O1 ANTIOXIDATIVE AND CYTOPROTECTIVE EFFECTS OF *PHYLLANTHUS URINARIA L.* ON DOXORUBICIN-INDUCED CARDIOTOXICITY

Linda Chularojmontri[1], Suvara K. Wattanapitayakul[2], Angkana Herunsalee[3], Suphan Charuchongkolwongse[3], Somchit Niumsakul[3], Supatra Srichairat[4]

[1] *Interdepartment of Pharmacology, Graduate School, Chulalongkorn University,*
[2] *Department of Pharmacology, Faculty of Medicine, Srinakharinwirot University, Bangkok,*
[3] *Medicinal Plant Research Institute, Department of Medical Science, Ministry of Public Health, Nonthaburi,*
[4] *Department of Pharmacology, Faculty of Veterinary, Chulalongkorn University, Bangkok.*

Cardiac toxicity is a major adverse effect caused by doxorubicin (DOX) therapy. DOX toxicity involves generation of reactive oxygen species (ROS). In this study, we investigated the antioxidative and cytoprotective effect of *Phyllanthus urinaria* (PU) against DOX toxicity using H9c2 cardiac myoblasts. Total antioxidant capacity of PU (1 mg/mL) was 5,306.75±461.62 μM FRAP value. DOX IC50s were used to evaluate cytoprotective effect of PU ethanolic extract (1 or 10 μg/mL) in comparison with ascorbic acid (VIT C, 100 μM) and N-acetylcysteine (NAC, 100 μM). PU treatments (1 or 10 μg/mL) dose dependently caused rightward-shifted of DOX IC50 to 2.8- and 8.5-fold, respectively, while treatments with VIT C and NAC increased DOX IC50 by 3.3- and 4.2-fold, respectively. Further evaluation of cytoprotective effect showed that PU and the pure antioxidants completely inhibited cellular lipid peroxidation and caspase-3 activation induced by DOX (1 μM). Endogenous antioxidant defense such as total glutathione (tGSH), catalase and SOD activity was also modulated by the antioxidants. PU treatment alone dose-dependently increased tGSH and this effect was retained in the presence of DOX. Similar effect was observed in catalase and SOD enzyme activity. The NFκB transcription factor assay demonstrated that all antioxidants significantly inhibited DOX-induced NFκB activation. Our results suggest that PU protected against DOX cardiotoxicity was mediated through multiple pathways and this plant may serve as alternative source of antioxidants for prevention of DOX cardiotoxicity.