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Mini Review

Allergens derived from shrimp

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Abstract

Allergy caused by food is usually type 1 allergy of four types of allergic reactions. One of the most widespread allergic is those that are caused by crustacean shellfish. Crustaceans are classified among arthropods which include crab, crayfish, lobster, prawn and shrimp. Shrimp which are broadly consumed as nutritional food is one of the most important food that contribute to allergy. Thus, reducing the allergenicity of shrimp allergen will be helpful to individuals who are sensitive to shrimp and for this reason the characteristics of each allergen need to be studied. Those sensitized individuals can develop urticaria, angiodema, laryngospasm, asthma and life threatening anaphylaxis. To date, four main allergens contribute to allergic reactions. They are tropomyosin (TM), a highly conserved and heat stable myofibrillar protein of 35-38 kDa followed by arginine kinase (AK) which is also known as Pen m 2 or Lit v 2 with 40 kDa. Two other contributing allergens are sarcoplasmic calcium-binding protein (SCP) also known as Lit v 4 with 22 kDa and myosin light chain (MLC) which is also termed as Lit v 3 with 20 kDa. This mini-review will provide a better understanding of each allergen derived from shrimp which subsequently will help to reduce the allergenicity.

Introduction

Food allergy or hypersensitivity disorders are defined as unfavorable immune responses to food proteins and differ from many adverse food reactions that have non immune causes or origins (Sicherer and Sampson, 2009). Food allergy is also the fastest growing allergy than any other allergic disorder (Gupta *et al*., 2007). Crustacean shellfish, peanuts, fish and tree nuts are the common foods that cause allergic reaction in adults while children are mostly affected by consumption of cow's milk, egg white, wheat and soy (Ebo and Stevens, 2001; Thong *et al.*, 2007; Ben-Shoshan *et al*., 2010). However, the most widespread IgE mediated food allergies which will cause severe reactions are allergies caused by crustacean shellfish (Crespo and Rodriguez, 2003; Vilalta *et al*., 2010). According to a research conducted in 2011, shellfish refers to those with a shell like exoskeleton like crustacean and mollusks that are classified among arthropods which include crab, crayfish, lobster, prawn and shrimp (Woo and Bahna, 2011). Shrimp which are broadly consumed as nutritional food is one of the most important crustacean shellfish that contribute to allergy (Lu *et al*., 2007). Thus, reducing the allergenicity of shrimp allergen will be helpful to those who are sensitive to shrimp (Zhenxing *et al*., 2006). Those sensitized individuals can develop urticaria, angioedema, laryngospasm, asthma and life threatening anaphylaxis (Yu *et al*., 2003).

There are four allergens from shrimp that have been discovered to be the major contributor to allergenicity including tropomyosin (TM), arginine kinase (AK), sarcoplasmic calcium-binding protein (SCP) and myosin light chain (MLC). Hoffman's study revealed that TM, a highly conserved and heat stable myofibrillar protein serves as a major allergen from crustaceans (Liang *et al*., 2008; Zheng *et al.*, 2011; Zailatul *et al*., 2012). Tropomyosin also present in other crustaceans (Motoyama *et al*., 2007), mollusks (Leung *et al*., 1996), house dust mites, cockroach and squid (Luis and Nathalie, 2011). Whereas, in a study conducted by Yu *et al.*, (2003) on black tiger shrimp *(Penaeus monodon)* they encountered that Pen m 2, an AK represents a new class of shrimp allergen and serves as a cross-reactive crustacean allergen with 40 kDa allergen protein. On the other hand, Lit v 2 was disclosed as arginine kinase from pacific white shrimp *(Litopenaeus vannamei)* species with 96% identity to Pen m 2 from black tiger shrimp (Garcia-Orozco *et al*., 2007). Subsequently, researchers have came across another two new allergens, MLC also known as Lit v 3 derived from pacific white shrimp species (Ayuso *et al*., 2008) and SCP also known as Lit v 4 which is also from the same species of shrimp (Ayuso *et al*., 2009).

