

Ferulsinaic acid attenuation of advanced glycation end products extends the lifespan of *Caenorhabditis elegans*

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Abstract

Objectives Ferulsinaic acid is the first member of a new rearranged class of sesquiterpene coumarins of the genus *Ferula*. The genus *Ferula* can be used for the treatment of skin infections, hysteria and for stomach disorders, such as a febrifuge and a carminative agent. The effect of ferulsinaic acid on the lifespan of the nematode *Caenorhabditis elegans* has been examined. Novel data explaining the effect of ferulsinaic acid on the lifespan of *C. elegans* and its antioxidant power were obtained.

Methods *C. elegans* was cultivated under standard laboratory conditions in absence and presence of different ferulsinaic acid. Also, animals were cultivated under heat and chemical stress conditions in absence and presence of ferulsinaic acid. Life span assay, determination of protein concentration, assay of malondialdehyde and ELISA for determination of AGEs were performed.

Key findings Under standard laboratory conditions and in presence of ferulsinaic acid (500 nM, 10 μ M and 100 μ M), mean life span of wild type animals was significantly lengthened in a dose-dependent manner from 18.64 ± 0.19 days (control) to 19 ± 0.19 ($P = 0.695$), 20.76 ± 0.25 ($P = 0.043$) and 22.3 ± 0.29 ($P = 0.0291$), respectively. Interestingly, in *C. elegans* resistance for heat stress at 35°C and oxidative stress induced by paraquat were significantly improved with ferulsinaic acid. Ferulsinaic acid was found to significantly attenuate both lipid peroxidation and the formation of advanced glycation end products in the wild-type animals under standard laboratory conditions.

Conclusions Ferulsinaic acid had therapeutic efficacy as an antioxidant with the possibility of its use as an antioxidant drug.

Keywords advanced glycation end products; *Caenorhabditis elegans*; ferulsinaic acid; lifespan

Introduction

Many plants synthesize an array of chemical compounds that are not involved in their primary metabolism. These 'secondary compounds' instead of serving a variety of ecological functions, they ultimately enhance the plant's survival during stress.^[1] In addition, these compounds may be responsible for the beneficial effects of fruits and vegetables on an array of health related measures.^[2]

Herbal medicine has existed for more than 5000 years. Today there are more than 3000 kinds of medicinal herbs. These herbal combinations are believed to act synergistically to harmonize beneficial effects and to neutralize or minimize the toxic or adverse effects of individual constituent herbs. Recently, numerous efforts have been made to investigate the mechanisms of action of Chinese herbal formulae using modern scientific methodology.^[3–5] In-vitro and in-vivo studies on the individual herbs or constituents of classic formulae have been reported and many herbal medicines have immunomodulatory or antioxidant effects that may offer clinically relevant therapeutics for patients with disorders associated with ageing.^[6,7]

The exclusively old-world genus *Ferula*, belonging to the family Apiaceae, has some 130 species distributed throughout the Mediterranean area and Central Asia. These plants are often used as spices and in the preparation of local drugs. The resins are reported to be used for stomach disorders, such as a febrifuge and carminative agent. Some species are used in traditional medicine for the treatment of skin infections and hysteria.^[8] Previous work on members of this genus revealed that the main constituents are sesquiterpenes and sesquiterpene coumarins.^[9]

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