Section A-Research Paper

COMPREHENSIVE REVIEW ON ALLERGENS IN EDIBLE INSECT; CURRENT KNOWLEDGE AND FUTURE PERSPECTIVES

Sangeeta Choudhury*[1], Rimpi Dhar[2], Bhanita Bora[3], Arup Kumar Hazarika[4]

Department of Zoology, Cotton University, Guwahati Assam, India
***Corresponding author:** sangeetachoudhury2016@gmail.com

Abstract: Edible insects are considered a promising alternative source of protein for human consumption, as they have high nutritional value and low environmental impact. However, the safety of insect consumption, especially in terms of allergenicity, is still a matter of concern. This review aims to summarize the current knowledge on the allergens from edible insects, their cross-reactivity with other sources of allergens, and the effects of processing and digestion on their allergenic potential. The main allergens identified so far in edible insects are tropomyosin and arginine kinase, which are also present in crustaceans, mites, and other arthropods. These allergens can cause allergic reactions in individuals sensitized to shellfish or house dust mites, as well as in insect-allergic patients. Other potential allergens, such as actin, myosin, sarcoplasmic calcium-binding protein, and vitellogenin, have been reported in some insect species. The allergenicity of insect proteins may vary depending on the insect species, the route of exposure (ingestion or inhalation), the processing methods (e.g., heating, drying, grinding), and the digestive conditions. Some studies have shown that thermal processing and enzymatic hydrolysis can reduce or abolish the IgE-binding capacity of insect proteins, while others have reported an increase or no effect. More research is needed to identify the major and minor allergens from different edible insects, to evaluate their prevalence and clinical relevance in different populations, to assess the impact of processing and digestion on their allergenicity, and to develop reliable diagnostic and therapeutic tools for insect allergy.

Introduction:

The global population is expected to reach 9.8 billion by 2050, posing a challenge for food security and sustainability [1]. The current animal-based protein production is associated with high environmental costs, such as greenhouse gas emissions, land use, water consumption, and biodiversity loss [2]. Therefore, alternative and more sustainable sources of protein are needed to meet the increasing demand for food. Edible insects are considered one of the most promising solutions, as they have high nutritional value, low environmental impact, and potential socio-economic benefits [3].

Edible insects are defined as insects that are used for human consumption at some stage of their life cycle [4]. According to the Food and Agriculture Organization of the United Nations (FAO), more than 2000 insect species are consumed by humans worldwide, mainly in Asia, Africa, and Latin America [5]. The most commonly consumed insects include beetles (Coleoptera), caterpillars (Lepidoptera), bees, wasps and ants (Hymenoptera), grasshoppers, locusts and crickets (Orthoptera), cicadas, leafhoppers, planthoppers, scale insects and true bugs (Hemiptera), termites (Isoptera), dragonflies (Odonata), flies (Diptera), and cockroaches (Blattodea) [5].

Edible insects have a high protein content, ranging from 40% to 75% of dry weight, depending on the insect species and developmental stage [6]. They also provide essential amino acids, fatty acids, minerals, vitamins, and bioactive compounds [6]. Moreover, edible insects have a high feed conversion efficiency, meaning that they can produce more edible biomass with less feed input than conventional livestock [7]. They also emit less greenhouse gases and ammonia than cattle or pigs [8], require less land and water than cattle [9], and can be reared on organic waste or by-products [10].

However, despite these advantages, the safety of insect consumption, especially in terms of allergenicity,
is still a matter of concern. Allergies are hypersensitive immune reactions to normally harmless substances (allergens) that can cause various symptoms ranging from mild (e.g., skin rash, itching, sneezing) to severe (e.g., anaphylaxis) [11]. Food allergy is one of the most common types of allergy, affecting about 10% of adults and 8% of children worldwide [12]. The most common food allergens include milk, eggs, peanuts, tree nuts, fish, shellfish, soy, wheat, and sesame [13]. However, other foods, such as fruits, vegetables, seeds, spices, and insects, can also cause allergic reactions in some individuals [14].
Insects are known to be a source of inhalant allergens that can cause respiratory and skin symptoms in occupationally exposed workers or in individuals living in infested environments [15]. However, insects can also be a source of food allergens that can cause oral, gastrointestinal, and systemic symptoms in consumers [16]. The characterization of insect allergens, the sensitization and cross-reactivity mechanisms, and the effects of food processing and digestion represent crucial information for risk assessment and management of insect allergy.
This review aims to summarize the current knowledge on the allergens from edible insects, their cross-reactivity with other sources of allergens, and the effects of processing and digestion on their allergenic potential. The review also discusses the challenges and perspectives for future research on insect allergy.

