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TOX/2025/35

Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment

EFSA draft scientific opinion on risks for human health related to the presence of plant lectins in food

Introduction

1. The European Food Safety Authority (EFSA) published a public consultation on a draft Opinion on the risks for human health related to the presence of plant lectins in food on 24th of July 2025 (see Annex A for link). The COT are being asked to review the draft opinion and provide any comments they may have; the Secretariat will then submit the Committee's comments to EFSA.

2. A document has been provided in the Teams folder for Members to provide comments before and after the Meeting but Members can also send any additional comments directly to the Secretariat. The closing date for the public consultation is the 18th of September 2025. Please provide any comments latest by **Friday the 12th of September, comments received after this deadline will not be included**. Please add the section and/or line number where possible.

3. The following paper provides a brief overview of the draft EFSA Opinion.

Background

4. EFSA were asked by the European Commission (EC) to assess the risk posed by the consumption of plant lectins in food. EFSA have not previously performed a risk assessment of plant lectins.

5. Following a request from the Federal Ministry of Food and Agriculture (BMEL), the German Federal Institute for Risk Assessment (BfR) published a statement on the health risks related to lectins in plant-based food in 2024 (BfR, 2024). The BfR highlighted several potential adverse effects that could arise from the consumption of plant lectins, especially in children, including nausea, abdominal pain, and diarrhoea. As lectins can be deactivated through heat treatment, cooking and preparation techniques can influence the adverse effects of lectins. The BfR also highlighted the potential allergy risk from lectin consumption and recommended that the mechanism be investigated further.

6. The EFSA opinion defined lectins as 'proteins involved in the specific and reversible binding to simple and complex carbohydrates'. Whilst there are up to 13 groups of identified plant lectins, only five groups were considered within the EFSA opinion as these were regarded to have a potential risk to human health. The five groups were:

- Legume lectins: This groups includes *Lens culinaris* agglutinin (LGA) from lentil (Loris et al., 1994), Pisum sativum agglutinin (PSA) from pea (Prasthofer et al., 1989), favin from broad bean (Reeke and Becker, 1986), phytohaemagglutinin-L (PHA-L) and phytohaemagglutinin-E (PHA-E) from kidney bean (Hamelryck et al., 1996 and (Nagae et al., 2016), concanavalin A (Con A) from jack bean, soybean agglutinin (SBA) from soybean (Olsen et al., 1997), and peanut agglutinin (PNA) from peanut (Banerjee et al., 1996).

- Galanthus nivalis agglutin (GNA)-related lectins: The name for the group is derived from the snowdrop (*Galanthus spp*.) (Hester et al., 1995). The main lectins of this group relevant to the opinion were *Allium sativum* agglutinin (ASA) from garlic (Van Damme et al., 1992; Chandra et al., 1997), *Allium cepa* agglutinin (ACA) from onion, and *Allium porrum* agglutinin (APA) from leek (Van Damme et al., 1998).

- Jacalin-related lectins (JRL): This group of lectins can be found in plants of the Moraceae family and include jacalin from jackfruit (Sankaranayanan et al., 1996), artocarpin from chempedak (Pratap et al., 2002), *Maclura pomifera* agglutinin (MPA) from Osage orange (Huang et al., 2010).

- Hevein-like domain-containing lectins: this group was represented in the opinion by pokeweed mitogen PWM (Börjeson et al., 1966), and wheat germ agglutinin (WGA) from wheat (Wright, 1990).

- Type 2 ribosome-inactivating proteins (RIP-2): this group contains toxic lectins including ricin (castor bean), arbin (jequirity bean). While these are toxic and inedible, EFSA considered them as they could be consumed accidentally or intentionally.

7. In general, there were limited data available on the occurrence and consumption of active lectins within food.

Summary of 2025 EFSA draft evaluation

Toxicokinetics

8. Limited toxicokinetic studies were available in rodents.

9. Over a period of 10 days, Pusztai et al. (1990) exposed rats to 470 mg/kg bw/day of plant lectins (PHA, SBA, SNA I, SNA II (from elderberry), VFL (from broad bean)) demonstrating that around 90% of PHA travelled through the digestive tract and remained functionally active. With the exception of VFL, all lectins caused decreased body weight gain.

