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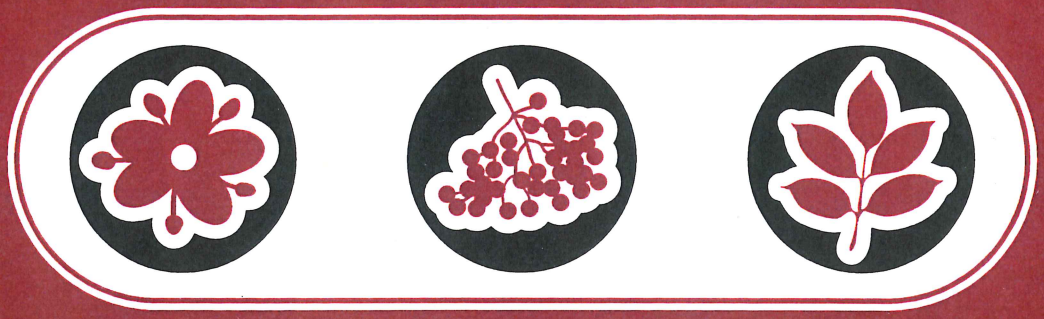

PROCEEDINGS

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Bioactive Compounds of Elder (*Sambucus nigra* L.) with Focus on their Potential Anti-diabetic Effects

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Preparations of elder (*Sambucus nigra*) are used in traditional medicine as diuretics and to treat colds, influenza, inflammation, and diabetes. Elderberries and elderflowers are rich in polyphenols such as phenolic acids, flavonol glycosides, and anthocyanins. Polyphenols are known for their antioxidant activity and are believed to prevent oxidative stress, a condition that may lead to serious diseases such as cancer, cardiovascular diseases, inflammation and type-2 diabetes (T2D). Hence, polyphenols have been pointed out as beneficial agents in both elderflowers and elderberries. Epidemiological investigations tend to confirm the protective effects of polyphenols against cardiovascular diseases and T2D but the mechanisms by which they exert their protective effects are far from understood. The reported beneficial effects of polyphenols against cancers and inflammation are mainly based on *in vitro* studies. The disparity between an excellent *in vitro* activity related to a specific disease(s) and a weaker *in vivo* effect of polyphenols may be due to pharmacokinetic properties such as poor bioavailability, low absorbability, and/or metabolism. Therefore the health effects of elder could be due to (1) polyphenols whose modes of action differ from the traditional one proposed for exogenous antioxidants or (2) other types of biomolecules not identified yet.

Extracts of elderflowers have been found to exert insulin-like and insulin-releasing actions *in vitro* and to activate PPARγ as well as to stimulate insulin-dependent glucose uptake. This indicates that elderflowers may be used in the prevention and/or treatment of insulin resistance. In the search for an explanation of the anti-diabetic effects of elderflowers we undertook an investigation of a methanol extract of elderflowers. A bioassay-guided fractionation of the extract by reverse phase flash column chromatography and semi-preparative HPLC resulted in the isolation of several compounds being able to activate PPARγ, including linoleic acid and linolenic acid, and the flavanone aglycone naringenin. However, major elderflower metabolites such as quercetin-3-O-rutinoside, quercetin-3-O-glucoside, kaempferol-3-O-rutinoside, isorhamnetin-3-O-rutinoside, isorhamnetin-3-O-glucoside, and 5-O-caffeoylquinic acid were unable to activate PPARγ *in vitro*. Several compounds with structures similar to that of naringenin have been identified previously as activators and/or agonists of PPARγ. These include among others the flavonol aglycone kaempferol, which indicates that flavonoid aglycones are relatively good ligands for PPARγ in contrast to their respective glycosides. Further investigations are, however, needed to demonstrate the bioavailability, absorption, and metabolism of elderflower flavonoids in order to determine their potential anti-diabetic or other health-promoting effects.