

# Novel Withanolides from *Tubocapsicum anomalum* Suppress Triple-Negative Breast Cancer by Triggering Apoptosis and p53-ASCT2-SLC7A11-mediated ferroptosis

Lili Huang <sup>1</sup>, Yingying Wei <sup>1</sup>, Maowei Ni <sup>2</sup>, Hongtao Hu <sup>1</sup>, Luyi Xi <sup>1</sup>, Chen Wang <sup>1</sup>, Zhihui Zhu <sup>1</sup>, Bo Yang <sup>1,\*</sup> and Huajun Zhao <sup>1,3,\*</sup>

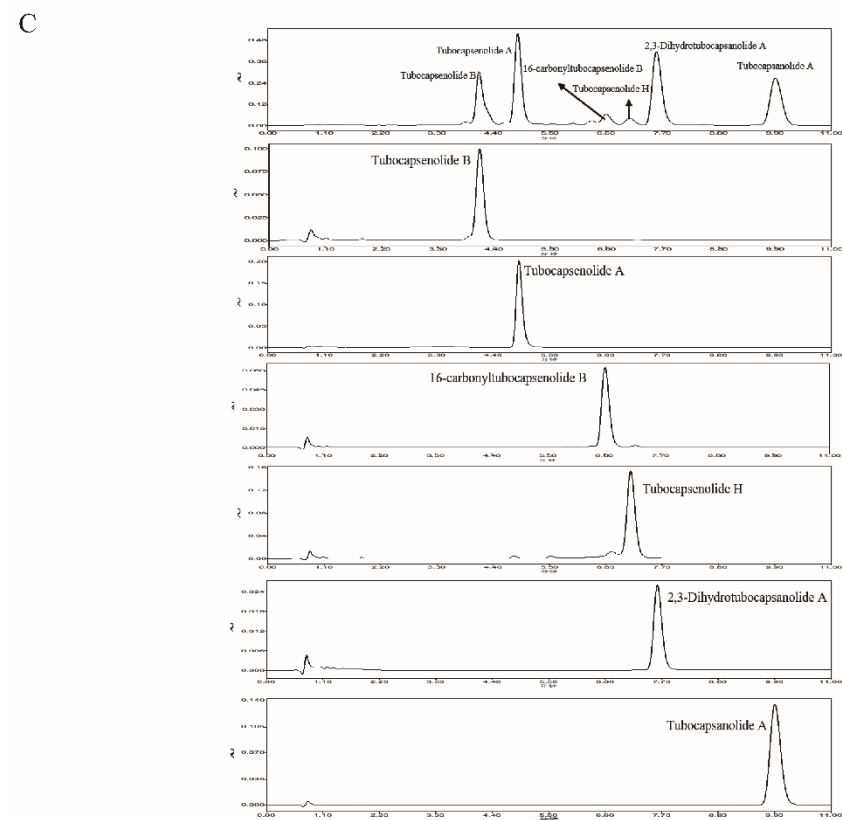
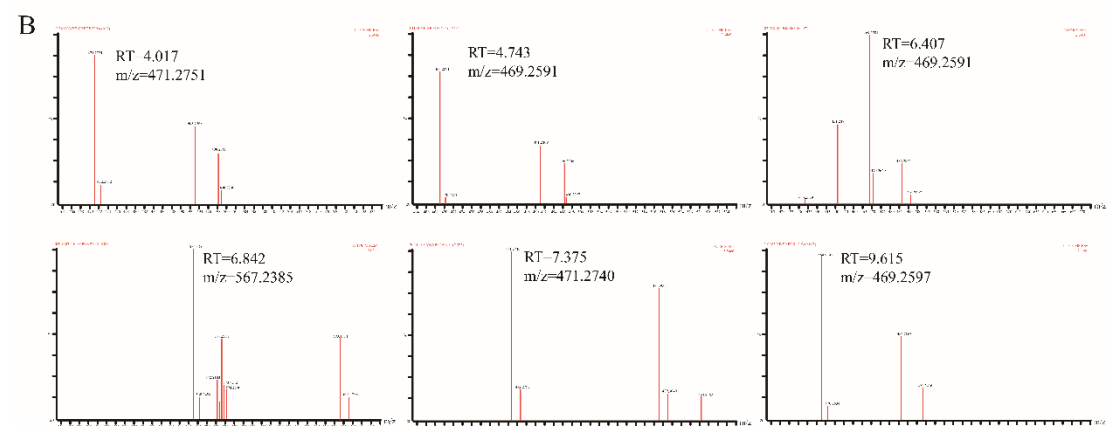
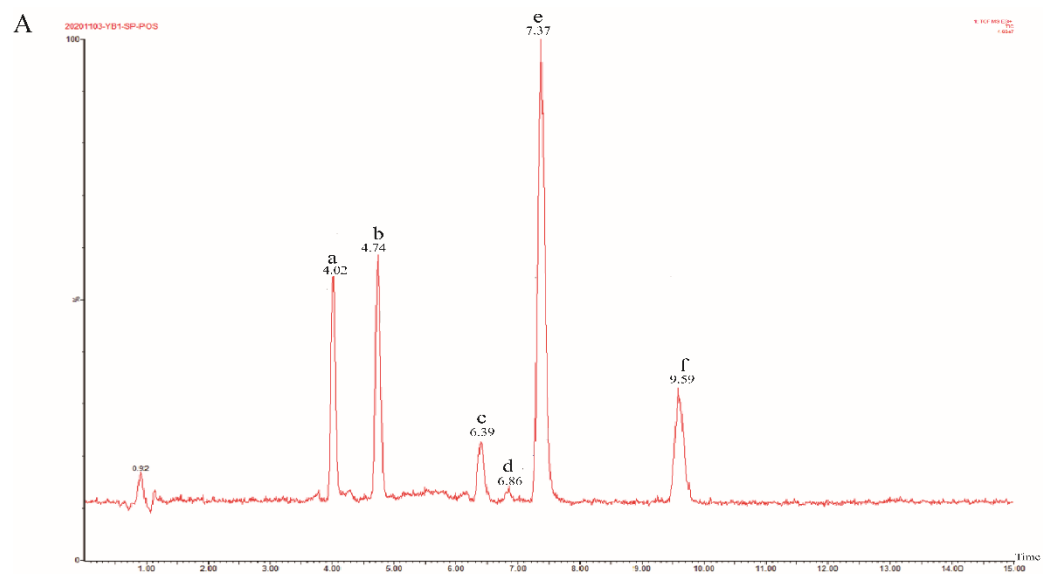
<sup>1</sup> School of Pharmaceutical Sciences, Zhejiang Chinese Medical University, Gaoke Rd., Hangzhou 311402, China

