TITLE: Repositioning Sodium Valproate for Amelioration of Bleomycin-Induced Scleroderma

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ABSTRACT (up to 300 words)

Skin fibrosis (Scleroderma) is one of the connective tissue disorders characterized by skin and systemic fibrosis. The pathogenesis of scleroderma involves multiple interrelated processes of autoimmunity, vasculopathy, inflammation and oxidative stress. Sodium valproate is used for treatment of many types of epilepsy and is known as an inhibitor of histone deacetylase enzyme. Recent studies had proven its promising role as an antifibrotic agent in different body organs such as the lung, peritoneum, liver, and kidney. The aim of this study was to explore the possible ameliorative effect of sodium valproate on the experimental model of scleroderma induced by bleomycin. Forty male BALB/c mice were divided into four equal groups as follows: control group, bleomycin group, bleomycin + sodium valproate group, and sodium valproate group. Mice were assessed for their body weight every 3 days throughout the whole study. Skin tissues were used to evaluate the oxidative stress parameters, transforming growth factor beta 1 (TGF-β1), tumor necrosis factor alpha, interleukin 15, and mammalian target of rapamycin (mTOR). Skin fibrosis was evaluated by measuring dermal thickness and staining the skin tissues with Masson trichrome stain. Furthermore, the skin tissues were immunostained with alpha smooth muscle actin (α-SMA). Administration of sodium valproate to bleomycin-treated mice resulted in the restoration of the body weight with significant decrease in the dermal thickness, amelioration of oxidative stress, suppression of TGF-β1 and mTOR expression, and significant reduction of the percentage of α-SMA immunostaining and the proinflammatory cytokine levels compared to mice treated with bleomycin alone. In conclusion, sodium valproate has an antifibrotic effect on skin fibrosis which may represent a beneficial therapeutic modality for management of scleroderma.

BIOGRAPHY (up to 200 words)

Dr. Ahmed M. Kabel had the Ph.D. degree in Pharmacology in 2013 from Faculty of Medicine, Tanta University, Egypt. He was involved in teaching undergraduate and postgraduate students as well as supervised master and Ph.D. students. He published more than 120 research articles in reputable international peer reviewed journals that have been cited over 1900 times, and his publication h-index is 23. He has been serving as an editorial board member of several reputed journals. Areas of research interests include oncology, dermatology, and therapeutics.

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