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Table 1. Allergenic proteins characterized in shrimp

Group	TM	AK	SCP	MLC
Crustacean (Shrimp)	North Sea Shrimp (Cra c 1) Pacific white shrimp (Lit v 1) Brown shrimp (Pen a 1) Indian prawn (Pen i 1) Black tiger shrimp (Pen m 1)	Pacific white shrimp (Lit v 2) Black tiger shrimp (Pen m 2)	Pacific white shrimp (Lit v 4) Black tiger shrimp (Pen m 4)	Pacific white shrimp (Lit v 3)
Characterization technique	RAST, MG, MS	MG, MS	ELISA, Edman, WB, LC-MS/MS, MG	MS, Edman, MG,WB, Peptide microarray
Quantification technique	ELISA, MS	MS	N/A	N/A

AK = Arginine kinase, ELISA = Enzyme-linked immunosorbent assay, LC-MS/MS = Liquid chromatography-tandem mass spectrometry, MG = Molecular genetics, MLC = Myosin light chain, MS = Mass spectrometry, N/A = Not available, RAST = Radioallergosorbent test, SCP = sarcoplasmic calcium-binding protein, TM = Tropomyosin, WB = Western blotting. Adapted from Woo and Bahna (2011).

Four major allergens

Tropomyosin (TM)

Tropomyosin, a muscle protein is the major shrimp allergen identified and also termed as Pen a 1 (identified in brown shrimp, *Penaeus aztecus*) (Reese *et al*., 1997), Pen i 1 (identified in Indian prawn, *Penaeus indicus*), Pen m 1 (identified in black tiger shrimp, *Penaeus monodon*), Lit v 1 (identified in pacific white shrimp, *Litopenaeus vanamei*) (Gamez *et al*., 2011) and Cra c 1 (identified in North Sea Shrimp) (Woo and Bahna, 2011). This heat-stable allergen initially was found in crustacean in the year 1981 by Hoffman and his team (1993) and Shanti *et al*. (1993) found it has 86% of similarity in amino acid sequence with muscle protein, TM from fruit fly, *drosophila melanogaster*. Tropomyosin is a diverse group of protein with different isoforms which are found in both muscle and non-muscle cells. The tissue-specific functions of TM are seen in both vertebrates and in crustaceans (Smillie, 1979; Miyazaki *et al*., 1992). Detailed studies on this allergen showed that TM is a major cross-reactive allergen among crustaceas and mollusks (Leung *et al*., 1996). In a study done by Motoyama *et al.* (2007) concluded that tropomyosin can be classified into three categories which are fast, slow-twitch and slow-tonic (based on muscle fiber) and majority of shrimp tropomyosin is known as fast type and they do not have much alteration in their amino acid sequences. The molecular weight is between 34 kDa to 38 kDa and it serves as the major allergen in almost all crustaceans (Zheng *et al*., 2011; Zailatul *et al*., 2012). Moreover, mite allergen patients who consumed shrimp can experience severe asthma symptoms and patients treated with immunotherapy with mite extracts can become sensitized with mite tropomyosin and react to shrimp (Luis and Nathalie, 2011). The characterization of this allergen was mainly used by using three main techniques which Radioallergosorbent test (RAST), Molecular genetics (MG) and Mass spectrometry (MS) (Garcia-Orozco *et al*., 2007; Abdel Rahman *et al*., 2012).

Arginine kinase (AK)

Arginine kinase is a monomeric phosphagen ATP phosphotransferase which is generally found in invertebrates and is the key to energy metabolism (Yao *et al*., 2005). Pen m 2, an allergen from black tiger shrimp, is an AK obtained from shrimp which is anticipated to plays an essential role as a cross-reactive crustacean allergen and in rousing hypersensitivity responses (Yu *et al*., 2003). AK is also rich in pacific white shrimp muscle and is anticipated to be the next major allergen (Garcia-Orozco *et al*., 2007). It has been reported AK from pacific white shrimp is known as Lit v 2 and has 96% identity to Pen m 2 from black tiger shrimp. Both researchers disclosed that AK is located at 40 kDa. Characterization of AK can be done by Molecular genetics and Mass spectrometry techniques (Garcia-Orozco *et al*., 2007; Abdel Rahman *et al.*, 2012).

Sarcoplasmic calcium-binding protein (SCP)

Sarcoplasmic calcium-binding protein is acquired from pacific white shrimp. It is known as Lit v 4 with 22 kDa allergen, 194 amino acids, isoelectric point of 4.7 and also a muscle protein (Ayuso *et al.*, 2009). The research team also revealed that sensitization to SCP appear to be involved in cross-reactivity among crustaceans only and SCP is the major culprit in pediatric population. In other study, during the process of purification of arginine kinase, it has been discovered that SCP is also found in black tiger shrimp (Pen m 4), kuruma shrimp *(Penaeus japonicus)*, American lobster *(Homarus americanus)*,

pink shrimp *(Pandalus eous)*, king crab *(Paralithodes camtschaticus)* and snow crab *(Chionoecetes opilio)* (Shiomi *et al*., 2008). To characterize this allergen few methods can be employed such as ELISA, Edman, Western blotting, Liquid chromatography-tandem mass spectrometry (LC-MS), Mass spectrometry or Molecular genetics (Garcia-Orozco *et al*., 2007; Abdel Rahman *et al*., 2012).

