Abstract

Introduction: Ifosfamide (IFA) is an alkylating chemotherapy drug used to treat several neoplasms such as testicular, head and neck cancers, sarcoma and lymphoma. Common side effects of IFA are alopecia, nausea and vomiting, hemorrhagic cystitis, and nephrotoxicity. In addition, IFA administration is associated with neurotoxicity and encephalopathy in 10-40%. IFA metabolites, particularly chloroacetaldehyde (CAA) as a toxic metabolite with mitochondrial dysfunction and oxidative stress cause neurotoxicity. Among plant flavonoids, betanin is a biologically active compound found in many fruits, including red beets. This compound has various medicinal activities such as antioxidant, anti-inflammatory, light protection, anti-cancer and anti-diabetic. Recent studies have shown the protective effects of betanin against various metabolic disorders and neurodegenerative diseases.

Materials and Methods: Male Wistar rats were randomly divided into four groups: control group, IFA group, IFA + betanin group and betanin group. Betanin (50 mg / kg, intraperitoneally) was administered to rats once daily for 2 consecutive days. IFA was then injected intraperitoneally at a dose of 500 mg / kg to induce acute neurotoxicity on the third day, and mitochondrial parameters, oxidative stress, cholinergic enzymes, and histopathological damage to brain tissue were evaluated.

Results: Our results showed that betanin significantly improved mitochondrial parameters including mitochondrial edema, succinate dehydrogenase (SDH) activity, mitochondrial membrane potential depletion (MMP) and reactive oxygen species (ROS). But it failed to restore altered levels of acetylcholinesterase (AChE), butyrylcholinesterase (BChE), histopathological parameters, reduced glutathione (GSH) and oxidized (GSSG) and malondialdehyde (MDA). Rats receiving concomitant IFA + betanin were also killed.

Discussion & Conclusion: Despite strong antioxidant effects and reported neuroprotection, betanin could not prevent acute neurotoxicity caused by ifosfamide and IFA + betanin administration resulted in loss of rats.

Keywords: Betanin, Ifosfamide, Neurotoxicity, Mitochondria, Reactive oxygen species (ROS), Oxidative stress