

8-prenylnaringenin was selected as Poison of the Month for July by the working group endocrine activity

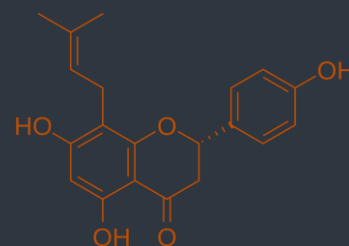
...because it is one of the most potent phytoestrogens known and illustrates how markedly intrinsic hormonal activity and actual human exposure can differ.

Endocrine disruptors – why concern is growing

Humans are simultaneously exposed to a wide range of hormonally active substances from the environment, food, cosmetics, and other everyday products. For individual substances, exposure levels are often below known effect thresholds. More difficult to assess, however, are long-term exposure, sensitive developmental windows, and possible combination effects of several substances acting on the same hormonal signalling pathway.

Pregnancy, early childhood, and puberty are particularly relevant because hormones regulate growth, development, and maturation during these stages. Absorption, distribution, metabolism, and individual susceptibility also vary considerably between people. Therefore, hormonal activity demonstrated in a laboratory test does not automatically imply a health risk under realistic exposure conditions.

A meaningful assessment must consider the intrinsic potency of a substance, the concentrations actually reached in the body, the duration of exposure, and the target tissue involved. The need to integrate all of these factors is what makes the risk assessment of endocrine-active substances particularly challenging.



8-prenylnaringenin

8-Prenylnaringenin from hops – hormonal activity from a glass of beer?

Hops (*Humulus lupulus*) give beer its characteristic bitter taste and distinctive aroma. In addition to bitter compounds and essential oils, the hop cones used in brewing contain prenylated flavonoids. One of these is 8-prenylnaringenin, commonly abbreviated as 8-PN. This compound is considered one of the most potent phytoestrogens identified to date.

Phytoestrogens are plant-derived substances that interact with estrogen receptors and can elicit hormone-like effects. 8-PN binds to both estrogen receptor subtypes, ER α and ER β , but, compared with many other phytoestrogens, shows pronounced activity mediated through ER α . This receptor is expressed, among other tissues, in the uterus, mammary gland, bone, and various neuroendocrine tissues. In several *in vitro* test systems, 8-PN was markedly more potent than the well-characterised soy-derived phytoestrogens genistein and daidzein. However, compared with the endogenous female sex hormone 17 β -estradiol, 8-PN is approximately 70-fold less potent.

The direct concentration of 8-PN in beer is comparatively low and varies considerably between beer types. Isoxanthohumol is therefore particularly relevant to overall exposure. This precursor is formed from xanthohumol during the brewing process and is often present in beer at substantially higher concentrations than 8-PN. Isoxanthohumol can subsequently be O-demethylated to 8-PN by the cytochrome P450 enzyme CYP1A2 in the liver and by certain intestinal bacteria. Thus, part of the more hormonally active compound is formed only after ingestion.

The efficiency of this bioactivation varies markedly between individuals. A recent study using human faecal samples found differences in microbial 8-PN formation spanning several orders of magnitude. In one donor sample, approximately 600 times more 8-PN was formed than in most of the other samples, whereas no measurable conversion was detected in another sample.



Hop pickers and the early suspicion of hormonal effects

Long before 8-PN was identified, hops were already suspected of exerting hormonal effects. Historical reports from the period of manual hop harvesting describe menstrual disturbances among female hop pickers during the harvest season. Hop baths and hop-based preparations were also traditionally used for gynaecological complaints and, later, for the relief of hot flushes.

These historical observations were non-specific and could not initially be explained scientifically. Early studies investigating the estrogenic activity of hops produced conflicting results, most likely because different extracts and test systems were used. It was not until the late 1990s that bioactivity-guided fractionation of hop extracts led to the identification of 8-prenylnaringenin as the principal estrogenically active constituent.

A physiologically based kinetic model extended to include the gut microbiome predicted that high metabolisers would experience approximately twice the internal exposure to 8-PN observed in low metabolisers.

Despite its high intrinsic estrogenic potency, 8-PN appears to result in only low internal concentrations following typical beer consumption. After daily beer intake, predicted uterine concentrations ranged from approximately 0.0004 to 0.002 nM. These values were well below the lowest effective concentration of approximately 1 nM identified in the *in vitro* assay.

High-dose hop extracts and dietary supplements require a different assessment. They are marketed, among other purposes, for the relief of menopausal symptoms and may contain substantially higher amounts of 8-PN and isoxanthohumol than beer. Some products declare defined concentrations of selected hop constituents, whereas the actual contents of other products remain unclear. Evidence suggesting a possible reduction in hot flushes must therefore be weighed against unresolved questions concerning long-term effects, hormone-sensitive tissues, and potential interactions with medicinal products.

The currently available data do not allow safe intake levels to be established for 8-PN and isoxanthohumol when consumed as dietary supplements. Their use should therefore be discouraged.

By Ute Haßmann

Literature and links:

- [Oestrogenic activity of the hop phyto-oestrogen, 8-prenylnaringenin | Reproduction | Oxford Academic](#)
- [Therapeutic Perspectives of 8-Prenylnaringenin, a Potent Phytoestrogen from Hops](#)
- [The Potent Phytoestrogen 8-Prenylnaringenin: A Friend or a Foe?](#)
- [The pharmacognosy of *Humulus lupulus* L. \(hops\) with an emphasis on estrogenic properties - ScienceDirect](#)
- [Interindividual variability in gut microbial formation of the hop phytoestrogen 8-prenylnaringenin results in elevated but sub-toxic internal exposures - PubMed](#)
- [Jahresbericht 2015](#)
- Foto of [Fábio Alves](#) on [Unsplash](#)

