′′	134.6	CH_2	7.60, t (7.2)

The assignments were aided by ^1H, ^{13}C, NOESY, HMQC, and HMBC

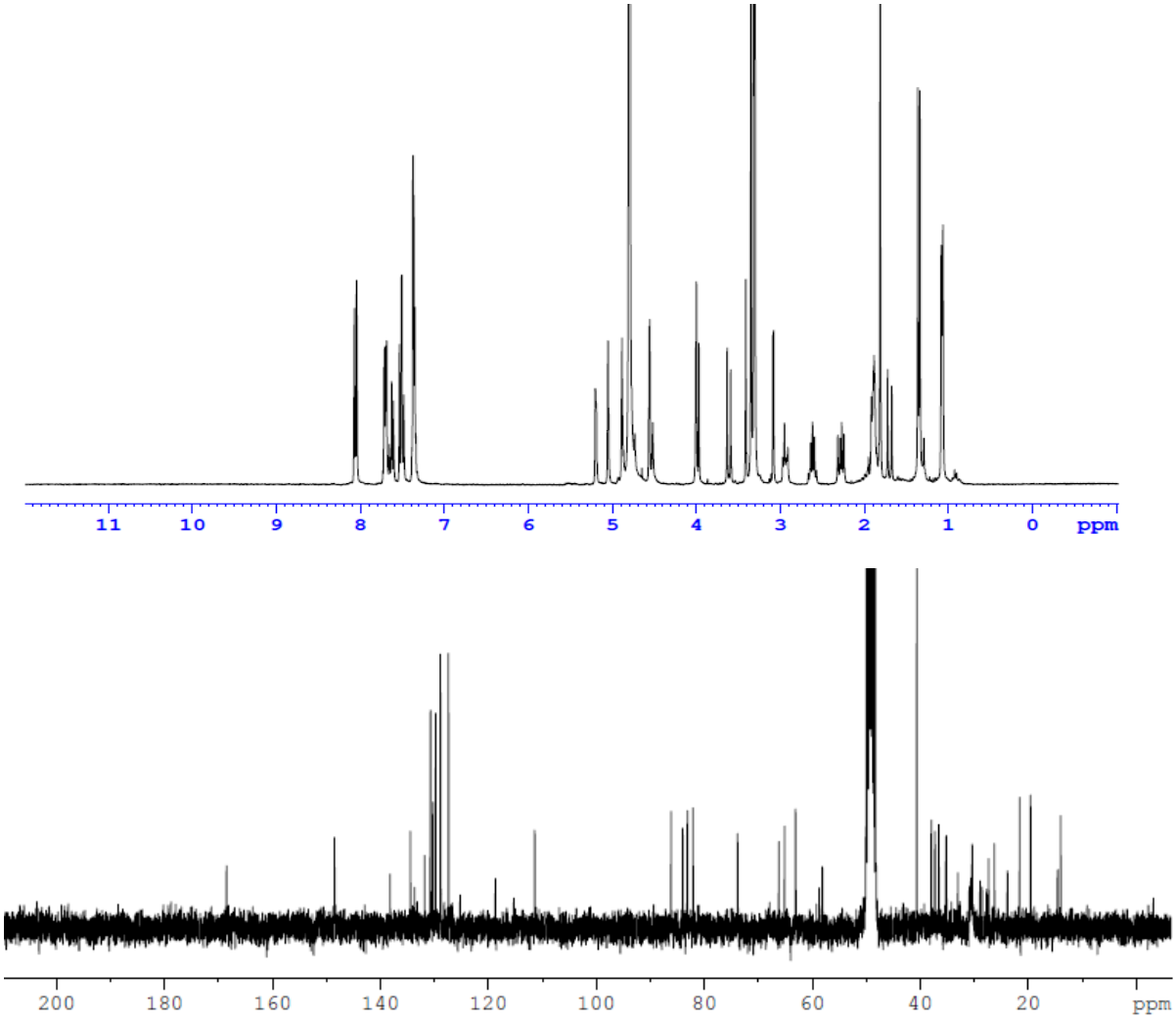

Figure S3. ^{1}H and ^{13}C NMR spectra of **1** in CD_3OD measured at 300 and 75 MHz, respectively.

