INTRODUCTION

Programmed cell death plays a role in the homeostasis of the normal epidermis as well as in the terminal differentiation of keratinocytes resulting in a cornified layer formed by dead keratinocytes that is finally shed from the skin surface ***(Candi et al., 2005)***.

The regulation of apoptosis involves a dynamic interaction between death-accelerator and death-depressor proteins. Many molecules or genes involved in the regulation of apoptosis have been identified either by preventing or by promoting apoptosis. The ratio of antiapoptotic versus pro-apoptotic proteins determines the inherent susceptibility of a given cell to respond to apoptotic signals (***Elmore, 2007***).

The Fas, Bcl-2, nuclear factor kappa B (NF-κB) and p53 proteins are known to play a central role in the regulation of apoptosis. Fas is a cell surface receptor belonging to the nerve growth factor ⁄ tumor growth factor (TNF) receptor family, and is highly expressed on a variety of cells of lymphoid or nonlymphoid origin. FasL is a membrane protein, usually restricted to activated T cells and natural killer cells. Binding of FasL to Fas on Fas-sensitive target cells causes apoptosis of the target cells by triggering a caspase cascade ***(Choi et al., 2006).***

p53 is a tumor-suppressor gene that controls cellular proliferation and can eliminate the cells by sending them down an irreversible apoptotic pathway ***(McNutt et al., 1994).*** On the other hand, NF-κB and Bcl-2 are protooncogenes that protect cells from apoptosis ***(Hockenbery et al., 1990).***

Spongiosis refers to intercellular edema between the keratinocytes of the stratum malpighii. It is characterized by condensation of cells, widening of the intercellular space, and stretching of remaining intercellular contacts, resulting in a sponge like appearance of the epidermis. Spongiotic dermatitis is a broad category of inflammatory skin disease in which spongiosis is the microscopic hallmark ***(Elder et al., 2005).***

Although spongiosis refers only to serum between keratinocytes, the serous fluid is usually accompanied by exocytosis of inflammatory cells. In its common forms, including atopic dermatitis, allergic contact dermatitis and nummular dermatitis, spongiosis is usually accompanied by lymphocytes (lymphocytic spongiosis). In other forms, spongiosis may be accompanied by eosinophils or neutrophils ***(Machado-Pinto et al., 1996).***

Apoptosis of keratinocytes has recently been implicated as a key mechanism of spongiosis which represents a main histopathologic feature in many dermatoses. In this process, caspases may play a role. Caspases are present in the cells as inactive zymogens that must be cleaved to generate free catalytic subunits able to associate and form active heterotetramers ***(Martinon & Tschopp, 2004)***.

Apoptosis of keratinocytes has been shown to be associated with cleavage of E-cadherin, an important component of adherence junctions. Therefore, cleavage of E-cadherin likely contributes to spongiosis formation. Because E-cadherin is a proteolytic target of caspase-3, it has been suggested that active caspase-3 cleaves E-cadherin in spongiotic disorders ***(Simon et al., 2006)***.