Myosin light chain (MLC)

Myosin light chain from pacific white shrimp termed as Lit v 3 was recognized as a new shrimp allergen (Ayuso *et al*., 2008). In their study, they concluded that despite TM being the major allergen, some patients are exclusively sensitive to MLC only; hence MLC is also a major shrimp allergen. It is a muscle protein with 20 kDa (Ayuso *et al*., 2008). Due to the fact that MLC has a similar molecular weight, 20 kDa and similar isoelectric point, 4.2 to SCP, provoking difficulties to recognize which protein is responsible for allergic reactions in particular patient's IgE antibodies by using standard laboratory methods. Ayuso *et al*. (2008) also found that patients with IgE binding to the boiled form of MLC appear to be greater in adults compared with children who tend to recognize the MLC in the raw extract with higher intensity. But, interestingly some children has asthmatic episodes when exposed to the steam boiling shrimp; suggesting that MLC is aerosolized and might contribute to respiratory symptoms in such patients. However, they recommended for further studies to be done finding out if MLC played the most important role in causing asthmatic reactions. Table 1 summarizes four major shrimp allergens and the proposed characterization and quantification techniques.

Conclusions

Nowadays, the seafood allergy is becoming more common and increasing among the adults. However, the identification and characterization of clinically relevant seafood allergen are still incomplete and thus limiting the understanding of their role in the immunopathogenic mechanisms involved in hypersensitivity reaction. In addition, it is essential that the correct diagnosis of food allergy is made to avoid false positive diagnosis which will lead to unnecessary dietary intake restriction that will cause nutritional deficiency.

References

Abdel Rahman, A.M., Helleur, R.J., Jeebhay, M.F. and Lopata, A.L. 2012. Characterization of seafood proteins causing allergic diseases, allergic diseases - highlights in the clinic, mechanisms and treatment, (Pereira, C., ed.), InTech, 2012, ISBN: 978-953-51-0227-4.

Ayuso, R., Grishina, G., Bardina, L., Carrilo, T., Blanco, C., Ibanez, M.D., Sampson, H.A. and Beyer, K. 2008. Myosin Light Chain is a novel shrimp allergen, Lit v 3. J. The Journal of Allergy and Clinical Immunology 122: 795-802.

Ayuso, R., Grishina, G., Ibanez, M.D., Blanco, C., Carrilo, T., Bencharitiwong, R., Sanchez, S., Nowak-Wegrzyn, A. and Sampson, H.A. 2009. Sarcoplasmic Calcium-binding protein is an EF-hand-type protein identified as a new shrimp allergen. The Journal of Allergy and Clinical Immunology 124: 114-120.

Ben-Shoshan, M., Harrington, D.W., Soller, L., Fragapane, J., Joseph, L., Pierre, Y., S., Godefroy, S., B. and Eliot, S.J. 2010. A population-based study on peanut, tree nut, fish, shellfish, and sesame allergy prevalence in Canada. The Journal of Allergy and Clinical Immunology 125: 1327-1335.

Crespo, J.F. and Rodriguez, J. 2003. Review Article Food allergy in adulthood. European Journal of Allergy and Clinical Immunology 58: 98-113.

Ebo, D.G. and Stevens, W.J. 2001. IgE-Mediated Food Allergy-Extensive Review of the Literature. Acta Clinica Belgica 56: 234-247.

Gamez, C., Sanchez-Garci, S., Ibanez, M.D., Lopez, R., Aguado, E., Lopez, E., Sastre, B., Sastre, J. and Pozo, V.D. 2011. Tropomyosin IgE-positive results are a good predictor of shrimp allergy. European Journal of Allergy and Clinical Immunology 66: 1375-1383.

García-Orozco, K.D., Aispuro-Hernández, E., Yepiz-Plascencia, G., Calderón-de-la Barca, A. and Sotelo-Mundo, R. 2007. Molecular characterization of arginine kinase, an allergen from the shrimp *Litopenaeus vannamei*. International Archives of Allergy and Immunology 144: 23-28.

Gupta, R., Sheik, A., Strachan, D.P. and Anderson, H.R. 2007. Review: Time trend in allergic disorders in the UK. Thorax 62: 91-96.

Hoffman, D., Day Jr, E. and Miller, J. 1981. The major heat stable allergen of shrimp. Annals of Allergy 47: 17-22.