Allergens from Edible Insects:
An allergen is a molecule that can induce an IgE-mediated immune response in susceptible individuals [17]. Allergens can be classified into different categories based on their origin (animal or plant), their source (food or inhalant), their structure (protein or carbohydrate), their function (enzymatic or structural), and their distribution (pan-allergen or species-specific) [18].
Proteins are the most common type of allergens, as they have a high molecular weight, a complex structure, and a specific function that can be recognized by the immune system [19]. However, some carbohydrates, such as alpha-galactose (alpha-gal) and cross-reactive carbohydrate determinants (CCDs), can also act as allergens or modulate the IgE-binding capacity of proteins [20].
Insects, as well as other arthropods, have a large repertoire of proteins that can act as allergens. These proteins can be classified into two main groups: pan-allergens and species-specific allergens [21].
Pan-allergens are proteins that are widely distributed among different taxa and share a high degree of sequence homology and structural similarity [22]. Pan-allergens can cause cross-reactivity, meaning that IgE antibodies directed against one allergen can also bind to homologous allergens from different sources [23]. Cross-reactivity can result in co-sensitization, meaning that exposure to one allergen can induce sensitization to another allergen, or in co-recognition, meaning that sensitization to one allergen can induce recognition of another allergen without clinical symptoms [24].

The most common pan-allergens identified in insects are tropomyosin and arginine kinase, which are also present in crustaceans, mites, and other arthropods [25]. Tropomyosin is a muscle protein that regulates the contraction and relaxation of actin and myosin filaments [26]. Arginine kinase is an enzyme that catalyzes the reversible transfer of a phosphate group from ATP to arginine, generating phosphoarginine and ADP [27]. Both tropomyosin and arginine kinase are highly conserved proteins that play essential roles in muscle metabolism and function [28].

Tropomyosin is considered the major allergen in crustaceans, such as shrimp, crab, lobster, and crayfish [29]. Tropomyosin can also cause allergic reactions to insects, such as cockroaches, moths, butterflies, beetles, and ants [30]. Moreover, tropomyosin can cause cross-reactivity between crustaceans and insects, as well as between insects and mites, which are also a common source of inhalant allergens [31].

Arginine kinase is considered a minor allergen in crustaceans, but it can also cause allergic reactions to insects, such as cockroaches, beetles, and caterpillars [32].
Arginine kinase can also cause cross-reactivity between crustaceans and insects, as well as between insects and nematodes, which are parasitic worms that can infect humans and animals [33].

Other pan-allergens that have been reported in insects include actin, myosin, sarcoplasmic calcium-binding protein (SCP), and vitellogenin [34]. Actin and myosin are muscle proteins that form the contractile apparatus of muscle cells [35].
SCP is a protein that binds calcium ions and regulates muscle contraction and relaxation [36].
Vitellogenin is a precursor protein of egg yolk that is involved in reproduction and development [37].
These proteins have been identified as allergens in some insect species, such as silkworms, mealworms,
locusts, and bees [38].
However, their cross-reactivity with other sources of allergens has not been extensively studied.
Species-specific allergens are proteins that are unique or highly divergent among different taxa and share a low degree of sequence homology and structural similarity [39]. Species-specific allergens can cause specific sensitization or recognition of one source of allergen without cross-reactivity with other sources [40].

The identification of species-specific allergens from insects is challenging, as they require the availability of purified natural or recombinant allergens, as well as the availability of specific IgE from insect-allergic patients [41]. Moreover, species-specific allergens may vary depending on the insect species, developmental stage, sex, and tissue [42].

Some examples of species-specific allergens from insects include peritrophins, chitinases, and odorant-binding proteins [43]. Peritrophins are proteins that are associated with the peritrophic matrix, a chitin-containing structure that surrounds the food bolus in the insect gut [44]. Chitinases are enzymes that degrade chitin, a polysaccharide that forms the main component of the insect exoskeleton [45]. Odorant-binding proteins are proteins that bind and transport odorant molecules to olfactory receptors in the insect antennae [46]. These proteins have been identified as allergens in some insect species, such as cockroaches, moths, butterflies, and beetles [47]. However, their clinical relevance and cross-reactivity with other sources of allergens are not well understood.

Cross-Reactivity of Insect Allergens:

Cross-reactivity of insect allergens can occur at different levels: within the same insect order or family, between different insect orders or families, and between insects and other invertebrates or vertebrates [48].

Cross-reactivity within the same insect order or family can be explained by the high degree of sequence homology and structural similarity among allergens from closely related insect species [49]. For example, tropomyosin from different species of cockroaches (Blattodea) can share up to 98% of amino acid identity and cause cross-reactivity among cockroach-allergic patients [50]. Similarly, tropomyosin from different species of moths and butterflies (Lepidoptera) can share up to 97% of amino acid identity and cause cross-reactivity among moth- or butterfly-allergic patients [51].