10. A study by Nakata and Kimura (1985), exposed Wistar rats to Con A (2%) for 24 hours before resuming a normal diet. After 72 hours approximately 63% of the Con A was detected in faeces. A second study by

the same authors exposed rats to 50 mg Con A in 5 g feed before fasting for 24 hours and then returning to a normal diet. Faeces were collected at 24-hour intervals until 120 hours and results indicated that >89% of Con A passed unchanged through the digestive tract.

11. Kilpatrick et al. (1985) studied the absorption of tomato lectins by feeding Lister rats fresh tomato (5% tomato lectin) over 10 days and active tomato lectin could be identified within the faeces. In a follow up study, rats were fed I^{125}-labelled tomato lectin and lectin was found to be the highest in the stomach and epithelium directly after consumption, with up to 60% of the tomato lectin being in the small intestine and epithelium after 1.5 hours, and 25% identified within the colon and epithelium after 3 hours. The authors concluded that most of the tomato lectin remained unchanged and passed through the gastrointestinal (GI) tract, this was further supported by the results showing that only 3% of the radioactive labelled tomato lectin was found within the body 3 hours after consumption, mainly within the serum and liver.

12. EFSA concluded that based on the studies available absorption of lectins was low and lectins remained structurally intact when passing through the GI tract. Within rodents there was no evidence of degradation of lectins as the lectins were found to retain biological activity and be functionally active after passing through the digestive tract.

13. Whilst there were limited studies available on the toxicokinetics of active lectins in humans, EFSA concluded that the evidence available on peanut agglutin (PNA) and wheat germ agglutin (WGA) suggested that absorption occurred in the upper GI tract. Studies also highlighted immunoglobulin G (IgG) and immunoglobulin M (IgM) responses which correlated with the consumption of lectins or proteins, suggesting that consumption of lectins may lead to increased translocation of dietary antigens.

Acute toxicity studies

14. In a study by Nakata and Kimura (1985) Wistar rats were given reduced feed for 48 hours before being fed 5 g of diet food with 25 mg Con A. The study demonstrated that intestinal enzyme activities remained the same or were reduced after Con A exposure, when compared to the control subjects, while the activity of enzymes such as sucrase and leucine aminopeptidase were shown to increase. The authors considered that Con A binds to the surface of the small intestine and disturbs the brush border membrane. A study by Larue-Achagiotis et al. (1992) exposing Wistar rats to Con A reported reduced food consumption when animals were given an equivalent dose of 3600 mg/kg bw.

15. There were no acute studies on PHA or soybean agglutin (SBA) available.

16. The lectins evaluated by EFSA exhibited similar toxic effects, i.e. as a result of lectin consumption animals demonstrated reduced body weight gain or reduced feed intake. EFSA highlighted that reduced body weight gain may be a side effect of reduced feed intake or digestibility. The studies also indicated that the retention of nitrogen may be lowered which could contribute to antinutritive effects.

Repeat dose toxicity studies

General toxicity

17. Zang et al. (2006a and 2006b), and Li et al (2003a and 2003b) conducted dose response studies exposing SD rats to SBA at doses between 10 and 187 mg/kg bw/day and found that pancreas weight increased at doses of 44 mg/kg bw/day and above. Kelsall et al. (2002) conducted a 24-week study on PNA in rats at 0.1 mg/kg and found a relative pancreas weight increase (+18%) while Bardocz et al. (1995) studied the effect of PHA on Lister rats and found the pancreas weight increased at doses of 32.5 mg/kg bw/day and above. In addition to this Bardocz et al. (1995; 1996) conducted

studies in rats which reported reduced body weight gain at PHA levels of 7 mg/kg and above.

18. EFSA identified two endpoints as the most sensitive, increased weight of the pancreas, and hypertrophy of the exocrine pancreas.