<sup>2</sup> The Cancer Hospital of the University of Chinese Academy of Sciences (Zhejiang Cancer Hospital), Institute of Basic Medicine and Cancer (IBMC), Chinese Academy of Sciences, Hangzhou 310022, China

<sup>3</sup> Academy of Chinese Medical Sciences, Zhejiang Chinese Medical University, Binwen Rd., Hangzhou 310053, China

\* Correspondence: [ybtcm@zcmu.edu.cn](mailto:ybtcm@zcmu.edu.cn) (B.Y.); [zhj@zcmu.edu.cn](mailto:zhj@zcmu.edu.cn) (H.Z.);  
Tel.: +86-0571-61768535 (B.Y.); +86-0571-61768535 (H.Z.)

**Suppl. Figure S1**



**Figure S1.** (related to figure 1) Structures and analysis of TAMEWs. (A) Total ions chromatogram of TAMEWs. IUPAC names are as follows: **a**: (2R,6S,7R,9R,14R,15S)-15-[(1S)-1-(4,5-dimethyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl]-6,14-dihydroxy-2,15-dimethyl-8-oxapentacyclo[9.7.0.0<sup>2,7</sup>.0<sup>7,9</sup>.0<sup>12,16</sup>]octadec-12(16)-en-3-one; **b**: (2R,6S,7R,9R,14R,15S)-15-[(1S)-1-(4,5-dimethyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl]-6,14-dihydroxy-2,15-dimethyl-8-oxapentacyclo[9.7.0.0<sup>2,7</sup>.0<sup>7,9</sup>.0<sup>12,16</sup>]octadeca-4,12(16)-dien-3-one; **c**: (1S,2R,6S,7R,9R,11R,14R,15S)-15-[(1S)-1-[(2R)-4,5-dimethyl-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl]-6,14-dihydroxy-2,15-dimethyl-8-oxapentacyclo[9.7.0.0<sup>2,7</sup>.0<sup>7,9</sup>.0<sup>12,16</sup>]octadec-12(16)-en-3-one; **d**: (1S,2R,6S,7R,9R,11S,12S,14R,16S,17S)-16-[(1R)-1-[(2R)-4,5-dimethyl-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl]-6-hydroxy-2,17-dimethyl-8,15-dioxahexacyclo[9.8.0.0<sup>2,7</sup>.0<sup>7,9</sup>.0<sup>12,17</sup>.0<sup>14,16</sup>]nonadecan-3-one; **e**: (1R,2S,6S,7R,10R,12S,17S,21R)-6-[(1S)-1-[(2R)-4,5-dimethyl-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl]-7,21-dihydroxy-1,6-dimethyl-16-oxa-13-thiapentacyclo[10.8.1.0<sup>2,10</sup>.0<sup>5,9</sup>.0<sup>17,21</sup>]henicosa-5(9),18-dien-20-one; **f**: (1S,2R,6S,7R,9R,11S,12S,14R,16S,17S)-16-[(1R)-1-[(2R)-4,5-dimethyl-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl]-6-hydroxy-2,17-dimethyl-8,15-dioxahexacyclo[9.8.0.0<sup>2,7</sup>.0<sup>7,9</sup>.0<sup>12,17</sup>.0<sup>14,16</sup>]nonadec-4-en-3-one. (B) The secondary mass spectrometry fragment data of the six withanolides. (C) UPLC analysis of TAMEWs with standards.