ACNE, ROSACEA, AND RELATED DISORDERS (INCLUDING HIDRADENITIS SUPPURATIVA)

METFORMIN EXERTS SEBOSTATIC EFFECT ON HUMAN SEBOCYTES VIA AMPK/TSC1/MTORC1 PATHWAY

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Background: Acne vulgaris is a most common skin condition which could impose significant emotional morbidity on patients. Excessive sebum production is one major factor contributive to acne pathogenesis. Metformin regulates multiple physiological processes, especially energy metabolism. However, the effect of metformin on lipogenesis in human sebaceous gland has not been reported yet. Given its safety profile, metformin would be a promising anti-acne agent in clinical practice.

Objective: The present study is to explore the effects of metformin on lipid metabolism in human sebaceous gland and determine whether it may behave as an effective sebostatic agent.

Materials and Methods: Human SZ95 sebocytes and normal human skin explants were treated by metformin with or without insulin-like growth factor 1 (IGF-1). Lipid synthesis was determined by Oil red O staining or Nile red staining. Intracellular adenine nucleotide levels were determined at different time points. Western blot was used to study the expression of key components in AMP-activated protein kinase (AMPK)/mTORC1 signaling pathway.

Results: Administration of metformin to cultured human sebocytes and human skin explants effectively inhibited lipogenesis induced by IGF-1. In response to metformin treatment, human sebocytes showed robust activation of AMPK and suppression of mTORC1 signaling followed by a significant rise of cellular AMP:ATP ratio. However, cells silenced of either AMPK or tuberous sclerosis complex 1 (TSC1) protein complex (TSC1 complex) expression were resistant to metformin-induced suppression of mTORC1 signaling and lipogenesis. These data demonstrated an AMPK/TSC1-dependent mechanisms of metformin that inhibited sebum production in sebaceous glands.

Conclusions: Metformin could be a potential anti-acne agent due to its lipostatic effect on sebaceous gland via AMPK/TSC1/mTORC1 signaling pathway.