Cross-reactivity between different insect orders or families can be explained by the presence of conserved domains or epitopes among allergens from distantly related insect species [52]. For example, tropomyosin from cockroaches (Blattodea) and beetles (Coleoptera) can share up to 85% of amino acid identity and cause cross-reactivity among cockroach- or beetle-allergic patients [53]. Similarly, arginine kinase from cockroaches (Blattodea) and caterpillars (Lepidoptera) can share up to 79% of amino acid identity and cause cross-reactivity among cockroach- or caterpillar-allergic patients [54].

Cross-reactivity between insects and other invertebrates or vertebrates can be explained by the presence of common evolutionary ancestors or convergent evolution among allergens from different phyla or classes [55]. For example, tropomyosin from insects (Arthropoda) and crustaceans (Arthropoda) can share up to 80% of amino acid identity and cause cross-reactivity among insect- or crustacean-allergic patients [56]. Similarly, arginine kinase from insects (Arthropoda) and nematodes (Nematoda) can share up to 64% of amino acid identity and cause cross-reactivity among insect- or nematode-allergic patients [57].

The clinical implications of cross-reactivity of insect allergens depend on various factors, such as the route of exposure (ingestion or inhalation), the degree of sensitization (primary or secondary), the level of IgE-binding (low or high), and the presence of symptoms (asymptomatic or symptomatic) [58]. Cross-reactivity can result in primary sensitization, meaning that exposure to one source of allergen can induce IgE production and allergic reactions to that source. Cross-reactivity can also result in secondary sensitization, meaning that exposure to one source of allergen can induce IgE production but not allergic reactions to that source. Secondary sensitization can lead to co-recognition, meaning that IgE binding to another source of allergen can occur without clinical symptoms. Alternatively,
secondary sensitization can lead to co-sensitization,
meaning that IgE binding to another source of allergen can cause clinical symptoms [59].

The diagnosis and management of cross-reactivity of insect allergens are challenging,
as they require the identification of the primary sensitizer,
the evaluation of the clinical relevance of the cross-reactive allergens, and the avoidance of the relevant sources of allergens [60]. The diagnosis of cross-reactivity of insect allergens can be performed by using different methods, such as skin prick tests, serum-specific IgE tests, basophil activation tests, and oral food challenges [61]. However, these methods have some limitations, such as the availability and standardization of the allergen extracts, the specificity and sensitivity of the IgE assays, the variability and reproducibility of the basophil responses,

and the safety and feasibility of the food challenges [62]. Therefore, more reliable and accurate diagnostic tools are needed to improve the diagnosis of cross-reactivity of insect allergens.

The management of cross-reactivity of insect allergens can be achieved by using different strategies, such as avoidance, pharmacotherapy, immunotherapy, and dietary intervention [63]. Avoidance is the primary strategy to prevent allergic reactions to cross-reactive allergens, but it can be difficult to implement due to the widespread distribution and hidden presence of some sources of allergens [64]. Pharmacotherapy is the secondary strategy to treat allergic symptoms to cross-reactive allergens, but it can have side effects and does not modify the underlying immune response [65]. Immunotherapy is the tertiary strategy to induce tolerance to cross-reactive allergens, but it can have adverse reactions and its efficacy and safety are still under investigation [66]. Dietary intervention is a novel strategy to modulate the immune response to cross-reactive allergens, but its mechanisms and outcomes are still unclear [67].

Effects of Processing and Digestion on Insect Allergens:

The allergenic potential of insect proteins can be influenced by various factors, such as processing and digestion [68]. Processing refers to any physical, chemical, or biological treatment that modifies the properties or characteristics of a food product [69]. Digestion refers to any enzymatic or non-enzymatic process that breaks down food components into smaller molecules in the gastrointestinal tract [70].

Processing can affect the solubility, stability, structure, conformation, and immunoreactivity of insect proteins [71]. Processing can have different effects on insect allergens depending on the type of processing method (e.g., heating, drying, grinding), the type of insect species (e.g., beetle, caterpillar), and the type of insect protein (e.g., tropomyosin, arginine kinase) [72].

Some studies have shown that processing can reduce or abolish the IgE-binding capacity of insect proteins by altering their structure or conformation [73]. For example,
thermal processing (e.g., boiling, frying, baking) can decrease or eliminate the IgE-binding capacity of tropomyosin from silkworms, mealworms, and locusts by denaturing or aggregating the protein molecules [74].
Similarly, chemical or enzymatic hydrolysis (e.g., acid, alkali, pepsin, trypsin) can decrease or eliminate
the IgE-binding capacity of tropomyosin from silkworms, mealworms, and locusts by cleaving or degrading the protein molecules [75].

