Supplementary Materials

Anti-Diabetic Effect of a Shihunine-Rich Extract of *Dendrobium loddigesii* on 3T3-L1 Cells and db/db Mice by Up-Regulating AMPK/GLUT4 /PPAR α

Xue-Wen Li¹⁺, Meixiang Huang¹⁺, Kakei Lo¹, Wei-Li Chen¹, Ying-Yan He¹, Yongli Xu¹, Huizhen Zheng¹, Haiyan Hu^{1,*} and Jun Wang^{1,*}

- ¹ School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou, 510006, China
- * Correspondence: lsshhy@mail.sysu.edu.cn (H.H.); wjun@mail.sysu.edu.cn (J.W.); Tel.: +86-203-933-6119 (H.-Y.H); +86-203-994-3090 (J.W.)

⁺ Those authors contribute equally to this work.

Figure Legends:

Figure S1. Structure of shihunine

Figure S2. ¹H NMR for shihunine from *D. loddigesii*

Figure S3. ¹H NMR for qNMR of shihunine-rich extract of *D. loddigesii* (DLS)

Figure S4. 1H NMR of salicylic acid for the external standard

Figure S5. Effect of shihunine-rich extract of D. loddigesii on gastric mucosa morphological changes in C57 mice

Figure S6. Effect of shihunine-rich extract of *D. loddigesii* on gastric mucosa morphological changes in db/db mice

Figure S7. Effect of shihunine-rich extract of D. loddigesii on the cell viability of 3T3-L1 preadipocytes



Figure S1. Structure of shihunine



Figure S3. ¹H NMR for qNMR of shihunine-rich extract of *D. loddigesii* (DLS); SHN: shihunine; I.S: salicylic acid



Figure S4. ¹H NMR of salicylic acid for an external standard



Figure S5. Effect of shihunine-rich extract of *D. loddigesii* (DLS) on the gastric mucosa morphological changes in the C57 mice. The atrophy areas of gastric mucosa were indicated via red arrows

(a): Control group, no-treatment C57BL/6 mice, which gastric mucosa was in normal states.

(**b**): DLS200 group, DLS-treatment C57BL/6 mice at a dose of 200 mg/kg, which gastric mucosa was partial atrophy; its numbers of main and parietal cells were decreased by 21% to 40%.



Figure S6. Effect of shihunine-rich extract of *D. loddigesii* (DLS) on the gastric mucosa morphological changes in db/db mice. The atrophy areas of gastric mucosa were indicated via red arrows

(a): MD group, no-treatment db/db mice, which gastric mucosa was partial atrophy, and the numbers of main and parietal cell were decreased by 41% to 75%.

(**b**): MDMET130 group, metformin-treatment db/db mice at a dose of 130 mg/kg, which gastric mucosa was partial atrophy, and the numbers of main and parietal cells were decreased by 41% to 75%.

(c): MDDLS25 group, DLS-treatment db/db mice at a dose of 25 mg/kg, which gastric mucosa was partial atrophy, and the numbers of main and parietal cells were decreased by 21% to 40%.

(d): MDDLS50 group, DLS-treatment db/db mice at a dose of 50 mg/kg, which gastric mucosa was partial atrophy, and the numbers of main and parietal cells were decreased by 21% to 40%.

(e): MDDLS100 group, DLS-treatment db/db mice at a dose of 100 mg/kg, which gastric mucosa was partial atrophy, and the numbers of main and parietal cells were decreased by 21% to 40%.



Figure S7. Effect of shihunine-rich extract of D. loddigesii (DLS) on the cell viability of 3T3-L1 preadipocytes