Sunflower Pollen Allergy: A Brief Review

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Abstract—*Sunflower (Helianthus annuus) belongs to Asteraceae family, which embraces genera of great allergologic interest. Respiratory allergy caused by pollen allergens is increasing worldwide at an alarming rate. About 15-30% of people worldwide suffer from respiratory allergy caused due to pollen grains. Several instances of pollen allergies have been reported from other members of the Asteraceae family, such as Ambrosia artemisifolia, Artemisia vulgaris and Parthenium hyserophorus. Sunflower in spite of being the most important crop of the Asteraceae family was underexplored for the allergologic properties of its pollen grains until recently. Recently, mass spectrometry based proteomics studies have revealed seven pollen allergens having molecular weight 32.7 kDa, 34.2 kDa, 37.8 kDa, 41.2 kDa, 42.7 kDa, 44.2 kDa and 49.5 kDa. Major pollen allergens have been found to be glycoproteins in nature. Sunflower pollen contains two novel allergens: one belonging to tubulin FtsZ superfamily and another one belonging to GluZincin superfamily containing a highly conserved zinc binding metalloprotease (M36). Sunflower pollen cross reacts with pollen of other compositae species. Future studies on purification, recombinant expression and epitope mapping of these allergens will be instrumental in catalyzing the diagnosis and immunotherapy of pollen allergy.*

1. INTRODUCTION

Allergy is an abnormally high sensitivity to certain substances collectively known as allergens, such as pollen grains, variety of food materials, medicines and microorganisms. It occurs upon the reaction of person's immune system to a previously encountered allergen introduced in the body of the individuals through inhalation, ingestion, injection and through skin contact. Allergic reactions are often manifested in various ways, which includes itchy eyes, runny nose, wheezing, skin rashes and sometimes, diarrhea. Both environmental antigens and allergens trigger the abnormal immune reactions which are mediated by IgE antibodies.

Pollen grains contain various factors that can lead to the stimulation of an innate immune response. Among intrinsic factors, nicotinamide adenine dinucleotide phosphate oxidases (NADPO), proteases, aqueous pollen proteins, lipids, and antigens, play significant role [1]. Each of these components is responsible for stimulation of innate immune response in a specific manner. Pollen NADPO induces reactive oxygen species (ROS) generation and recruits neutrophils that stimulate subsequent allergic inflammation. Pollen proteases are known to damage epithelial barrier function which subsequently leads to an increased antigen uptake. The proteins present in the aqueous pollen extract and pollen lipids have been implicated in the modulation of dendritic cell function and induction of Th2 polarization.

The treatment of airborne allergy exploits antihistamines, nasal steroids, decongestants and corticosteroids in acute cases which lead to severe side effects. Allergen-specific immunotherapy is a potentially disease-modifying therapy effectively used for the treatment of allergic rhinitis/conjunctivitis and allergic asthama. It exploits allergy inducing molecule i.e. the allergen itself for vaccination [2]. Purified allergens are used for the clinical diagnosis of allergy for accuracy. Proper identification and characterization of allergens are essential for effective utilization of diagnostic and therapeutic tools.

Sunflower (*Helianthus annuus L.*) belongs to the family Asteraceae (Compositae) which comprises over 20,000 species. This family is distributed throughout the world and contains several genera of great allergologic interest. Amongst these genera, such as *Ambrosia artemisiifolia* (short ragweed) [3-5] and *Artemisia vulgaris* (mugwort) [6, 7] and *Parthenium hysterophorus* [8, 9] have been studied intensively and have been reported as important sources of pollen allergy. Several allergens from mugwort and ragweed have been cloned and characterized at the molecular level [10]. Though, sunflower is the most economically important plant of the Asteraceae family (being agriculturally important oilseed crop and an important ornamental plant) fewer studies were reported on pollinosis. The occurrence of sunflower pollen allergy has been reported from various parts of the world [11, 12]. Present article highlights the research done so far in identification and elucidating the nature of various allergens present in the pollen grains of sunflower.

