Soybean oil production residue can be used to make product that treats symptoms of menopause

December 11 2023, by Karina Ninni

Credit: CC0 Public Domain

Consuming soy foods is often said to be good for women's health, and much research has been conducted in recent decades to find out whether it can explain why Asian women, whose diet contains plenty of soy foods, have few or none of the usual symptoms of menopause reported by women in the West, such as hot flushes, insomnia, irritability, and depression.

"Soy isoflavones are important sources of bioactive compounds and belong to the class of phytoestrogens—substances similar to estrogen and beneficial to health. However, they're normally found in glycosylated [sugar-coated] form and aren't easily absorbed by the gastrointestinal tract."

"To have an effect on human health, they need to be metabolized by gut microbiota and become aglycone [non-sugar] isoflavones and their bioactive secondary metabolites, such as equol, which has a very similar structure to estrogen," said Gabriela Alves Macedo, a professor at the State University of Campinas's School of Food Engineering (FEA-UNICAMP) in São Paulo, Brazil.

The first author of an article on the study published in the journal *Foods*, Macedo recalled that falling production of estrogen during menopause is responsible for various physiological and behavioral changes in women.

Equol and other phytoestrogens are believed to be capable of mitigating the unpleasant symptoms of menopause. "However, some women's gut microbiota just can't manage to metabolize soy isoflavones," she said. "With the help of colleagues, I've been working to obtain a product that contains bioavailable equol and can benefit such women."

In the study, the researchers mimicked human gut microbiota in vitro to understand how soy isoflavones are metabolized by these microorganisms. According to Macedo, soy isoflavones can be obtained

from okara (also called soy pulp or tofu dregs), an insoluble residue remaining from the production of soybean oil.

"Both protein and phenolic compounds can be extracted from okara. As a food engineer, I'm always interested in ways of using such residues. In Brazil, I know of no more promising source than soybeans to obtain the extract on an industrial scale, although in principle, equol can be obtained from all isoflavone-rich plants," she said.

Methods

The researchers produced a soy milk extract with the correct initial concentration of isoflavones for their experiments. "The industrial process used to obtain the extract for soy-based drinks sold in supermarkets doesn't have sufficient phenolic content because they're designed to serve as a source of non-animal protein," Macedo explained.

The group used different processes to obtain equol by mimicking the metabolization of the isoflavones in the extract. "In the first, we deployed enzymes to remove glucose from glycosylated isoflavones. In this case, we performed measurements to find out whether a metabolite of interest could be obtained using enzymes and to quantify the glycosylated and aglycone isoflavones at the end of the process," Macedo said.

The second strategy entailed fermenting the extract with a mixture of lactobacilli. The researchers inoculated the extract with lactic bacteria in the absence of oxygen (anaerobiosis) and analyzed the isoflavones before and after fermentation.

In the third process, they combined enzymes with probiotics. "After the enzymatic action, I inoculated the mix of probiotics. The aim was to facilitate the work of the lactobacilli by meeting them halfway with the

enzymes in an attempt to speed up the process and obtain more metabolites at the end."

"We found that this combination did indeed work better. It enhanced anti-oxidant capacity, production of metabolites, and conversion of glycosylated into aglycone isoflavones. Both treatments combined had synergistic effects on soy-based products," Macedo said.

The group made a point of testing processes that can be replicated on an industrial scale, working with commercial enzymes and probiotics. "We have to develop solutions that make sense from a technological standpoint," she said.

Effects and contraindications

Because equol is very similar to estrogen, receptors of this hormone in the ovaries, womb, and breasts do not detect any difference, and in menopausal women, the organism does not react to lack of estrogen, which appears to be present, minimizing the symptoms.

"This is the point of obtaining compounds that mimic estrogen. They're also found in blackberry leaves, yams, and other plants. I don't know if they're more bioavailable or also require some kind of transformation to be absorbable by the organism," Macedo said.

According to existing knowledge, she added, phytoestrogen acts similarly to estrogen taken for hormone replacement therapy, albeit in far smaller doses.

"There are already products on the market based on soy extract or soy milk, and some are indicated for menopause symptoms, but they aren't effective for everyone. Every gut microbiota is different. We aim to develop a product to treat menopause symptoms that are based on

phytoestrogen and sufficiently bioavailable to be digested easily," Macedo explained.

Some cancer patients cannot take the hormone, however: breast, ovarian, and endometrial (uterine) cancer rely on estrogen to develop and grow. "Some types of prostate cancer also respond to estrogen. People with these ailments won't be able to use the products we're developing," she noted.

Next steps

According to Macedo, equol can exist in two forms: R-equol and S-equol. "Only the latter is highly absorbed, but in the process used to obtain the metabolite, we couldn't find a way to separate them, so we opted for two routes. One was identification by chromatography, which distinguishes between equol and other metabolites of interest. However, the concentration is too low to enable us to detect the two forms of the molecule separately. The other was in vitro studies involving human cancer cells to test the estrogenic effects of the extracts obtained," she said.

The cells were treated with soy extract processed using enzymes and fermentation. If they multiplied, the extract was deemed to have estrogenic effects. "The findings from the assays involving cancer cells aren't included in the latest article in *Foods*, which wasn't our first on this topic, but we plan to publish them soon," she said.

Nevertheless, the results of in vitro digestion simulation confirmed that the anti-oxidant effects and other benefits of isoflavones persisted. "We wanted to find out which process was most efficient in terms of isoflavone biotransformation and whether it was good enough to assure bioavailability and absorption by the organism. Theoretically speaking, if we simulated the digestive process effectively, the metabolite was

absorbed and circulated in the bloodstream, so I believe we're close to our goal. I want to obtain a food supplement that benefits menopausal women who don't metabolize isoflavones," Macedo concluded.

More information: Gabriela Alves Macedo et al, Bioaccessibility Evaluation of Soymilk Isoflavones with Biotransformation Processing, *Foods* (2023). DOI: 10.3390/foods12183401

Provided by FAPESP