Gastrointestinal toxicity

19. The toxicological effects of lectins are dependent on binding specificity. PHA was reported to damage microvilli, villi and crypts at doses of 3mg/kg bw/day, and Con A was shown to damage microvilli, villi and crypts at doses of 8 mg/kg bw/day. Bardocz et al. (1995) reported an increase of small intestine weights when rats were dosed with PHA at levels of 32.5 mg/kg bw/day and above. In PND14 rats at dosage levels of 50 mg/kg and above, PHA has shown to affect body weight gain, liver and pancreas weights, maturation of the gastrointestinal tract and the immune system. At levels of 2 mg/kg bw/day, PHA has been shown to alter small intestine morphology. SBA has also been associated with increased small intestine length at doses of 112 mg/kg bw/day and above. Pita-Lopez et al. (2020) studied SD rats over 6 weeks with an average dose of tepary bean lectin fraction of approximately 20 mg/kg bw/day. Results showed a decrease in the microbial diversity of the faeces. EFSA noted that the omission of lectin from the diet would reverse many of the effects on the gut.

20. EFSA highlighted that consumption of lectins may lead to an antibody response which could trigger an allergic response. This had been shown after administration of PHA (0.5 mg/kg bw) and SBA (60 mg/kg bw/day) in rodents.

21. There were few studies investigating the carcinogenic potential of lectins. Kelsall et al. (2002) investigated intestinal carcinogenesis of PNA, and no evidence was found, supporting EFSAs conclusion that genotoxicity would not be expected via direct DNA interaction as lectins are proteins.

Observations in Humans

22. The limited number of human studies available studied the exposure to non-purified lectins and their effect on metabolism, allergy and gastrointestinal system. None of the studies were quantitative and they all had limitations, including a lack of relevant control groups and no quantitative lectin identification. Allergenicity studies on lectin consumption were either skin prick tests or IgE antibody assays.

23. EFSA stated that cross reactivity may occur from lectins in edible plants or consumers allergic to other lectins.

Mode of action

24. The adverse effects of lectins are dependent on a) structure and carbohydrate binding activity, b) number of carbohydrate binding sites, c) overall lectin content, and d) arrangement of sub-units and their interaction with glycans. By binding to carbohydrate moieties within the gut epithelial cells, lectins can affect the microvilli, villi and crypts. It has further been suggested that as a result of lectin consumption, the exocrine pancreas may produce digestive juice and grow due to the release of cholecystokinin from enteroendocrine cells into the bloodstream.

25. Lectins have demonstrated that they are capable of binding to the gut epithelial cells. Lectins have also been thought to be involved in the induction of autoimmune and allergic responses as a result of their effect on the gut barrier and microbiota. The animal species and the amount of lectin within the circulation would thereby affect the type of immune response.

26. EFSA considered that lectins could modulate intracellular/intercellular signalling pathways by binding to gut receptors which may affect viability.

Occurrence data and dietary exposure assessment for the European population

27. Due to the lack of toxicological information on most lectins, the dietary exposure assessment focused on phytohaemagglutinin (PHA) only. The occurrence data used in EFSA's exposure assessment came thereby from a study by Bognolia et al. (2008) which identified PHA within kidney beans at a level of 24.9 mg/g. The authors believed this concentration to be representative of all beans within the *Phaseolus sp.* including runner beans and French beans. EFSA considered this value appropriate/representative as Bognolia et al. used enzyme-linked immunosorbent assay (ELISA) to only quantified active lectins, for an acute dietary exposure calculation the highest end of the concentration data was required.

28. The EFSA Comprehensive European Food Consumption Database was used to calculate the highest acute dietary exposure to PHA, which in this assessment was for 'other children' and 'toddlers'. The exposure was estimated for separate food items, i.e. lima beans, borlotti or other common beans, beans and vegetables meal, within different population categories and consumption days.

