Thymoquinone-rich fraction nanoemulsion (TQRFNE) decreases Aβ40 and Aβ42 levels by modulating APP processing, up-regulating IDE and LRP1, and down-regulating BACE1 and RAGE in response to high fat/cholesterol diet-induced rats

ABSTRACT

Though the causes of Alzheimer's disease (AD) are yet to be understood, much evidence has suggested that excessive amyloid-β (Aβ) accumulation due to abnormal amyloid-β precursor protein (APP) processing and Aβ metabolism are crucial processes towards AD pathogenesis. Hence, approaches aiming at APP processing and Aβ metabolism are currently being actively pursued for the management of AD. Studies suggest that high cholesterol and a high fat diet have harmful effects on cognitive function and may instigate the commencement of AD pathogenesis. Despite the neuropharmacological attributes of black cumin seed (Nigella sativa) extracts and its main active compound, thymoquinone (TQ), limited records are available in relation to AD research. Nanoemulsion (NE) is exploited as drug delivery systems due to their capacity of solubilising non-polar active compounds and is widely examined for brain targeting. Herewith, the effects of thymoquinone-rich fraction nanoemulsion (TQRFNE), thymoquinone nanoemulsion (TQNE) and their counterparts' conventional emulsion in response to high fat/cholesterol diet (HFCD)-induced rats were investigated. Particularly, the Aβ generation; APP processing, β-secretase 1 (BACE1), γ-secretases of presenilin 1 (PSEN1) and presenilin 2 (PSEN2), Aβ degradation; insulin degrading enzyme (IDE), Aβ transportation; low density lipoprotein receptor-related protein 1 (LRP1) and receptor for advanced glycation end products (RAGE) were measured in brain tissues. TQRFNE reduced the brain Aβ fragment length 1–40 and 1–42 (Aβ40 and Aβ42) levels, which would attenuate the AD pathogenesis. This reduction could be due to the modulation of β- and γ-secretase enzyme activity, and the Aβ degradation and transportation in/out of the brain. The findings show the mechanistic actions of TQRFNE in response to high fat and high cholesterol diet associated to Aβ generation, degradation and transportation in the rat's brain tissue.

Keyword: Thymoquinone-rich fraction; Thymoquinone; Nigella sativa; Nanoemulsion; Amyloid-β; High fat/cholesterol diet