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Inhibition of Apoptosis-Driven Regression of Hair Bulb

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Hair exerts a range of functions including thermoregulation, physical protection, sensory activity. Mature and actively growing hair follicles become anchored in the subcutis, and regenerate by spontaneous repetitive cycles of growth (anagen), apoptosis-driven regression (catagen), and quiescence (telogen). HF regression is characterized by activation of pathways that induce apoptosis in HF cells. We focused our study on investigating the effect of new therapeutic molecules capable of counteracting the regression phase. HFDPC cells, grown in culture, were incubated for 24 hours incubation with 1 μ M staurosporin and apoptosis was monitored. There was a marked activation of Caspase-3 accompanied by cytoskeletal degradation, nuclear blebbing, and cellular fragmentation. The addition of spermidin or rutine in the micromolar range concentration reduced staurosporin-induced caspase activity by over 50%, when the two agents were added simultaneously equal levels of caspase-3 inhibition was achieved with concentration 10 fold lower. Zeaxantine alone was ineffective, however when added to the combined spermidin and rutine treatment, the staurosporin-induced caspase activity was almost totally counteracted and the enzymatic activity was significantly reduced. These combined treatment were also effective in preventing staurosporin-mediated cellular damage. The extent of cell loss was greatly reduced with preservation of cell shape and actin-tubulin cytoskeleton. The combined treatment also counteracted staurosporin-induced caspase-3 and PARP over-expression, and prevented the inhibition of Akt/PKB and MAP kinase ERK1/2 activities. The protective effects of our agents was also observed in ex vivo bulbs. After 24 hours in vitro culture of bulbs there is a dramatic loss of Akt and ERK phosphorylation. This is totally prevented by co-incubation with our combined treatment. Thus, here we report that concomitant exposure of spermidine, rutine and zeaxantine blocks the degradation of vital intracellular pathways and structure of vital importance for the prevention of catagen.