Xanthohumol and related prenylflavonoids in hops and beer:
To your good health!

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Xanthohumol and related prenylated flavonoids from hops (*Humulus lupulus*): Dietary supplements and potential health benefits
Chemical changes of hop compounds during the brewing process: isomerization

Humulone (α-bitter acid)

Xanthohumol

Isomerization in the brew kettle

Isohumulone (iso-α-acid)

Isoxanthohumol

Courtesy of Hopsteiner

Courtesy of Hopsteiner
Novel XN-related flavonoids from hops

XN and isoXN detected in beer

Properties of XN reported

XN featured as a ‘Molecule of Interest’ in Phytochemistry


Xanthohumol: Publications over time
(Source: gopubmed.org)

XN bioactivity studies
- estrogenic effects (HRT)
- cancer chemoprevention
- inhibition of tumor angiogenesis
- effects on glucose and lipid metabolism
- hepatic and intestinal metabolism

Xanthohumol supplements on the market
Xanthohumol: Network of top authors
(Source: gopubmed.org)
Prenylflavonoid variation in *Humulus lupulus*: distribution and taxonomic significance of xanthogalenol and 4'-O-methylxanthohumol

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Available online at www.sciencedirect.com

Molecules of Interest

Xanthohumol and related prenylflavonoids from hops and beer: to your good health!

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Estrogens and Congeners from Spent Hops (*Humulus lupulus*)

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2004


The alphabet xanthohumols
How it all started…

How much is there in beer?

<table>
<thead>
<tr>
<th></th>
<th>Xanthohumol</th>
<th>Isoxanthohumol</th>
<th>8-prenylNaringenin</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. Major brand</td>
<td>0.034 mg/l</td>
<td>0.5 mg/l</td>
<td>0.013 mg/l</td>
</tr>
<tr>
<td>Northwest microbrew</td>
<td>0.24</td>
<td>3.4</td>
<td>0.11</td>
</tr>
<tr>
<td>European pilsner</td>
<td>0.012</td>
<td>1.1</td>
<td>0.008</td>
</tr>
</tbody>
</table>
The endocrine activities of 8-prenylnaringenin and related hop (Humulus lupulus L.) flavonoids

Interaction of 8-prenylnaringenin with the estradiol binding site of ERα
Metabolism of xanthohumol

Metabolism of xanthohumol

Metabolism of xanthohumol
LC-MS/MS Analysis of xanthohumol and metabolites in plasma samples from male jugular vein-cannulated Sprague-Dawley rats (LC run time: 5 minutes)

Figure 2. Representative LC-MS chromatograms of (A) a 0.2 mM standard and (B) a 24 hour plasma sample from an oral high (16.9 mg / kg BW) dosed animal. The standard contained xanthohumol (XN) and its metabolites (isoxanthohumol – IX, 8-prenylnarigenin – 8PN, and 6-prenylnarigenin – 6PN) as well as an internal standard (4, 2'-dihydroxychalcone – DHC).

**Bioavailability of xanthohumol**

**Figure 3.** Semilogarithmic plot of mean plasma concentration–time data of xanthohumol obtained from Sprague Dawley rats (n = 12) given a single intravenous injection dose of 1.86 mg/kg BW.

**Figure 4.** Semilogarithmic plot of mean plasma concentration–time data of xanthohumol obtained from Sprague Dawley rats (n = 12/dose) given a single oral low, med, or high dose (1.86, 5.64 or 16.9 mg/kg BW).

<table>
<thead>
<tr>
<th>Dose (equivalent human dose)</th>
<th>1.86 mg/kg (20 mg)</th>
<th>5.64 mg/kg (60 mg)</th>
<th>16.9 mg/kg (180 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioavailability</td>
<td>30%</td>
<td>13%</td>
<td>11%</td>
</tr>
</tbody>
</table>

Causal factors in the development of Metabolic Syndrome

- Genetic factors
- Insulin resistance
- Elevated blood pressure
- Dyslipidemia
- Central obesity
- Chronic inflammation
- Cigarette smoking
- Lack of physical activity
- Overnutrition

*Adapted from Perez-Martinez et al. Mol. Nutr. Food Res. 2011, 55*
Effect of xanthomol (XN) on markers of Metabolic Syndrome in Zucker fa/fa rats, a rodent model of obesity

- 12 rats (6 male/6 female)
  - Eq. human dose of **0 mg XN** daily for 6 weeks

- 12 rats (6 male/6 female)
  - Eq. human dose of **20 mg XN** daily for 6 weeks

- 12 rats (6 male/6 female)
  - Eq. human dose of **60 mg XN** daily for 6 weeks

- 12 rats (6 male/6 female)
  - Eq. human dose of **180 mg XN** daily for 6 weeks

Endpoints
- Body weight
- Fasting plasma glucose
- Cholesterol
- Insulin
- Triglycerides
- Metabolome profile

High fat (60% kcal) AIN-93G diet

Normal fat (15% kcal) AIN-93G diet

0 1 2 3 4 5 6 weeks
Steady-state plasma concentrations
(0.9 μM at 16.9mg/kg)

Xanthohumol lowers body weight in obese male Zucker fa/fa rats ($n=6$ per group)

No difference in food intake between groups

Xanthohumol lowers fasting plasma glucose in obese male Zucker fa/fa rats ($n=6$ per group)

Pharmacological activities of xanthohumol in vivo

- Pharmacologically relevant concentrations cannot be reached by consumption of beer
- Pharmacological relevant concentrations can be reached by oral administration of supplements (rats, humans)
- Xanthohumol **attenuates weight gain** in Zucker rats, a model of obesity and type II diabetes (eq. human dose 180 mg/day)
- Xanthohumol **lowers fasting plasma glucose** in Zucker rats at equivalent human dose of 180 mg/day
- Xanthohumol lowers plasma acylcarnitines and free fatty acids in Zucker rats (eq. 180 mg/day), thereby **improving mitochondrial β-oxidation and lipid homeostasis**
Der erschaute Mensch

Anti Aging
Bier

für Körper, Geist und Seele

Xanthohumol: To your good health!
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