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Abstract

The Role of Vitamin K Family in Obesity †

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Abstract: Environmental and lifestyle adaptations over the last decades have contributed to enhanced man´s longevity, however it also paved the ground for different diseases to unfold. Today one of the main public health challenges is obesity and its related metabolic dysfunctions. In recent years, the pharmacological options are reported as being insufficient, therefore, the discovery and pharmacological development of new therapeutic approaches are required to overcome this epidemic. Vitamin K are a fat-soluble family of compounds implicated in a number of essential biological functions. Vitamin K1 and K2 are two naturally occurring compounds, while vitamin K3 is the most common synthetic form. A bioactivity-guided approach was used with the Nile red fat metabolism assay in zebrafish larvae to successfully isolate an analog of vitamin K1 for the first time from Tychonema sp. LEGE 07196. The structure confirmation was based on NMR spectroscopy and mass spectrometry. This analog was first isolated in 1965 from the cyanobacteria *Synechococcus elongatus*, but little is known on its bioactivity. The anti-obesity effects of all vitamin K forms, including the K1-analog, were studied. The compounds did not cause any general toxicity or malformations and showed significant neutral lipid-reducing activity after 48 h of exposure. The different vitamin forms displayed different levels of activity which shows the importance of the naphthoquinone ring, as well as the impact of the saturation and polarity of the aliphatic side-chain for the structure–activity relationship. Metabolomics approaches were employed to establish the distinct bioavailability and biotransformation of the different forms of vitamins in the organisms. The metabolite profiling was achieved using different databases and MetaboAnalyst was used for associated analysis. The organism has a clear preference to transform the various vitamins into K1 and K1-analog forms, regardless of the supplementation, and each exposed vitamin significatively altered the expression of different metabolites indicating that different metabolic targets are involved. This work is ongoing, and the final aim is to understand the effects of vitamin K family on obesity and related co-morbidities, which could lay the ground to develop a future nutraceutical with lipid reduction activity.

Keywords: vitamin K family; obesity; metabolic dysfunctions; Nile red fat metabolism assay; metabolomics

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