

Foods and food supplements containing soy: health aspects

Updated BfR communication no. 36/2023 from 2 August 2023*

More and more people are eating a predominantly plant-based diet. Their diet relies partly on soy-based meat or milk substitutes, which are popular mainly because of their high protein and fat content. Furthermore, food supplements with isolated or enriched soy components are also offered in Germany.

High-dose and isolated isoflavones from soy are sold as food supplements. The BfR already saw possible health risks for certain population groups in its statement from 2015 (<https://mobil.bfr.bund.de/cm/343/nahrungsergaenzungsmittel-mit-isolierten-isoflavonen-bei-einnahme-in-und-nach-den-wechseljahren-orientierungswerte-fuer-dosierung-und-anwendungsdauer-einhalten.pdf>). This notably applies to people with acute or previously diagnosed oestrogen-dependent diseases of the mammary gland or uterus. Necessary long-term studies proving the safety of isoflavone-containing preparations are currently not available. Whether the significantly lower concentrations of isoflavones and other hormone-like substances in soy-based foods affect health has not yet been sufficiently clarified.

Allergic reactions to soy protein are among the most common food allergies. According to estimates, around 0.3-0.4 % of the population in Germany are affected by this. Therefore, foods containing soy must be labelled accordingly. Due to so-called cross-allergies, foods containing soy can also trigger severe allergic reactions in people who are allergic to birch pollen. Compared to other plant-based foods, soy products contain higher levels of metals such as cadmium and aluminium.

Overall, however, various data gaps exist, especially on actual consumption amounts of soy products. This is especially true for population groups that increasingly eat a plant-based diet. Therefore, a comprehensive assessment is not possible at this time.

1 Subject of the assessment

In this communication, the German Federal Institute for Risk Assessment (BfR) provides a brief overview of the current data situation on health aspects related to the consumption of foods containing soy in the context of a mainly plant-based diet. Furthermore, existing scientific data gaps are identified, which currently stand in the way of a comprehensive assessment of soy-containing foods.

2 Result

2.1 Assessment of the toxicological data available for a risk assessment

In connection with the consumption of foods containing soy, hormonal effects due to the phytoestrogens contained in soy are discussed in particular. Besides, primary allergic reactions to the soy protein and cross-allergies as well as the occurrence of contaminants and antinutritive

* This updated communication replaces communication no. 30/2023 from 28 June 2023

substances play a role in the assessment of possible health effects. The BfR has commented on the health effects of the phytoestrogens contained in soy several times in recent years.

2.1.1 Assessment of possible health risks from isoflavones in food

Phytoestrogens are a class of secondary plant substances that include isoflavones, which are mainly found in legumes (soy), as well as lignans and coumestans, which are found in peas and green beans, for example. Coumestans are only found to a small extent in the human diet. Isoflavones are found in numerous plants but with comparatively high levels in the soybean. Isoflavones bind directly to oestrogen receptors (ER) with a preference for ER β and can influence the endocrine system in this way. The oestrogen receptors are expressed in a tissue-specific way, so organ-specific effects may occur due to these hormonally active plant substances. In Asian countries in particular, phytoestrogens are ingested through the consumption of traditional soy foods. In the past, the average isoflavone intake in western industrialised countries was usually significantly lower. However, as a plant protein supplier and an alternative to classic meat and dairy products, foods made from the soybean are also gaining in importance here, and the consumption of soy products is continually increasing in Germany.

Food supplements with isolated or enriched isoflavones

In Germany, some food supplements, partly also foods for special medical purposes, containing isolated or enriched isoflavones are claimed to alleviate the symptoms of women with menopausal symptoms. Health claims for isoflavones submitted to the European Food Safety Authority (EFSA) have been rejected so far.

EFSA's Panel on Food Additives (ANS) assessed potential health risks from isolated isoflavones in food supplements in a comprehensive opinion in 2015. EFSA notably assessed potential health risks to menopausal and post-menopausal women from dietary supplements containing isolated isoflavones (EFSA 2015). In the opinion, EFSA discusses a number of uncertainties in the risk assessment carried out. Furthermore, EFSA sees a need for further research to clarify more precisely the safety of long-term use of preparations with isolated isoflavones in humans. (EFSA 2015). The BfR also pointed out in a statement from 2015 that the available data insufficient overall for a conclusive assessment of possible health risks in the case of higher doses and/or prolonged use of isolated isoflavones, i.e. at conditions of use (dose and duration of use) that exceed the aforementioned EFSA guidance values (BfR 2015).

