SHORT COMMUNICATION

Topical pimecrolimus lacks genotoxicity and cytotoxicity by means of micronucleus erythrocyte rodent assay

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Abstract
Topical pimecrolimus is an alternative treatment of atopic dermatitis. However, rare cases of malignancy have been reported with their use. This study was performed to investigate the possible geno- or cytotoxic effect in mouse bone marrow caused by systemic absorption of pimecrolimus 1% cream. In order to determine this, induction of micronucleated erythrocytes (MNE) in mouse peripheral blood was determined after the cutaneous application of three different doses, daily for 5 consecutive days. No differences were found in frequencies of polychromatic erythrocytes, MNE, and micronucleated polychromatic erythrocytes in the different groups of study. In conclusion, under described conditions, no geno- or cytotoxic effects were detected after the cutaneous application of pimecrolimus.

Keywords: DNA damage, calcineurin inhibitor, atopic dermatitis, blood, mouse

Introduction
Pimecrolimus (PIM), an ascomycin-derived immunosuppressant, is a calcineurin inhibitor that selectively targets T cells and mast cells. By inhibiting the action of calcineurin, PIM blocks the transcription of Th1- (e.g., interleukin [IL]-2 and interferon gamma; IFN-γ) and Th2 (e.g., IL-4, IL-10)-type cytokines (Mrowietz, 2001). In addition, it prevents the transcription of cytokines and the release of inflammatory preformed mediators from mast cells (Gupta and Chow, 2003).

PIM is marketed as an alternative treatment for mild to moderate atopic dermatitis and is administered topically as a 1% cream preparation (Hebert, 2006). Conventional treatment for atopic dermatitis has been topical corticosteroids; nevertheless, they carry the risk of local adverse effects, such as skin atrophy (Olkininen et al., 1998). In contrast, PIM is a potent anti-inflammatory substance without the adverse effects associated with corticosteroids (Quelle-Roussel et al., 2001; Grassberger et al., 2004). Topical PIM is used in the management of pediatric patients with atopic dermatitis who do not achieve satisfactory treatment with other topical pharmacologic treatments (Yang and Curran, 2009).

However, there is ongoing controversy, because the U.S. Food and Drug Administration (FDA) raised concerns about the use of topical PIM in atopic dermatitis, suggesting that there is a potential risk of development of malignancy, in terms of lymphoma and skin cancer.