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PPARγ agonists identified in extracts of elderflowers (*Sambucus nigra*) by bioassay-guided fractionation

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Methanolic extract of elderflowers

Background

Black elder (*Sambucus nigra* L.) have been used traditionally to treat various diseases such as colds, influenza, inflammation, and diabetes. Most studies on the health-promoting effects of black elder have been performed on elderberries, although elderflowers also produce many potential bioactive metabolites such as flavonoids and phenolic acids. It has been found that aqueous extracts of elderflowers exhibit insulin-like and insulin-releasing actions *in vitro*. The bioactive metabolites were not identified and major elderflower metabolites such as quercetin-3-*O*-rutinoside, lupeol, and β-sitosterol did not individually stimulate insulin secretion [1].

In this study 3 kg of elderflowers (cv. Haschberg) was macerated and extracted twice overnight with methanol. The dried extract was separated by RP flash CC to give 12 fractions. Fractions B+C contained phenolic acids, primarily 3-, 4-, and 5-*O*-caffeoylquinic acid. Fractions D-H contained mostly the phenolics quercetin 3-*O*-rutinoside, kaempferol 3-*O*-rutinoside, isorhamnetin 3-*O*-rutinoside, and 1,5-di-*O*-caffeoylquinic acid. In fractions I+J the flavanone naringenin was the major constituent. Fractions K and L were dominated by α-linolenic acid and linoleic acid. All metabolites were purified by RP semi-preparative HPLC and identified by HPLC-DAD, LC-MS, and standard addition.

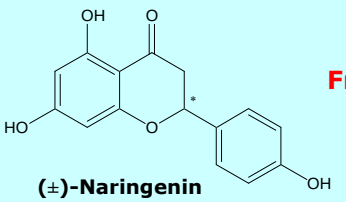
C_{18}-RP Flash CC (Ø70) with MeCN-H_2O gradient

PHENOLIC ACIDS

FLAVONOIDS

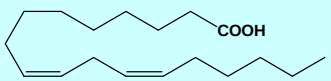
Fractions I + J

C_{18}-RP semi-prep HPLC with MeCN-H_2O gradient



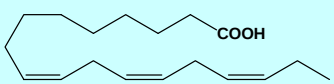
(±)-Naringenin

Fraction L



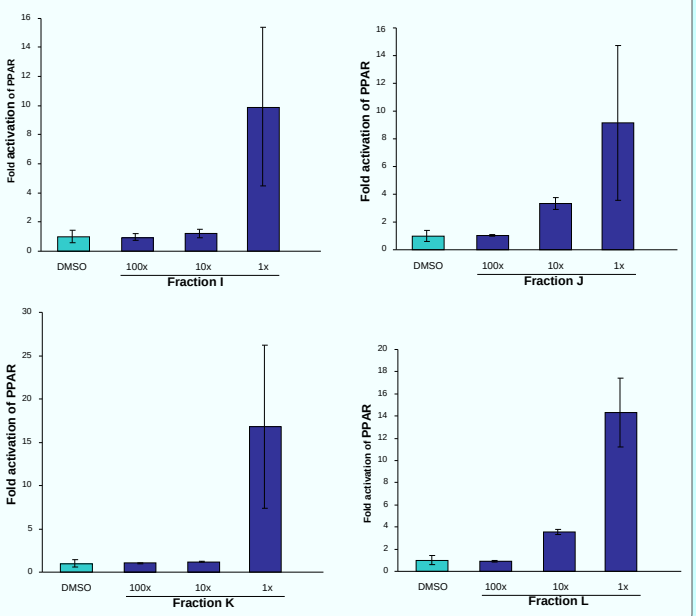
Linoleic acid 18:2 (9c, 12c)

Fraction K



α-Linolenic acid 18:3 (9c, 12c, 15c)

Activation of PPAR by elderflower fractions



Bioactivity and perspectives

Bioassay-guided chromatographic fractionation of the elderflower extract yielded four bioactive fractions (marked with pink) and the major metabolites in these were naringenin, α-linolenic acid, and linoleic acid. Bioactivity was assessed using a PPARγ transactivation assay and results obtained are shown to the left for the four fractions I, J, K, and L. Rosiglitazone (1 μM) was used as positive control and the results are given as fold activation when DMSO is set to 1. Fatty acids are well-known activators of PPARγ, but naringenin is not and will have to be further tested to establish its potential as an anti-diabetic compound.

Large differences in the content of the active compounds and other metabolites was found among elderflower varieties. This indicates the importance of choosing the optimal elder variety in order to develop effective functional foods/herbal products for prevention/treatment of type 2 diabetes.

References: [1] Gray, A. M. *et al.* (2000) The traditional plant treatment, *Sambucus nigra* (elder), exhibits insulin-like and insulin-releasing actions *in vitro*, *J. Nutr.* **130**, 15-20.

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