Hepatoprotective phenylethanoid glycosides from *Cirsium setosum*

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**Abstract:** Two new phenylethanoid glycosides, namely \(\beta\)-D-glucopyranoside, \(1''\)-O-(7S)-7-(3-methoxyl-4-hydroxyphenyl)-7-methoxyethyl-3''\)-\(\alpha\)-L-rhamnopyranosyl-4''\)-[(8E)-7-(3-methoxyl-4-hydroxyphenyl)-8-propenoate] (1) and \(\beta\)-D-glucopyranoside, \(1''\)-O-(7S)-7-(3-methoxyl-4-hydroxyphenyl)-7-methoxyethyl-3''\)-\(\alpha\)-L-rhamnopyranosyl-4''\)-[(8E)-7-(4-hydroxyphenyl)-8-propenoate] (2), together with six phenylethanoid glycosides were isolated from *Cirsium setosum*. Their structures were elucidated by their spectroscopic data and references. Compounds 2, 4, 5, 7, and 8 (10μM) exhibited moderate hepatoprotective activities. Compounds (3-8) were obtained from this plant for the first time.

**Keywords:** *Cirsium setosum*; phenylethanoid glycoside; hepatoprotective activity
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Figure S1. Structures of compounds 1-8
Figure S2. Key HMBC (H→C), NOESY, and $^1$H-$^1$H COSY correlations of compounds 1 and 2
Table S1. $^1$H NMR (400 MHz, CD$_3$OD), $^{13}$C NMR (100 MHz, CD$_3$OD) and key HMBC correlations of compounds 1 and 2

| No. | $^1$H NMR | $^{13}$C NMR | HMBC($^1$H-$^{13}$C) | $^1$H NMR | $^{13}$C NMR | HMBC($^1$H-$^{13}$C) |
|-----|-----------|-------------|-------------------|-----------|-------------|-------------------|
| 1   | -         | 130.9       | -                | -         | 130.7       | -                |
| 2   | 6.79(1H,d,1.5) | 113.6       | -                | 6.81(1H,d,1.5) | 113.5       | -                |
| 3   | -         | 148.7       | -                | -         | 149.0       | -                |
| 4   | -         | 147.1       | -                | -         | 146.9       | -                |
| 5   | 6.68(1H,d,8.0) | 116.7       | -                | 6.67(1H,d,8.0) | 116.5       | -                |
| 6   | 6.63(1H,dd,8.0,1.5) | 122.2       | C-4              | 6.64(1H,dd,8.0,1.5) | 122.3       | C-4              |
| 7   | 4.46(1H,d,7.5) | 83.4        | C-2,C-6          | 4.46(1H,d,7.5) | 83.6        | C-2,C-6          |
| 8   | 3.95(2H,m) | 72.9        | -                | 3.96(2H,m) | 73.1        | -                |
| 1'  | -         | 127.5       | -                | -         | 127.9       | -                |
| 2'  | 7.16(1H,d,1.5) | 111.6       | -                | 7.40(2H,d,8.0) | 132.0       | C-4'             |
| 3'  | -         | 149.3       | -                | 6.78(2H,d,8.0) | 117.8       | -                |
| 4'  | -         | 151.9       | -                | -         | 160.5       | -                |
| 5'  | 6.80(1H,d,8.0) | 117.0       | -                | 6.78(2H,d,8.0) | 117.8       | -                |
| 6'  | 7.02(1H,dd,8.0,1.5) | 123.9       | C-4'             | 7.40(2H,d,8.0) | 132.0       | C-4'             |
| 7'  | 7.64(1H,d,15.8) | 146.2       | C-6', C-9'       | 7.63(1H,d,15.8) | 147.1       | C-6', C-9'       |
| 8'  | 6.39(1H,d,15.8) | 116.0       | -                | 6.40(1H,d,15.8) | 115.8       | -                |
| 9'  | -         | 169.1       | -                | -         | 169.2       | -                |
| 1'' | 4.56(1H,d,7.8) | 103.8       | C-8              | 4.53(1H,d,7.8) | 103.9       | C-8              |
| 2'' | 3.37(1H,m) | 75.2        | -                | 3.35(1H,m) | 75.6        | -                |
| 3'' | 3.60(1H,m) | 83.3        | -                | 3.58(1H,m) | 83.6        | -                |
| 4'' | 3.53(1H,m) | 71.0        | C-9'             | 3.53(1H,m) | 71.1        | C-9'             |
| 5'' | 3.56(1H,m) | 75.4        | -                | 3.57(1H,m) | 75.6        | -                |
| 6a''| 3.93(1H,dd,11.5,2.4) | 62.6       | C-5''            | 3.94(1H,dd,11.5,2.4) | 62.5       | C-5''            |
| 6b''| 3.68(1H,dd,11.5,5.6) | 62.6       | C-5''            | 3.68(1H,dd,11.5,5.6) | 62.5       | C-5''            |
| 1'''| 5.01(1H,d,1.5) | 101.8       | C-3''            | 5.03(1H,d,1.5) | 101.5       | C-3''            |
| 2'''| 3.68(1H,m) | 72.3        | -                | 3.67(1H,m) | 72.3        | -                |
| 3'''| 3.70(1H,m) | 72.4        | -                | 3.71(1H,m) | 72.5        | -                |
| 4'''| 3.39(1H,t,9.0) | 74.0        | -                | 3.40(1H,t,9.0) | 73.9        | -                |
| 5'''| 3.96(1H,m) | 70.1        | -                | 3.95(1H,m) | 70.3        | -                |
| 6'''| 1.24(3H,d,6.2) | 18.1        | -                | 1.24(3H,d,6.2) | 18.2        | -                |
| 3-OCH$_3$ | 3.86(3H,s) | 56.8        | -                | 3.85(3H,s) | 56.6        | -                |
| 3'-OCH$_3$ | 3.86(3H,s) | 56.8        | -                | -        | -            | -                |
| 7-OCH$_3$ | 3.23(3H,s) | 56.5        | -                | 3.24(3H,s) | 56.6        | -                |
Table S2. Hepatoprotective effects of selective compounds (10μM)

| Compound | Cell survival rate (% of normal) | Inhibition (% of control) |
|----------|----------------------------------|---------------------------|
| normal   | 100.0 ± 4.5                      | -                         |
| control  | 51.1 ± 5.9                       | -                         |
| bicyclol | 62.9 ± 7.2^a                      | 24.1                      |
| 2        | 67.7 ± 6.0^a                      | 33.9                      |
| 4        | 70.6 ± 3.6^a                      | 39.9                      |
| 5        | 61.0 ± 5.7^a                      | 20.2                      |
| 7        | 79.8 ± 7.1^a                      | 58.7                      |
| 8        | 75.2 ± 5.2^a                      | 49.3                      |

Results were expressed as means ± SD (n=3; for normal and control, n = 6); bicyclol was used as positive control (10μM). ^p< 0.05.