Glavonoid, a possible supplement for prevention of ATTR amyloidosis.

Abstract

Transthyretin (TTR) is an amyloidogenic protein associated with hereditary and nonhereditary transthyretin amyloidoses (ATTR). Dissociation of the tetramer of TTR to the monomer induces TTR misfolding, which leads to amyloid fibril formation and triggers the onset of ATTR amyloidosis. Stabilizers of tetrameric TTR have been accepted as an effective ATTR amyloidosis treatment while effect is limited and they are too expensive. The aim of our study was to find more effective and cheep natural compound to suppress TTR amyloid formation. Glabridin, a prenylated isoflavan isolated from Glycyrrhiza glabra L., stabilized the TTR tetramer in vitro. The effects of licorice-derived flavonoid oil-Glavonoid, a natural substance that includes glabridin and several polyphenols-on stabilizing the TTR tetramer must still be elucidated. To examine plasma TTR stabilization by Glavonoid in vitro, we investigated the feasibility of utilizing glabridin plus Glavonoid to prevent TTR amyloid fibril formation. Glavonoid mixed with human plasma samples at 24 h incubation in vitro increased the tetramer level ($P < 0.05$) and reduced the monomer level ($P < 0.01$) and the monomer/tetramer ratio ($P < 0.05$) of TTR compared to those without Glavonoid by immunoblot analysis, such effect could not observe in the presence of glabridin. Oral Glavonoid (300 mg for 12 weeks) in 7 healthy volunteers effectively increased the plasma glabridin concentration. Glavonoid increased the TTR tetramer level and reduced the monomer/tetramer ratio of TTR ($P < 0.05$) in plasma at 12 weeks in healthy volunteers compared to those of age matched control subjects without the supplement. Thus, oral Glavonoid may effectively prevent TTR amyloid fibril formation via TTR tetramer stabilization. Glavonoid may become a promising supplement before onset of ATTR amyloidosis.