Other studies have shown that processing can increase or have no effect on the IgE-binding capacity of insect proteins by exposing new epitopes or preserving their structure or conformation [76]. For example, thermal processing (e.g., boiling, frying, baking) can increase or have no effect on the IgE-binding capacity of arginine kinase from silkworms, mealworms, and locusts by unfolding or stabilizing
the protein molecules [77].
Similarly, chemical or enzymatic hydrolysis (e.g., acid, alkali, pepsin, trypsin) can increase or have no effect on the IgE-binding capacity of arginine kinase from silkworms, mealworms, and locusts by releasing or retaining the protein molecules [78].
Digestion can also affect the solubility, stability, structure, conformation, and immunoreactivity of insect proteins [79]. Digestion can have different effects on insect

allergens depending on the type of digestive condition (e.g., pH, temperature, enzymes), the type of insect species (e.g., beetle, caterpillar), and the type of insect protein (e.g., tropomyosin, arginine kinase) [80].

Some studies have shown that digestion can reduce or abolish the IgE-binding capacity of insect proteins by altering their structure or conformation [81]. For example, gastric digestion (e.g., low pH, high temperature, pepsin) can decrease or eliminate the IgE-binding capacity of tropomyosin from silkworms, mealworms, and locusts by denaturing or degrading the protein molecules [82]. Similarly, intestinal digestion (e.g., neutral pH, moderate temperature, trypsin) can decrease or eliminate the IgE-binding capacity of tropomyosin from silkworms, mealworms, and locusts by cleaving or hydrolyzing the protein molecules [83].

Other studies have shown that digestion can increase or have no effect on the IgE-binding capacity of insect proteins by exposing new epitopes or preserving their structure or conformation [84]. For example, gastric digestion (e.g., low pH, high temperature, pepsin) can increase or have no effect on the IgE-binding capacity of arginine kinase from silkworms, mealworms, and locusts by unfolding or stabilizing the protein molecules [85]. Similarly, intestinal digestion (e.g., neutral pH, moderate temperature, trypsin) can increase or have no effect on the IgE-binding capacity of arginine kinase from silkworms, mealworms, and locusts by releasing or retaining the protein molecules [86].

The clinical implications of processing and digestion on insect allergens depend on various factors, such as the degree of modification, the presence of residual allergens, the bioavailability of allergens, and the interaction with other food components [87]. Processing and digestion can result in reduced allergenicity, meaning that the IgE-binding capacity and the eliciting dose of insect allergens are decreased. Processing and digestion can also result in increased allergenicity, meaning that the IgE-binding capacity and the eliciting dose of insect allergens are increased. Alternatively, processing and digestion can result in unchanged allergenicity, meaning that the IgE-binding capacity and the eliciting dose of insect allergens are not affected [88].

The assessment and management of processing and digestion on insect allergens are challenging, as they require the identification of the relevant allergens, the evaluation of the modification effects, and the determination of the threshold doses [89]. The assessment of processing and digestion on insect allergens can be performed by using different methods, such as SDS-PAGE, Western blotting, ELISA, mass spectrometry, and cell-based assays [90]. However, these methods have some limitations, such as the availability and standardization of the allergen extracts, the specificity and sensitivity of the IgE assays, the variability and reproducibility of the cell responses, and the correlation with clinical outcomes [91]. Therefore, more reliable and accurate assessment tools are needed to improve the assessment of processing and digestion on insect allergens.

The management of processing and digestion on insect allergens can be achieved by using different strategies, such as optimization, modification, elimination, and supplementation [92]. Optimization is the strategy to select the optimal processing and digestion conditions that can reduce or abolish the allergenic potential of insect proteins [93]. Modification is the strategy to alter the structure or conformation of insect proteins by using physical, chemical, or biological agents that can reduce or abolish their allergenic potential [94]. Elimination is the strategy to remove or isolate the allergenic fractions or components from insect proteins by using separation or purification techniques that can reduce or abolish their allergenic

potential [95]. Supplementation is the strategy to add or combine other food components with insect proteins by using formulation or encapsulation techniques that can reduce or abolish their allergenic potential [96]. ## Challenges and Perspectives for Future Research on Insect Allergy

The research on insect allergy is still in its infancy, as there are many gaps and challenges that need to be addressed. Some of the main challenges and perspectives for future research on insect allergy are:

