Chapter 1

Introduction
Food is essential for the sustenance of life, but occasionally it can turn out to be a foe and may result into life threatening conditions in the form of food allergies, intolerances and toxicities due to its various components. Though the mechanisms involved in food intolerances and toxicities are well understood, the molecular basis of food allergy is poorly understood because of the involvement of a multifaceted interplay between host immune system and the dietary antigens. Food allergies by and large entail an adverse immunological (hypersensitivity) response to proteins present in food. As such food allergy is not a single disease nor is it caused by single pathophysiological condition, rather it encompasses a range of disorders including a wide spectrum, ranging from chronic situations affecting gastro-intestinal tract and skin to acute and potentially fatal manifestations. Most of the research till this date is based on the epidemiological, clinical and immunological aspects of the disorder. Though well addressed in case of small molecular weight xenobiotics-like drugs, the basic understanding of the structural contributions of the macromolecular allergens in the generation of allergic reaction is very rudimentary.

It is very well established that not all the proteins are allergenic. The allergy associated proteins belong to very few specific protein families. Thus, involvement of structure specific features influencing the allergenic potency of a protein is highly plausible. The main challenge is to identify the common structural features that could be associated with protein allergenicity. To achieve this goal we took the approach of comparative structural proteomics, involving an analysis of allergy related proteins by structure-based comparison in the context of their allergy potentials.

It is interesting that majority of the plant food allergens are clustered within a few protein families. In most cases they are the proteins that ensure survival of the
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species as either seed storage proteins or proteins that are actively involved in the
defence of the organism. The seed storage family of proteins are broadly classified
into 2S albumins, 7S vicilins and 11S globulins. The storage proteins are highly
polymorphic and functionally diverse (Shewry et al., 1995). Besides studying the
seed proteins for allergenicity, they present a diverse pool of novel protein folds
study of which will enhance the basic understanding of these proteins in
physiological and evolutionary context.

Among the 8 major sources of food allergy, legume seeds and tree nuts are
the leading causes. In comparison to animal sources plant sources are rich in variety
of proteins associated with allergy. Much of the interest in proteins from seeds is
driven by their importance in food, either their nutritional quality for livestock or
their functional properties for food processing. Being a very rich source of proteins
the tree nuts and legume seeds are good source of experimentation. The present study
is directed towards understanding of the architecture of the seed proteins with allergy
potential. The thesis is an endeavour towards structure-based understanding of
regular physiological functions and evolutionary implications of the seed proteins in
addition to correlating structure with the determinants of protein allergenicity.

This thesis addresses two major classes of the seed proteins: albumins and
globulins. It is organized into 7 chapters including the present one. The next chapter
provides an overview of food allergens and the efforts to delineate various aspects
related to it. This chapter also provide a review on seed storage proteins, highlighting
the structural and physiological studies and their association with allergy. Chapter 3
outlines the experimental procedures employed during the course of this study.
Chapter 4 and chapter 5 deal with the albumin class of seed proteins highlighting the
protein structural fold and its association with plant physiology. While chapter 4 describes the normal physiological role of albumin proteins, chapter 5 for the most part deals with the evolutionary divergence of the albumin proteins and their physiological implications. Chapter 6 highlights the globular protein, presenting the structural features associated with the allergy potential of a globular plant seed protein. Finally, the insights provided by these studies in understanding the physiology and facets allergenic properties are discussed in the concluding chapter.