SUPPLEMENTARY MATERIAL

Three new phenylacetamide glycosides from *Dracocephalum tanguticum* Maxim
and their anti-hyperglycemic activity

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ABSTRACT

Three new phenylacetamide glycosides (1–3) together with one known phenylacetamide glycoside (4) and two known flavonoid glycosides (5–6) were isolated from whole plants of *Dracocephalum tanguticum*. The structure of all compounds were elucidated based on spectroscopic data analysis and comparison with data reported in related literature. Compounds (1–3) were evaluated for their anti-hyperglycemic and anti-fungal (*Candida albicans*) activities, the results revealed that all of them showed moderate activity with 3T3-L1 adipocytes glucose consumption rate of 20.80±1.47%, 21.48±2.44%, and 21.57±1.35%, respectively at the final concentration of 25 μM. However, none of them showed obvious *Candida albicans* inhibitory activity.

Keywords; *Dracocephalum tanguticum*, phenylacetamide glycosides, anti-hyperglycemic activity
| position | \( \delta_C \) (mult.) | \( \delta_H \) (mult, \( J \), Hz) | \( \delta_C \) (mult.) | \( \delta_H \) (mult, \( J \), Hz) | \( \delta_C \) (mult.) | \( \delta_H \) (mult, \( J \), Hz) |
|----------|----------------|----------------|----------------|----------------|----------------|----------------|
| 1        | 134.3 s        | 134.5 s        | 134.4 s        | 134.4 s        | 134.4 s        | 134.4 s        |
| 2,6      | 130.8 d        | 7.16 (d) 8.3   | 130.8 d        | 7.19 (d) 8.7   | 130.8 d        | 7.05 (d) 8.6   |
| 3,5      | 117.5 d        | 6.85 (d) 8.4   | 117.7 d        | 7.03 (d) 8.7   | 117.6 d        | 6.97 (d) 8.7   |
| 4        | 155.9 s        | 156.2 s        | 156.2 s        | 156.2 s        | 156.2 s        | 156.2 s        |
| 7        | 35.7 t         | 2.88, overlap  | 35.7 t         | 2.82 (t) 7.3   | 35.7 t         | 2.65 (t) 7.2   |
| 8        | 42.8 t         | 3.59 (t) 7.4   | 42.3 t         | 3.51 (t) 7.3   | 42.1 t         | 3.30, overlap  |
| 1'       | 135.8 s        | 136.3 s        | 132.8 s        | 132.8 s        | 132.8 s        | 132.8 s        |
| 2',6'    | 128.2 d        | 7.77 (d) 7.5   | 128.8 d        | 7.53 (d) 8.5   | 130.4 d        | 7.01 (d) 8.6   |
| 3',5'    | 129.6 d        | 7.43 (d) 7.4   | 129.9 d        | 7.36 (d) 8.5   | 116.2 d        | 6.70 (d) 8.4   |
| 4'       | 132.6 d        | 7.50 (d) 7.1   | 130.9 d        | 7.36 m         | 156.8 s        | 2.88, overlap  |
| 7'       | 170.3 s        | 141.7 d        | 7.50 (d) 15.8  | 32.2 t         | 2.78 (t) 7.5   |
| 8'       | 121.8 d        | 6.56 (d) 15.8  | 39.3 t         | 2.38 (t) 7.6   | 175.4 s        | 2.38 (t) 7.6   |
| 9'       | 168.6 s        | 175.4 s        | 175.4 s        | 175.4 s        | 175.4 s        | 175.4 s        |
| 1''      | 98.3 d         | 5.60 (d) 1.7   | 99.7 d         | 5.43 (d) 1.7   | 99.6 s         | 5.40 (d) 1.5   |
| 2''      | 82.8 d         | 4.00, overlap  | 79.7 d         | 4.13 (dd) 9.8, 3.3 | 82.7 d | 3.94 (dd) 9.1, 3.2 |
| 3''      | 80.3 d         | 4.41, overlap  | 71.8 d         | 4.31 (dd) 3.2, 1.9 | 71.4 d | 4.29 (dd) 3.0, 1.9 |
| 4''      | 72.2 d         | 3.32, overlap  | 73.7 d         | 5.14 (t) 9.9   | 72.7 d         | 3.62, overlap  |
| 5''      | 70.1 d         | 3.64, overlap  | 68.5 d         | 3.85, overlap  | 70.2 d         | 3.68, overlap  |
| 6''      | 18.1 q         | 1.19 (d) 4.8   | 17.9 q         | 1.10 (d) 6.3   | 18.1 q         | 1.23 (d) 6.0   |
| 1'''     | 105.7 d        | 4.52 (d) 7.6   | 106.2 d        | 4.47 (d) 7.8   | 105.8 d        | 4.60 (d) 7.6   |
| 2'''     | 75.33 d        | 3.21, overlap  | 74.8 d         | 3.22, overlap  | 75.4 d         | 3.32, overlap  |
| 3'''     | 77.9 d         | 3.27, overlap  | 77.9 d         | 3.34, overlap  | 77.6 d         | 3.40, overlap  |
| 4'''     | 70.7 d         | 3.34, overlap  | 71.1 d         | 3.35, overlap  | 71.0 d         | 3.38, overlap  |
| 5'''     | 77.5 d         | 2.89, overlap  | 77.7 d         | 3.30, overlap  | 77.7 d         | 3.33, overlap  |
| 6''''a   | 61.8 t         | 3.49, overlap  | 62.3 t         | 3.83, overlap  | 62.2 t         | 3.85 (dd) 9.3, 2.4 |
| 6''''b   | 3.38, overlap  | 3.73 (dd) 11.9, 4.6 | 3.73 (dd) 10.6, 3.1 |
| 1''''    | 106.4 d        | 4.64 (d) 7.7   | 21.2 q         | 2.09 (s)       | 3.73 (dd) 10.6, 3.1 |
| 2''''    | 75.3 d         | 3.36, overlap  | 172.6 s        |                |                |                |
| 3''''    | 77.6 d         | 3.46, overlap  |                |                |                |                |
| 4''''    | 72.3 d         | 3.63, overlap  |                |                |                |                |
| 5''''    | 75.6 d         | 3.76, overlap  |                |                |                |                |
| 6''''''a | 66.1 t         | 4.70 (d) 11.2  |                |                |                |                |
| 6''''''b | 4.40, overlap  |                |                |                |                |                |
| 1''''''  | 130.9 s        |                |                |                |                |                |
| 2''''''  | 130.5 d        | 7.96 (d) 7.7   |                |                |                |                |
| 3''''''  | 129.7 d        | 7.08 (t) 7.7   |                |                |                |                |
| 5''''''  | 134.3 d        | 7.24 (t) 7.4   |                |                |                |                |

