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Investigation of the interaction of allergens of *Glycine max* with IgE-antibody for designing of peptidomimetics based anti-allergen

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ABSTRACT

Allergen induced IgE dependent type I hypersensitivity is the main cause of the allergy, which would be a burden on medical setup in coming years. Allergens of *Glycine max* have been isolated, and their disease relationships are documented. Therefore, it becomes important to investigate the interaction of different allergens of *Glycine max* with IgE and also screen suitable therapeutics to prevent this interaction. The amino acid sequences of all allergens of *Glycine max* and their isoallergens have been taken, and 3D structure of allergens (Gly m 3, Gly m 4, Gly m 5, Gly m 6 and Gly m 8) and their isoallergens were generated using Modeller v9.17. The modeled structures were further validated using PSVS, ProSA, RAMPAGE, and PDBsum. HL domain of Fab region of human IgE (PDBID: 2R56) was generated using UCSFchimera. The HL domain was minimized by Schrodinger software using the OPLS_2005 force field. SiteMap identified epitope binding site of the minimized domain. All the predicted epitopes of different allergens were docked to the binding site of HL domain using the Patchdock server. We have also designed a peptidomimetics based inhibitor targeted at interaction interface of Gly m8 and IgE, using *in-silico* virtual screening, molecular mechanics, and molecular dynamics simulation studies. These studies identified BDE32166344 ((N-(1-{[1-(1-aminocyclopentanecarbonyl)-3-hydroxypyrrolidin-3-yl]methyl} piperidin-4-yl)acetamide) as a peptidomimetics based lead with binding energy of −72.77 kcal/mol. Therefore, the present study investigates the interaction between different Gly m allergens and IgE antibody and identifies peptidomimetics based lead that might be developed as a suitable therapeutics against allergy caused by allergen of *Glycine max*.

1. Introduction

Allergy is an overreaction of the immune system against antigen or molecules, which are otherwise considered harmless. Allergen induces IgE dependent type I hypersensitivity and is the leading cause of allergy in an individual. They indeed have grown in number with many allergens having been isolated from plants and animal alike. Allergens have evolved along with time and now have a much more crucial influence on human health alongside climate change [20]. It is responsible for a number of varied symptoms extending from boils, rashes, eczema, asthma and in some instances violent anaphylactic shocks leading to death. Not always life-threatening but allergies are no less a grave danger than any disease. Allergy can be contributed to a number of sources that range from plants, animals, and even dust. Miniscule in size, allergens have been identified as an emerging burden upon the health economy across not only developing countries but also developed countries as individuals afflicted with allergy have to carry on with medications throughout their life. Several methods aimed at curbing this menace have been described [35]. Owing to the unique identification of different forms of allergens and their varied sources, to streamline the nomenclature of these allergens, the International Union of Immunological Societies (IUIS) has defined the nomenclature of allergens identified and has categorically listed them on allergen database www.allergen.org. [39].

Among the total number of listed and identified allergens around the world, nearly all the pollen allergens are ambiguously distributed in 29 protein families among the 2615 seed plant families [5]. The maximum number of allergens have been isolated from plants and range from grapes to climbers. Not only the plants but their products are equally susceptible to sensitizing Type I hypersensitivity among individuals [5]. Several allergen structures have been made available in the Protein Data Bank [4,19,25,32]. The allergenicity can be attributed in most cases to the structural aspects of the allergen. Allergens also have various isoforms, termed as isoallergens that show nearly 70% sequence similarity with the allergen and similar cross-reactivity with IgE. Till date, only two-documented interaction [23,31] studies