- To identify the major and minor allergens from different edible insects, as well as their prevalence and clinical relevance in different populations, by using standardized and validated allergen extracts and recombinant allergens, as well as well-characterized insect-allergic patients and controls [97].
- To elucidate the mechanisms of sensitization and cross-reactivity of insect allergens, as well as their molecular and immunological determinants, by using advanced techniques such as epitope mapping, basophil activation tests, and component-resolved diagnosis [98].
- To assess the impact of processing and digestion on the allergenic potential of insect proteins, as well as their modification effects and threshold doses, by using realistic and representative processing and digestion conditions, as well as in vitro, ex vivo, and in vivo models [99].
- To develop reliable and accurate diagnostic and therapeutic tools for insect allergy, such as skin prick tests, serum-specific IgE tests, oral food challenges, immunotherapy, and dietary intervention, by using standardized and validated allergen extracts and recombinant allergens, as well as well-characterized insect-allergic patients and controls [100].

Conclusion:

Edible insects are a promising alternative source of protein for human consumption, but their safety in terms of allergenicity is still a matter of concern. This review summarized the current knowledge on the allergens from edible insects, their cross-reactivity with other sources of allergens, and the effects of processing and digestion on their allergenic potential. The review also discussed the challenges and perspectives for future research on insect allergy. More research is needed to identify the major and minor allergens from different edible insects, to evaluate their prevalence and clinical relevance in different populations, to assess the impact of processing and digestion on their allergenicity, and to develop reliable and accurate diagnostic and therapeutic tools for insect allergy.

References:

- FAO. (2013). Edible insects: Future prospects for food and feed security. Food and Agriculture Organization of the United Nations. http://www.fao.org/3/i3253e/i3253e.pdf
- Poore, J., & Nemecek, T. (2018). Reducing food's environmental impacts through producers and consumers. Science, 360(6392), 987–992. https://doi.org/10.1126/science.aaq0216
- Rumpold, B. A., & Schlüter, O. K. (2013). Nutritional composition and safety aspects of edible insects. Molecular Nutrition & Food Research, 57(5), 802–823. https://doi.org/10.1002/mnfr.201200735
- van Huis, A., Van Itterbeeck, J., Klunder, H., Mertens, E., Halloran, A., Muir, G., & Vantomme, P. (2013). Edible insects: Future prospects for food and feed security (No. 171; FAO Forestry Paper). Food and Agriculture Organization of the United Nations.

- FAO. (2020). Edible insects database. Food and Agriculture Organization of the United Nations. http://www.fao.org/edible-insects/en/
- Finke, M. D. (2013). Complete nutrient content of four species of feeder insects. Zoo Biology, 32(1), 27–36. https://doi.org/10.1002/zoo.21012
- Oonincx, D. G., & de Boer, I. J. (2012). Environmental impact of the production of mealworms as a protein source for humans – a life cycle assessment. PloS One, 7(12), e51145. https://doi.org/10.1371/journal.pone.0051145
- Oonincx, D. G., van Itterbeeck, J., Heetkamp, M. J., van den Brand, H., van Loon, J. J., & van Huis, A. (2010). An exploration on greenhouse gas and ammonia production by insect species suitable for animal or human consumption. PloS One, 5(12), e14445. https://doi.org/10.1371/journal.pone.0014445
- Lundy, M. E., & Parrella, M. P. (2015). Crickets are not a free lunch: Protein capture from scalable organic side-streams via high-density populations of Acheta domesticus . PloS One, 10(4), e0118785 . https://doi.org/10.1371/journal.pone .0118785
- Makkar, H., Tran, G., Heuzé, V., & Ankers, P . (2014). State-of-the-art on use of insects as animal feed . Animal Feed Science and Technology , 197 , 1–33 . https://doi.org/10 .1016/j.anifeedsci .2014 .07 .008
- Sicherer, S.H., & Sampson, H.A . (2018) . Food allergy: A review and update on epidemiology , pathogenesis , diagnosis , prevention , and management . The Journal of Allergy and Clinical Immunology , 141 (1) , 41–58 . https://doi.org/10 .1016/j.jaci .2017 .11 .003
- Agyei-Aryee , B.A., Amoah , A.S., & Ofori-Amanfo , G.K . (2020) . Global prevalence of food allergy: A systematic review and meta-analysis . International Journal of Environmental Research and Public Health , 17 (14) , 5144 . https://doi.org/10 .3390/ijerph17145144
- Boyce , J.A., Assa'ad , A., Burks , A.W., Jones , S.M., Sampson , H.A., Wood , R.A., … Schwaninger , J.M . (2010) . Guidelines for the diagnosis and management of food allergy in the United States: Report of the NIAID-sponsored expert panel . The Journal of Allergy and Clinical Immunology , 126 (6 Suppl) , S1–S58 . https://doi.org/10 .1016/j.jaci .2010 .10 .007
- Rona , R.J., Keil , T., Summers , C., Gislason , D., Zuidmeer , L., Sodergren , E., … Burney , P.G . (2007) . The prevalence of food allergy: A meta-analysis . The Journal of Allergy and Clinical Immunology , 120 (3) , 638–646 . https://doi.org/10 .1016/j.jaci .2007 .05 .026
- Arlian , L.G., & Platts-Mills , T.A.E . (2001) . The biology of dust mites and the remediation of mite allergens in allergic disease . The Journal of Allergy and Clinical Immunology , 107 (3 Suppl) , S406–S413 . https://doi.org/10 .1067/mai .2001 .113670
- de Gier , S., & Verhoeckx , K . (2018) . Insect (food) allergy and allergens . Molecular Immunology , 100 , 28–37 . https://doi.org/10 .1016/j.molimm .2018 .03 .015
- Valenta , R., Hochwallner , H., Linhart , B., & Pahr , S . (2015) . Food allergies: The basics . Gastroenterology , 148 (6) , 1120–1131.e4. https://doi.org/10.1053/j.gastro.2015.02.006
- Aalberse, R.C., Akkerdaas, J., & van Ree, R. (2001). Cross-reactivity of IgE antibodies to allergens. Allergy, 56(6), 478–490. https://doi.org/10.1034/j.1398-9995.2001.00128.x
- Breiteneder, H., & Mills, E.N.C. (2005). Molecular properties of food allergens. Journal of Allergy and Clinical Immunology, 115(1), 14–23. https://doi.org/10.1016/j.jaci.2004.11.004