29. EFSA considered different exposure scenarios in their assessment, focussing on the processing of lectins. Exposure scenario one considered beans within the *Phaseolus sp* that had been adequately processed, mainly through soaking and boiling. EFSA assumed that if correct processing procedures had been followed, the lectins would no longer be active and therefore no risk would arise from consumption. Therefore, no dietary exposure was estimated for scenario one. The second scenario considered that adequate processing practices had not been applied, and therefore the lectins remained active. Within scenario 2, EFSA chose a value of 50% to represent the lectins that would remain active. EFSA therefore estimated that the highest mean exposure would be 23.5 mg/kg bw day and 35.0 mg/kg bw per day for 'Borlotti or other common beans (dry)', and 'Lima beans (dry)', respectively.

Risk characterisation

30. For lectins, EFSA agreed that a health-based guidance value (HBGV) would not be suitable as the available information on both toxicological and occurrence data were not sufficient. Hence, a margin of exposure (MOE) approach was applied. An MOE of 100 was considered to be safe as it would account for animal and human differences, as well as differences between humans.

31. Based on the limited data available on plant lectins, EFSA considered PHA the most toxic of the lectins of edible plants due to its specificity to bind complex glycans containing a bisecting N-acetylglucosamine and its high affinity to human enterocytes. Hence, the risk characterisation was performed on PHA only.

32. A $BMDL_{10}$ value of 22.9 mg/kg bw/day for an increase in small intestine dry weight was selected from a study by Bardocz et al. (1995) to use as the reference point for PHA. EFSA calculated an MOE of 0.3 based on the BMDL of 22.9 mg/kg bw/day and the highest percentile exposure of 75.8 mg/kg bw/day (from the consumption of 'beans and vegetables meal' in the category 'other children').

33. The MOE (0.3) for PAH was below the MOE considered to be safe (> 100). therefore, at a level of 50% deactivation of PHA would be considered a health risk. As no sufficient toxicological data was available for other lectins, no conclusions on their risk could be reached. However, EFSA agreed that for foods that had been prepared in line with adequate food preparation, there was no health concerns from exposure to deactivated lectins.

Uncertainty analysis

34. An uncertainty analysis was performed that concluded, with at least 95% certainty, that under the scenario of 50% deactivation, PHA would pose

a health concern. The Panel agreed that this would also be true for all age groups.

Recommendations

35. EFSA recommended that for the quantification of active and non-active lectins, the development and validation of analytical methods was needed. In addition to this, studies using PHA were needed for information on absorption, distribution, metabolism, and excretion (ADME), immunotoxicity, and gastrointestinal endpoints in humans and rodents. Further information was also required for an in-depth exposure assessment.

Questions on which the views of the Committee are sought

36. Members are invited to consider the following questions:

i). Do Members agree with the MOE approach used by EFSA?

ii). Do Members agree with the recommendations by EFSA?

iii) Do Members have any further comments?

Secretariat
September 2025

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List of Abbreviations

Abbreviation	Definition
ACA	*Allium cepa* agglutinin
ADME	Absorption, Distribution, Metabolism, and Excretion
APA	*Allium porrum* agglutinin
ASA	*Allium sativum* agglutinin
BfR	German Federal Institute for Risk Assessment
BMEL	Federal Ministry of Food and Agriculture
Con A	Concanavalin A
EC	European Commission
EFSA	European Food Safety Authority
ELISA	Enzyme-linked immunosorbent assay
GI	Gastrointestinal
GNA	Galanthus nivalis agglutin
IgG	Immunoglobulin G
IgM	Immunoglobulin M
JRL	Jacalin-related lectins
LGA	*Lens culinaris* agglutinin
PHA	Phytohemagglutinin
PHA-E	Phytohaemagglutinin-E
PHA-L	Phytohaemagglutinin-L
PNA	Peanut agglutinin
PSA	Pisum sativum agglutinin
RIP-2	Type 2 ribosome-inactivating proteins
SBA	Soybean agglutinin
WGA	Wheat germ agglutinin

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Annex A to TOX/2025/35

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

EFSA draft scientific opinion on risks for human health related to the presence of plant lectins in food

Link to the draft EFSA opinion:
Public Consultation

Secretariat

September 2025