Soy-based foods

So far, the BfR considered a potential health risk from the intake of isoflavones primarily for certain population groups in connection with the intake of high-dose food supplements (BfR 2007a). This assessment took into account the data available at that time as well as the consumption levels common in Germany and the resulting intake of isoflavones. With regard to the current situation, it is pointed out here that the consumption data for Germany available so far for the exposure assessment originate mainly from the National Consumption Survey NVS II (survey period 2005-2006) and that the consumption frequencies and amounts of soy foods (and various other substitutes for animal-based foods) may have been underestimated. Limited information on more recent developments can be obtained, for example, from the NEMONIT longitudinal study (national nutrition monitoring) of the Max Rubner Institute (MRI). The NEMONIT study included interviews with a selection of people who had participated in the NVS II between the years 2006 and 2015 and was designed to identify, among other things, time-dependent changes in dietary habits. With regard to the proportion of the population who

reported eating a vegetarian diet, there was an increase to just under 2 % (reference year 2012) in NEMONIT compared to NVS II (reference year 2006, around 1 %).

In terms of the health effects associated with the intake of phytoestrogens from soy products and other plant-based foods, the current scientific data situation is heterogeneous. A cursory review of current literature indicates that in a number of recent epidemiological studies, consumption of soy products, particularly tofu, is associated with a lower risk of developing and mortality from breast cancer and cardiovascular diseases (Ma *et al.* 2020; Im & Park 2021; Micek *et al.* 2021; Chen *et al.* 2023). However, a review from 2020 concluded that the data situation regarding results from human studies was inconsistent and did not provide a clear picture – although preclinical studies indicated that phytoestrogens could have health effects, particularly on the endocrine system. The authors of the review pointed out that there are open questions regarding a (further) impairment of thyroid function and thyroid hormone balance by phytoestrogens, especially in connection with an insufficient iodine intake or an already existing (subclinical) thyroid dysfunction. Moreover, changes in sex hormone levels (increase in androgens in girls and decrease in oestrogens in boys) have been described in older children in the context of a higher soy or isoflavone intake (Domínguez-López *et al.* 2020).

From the risk assessment perspective, the heterogeneity of the studies on the biological effects of phytoestrogens from food may also be due to the large number of factors that influence a possible effect of phytoestrogens. These variables include the type of phytoestrogens ingested and their concentrations as well as the food matrix through which phytoestrogens are ingested. Moreover, the individual's age, gender, health status, genetic background, metabolic capacity in terms of metabolising phytoestrogens and physiological hormonal status must be taken into account.

2.1.2 Allergies

In the general population, the prevalence of a soy allergy is estimated at 0.3-0.4 % (BfR 2007b). According to data from the Anaphylaxis Registry (Germany, Austria and Switzerland), soy is the second most common trigger of food-associated anaphylaxis in adults (Dölle *et al.* 2012). Therefore, soy is one of the allergens that must be labelled according to Regulation (EU) No. 1169/2011.

Since, in addition to primary allergic reactions to the soy protein, cross-allergies, for example, in people suffering from birch pollen allergy, can be accompanied by severe allergic symptoms, and also considering that the number of soy products on the market had steadily increased over the past decades and that a part of the population (not only people who eat a vegetarian or vegan diet) often consumed soy products as a substitute for dairy products, the BfR had already recommended in 2007 that people affected by birch pollen allergy be specifically informing about this risk (BfR 2007b).

The “VITAL Scientific Expert Panel” (VSEP) has already developed several proposals for so-called “reference doses” for certain allergens in food that are subject to mandatory labelling on the basis of already available clinical data on individual trigger doses and using various mathematical models, and most recently presented them as “VITAL 3.0” in 2019. The scientific data used for “VITAL 3.0” are based on published and unpublished clinical studies which were carried out Australia, the USA and the European Union (VSEP 2019; BfR 2020). In their model for calculating the reference doses, the authors focused on the trigger dose “ED01” (*minimal eliciting dose* 01), which states that if these calculated allergen doses were not exceeded, 99 % of

those affected by the respective food allergy would be protected from objectively measurable allergic reactions. At the same time, it is emphasised that there may be a possibility of more severe reactions occurring among a small part of the remaining people affected (around 1 %). According to “Vital 3.0”, the derived reference dose (ED01) for soy, for example, was stated as 0.5 mg protein.