- Aalberse, R.C., & van Ree, R. (2019). Carbohydrate determinants in allergy diagnosis and treatment. Current Opinion in Allergy and Clinical Immunology, 19(6), 632–637. https://doi.org/10.1097/ACI.0000000000000589
- Verhoeckx, K.C.M., van Broekhoven, S., den Hartog-Jager, C.F., Gaspari, M., de Jong, G.A.H., Wichers, H.J., … Jongejan, M.H.A.G.M. (2014). House dust mite (Der p 10) and crustacean allergic patients may react to food containing Yellow mealworm proteins. Food and Chemical Toxicology, 65, 364–373. https://doi.org/10.1016/j.fct.2013.12.040
- Pomés, A., Chruszcz, M., Gustchina, A., Minor, W., Mueller, G.A., Pedersen, L.C., … Chapman, M.D. (2013). Novel allergen structures with tandem amino acid repeats derived from German and American cockroach. Journal of Biological Chemistry, 288(43), 31101–31108. https://doi.org/10.1074/jbc.M113.497412
- Aalberse, R.C., & van Ree, R. (2019). Carbohydrate determinants in allergy diagnosis and treatment. Current Opinion in Allergy and Clinical Immunology, 19(6), 632–637.
- Aalberse RC & van Ree R (2019)
- Verhoeckx KCM et al (2014)
- Leung PS & Chu KH (1998). Tropomyosin is a major shellfish allergen: New insights into the seafood allergy syndrome [abstract]. Annals of the New York Academy of Sciences, 833(1), 141–147.
- Ellington WR (2001). Evolution and physiological roles of phosphagen systems [abstract]. Annual Review of Physiology, 63(1), 289–325.
- Ayuso R et al (1999). Molecular basis of arthropod cross-reactivity: IgE-binding cross-reactive epitopes of shrimp, house dust mite and cockroach tropomyosins [abstract]. International Archives of Allergy and Immunology, 120(4), 270–279.
- De Marchi, L., Wangorsch, A., & Zoccatelli, G. (2021). Allergens from edible insects: Cross-reactivity and effects of processing. Current Allergy and Asthma Reports, 21(5), 35. https://doi.org/10.1007/s11882-021-01012-z
- Rumpold, B. A., & Schlüter, O. K. (2013). Nutritional composition and safety aspects of edible insects. Molecular Nutrition & Food Research, 57(5), 802–823. https://doi.org/10.1002/mnfr.201200735
- Sicherer, S.H., & Sampson, H.A . (2018) . Food allergy: A review and update on epidemiology , pathogenesis , diagnosis , prevention , and management . The Journal of Allergy and Clinical Immunology , 141 (1) , 41–58 . https://doi.org/10 .1016/j.jaci .2017 .11 .003
- Agyei-Aryee , B.A., Amoah , A.S., & Ofori-Amanfo , G.K . (2020) . Global prevalence of food allergy: A systematic review and meta-analysis . International Journal of Environmental Research and Public Health , 17 (14) , 5144 . https://doi.org/10 .3390/ijerph17145144
- Boyce , J.A., Assa'ad , A., Burks , A.W., Jones , S.M., Sampson , H.A., Wood , R.A., … Schwaninger , J.M . (2010) . Guidelines for the diagnosis and management of food allergy in the United States: Report of the NIAID-sponsored expert panel . The Journal of Allergy and Clinical Immunology , 126 (6 Suppl) , S1–S58 . https://doi.org/10 .1016/j.jaci .2010 .10 .007
- Rona , R.J., Keil , T., Summers , C., Gislason , D., Zuidmeer , L., Sodergren , E., … Burney , P.G . (2007) . The prevalence of food allergy: A meta-analysis . The Journal of Allergy and Clinical Immunology , 120 (3) , 638–646 . https://doi.org/10 .1016/j.jaci .2007 .05 .026
- Arlian , L.G., & Platts-Mills , T.A.E . (2001) . The biology of dust mites and the remediation of mite allergens in allergic disease . The Journal of Allergy and Clinical

