

Alteration of circadian rhythm by UV exposure: Chronobiology is coming...

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Since ever, humans are submitted to day/night cycles. This alternation of light activates a 24-hours internal clock in our brain, generating a circadian rhythm, which synchronize cutaneous cells clock. At the molecular level, it consists of an autoregulatory feedback loop, inducing a 24-hour cycle in the expression of several genes. Thereby many proteins involved in skin functions are products of clock-controlled genes (CCG). Thus, circadian clock modulates skin properties such as hydration, pigmentation, sebum production, and participates in its well-being. Nevertheless, it has been proved that intense sun exposure alters skin physiology. The aim of this study is to evaluate the effect of UV exposure on the expression of genes involved in the circadian clock modulation.

To fulfill this purpose, human primary keratinocytes were synchronized before a UVB exposure. Expression of genes involved in circadian clock regulation was analyzed by qPCR on a 24-hours kinetic and results were compared to non UVB exposed condition. This study has demonstrated that UVB exposure alters expression of four genes involved in circadian clock modulation (Clock, Bmal1, Cry1 and Rora). Their expressions were significantly altered at 6 and 10 hours after exposure.

Moreover, we have studied the capacity of *Crocus sativus* extract to prevent these UVB effects on keratinocytes. The application of this botanical extract minimized UVB effects on those 4 genes, at 6 and 10 hours after exposure, restoring the rhythmicity in expression of genes which control circadian clock.

In conclusion, this study has identified a UVB exposure effect on skin cells: it modifies rhythmicity in expression of genes involved in the circadian cycle of keratinocytes. This is likely to alters both cell metabolism and physiology. Furthermore, *Crocus sativus* extract has proved its capacity to protect skin clock from UV damages, enabling to minimize those effects on genes. Other tests have been conducted and have shown that the same botanical extract has photo-protective effect: it protects skin from sunburn cells apparition and has SPF booster property.