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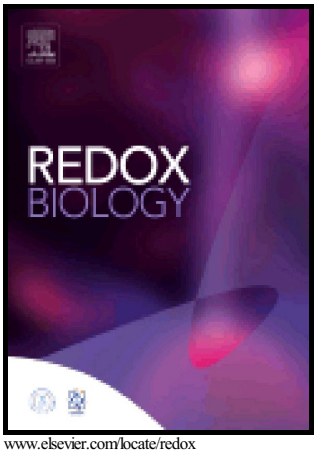

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Importance of ROS-mediated autophagy in determining apoptotic cell death induced by physapubescin B

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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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