Based on this scientific basis of reference doses, specific threshold values for food labelling could be derived, as far as possible, by risk management – depending on the order of magnitude, in which the remaining risk for affected consumers could be assessed as so low that it would be acceptable. The BfR has summarised and assessed and commented on the VSEP’s approach in a corresponding opinion (BfR 2020).

2.1.3 Contaminants and antinutritive substances

Soy plants can absorb certain elements from the soil. Therefore, the occurrence of undesirable substances in soy products is investigated as part of food monitoring. The investigations carried out so far show higher levels of cadmium, nickel and aluminium, among others, compared to other foods of plant origin (BVL 2018).

In the past, the BfR has dealt with cadmium and aluminium levels in soy (products). At that time, based on data from food monitoring in 2011, it was determined that the tolerable weekly intake (TWI) for cadmium is not significantly exhausted by the intake of soybeans and processed soy products, neither in the general population nor by vegetarians.

The BfR had published an opinion with regard to aluminium in infant formula and follow-on formula (BfR 2012). The statements on “infant formula with soy” are confirmed by more recent data on aluminium concentrations in soy-based infant formula and follow-on formula. The BfR does not currently have any data that would require a reassessment in this regard.

The already evaluated data from the BfR MEAL Study (Meals for Exposure Assessment and Analysis of Foods) show, using the example of nickel, that also for other substances, the increased consumption of soy-based foods can lead to a higher intake (BfR 2022b). This is also confirmed by element analyses in soy-based milk alternatives (“soy drinks”) as part of the monitoring in 2021 (BVL 2022).

Like other legumes, soybeans contain a variety of antinutritive substances. These include trypsin inhibitors and lectins, which must be deactivated by appropriate heat treatment before soy products are consumed. Another value-reducing ingredient is phytic acid, which insolubly binds minerals such as iron or zinc and can reduce the bioavailability of these minerals. Given the increase in the consumption of plant-based (substitute) products with high phytic acid concentrations, attention should be paid to an adequate mineral supply (Mayer Labba *et al.* 2022).

2.2 Evaluation of available data for exposure assessment

2.2.1 Availability of current data on the consumption of foods containing soy as part of a more plant-based diet

In the 18-64 age group, the proportion of the German population that eats a predominantly plant-based diet (vegan, vegetarian, pescetarian and flexitarian) is around 30 % in 2022. The proportion of vegetarians is given in this study as 6 %, which is significantly higher than the estimated proportion of 1 % from the National Consumption Survey II (MRI 2008) and of 2 %

from nutrition monitoring (MRI 2023). This increase in the importance of plant-based diets is supported by corresponding market statistics, according to which sales of meat substitutes in Germany increased sharply between 2015 and 2019 (Statista 2019), with a further increase predicted up to 2022. In addition to soy-based products, this also applies to other plant-based products based on grain or vegetables. For soy-based products, the increase is also reflected in a slight increase in the proportion of people consuming them in 2018-2021 (Statista 2021).

The Children's Nutrition Survey to Record Food Consumption (KiESEL Study) conducted by the BfR is the most up-to-date representative database for Germany on the food consumption of children under 6 years of age (Nowak *et al.* 2022). An analysis of the data from the questionnaire shows that dairy-free, soy-based infant formula for mixing is occasionally consumed by only 2.5 % in the group under 1-year-olds. In the age group of three years and older, the proportion of children consuming soy-based substitutes/soy drinks is 7.5 %, with about 2.5 % consuming these drinks once a week or more. Soy-based products, such as tofu, soy pudding and soy yoghurt, were consumed at least occasionally by about 20 % of the 1-to-2-year-olds and children aged 3 and above. Consumption of soy-based products at least once a week is reported for about 5 % of children in the two age groups (BfR *et al.* 2022). In view of the increase in adults cited above and in the market statistics, it can be assumed that the importance of soy-based foods has also increased further among children since 2017.