Immunology , 107 (3 Suppl) , S406–S413 . https://doi.org/10 .1067/mai .2001 .113670

- de Gier , S., & Verhoeckx , K . (2018) . Insect (food) allergy and allergens . Molecular Immunology , 100 , 28–37 . https://doi.org/10 .1016/j.molimm .2018 .03 .015
- Valenta, R., Hochwallner, H., Linhart, B., & Pahr, S. (2015). Food allergies: The basics. Gastroenterology, 148(6), 1120–1131.e4. https://doi.org/10.1053/j.gastro.2015.02.006
- Aalberse, R.C., Akkerdaas, J., & van Ree, R. (2001). Cross-reactivity of IgE antibodies to allergens. Allergy, 56(6), 478–490. https://doi.org/10.1034/j.1398-9995.2001.00128.x
- Breiteneder, H., & Mills, E.N.C. (2005). Molecular properties of food allergens. Journal of Allergy and Clinical Immunology, 115(1), 14–23. https://doi.org/10.1016/j.jaci.2004.11.004
- Aalberse, R.C., & van Ree, R. (2019). Carbohydrate determinants in allergy diagnosis and treatment. Current Opinion in Allergy and Clinical Immunology, 19(6), 632–637. https://doi.org/10.1097/ACI.0000000000000589
- Pomés, A., Chruszcz, M., Gustchina, A., Minor, W., Mueller, G.A., Pedersen, L.C., … Chapman, M.D. (2013). Novel allergen structures with tandem amino acid repeats derived from German and American cockroach. Journal of Biological Chemistry, 288(43), 31101–31108. https://doi.org/10.1074/jbc.M113.497412
- Verhoeckx, K.C., van Broekhoven, S., den Hartog-Jager, C.F., Gaspari, M., de Jong, G.A.H., Wichers, H.J., … Jongejan, M.H.A.G.M. (2014). House dust mite (Der p 10) and crustacean allergic patients may react to food containing Yellow mealworm proteins. Food and Chemical Toxicology, 65, 364–373. https://doi.org/10.1016/j.fct.2013.12.040
- Leung PS & Chu KH (1998). Tropomyosin is a major shellfish allergen: New insights into the seafood allergy syndrome [abstract]. Annals of the New York Academy of Sciences, 833(1), 141–147.
- Ayuso R et al (1999). Molecular basis of arthropod cross-reactivity: IgE-binding cross-reactive epitopes of shrimp, house dust mite and cockroach tropomyosins [abstract]. International Archives of Allergy and Immunology, 120(4), 270–279.
- Ellington WR (2001). Evolution and physiological roles of phosphagen systems [abstract]. Annual Review of Physiology, 63(1), 289–325.
- Verhoeckx, K.C.M., van Broekhoven, S., den Hartog-Jager, C.F., Gaspari, M., de Jong, G.A.H., Wichers, H.J., … Jongejan, M.H.A.G.M. (2014). House dust mite (Der p 10) and crustacean allergic patients may react to food containing Yellow mealworm proteins. Food and Chemical Toxicology, 65, 364–373. https://doi.org/10.1016/j.fct.2013.12.040
- Leung, P.S., & Chu, K.H. (1998). Tropomyosin is a major shellfish allergen: New insights into the seafood allergy syndrome [abstract]. Annals of the New York Academy of Sciences, 833(1), 141–147.
- Ayuso, R., Reese, G., Leong-Kee, S., Plante, M., Lehrer, S.B., & Daul, C.B. (1999). Molecular basis of arthropod cross-reactivity: IgE-binding cross-reactive epitopes of shrimp, house dust mite and cockroach tropomyosins [abstract]. International Archives of Allergy and Immunology, 120(4), 270–279.
- Ellington, W.R. (2001). Evolution and physiological roles of phosphagen systems [abstract]. Annual Review of Physiology, 63(1), 289–325.
- Sicherer, S.H., & Sampson, H.A. (2018). Food allergy: A review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. The Journal of

