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Protective Effect of Betanin Inhibits Inflammation and Apoptosis through Modulate PTEN/AKT Signaling Pathway in Doxorubicin-Induced Cardiotoxicity Rats

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SUMMARY. **Doxorubicin (DOX) is an effective anti-neoplastic mediator; however, the usage is limited owing to its cardiomyopathy. Betanin is an active radical scavenger widely used in the regulation of cerebrovascular blood supply. The present work was focused on investigating the effect of betanin (Pre-treated) in rats with cardiomyopathy induced by DOX. Cardiotoxicity was induced by IP injection of DOX (15 mg/kg) for two weeks in the rat. DOX treated rats showed an increase in lipid peroxidation (TBARS) and decreased antioxidants status (SOD, CAT, GST, GSH, GST, GR, and GPx). We observed irregular pathological structures in DOX-induced rats. The DOX treatment significant increase the myocardium biomarkers such as Ct-I, BNP, CK-MB in serum. Significantly enhanced activity of pro-inflammatory cytokines in DOX treated rats. Betanin treated rats show increased antioxidants, reduced cardiac damage biomarkers, and suppressed inflammatory cytokines in DOX-induced rats. Furthermore, a DOX-induced rat shows increased PTEN, PI3K, and decreased p-AKT, thereby enhancing pro-apoptotic protein Bax, Bad, Caspase 3 expression resulting in induced cell apoptosis. Whereas betanin treatment significantly down in the activation PTEN/AKT and pro-apoptotic protein, enhance Bcl-2 expression in DOX-mediated rats. The overall finding shows that betanin inhibits inflammation and cell apoptosis by modulating PTEN/AKT signaling in the DOX-induced rat.**

RESUMEN. La doxorrubicina (DOX) es un mediador antineoplásico eficaz; sin embargo, el uso es limitado debido a su miocardiopatía. La betanina es un eliminador de radicales activo ampliamente utilizado en la regulación del suministro de sangre cerebrovascular. El presente trabajo se centró en investigar el efecto de la betanina (pretratada) en ratas con miocardiopatía inducida por DOX. Se indujo cardiotoxicidad mediante inyección IP de DOX (15 mg/ kg) durante dos semanas en la rata. Las ratas tratadas con DOX mostraron un aumento en la peroxidación de lípidos (TBARS) y una disminución del estado de antioxidantes (SOD, CAT, GST, GSH, GST, GR y GPx). Observamos estructuras patológicas irregulares en ratas inducidas por DOX. El tratamiento con DOX incrementa significativamente los biomarcadores de miocardio como Ct-I, BNP, CK-MB en suero. La actividad de citocinas proinflamatorias está significativamente mejorada en ratas tratadas con DOX. Las ratas tratadas con betanina muestran un aumento de antioxidantes, una reducción de los biomarcadores de daño cardíaco y citocinas inflamatorias suprimidas en ratas inducidas por DOX. Además, ratas inducidas por DOX muestra un aumento de PTEN, PI3K y una disminución de p-AKT, lo que mejora la expresión de la proteína proapoptótica Bax, Bad, Caspasa 3, lo que da como resultado la apoptosis celular inducida. En tanto, el tratamiento con betanina reduce significativamente la activación de PTEN/AKT y la proteína proapoptótica, mejora la expresión de Bcl-2 en ratas mediadas por DOX. El hallazgo general muestra que la betanina inhibe la inflamación y la apoptosis celular modulando la señalización de PTEN/AKT en la rata inducida por DOX.

KEY WORDS: apoptosis, betanin, cardioprotective, doxorubicin, PTEN/AKT pathway.

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