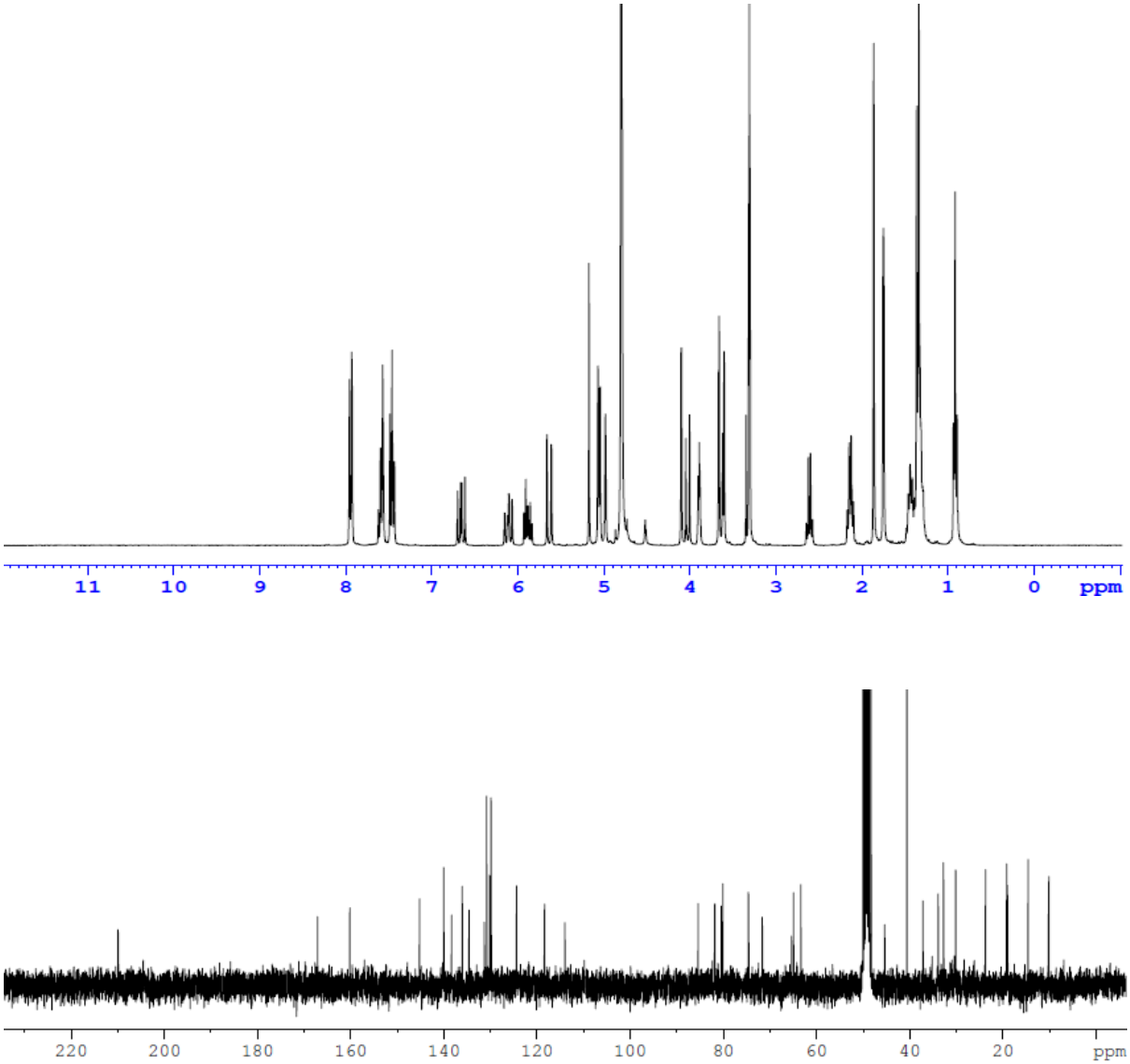

Figure S4. ^{1}H and ^{13}C NMR spectra of **2** in CD_3OD measured at 300 and 75 MHz, respectively.

Reference

(1) Olsson, M.; Nikkhah, G.; Bentlage, C.; Bjorklund, A. *J. Neurosci.* **1995**, *15*, 3863-3875.