Table S1. \(^{1}H\) and \(^{13}C\) NMR data of 1–3 in Methanol-\(d_4\) (400 and 100 MHz, \(J\) in Hz)
Table S2. Compounds (1–3) glucose consumption rate

| Sample | Final concentration (µM) | Glucose consumption rate (%) |
|--------|--------------------------|------------------------------|
| insulin| 0.1                      | 27.45±1.63                   |
| 1      | 25                       | 20.80±1.47                   |
| 2      | 25                       | 21.48±2.44                   |
| 3      | 25                       | 21.57±1.35                   |

Insulin was used as positive control.

Figure 1. The structures of compounds 1–6.
Supplemental file (Figure) Legend

Figure S1. $^1$H NMR spectrum of compound 1 recorded in CD$_3$OD at 400 MHz

Figure S2. $^{13}$C NMR spectrum of compound 1 recorded in CD$_3$OD at 100 MHz

Figure S3. Lift: $^{13}$C NMR spectrum of compound 1 benzene ring enlarge
Right: $^{13}$C NMR spectrum of compound 1 glycoside enlarge

Figure S4. HSQC spectrum of compound 1 recorded in CD$_3$OD at 500 MHz

Figure S5. HMBC spectrum of compound 1 recorded in CD$_3$OD at 500 MHz

Figure S6. COSY spectrum of compound 1 recorded in CD$_3$OD at 500 MHz

Figure S7. UV spectrum of compound 1 recorded in MeOH

Figure S8. IR spectrum of compound 1

Figure S9. HR-ESI-MS spectrum of compound 1

Figure S10. HPLC analysis of monosaccharide derivative of compound 1

Figure S11. Key HMBC correlations of compound 1.

Figure S12. $^1$H NMR spectrum of compound 2 recorded in CD$_3$OD at 400 MHz

Figure S13. $^{13}$C NMR spectrum of compound 2 recorded in CD$_3$OD at 100 MHz

Figure S14. HSQC spectrum of compound 2 recorded in CD$_3$OD at 500 MHz

Figure S15. HMBC spectrum of compound 2 recorded in CD$_3$OD at 500 MHz

Figure S16. HR- ESI-MS spectrum of compound 2

Figure S17. Key HMBC correlations of compound 2.

Figure S18. $^1$H NMR spectrum of compound 3 recorded in CD$_3$OD at 400 MHz

Figure S19. $^{13}$C NMR spectrum of compound 3 recorded in CD$_3$OD at 100 MHz

Figure S20. HR-ESI-MS spectrum of compound 3
Figure S1. $^1$H NMR spectrum of compound 1 recorded in CD$_3$OD at 400 MHz.

Figure S2. $^{13}$C NMR spectrum of compound 1 recorded in CD$_3$OD at 100 MHz.
Figure S3. Lift: $^{13}$C NMR spectrum of compound 1 benzene ring enlarge.

Right: $^{13}$C NMR spectrum of compound 1 glycoside enlarge.

Figure S4. HSQC spectrum of compound 1 recorded in CD$_3$OD at 500 MHz.
Figure S5. HMBC spectrum of compound 1 recorded in CD$_3$OD at 500 MHz.

Figure S6. COSY spectrum of compound 1 recorded in CD$_3$OD at 500 MHz.
**Figure S7.** UV spectrum of compound 1 recorded in MeOH.

**Figure S8.** IR spectrum of compound 1.
Figure S9. HR-ESI-MS spectrum of compound 1.

Figure S10. HPLC analysis of monosaccharide derivative of compound 1.
Figure S11. Key HMBC (→) correlations compound 1.
Figure S12. $^1$H NMR spectrum of compound 2 recorded in CD$_3$OD at 400 MHz.

Figure S13. $^{13}$C NMR spectrum of compound 2 recorded in CD$_3$OD at 100 MHz.
Figure S14. HSQC spectrum of compound 2 recorded in CD$_3$OD at 500 MHz.

Figure S15. HMBC spectrum of compound 2 recorded in CD$_3$OD at 500 MHz.
Figure S16. HR-ESI-MS spectrum of compound 2.

Figure S17. Key HMBC (→) correlations of compound 2.
Figure S18. $^1$H NMR spectrum of compound 3 recorded in CD$_3$OD at 400 MHz.
Figure S19. $^{13}$C NMR spectrum of compound 3 recorded in CD$_3$OD at 100 MHz.

Figure S20. HR-ESI-MS spectrum of compound 3.