# Modulation of Apoptosis in HaCaT keratinocytes via Differential Regulation of ERK Signaling Pathway by Flavonoids

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**Abstract**

In the present study, we have administered several flavonoids to human HaCaT keratinocytes, and determined that 3,4′-dihydroxy flavone (3,4′-DHF) exerts a slight stimulatory effect on cell growth, although other flavonoids, including keamferol, quercetin, and isohamnetin exhibited growth inhibitory properties. 3,4′-DHF was found to exert an anti-apoptotic effect on etoposide-induced cell death. We were also able to determine that sustained ERK activation was intimately associated with the etoposide-induced apoptosis of HaCaT cells, and treatment with 3,4′-DHF induced a significant suppression of etoposide-induced ERK activation, concomitant with the repression of PARP or the cleavage of pro-caspase 3. ERK overexpression significantly overrode the anti-apoptotic function of 3,4′-DHF, but this was not true of ERK-DN. Moreover, treatment with 3,4′-DHF resulted in the protection of cells from H2O2-induced cell death, and also exerted an apparent suppressive effect on the stress-induced generation of ROS. Finally, we showed that 3,4′-DHF almost completely abolished kaempferol-induced apoptosis, coupled with a concomitant suppression of both intracellular ROS generation and the activation of ERK. Taken together, our data clearly indicate that a host of phytochemicals, including etoposide and a variety of flavonoids, differentially regulate the apoptosis of human HaCaT keratinocytes via the differential modulation of intracellular ROS production, coupled with the concomitant activation of the ERK signaling pathway. According to these results, we are able to conclude the distinct structure-activity relationship (SAR) between several flavonoids.

## References

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