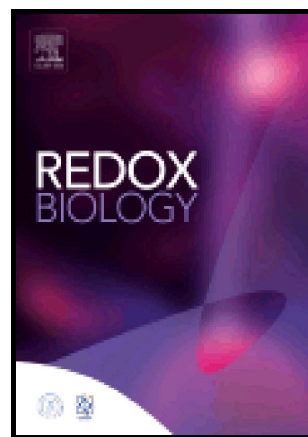


Author's Accepted Manuscript

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www.elsevier.com/locate/redox

PII: S2213-2317(17)30101-5
DOI: <http://dx.doi.org/10.1016/j.redox.2017.02.017>
Reference: REDOX586

To appear in: *Redox Biology*

Received date: 8 February 2017
Revised date: 22 February 2017
Accepted date: 23 February 2017

Cite this article as: Jian Xu, Yihua Wu, Guang Lu, Shujun Xie, Zhongjun Ma, Zhe Chen, Han-Ming Shen and Dajing Xia, Importance of ROS-mediated autophagy in determining apoptotic cell death induced by physapubescin B *Redox Biology*, <http://dx.doi.org/10.1016/j.redox.2017.02.017>

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Importance of ROS-mediated autophagy in determining apoptotic cell death induced by physapubescin B

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Abstract

Physapubescin B, a steroidal compound extracted from the plant *Physalis pubescens* L. (Solanaceae), has been reported to possess anti-cancer potential, whereas the molecular mechanism remains elusive. In this study, we first demonstrated that physapubescin B induced autophagy in human cancer cells based on the evidence that physapubescin B increased lipidation of microtubule-associated protein 1 light chain 3 (LC3) as well as number of GFP-LC3 puncta. We further examined the molecular mechanisms and found that physapubescin B enhanced the autophagic flux through promotion of reactive oxygen species (ROS)-mediated suppression of mammalian target of rapamycin complex I (mTORC1), the key negative regulator of autophagy. Additionally, excessive ROS caused by physapubescin B also induced p53-dependent apoptotic cell death. Furthermore, we provided evidence that inhibition of autophagy either by a chemical inhibitor or gene silencing promoted physapubescin B-induced apoptotic cell death, indicating that autophagy serves as a cell survival mechanism to protect cell death. Thus, our data provide a clue that inhibition of autophagy would serve as a novel

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