2. SUNFLOWER POLLEN AS AEROALLERGEN

Air-borne allergens, called as aeroallergens, play an important role in the pathogenesis of allergic diseases (mainly asthama and rhinitis) related to respiration. Fungal spores, pollen grains, house dust mites, insects' acts as an important trigger for allergies due to aeroallergens. Pollen grains from trees, weeds and grasses have been extensively studied as allergens and are important source of pollinosis. Epidemiological data

across the globe reports the prevalence of respiratory allergy from15% to 30% [13, 14].

The role played by pollen grains of sunflower as airborne allergen was controversial until recently. This controversy was mainly attributed to the larger size of the pollen grain (~40.2 x 37.9 μm^2) due to which they were thought to be incapable of flying in the air (Fig. 1). Development of rhinitis, conjunctivitis and asthama were reported in a person upon 5years of sunflower pollen exposure [15]. Jiménez et al., 1994 reported that the sensitization to sunflower pollen results in the occupational allergy in workers employed in the laboratories or sunflower fields working under sunflower pollen dust [16]. Furthermore, it was suggested that sunflower pollen not only acts as an occupational allergen but also responsible for allergic rhinitis and asthama in the population inhabiting the sunflower growing areas. Atis et al., 2002 reported a high rate of sensitization to sunflower pollen and impairement of lung function in sunflower processing workers as compared to control workers.

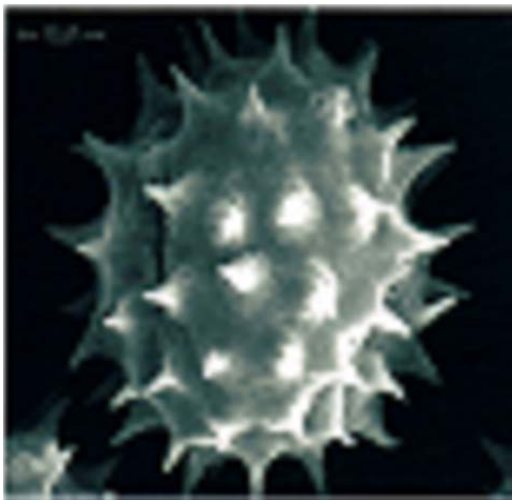

Fig. 1: Scanning electron micrograph (SEM) of sunflower pollen. Scale bar= 10 µm [17]

The concentration and nature of inhaled substances and working conditions within workplaces contribute to the development of occupational asthama and allergies. High exposure to the pollen leads to high prevalence of occupational asthama and allergy.

3. POLLEN ALLERGENS REPORTED IN SUNFLOWER

de la Hoz et al., have isolated and partially characterized allergens from sunflower pollen with apparent molecular masses of 32, 24 and 55kDa [18]. Until recentlyonly two allergens, Hela 1 (34 kDa) and Hel a 2 (14.7 kDa) were reported in International Union of Immunological Societies (IUIS) database. However, Ghosh et al., 2015 have reported seven pollen allergens from sunflower with molecular weight 32.7, 34.2, 37.8, 41.2, 42.7, 44.2 and 49.5 kDa by exploiting the immuno-biochemical and mass spectrometry techniques (Table 1).

Table 1: Sunflower Pollen allergens

S. No.	Pollen allergen (SPA)	Molecular weight (kDa)	Biological function
1	SPA 1	49.5	GTPase
2	SPA 2	42.7	Pectin degradation
3	SPA 3	44.2	Pectin degradation
4	SPA 4	34.2	peptidase
5	SPA 5	32.7	Pathogenesis related protein
6	SPA 6	37.8	Glyceraldehyde-3-phosphate dehydrogenase
7	SPA 7	41.2	Aldolase

3.1 Three major pollen allergens of sunflower are glycoproteins

Glycoproteins which bind to IgE are of widespread occurrence among pollen grains [19]. Among members of Asteraceae family, pollen grains of *Artemisia vulgaris* [20] and *Ambrosia artemisiifolia* [21] reportedly contain Art v 1 and Amb a 4 allergens with arabinogalactan-protein moiety, respectively. Of the seven pollen allergens reported from sunflower, four allergens have been found to be glycoproteinaceous in nature. These four pollen allergens have molecular weight of 44.2 kDa, 42.7 kDa, 34.2 kDa and 41.2 kDa and their carbohydrate moiety acts as determinant of antigenic properties. Amongst them three allergens (44.2 kDa, 42.7 kDa and 34.2 kDa) emerged as the major pollen allergens in about 95% cases [22].