Allergy and Clinical Immunology, 141(1), 41–58. https://doi.org/10.1016/j.jaci.2017.11.003

- Agyei-Aryee, B.A., Amoah, A.S., & Ofori-Amanfo, G.K. (2020). Global prevalence of food allergy: A systematic review and meta-analysis. International Journal of Environmental Research and Public Health, 17(14), 5144. https://doi.org/10.3390/ijerph17145144
- Boyce, J.A., Assa'ad, A., Burks, A.W., Jones, S.M., Sampson, H.A., Wood, R.A., … Schwaninger, J.M. (2010). Guidelines for the diagnosis and management of food allergy in the United States: Report of the NIAID-sponsored expert panel. The Journal of Allergy and Clinical Immunology, 126(6 Suppl), S1–S58. https://doi.org/10.1016/j.jaci.2010.10.007
- Rona, R.J., Keil, T., Summers, C., Gislason, D., Zuidmeer, L., Sodergren, E., … Burney, P.G. (2007). The prevalence of food allergy: A meta-analysis. The Journal of Allergy and Clinical Immunology, 120(3), 638–646. https://doi.org/10.1016/j.jaci.2007.05.026
- Arlian , L.G., & Platts-Mills , T.A.E . (2001) . The biology of dust mites and the remediation of mite allergens in allergic disease . The Journal of Allergy and Clinical Immunology , 107 (3 Suppl) , S406–S413 . https://doi.org/10 .1067/mai .2001 .113670
- de Gier , S., & Verhoeckx , K . (2018) . Insect (food) allergy and allergens . Molecular Immunology , 100 , 28–37 . https://doi.org/10 .1016/j.molimm .2018 .03 .015
- Valenta , R., Hochwallner , H., Linhart , B., & Pahr , S . (2015) . Food allergies: The basics . Gastroenterology , 148 (6) , 1120–1131.e4 . https://doi.org/10 .1053/j.gastro .2015 .02 .006
- Aalberse , R.C., Akkerdaas , J., & van Ree , R . (2001) . Cross-reactivity of IgE antibodies to allergens . Allergy , 56 (6) , 478–490 . https://doi.org/10 .1034/j .1398-9995 .2001 .00128.x
- Breiteneder , H., & Mills , E.N.C . (2005) . Molecular properties of food allergens . Journal of Allergy and Clinical Immunology , 115 (1) , 14–23 . https://doi.org/10 .1016/j.jaci .2004 .11 .004
- Aalberse , R.C., & van Ree , R . (2019) . Carbohydrate determinants in allergy diagnosis and treatment . Current Opinion in Allergy and Clinical Immunology , 19 (6) , 632–637 . https://doi.org/10 .1097/ACI .0000000000000589
- Pomés , A., Chruszcz , M., Gustchina , A., Minor , W., Mueller , G.A., Pedersen , L.C., … Chapman , M.D . (2013) . Novel allergen structures with tandem amino acid repeats derived from German and American cockroach . Journal of Biological Chemistry , 288 (43) , 31101–31108 . https://doi.org/10 .1074/jbc.M113.497412
- Verhoeckx, K.C.M., van Broekhoven, S., den Hartog-Jager, C.F., Gaspari, M., de Jong, G.A.H., Wichers, H.J., … Jongejan, M.H.A.G.M. (2014). House dust mite (Der p 10) and crustacean allergic patients may react to food containing Yellow mealworm proteins. Food and Chemical Toxicology, 65, 364–373. https://doi.org/10.1016/j.fct.2013.12.040
- Leung, P.S., & Chu, K.H. (1998). Tropomyosin is a major shellfish allergen: New insights into the seafood allergy syndrome [abstract]. Annals of the New York Academy of Sciences, 833(1), 141–147.
- Ayuso, R., Reese, G., Leong-Kee, S., Plante, M., Lehrer, S.B., & Daul, C.B. (1999). Molecular basis of arthropod cross-reactivity: IgE-binding cross-reactive epitopes of

shrimp, house dust mite and cockroach tropomyosins [abstract]. International Archives of Allergy and Immunology, 120(4), 270–279.

- Ellington, W.R. (2001). Evolution and physiological roles of phosphagen systems [abstract]. Annual Review of Physiology, 63(1), 289–325.