Role of pyrethroid derivatives in autophagy and apoptosis crosstalk signaling and potential risk for malignancies

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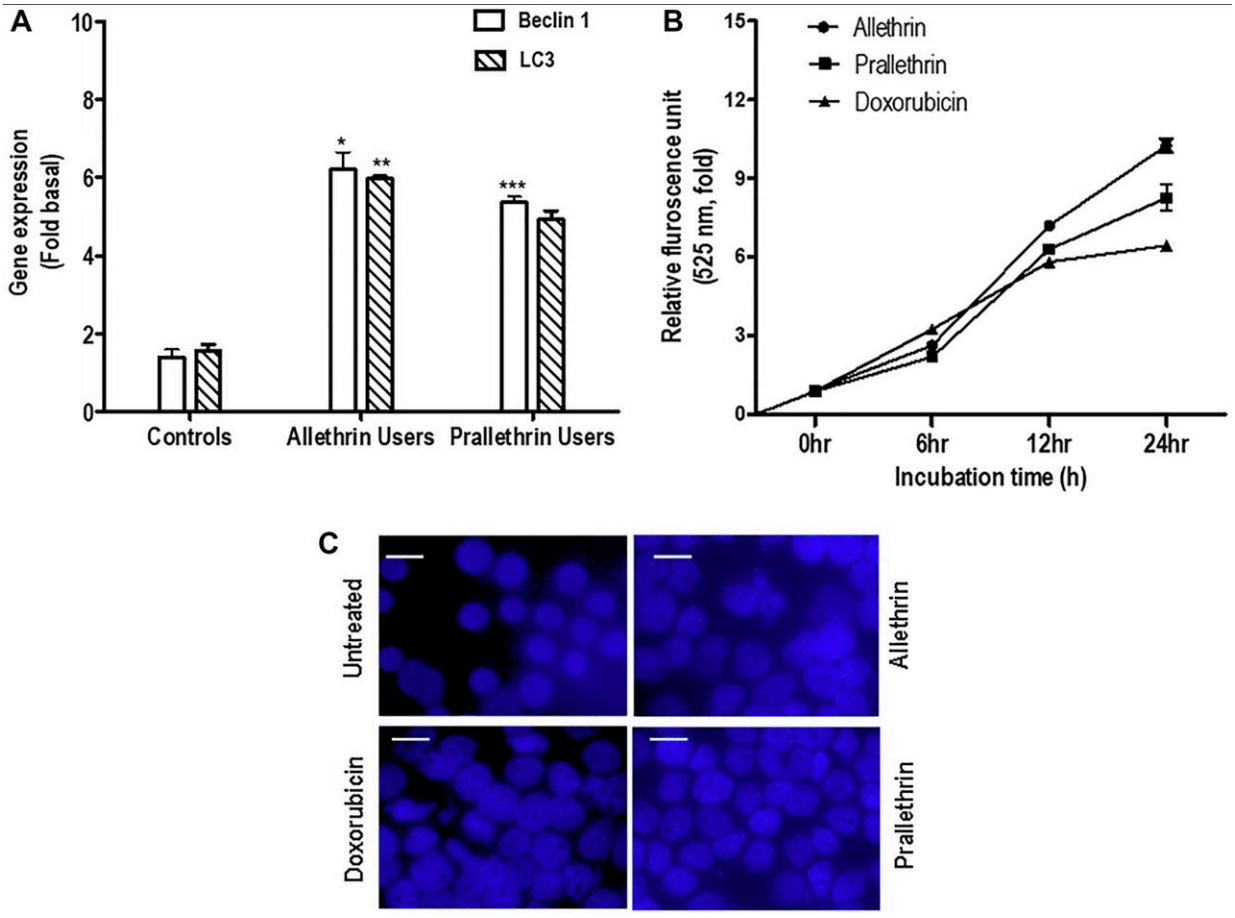

The effect of pyrethroid derivatives on induction of autophagy. Credit: 2022 Puvula et al.

Pyrethroids are extensively used insecticides by virtue of insecticidal activity potential in Asia, especially India, and in different nations worldwide to counter mosquitoes and insects for household or agricultural needs. The continuous widespread and uncontrolled use of pyrethroids and its derivatives have influenced multiple deleterious effects resulting in a potential risk factor causing damage to organ systems.

Allethrin and prallethrin are extensively used, yet their influences on human primary cells are very limited or under-reported. The potential mechanisms by which allethrin and prallethrin modulates human primary cells, especially the molecular mechanisms or interconnectivity of autophagy-apoptosis, and their clinical relevance in human subjects or patients are not well defined.

In a new research paper published in *Oncotarget* on December 17, 2022, researchers Jyothi Puvula, Narendra Maddu, Nagajothi Gutam, Asha Parimal, and Raghavendra B. Pongali from Sri Krishnadevaraya University, Queen Mary's College, Manipal University, and National Institute of Biomedical Genomics furnished the evidence that both allethrin and prallethrin user samples significantly induced Ccl2 mRNA expression, increased amount of reactive oxygen intermediate, inhibited membrane bound enzymes and altered membrane fluidity.

Pyrethroid derivative users had induced levels of lipid peroxidation and induced binding activities of transcription factors(tfs) like CEBP-β and NF-AT. Pyrethroid derivatives induced autophagy, elicited intracellular Ca2+ concentration, calcineurin and regulated proapoptotic genes, DAPK1, Bim.

"Our current study presumably comprises the initial investigation of a very new mechanism of pyrethroid derivatives-moderated programmed cell death in various cell sets or types, like human primary cells where-in

this is a late event, is documented," state the researchers.

Hence, the current research-study might be significant in the various pyrethroid derivatives-allied hematological-related cancers and immunosuppressant or auto-immune disorders. In the foremost instance, the researchers present data stating that pyrethroid derivatives induces multiple cell signaling cascades, like CEBP-β, NF-AT, ERK and MAPK having a role in autophagy thereby; synchronously effectively impact on the apoptosis, therefore causing hematological tumors and toxic or immune related disorders.

"Overall this current study might facilitate to formulate therapeutics or intervention targets that might serve to decrease the effect or impact of pyrethroids derivatives by targeting the signaling cascade that serves to minimize the modulation of autophagy mediated apoptosis," the researchers conclude.

More information: Jyothi Puvula et al, The role of pyrethroid derivatives in autophagy and apoptosis crosstalk signaling and potential risk for malignancies, *Oncotarget* (2022). DOI: 10.18632/oncotarget.28328

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