3.2 Nove l allergens in sunflower pollen

Two novel pollen allergens SPA1 and SPA5 corresponding to molecular weight of 49.5kDa and 32.7 kDa have been reported recently by Ghosh et al., 2015. SPA1 allergen has been suggested to contain a putative conserved domain characteristic of tubulin FtsZ superfamily, which was earlier reported as allergens from dust mites. SPA1 is the first plant specific tubulin which acts as respiratory allergen from pollen grains. SPA 5 has been assigned as the putative member of GluZincin superfamily and contains a highly conserved zinc binding metalloprotease (M36) domain with HEXXH and EXXXD motifs. Pathogenic molds, like *Aspergillus fumigates*, have been reported to contain such metalloproteases as allergen [23]. Biotic stress is believed to induce the translation of similar type of proteins in plants. These proteins belong to the PR-17 family and are considered as pathogenesis related protein. No such proteins have been reported to exhibit allergenic properties in plants.

3.3 Cross-reactivity of sunflower pollen with other Asteraceae members

Pollen allergens cross react with allergens present in the pollens of the same family and also with the allergens present in pollens and food material belonging to other families. The cross-reactivity between sunflower pollen and pollens of other members belonging to family Asteraceae has not been very well documented. Bousquet et al., 1985 demonstrated that sunflower pollen does not cross-react with pollen from members of Asteraceae family, such as ragweed. However, almost after a decade the homology between sunflower and other members of Asteraceae was reported [24]. Fernandez etal.,1994 tested five members of Asteracea family, namely, *Artemisia vulgaris* (mugwort), *Argyranthemum frutescens* (marguerite), *Taraxacum* (dandelion), *Solidago virgaurea* (golden rod) and *Ambrosia artemisiifolia* (short ragweed) for their cross-reactivity with sunflower pollen. High degree of allergenic homology was exhibited by *Artemisia vulgaris* pollen whereas *Ambrosia artemisiifolia* pollen was found to be less cross-reactive with sunflower pollen. It has been suggested that mostly primary sensitization occurs through exposure to *Artemisia vulgaris* pollen. However, another study conducted by Jimenez et al., have reported sunflower pollen as the trigger of primary sensitization in the population exposed to sunflower pollen. Thus, it can be suggested that other climatic factors, pollution and degree of exposure might play an instrumental role in determining the cross-reactivity and subsequently primary sensitization process.

4. SUMMARY

Sunflower pollen is an important source of inhalant allergens responsible for allergic rhinitis, severe lung impairment and conjuctivits. Sunflower pollen allergens are potent aeroallergen for the people inhabiting the vicinity of sunflower fields. Therefore, proper identification of these allergenic entities is crucial for understanding the immunological and molecular basis of pollinosis due to sunflower. Recent advances in the mass spectrometry based proteomics and bioinformatics has rendered identification procedure more accurate. Recently, mass spectrometry based proteomics, which relies on homology searching has led to the identification of seven allergens (32.7 kDa, 34.2 kDa, 37.8 kDa, 41.2 kDa, 42.7 kDa, 44.2 kDa and 49.5 kDa) from sunflower pollen. Further, characterization of these allergens have revealed the glycoproteinaceous nature of the major allergens (44.2 kDa, 42.7 kDa and 34.2 kDa) triggering sensitization in >95% of the individuals screened. Interestingly, the glycan moiety of these glycoproteins was found to be participating in IgE binding, thus, eliciting the allergenicity. Two novel allergens corresponding to molecular weight of 49.5kDa and 32.7 kDa have been reported as the aeroallergen from pollen. Further, purification, recombinant expression and epitope mapping of these pollen allergens is essential for the improvement of current diagnostic tools and immunotherapy of pollen allergy caused due to sunflower pollen.

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