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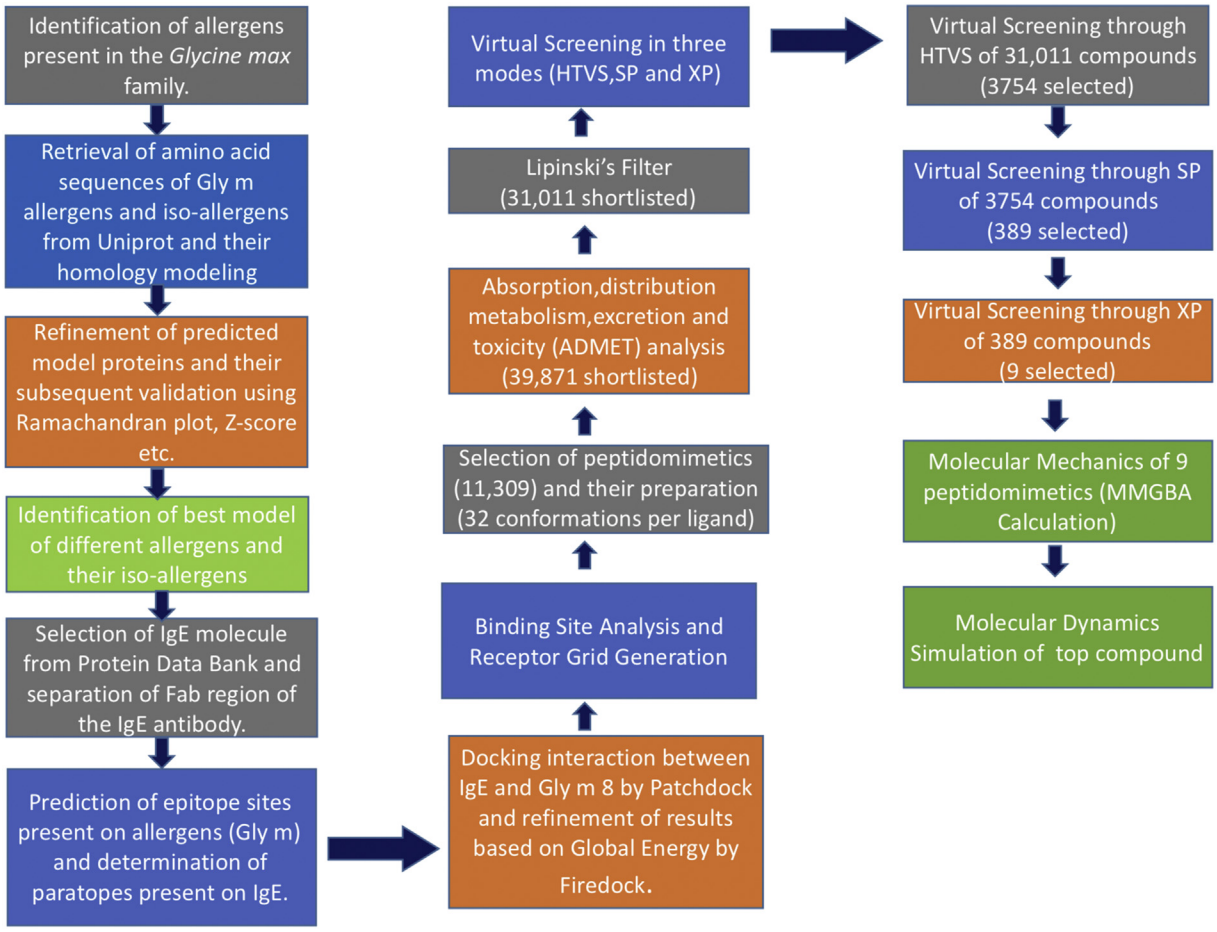

Fig. 1. The flowchart represents the outline of different steps of the methodology used in the present study.

Table 1
Results of refinement of modeled Gly m 8 using Galaxy web.

Model	GDT-HA	RMSD	MolProbity	Clash score	Poor rotamers	Rama favored	Z-score
Initial	1.0000	0.0000	3.378	89.6	3.4	89.7	
MODEL 1	0.9335	0.475	2.085	18.9	0.7	95.5	−3.23
MODEL 2	0.9383	0.458	1.939	13.1	0.7	95.5	−3.13
MODEL 3	0.9430	0.447	2.346	16.6	2.0	94.2	−3.17
MODEL 4	0.9446	0.432	2.204	17.8	1.4	94.9	−3.37
MODEL 5	0.9304	0.469	2.128	18.5	1.4	96.2	−3.19

between allergen and IgE have been made.

In the present study, we concentrate upon the soybean plant, a source of highly proteinaceous food. The plant *Glycine max* has been found to have different allergens. As specified by IUIS, the allergen present in the soybean plant has been named as Gly m followed by either one of the eight forms of iso-allergens [18]. Soybean allergy has already been reported before with well-documented cases for different allergens such as Gly m 1 [13], Gly m 2 [6], Gly m 3 [41], Gly m 4 [8], Gly m 5 [27,28], Gly m 6 [1,45], Gly m 7 [40] and Gly m 8 [10]. These allergens have been documented to show cross-reactivity [21]. A study conducted on the impression of soy allergy on individuals (with Gly m 8 allergen) indicates that it can occur at any age and the individuals with soy allergy are most certainly susceptible to peanut allergen (nearly 89% of tested individuals) [21].

In this fast-paced 21st century the need behind faster results has attributed to the success of bioinformatics which certainly outpaces experimental method and complements the experiment being conducted leading it to a number of avenues exclusively tailored to meet the demands of the experiment concerned. The sequences of most of the allergens of the *Glycine max* are known but their structures are not available in the database (WHO/IUIS). Homology modeling has provided to be a boon in allergen-specific research; this can be attributed to the importance of structural properties behind allergenic stimulation. Docking interactions help provide insights into the interaction between IgE and the allergen concerned. The study also uses the approaches for epitope prediction, which subsequently aid in protein interaction between IgE and Gly m allergens family found in *Glycine max*. Therefore, the present study aims to generate models of different protein allergens present in *Glycine max* and their subsequent interaction studies of allergens with human immunoglobin E (IgE). Gly m 8 has been selected because it showed the best clinical reactivity among the different allergens of *Glycine max* [21]. A comparative study of all other isoallergens found in *Glycine max* was also made. Using *in-silico* virtual screening, molecular mechanics, and molecular dynamics simulation approach, we have also designed peptidomimetics based lead, targeted at interaction interface of Gly m8 with Fab region of IgE.