**The protective effect of two types of Moroccan honeys against cyclophosphamide-induced toxicity in mice.**

Houssam Lakhmili1,2\*, Ahmed Khadra3 , Karima Warda4 , Abdelilah El-Abbassi1,2, Laila El Bouzidi1,2 , and Abdellatif Hafidi1,2

*1Laboratory of Agri-Food, Biotechnologies, and Valorization of Plant Bioresources. Faculty of Sciences Semlalia. Cadi Ayyad University, 40000 Marrakech, Morocco.*

*2Agrobiotechnology and Bioengineering Center, CNRST-labeled Research Unit (AgroBiotech-URL-CNRST-05 Center). Cadi Ayyad University, 40000 Marrakech, Morocco. E-mail:* [*houssam.lakhmili@ced.uca.ma*](mailto:houssam.lakhmili@ced.uca.ma)*\* ;* [*a.elabbassi@uca.ma*](mailto:a.elabbassi@uca.ma) *;* [*elbouzidimail@gmail.com*](mailto:elbouzidimail@gmail.com)*;* [*a.hafidi@uca.ma*](mailto:a.hafidi@uca.ma)

*3Faculty of Sciences Semlalia. Cadi Ayyad University, 40000 Marrakech, Morocco. E-mail:*[*khadraucam@gmail.com*](mailto:khadraucam@gmail.com)

*4Laboratory of Microbiology-Virology. Faculty of Medicine and Pharmacy, Cadi Ayyad University, 10 40000 Marrakech, Morocco. Email:* [*k.warda@uca.ma*](mailto:k.warda@uca.ma)

Cyclophosphamide (CP) is a common anticancer agent used for the treatment of various forms of cancer, autoimmune diseases and is also used as an immunosuppressant after organ transplants. However, upon treatment, it induces severe toxicity due to its oxidative stress capability. Honey, is a natural product collected by honey bees, has shown several biological activities, such as free radical scavenging and antioxidant agent. In this context, the present study aims to assess the protective effects of two types of Moroccan honeys against CP-induced genotoxic and cytotoxic effects in mouse bone-marrow cells. The ratio of polychromatic erythrocytes (PCE)/normochromatic erythrocytes (NCE) and the frequency of micro nucleated polychromatic erythrocytes (MNPCE) demonstrated that the tested concentration of CP alone or combined with sucrose, significantly induced an increase in the % MNPCE and significantly reduced PCE/NCE ratios demonstrating a potential genotoxic and cytotoxic effect of CP. While the cytotoxic and genotoxic effect was attenuated in the CP group pretreated with honey for 6 days. Also, the results indicated that the mice that were pretreated with honey have improved levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and creatinine concentrations in mice serum compared to the other groups. Moreover, the intake of honey also reduced the incidence of liver damage induced by CP. These results indicate that CP had a marked damaging effect on liver tissue including steatosis apoptosis, necrosis, and massive infiltration of inflammatory cells with irregular general pattern of the tissue. The tested Moroccan honeys showed a potential protective effect against cyclophosphamide-induced hepatotoxicity in mice.

Keywords: Cyclophosphamide; Moroccan honey; bioactive compounds; genotoxicity; micronucleus formation.