Leung, P.S.C., Chow, W.K., Duffey, S., Kwan, H.S., Gershwin, M.E. and Chu, K.H. 1996. IgE reactivity against a cross-reactive allergen in crustacean and mollusca: evidence from tropomyosin as the common allergen. The Journal of Allergy and Clinical Immunology 98: 954-961.

Liang, Y.L., Cao, M.J., Su, W.J., Zhang, L.J., Huang, Y.Y. and Liu, G.M. 2008. Identification and characterisation of the major allergen of Chinese mitten crab *(Eriocheir sinensis)*. Food Chemistry 111: 998-1003.

Lu, Y., Ohshima, T., Ushio, H., Hamada, Y. and Shiomi, K. 2007. Immunological characteristics of

monoclonal antibodies against shellfish major allergen tropomyosin. Food Chemistry 100: 1093-1099.

Luis, C. and Nathalie, A. 2011. Allergy in the tropics: the impact of cross-reactivity between mites and ascaris. Frontiers in Bioscience E3: 51-64.

Miyazaki, J.I., Makioka, T., Fujiwara, Y. and Hirabayashi, T. 1992. Tissue specificity of crustacean tropomyosin. Journal of Experimental Zoology 263:235–244.

Motoyama, K., Suma, Y., Ishizaki, S., Nagashima, Y. and Shiomi, K. 2007. Molecular cloning of tropomyosin identified as allergens in six species of crustaceans. Journal of Agriculture and Food Chemistry 55: 985-991

Reese, G., Jeoung, B., Daul, C. and Lehrer, S. 1997. Characterization of recombinant shrimp allergen pen a 1 (tropomyosin). International Archives of Allergy and Immunology 113: 240-242.

Shanti, K., Martin, B., Nagpal, S., Metcalfe, D. and Rao, P. 1993. Identification of tropomyosin as the major shrimp allergen and characterization of its IgE-binding epitopes. The Journal of Immunology 50: 153-159.

Shiomi, K., Sato, Y., Hamamoto, S., Mita, H. and Shimakura, K. 2008. Sarcoplasmic calcium-binding protein: Identification as a new allergen of the black tiger shrimp *(Penaeus monodon)*. International Archives of Allergy and Immunology 146: 91-98.

Sicherer, S.H. and Sampson, H.A. 2009. Food Allergy: Recent advances in pathophysiology and treatment. Annual Review of Medicine 60: 261-277.

Smillie, L.B. 1979. Structure and functions of tropomyosin from muscle and non-muscle sources. Trends Biochemical Science 4:151–155.

Thong, B.Y.H., Cheng, Y.K., Leong, K.P., Tang, C.Y. and Chong, H.H. 2007. Immediate food hypersensitivity among adults attending a clinical immunology/ allergy centre in Singapore. Singapore Medical Journal 48: 236-240.

Villalta, D., Tonutti, E., Visentini, D., Bizarro, N., Roncarolo, D., Amato, S. and Mistrello, G. 2010. Detection of a novel 20 kDa shrimp allergen showing cross-reactivity to house dust mites. European Annals of Allergy and Clinical Immunology 42: 20-24.

Woo, C.K. and Bahna, S.M. 2011. Not all shellfish "allergy" is allergy!. Clinical Translational Allergy 1: 1-7.

Yao, C. L., Wua, C. G., Xiang, J. H. and Dong, B. 2005. Molecular cloning and response to laminarin stimulation of arginine kinase in haemolymph in Chinese shrimp, Fenneropenaeus chinensis. Fish and Shellfish Immunology 19: 317-329.

Yu, C.J., Lin, Y.F, Chiang, B.L. and Chow, L.P. 2003. Proteomics and immunological analysis of a novel shrimp allergen, Pen m 2. The Journal of Immunology 170: 445-453.

Zailatul, H.M.Y., Rosmilah, M., Noormalin, A., Faizal, B., Masita, A. and Shahnaz, M. 2012. Identification of the major allergen of *(Macrobrachium rosenbergii)* giant freshwater prawn. Asian Pacific Journal of Tropical Biomedicine 2: 50-54.

Zheng, L.N., Lin, H., Pawar, R., Li, Z.X. and Li, M.H. 2011. Mapping IgE binding epitopes of major shrimp *(Penaeus monodon)* allergen with immunoinformatics tools. Food and Chemical Toxicology 49: 2954-2960.

Zhenxing, L., Linhong, C. and Khalid, J. 2006. Reduction of allergenic properties of shrimp *(Penaeus vannamei)* allergens by high intensity ultrasound. European Food Research and Technology 223: 639-644.