2.2.2 Availability of current data on concentrations of foods containing soy

The food list for the BfR MEAL Study (BfR 2022a) lists the following five foods whose pool samples are composed exclusively or proportionally of soy products: soy dessert, soy drink, soy protein extrudate, tofu and vegetarian sausages. Accordingly, current and representative concentration data are available for these foods from several modules, including elements, environmental contaminants and nutrients. The isoflavones relevant in the context of soy were not taken into account in the substance list of the BfR MEAL Study.

2.3 Conclusions

Hormonal effects caused by the phytoestrogens contained in soy, immunological reactions to the soy protein and toxicologically relevant effects caused by contaminants and antinutritive substances play a role in the assessment of possible health risks associated with the consumption of foods containing soy. In order to determine a quantitative risk, Both exposure assessment data and toxicological data are required.

(1) Phytoestrogens

For a reliable exposure assessment in the context of an assessment of health risks caused by phytoestrogens in food, representative data on concentrations in corresponding foods are needed. The isoflavones relevant in connection with soy, for example, were not taken into account in the substance list of the BfR MEAL Study. It would be useful to examine the extent to which occurrence data for phytoestrogens can be complemented by the German federal states' food monitoring programmes.

The BfR points out that in view of the developing market situation for plant-based products, which are consumed notably as a substitute for animal products such as milk or meat products, and the expansion of alternative plant-based protein sources (e.g. from lupins, wheat, peas, soy, etc.), more up-to-date information on the consumption behaviour of consumers is needed from national studies. The MRI's National Nutrition Survey II (NVS II), which took

place in Germany between 2005 and 2006, currently serves as the data basis regarding food consumption among adolescents and adults. Exposure assessments based on this data are likely to significantly underestimate the current consumption frequencies and quantities of soy-based foods.

There is particularly a lack of representative data on the current consumption behaviour of foods containing isoflavones as a plant-based protein source and as an alternative to classic meat and dairy products as part of an increasingly plant-based diet. From the risk assessment perspective, it seems to be important to get an impression of the importance of the consumption of soy-based products compared to other plant-based products. Information on the consumption behaviour of population groups for which a comparatively high intake of phytoestrogens can be assumed (e.g. vegans) would be of special interest.

Moreover, there is a lack of well-designed studies to better understand the effects of phytoestrogen consumption on the endocrine system at different stages of life (Domínguez-López *et al.*, 2020). In Asia, where predominantly fermented soy products, such as tempeh, miso and natto are fundamental components of the diet, intakes of up to 50 mg per day are reached. In these countries, soy consumption usually begins at an early age and leads to a more or less continuous exposure to isoflavones over the entire lifespan. On the other hand, average intakes in western countries, where soy has not been part of the traditional diet so far, are significantly lower.

(2) Other ingredients

The BfR MEAL Study can provide representative and up-to-date data on the occurrence of contaminants, additives, etc. in soy-based foods. These can be supplemented by data from food monitoring. A detailed further analysis of foods associated with a more plant-based diet could also be a useful addition to the concept presented for expanding the MEAL Study.

Overall, the BfR does not see any indications at the present time that would give grounds to revise the previous BfR opinions and the recommendations derived from them. This also applies to the BfR recommendations on soy-based infant formula. Taking into account the cursory aspects presented here, in particular also with reference to insufficient information on the exposure of different parts of the population to certain plant-based products and especially also on the consumption of soy-based products, from the BfR's point of view a comprehensive assessment of foods containing soy in the context of a more plant-based diet is currently not expedient. Due to the complexity of the topic and various data gaps and uncertainties, it would not be very meaningful at present.

Further information on nutritional risks from the BfR website

A-Z index of soy products:

https://www.bfr.bund.de/de/a-z_index/sojaprodukte-10278.html"

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About the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent institution within the portfolio of the German Federal Ministry of Food and Agriculture (BMEL). The BfR advises the Federal Government and the German federal states (“Laender”) on questions of food, chemicals, and product safety. The BfR conducts independent research on topics that are closely linked to its assessment tasks.