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Lectins-Robust and Quintessential Proteins of Nature: A Review

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ABSTRACT

Recent advances in glycobiology have proclaimed that cell surface saccharides play a pivotal role in recognition events. More accurately, these saccharides may be complexed by lectins. Lectins are saccharide binding proteins that are highly specific for sugar moieties of other molecules. They are ubiquitous in nature. They are diverse proteins with spectacular potential and overwhelming medical applications. Hence, there is quest for identification of new lectins and their precise mechanism of action with specific ligands. In this review, main features of lectins are succinctly described with emphasis on ligand binding and therapeutic applications.

Key words: Lectins, Lectin-sugar interactions, Oligomerisation, Therapeutic applications.

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Lectins are multivalent sugar binding proteins of non-immune nature. They play pivotal roles in various biological processes such as cell-cell recognition, host pathogen interactions, serum glycoprotein clearance, innate immune response, cancer metastasis, embryogenesis, tissue development and mutagenic stimulation (Rini *et al* 1999, Feizi 2000, Sharon 2007, Taylor and Drickamer 2011, Dam and Brewer 2010). Even though they are involved in many immune responses, they cannot be termed as antibodies. Lectins do not exhibit enzymatic activity towards their sugar ligands so carbohydrates are neither modified chemically nor metabolised by them. Lectin sugar interactions are reversible and highly specific (Vijayan and Chandra 1999 Loris 2002, Sharon and Lis 2004). Binding affinity of lectin and ligands is low; however, most of the lectins contain several binding sites per molecule and also form oligomers, thereby accomplishing high avidity interactions (Babu, *et al* 2007, Esko and Sharon 2009). Water bridges, variations in loop length and post translational modifications are the strategies deployed at molecular level to exhibit remarkable sugar specificity (Manoj, Surolia 2000, Abhinav and Vijayan 2014).

One of the defining features of lectins due to multivalency is their ability of agglutinate various cells and to precipitate polysaccharides and glycoproteins in solution (Kaltner 1998). Lectins can conjoin cells via interactions with carbohydrates on their surfaces. Their robust ability to agglutinate erythrocytes indeed led to the discovery of lectins at the end of the 19th century (Boyd and Shapleigh 1954, Gabius 2004). Lectins are ubiquitous in nature. They occur in all five kingdoms of life and are involved in many biological processes (Kaur and Singh 2006, Akkouh 2015, Moulei, Alexander *et al* 2015) .

The ubiquitous distribution of lectins affirms their significance *in situ*. Plant lectins have been studied extensively. In fact “ricin” the first lectin to be reported was isolated from plants (Olsnes 2004). Fascinatingly, of the six structural classes of plant lectins (Table 1.1) in three cases the lectin subunits cherish approximate three fold symmetry and each subunit is believed to have evolved through successive gene duplication, fusion and divergent evolution (Endo and Tsurugi 1987, Sankaranarayanan *et al* 1996).

The name lectin is derived from Latin word “legere” meaning to choose or select. Boyd and Shapleigh termed these proteins lectins because of their ability to distinguish between different erythrocytes. Lectins are also called hemagglutinins, phytoagglutinins or phytohemagglutinins because they were primarily discovered in plant extracts. Later the term lectin was generalized by Sharon and Lis in 1972 and now used as mentioned above, for all multivalent carbohydrate specific proteins of non-immune origin. However, the term “hemagglutinin” is still used in viral lectin nomenclature. The earliest report dates back to the year 1888, when Peter Stillmark demonstrated the toxicity and agglutination ability of ricin from castor seeds (*Ricinus communis*) as part of his doctoral work (Van Damme *et al* 2001). Later on many non-toxic proteins, which could agglutinate blood, were purified from natural sources. The ability of these “agglutinins” to bind carbohydrates present on the surface of erythrocytes was established as the reason behind the property of agglutination in 1952. Certain plant seed extracts had the ability to distinguish between different human blood group types.

Lectins have been classified based on several parameters like (Kumar and Reddy 2012)

1. Carbohydrate binding specificity; Ex: mannose, galactose, fucose, rhamnose, lactose specificity. Lectins with same specificity for simple sugars (eg: galactose lectins) show considerably different oligosaccharide binding preferences. Moreover, a large number of lectins have been found to have no affinity to simple saccharides.

2. Source organism: Ex: Plant, animal, virus, bacteria and other life forms.

3. Structural fold; Ex: jelly roll, β-prism, β-propeller and others. The fold based classification is used more extensively as it allows unambiguous classification of lectins. Molecular geometry based classification can be used for only those lectins for which 3d structures have been determined. Moreover, lectins with similar structures can belong to widely different species and can have varied saccharide specificities.

Plant Lectins

Lectins have been found in thousands of plant species and hundreds of them have been isolated and characterized. Indeed, plant lectins comprise of the most elaborately studied lectin superfamily. These proteins display a wide variety of tertiary and quaternary structures. Moreover, often the same tertiary structure is a part of plethora of quaternary structures (Hamelryck *et al.* 1999). Although, lectins have high specificities for their saccharide ligands, the variations in their secondary and tertiary structure remain very obtuse. Based on structural fold, plant lectins can be grouped into six classes such as legume lectin, hevein domain, β-trefoil, β-prism I, β-prism II and Cyanovirin-N folds respectively. This classification is illustrated in table below.

The major secondary structure component of most plant lectins is the β-sheet (Chandra *et al* 2001, Rini 1995). It is these mutual orientations of these β-sheets in the lectin subunit that christen them differently. The three main kinds of β-sheet structures found in plant lectins are the jelly roll, hevein domain and barrel structures (Sauerborn *et al* 1999, Gouget 2006). In legume lectins minor alterations in the amino acid sequences of protein subunits with nearly identical tertiary structures can give rise to varied modes of quaternary associations. The barrel type structures can be further sub classified into β-trefoil, β-prism I and β-prism II folds. The deviation in the quaternary structure of lectin within a particular category eventuates from the variations in the mutual orientations of subunits in the oligomers. β-trefoil fold is the sugar recognition motif of multidomain proteins and is not implicated in inter subunit interactions. A single subunit of any plant lectin is able to bind to ligand and oligomerisation is not cardinal to the process of recognition. However, it is still seen that all plant lectins found and studied till date exist as oligomers in nature. This suggests that there is inherent co-operativity in the ligand recognition process in these proteins. The diverse quaternary structure could lead to higher order sugar specificities and generate the mandated topology on the macromolecular surface to facilitate uninhibited recognition or binding. Legume lectin fold comprises of a curved 7-stranded front β-sheet, a flat 6-stranded back β-sheet and a short 5-stranded β-sheet connecting the front and back â-sheets. The loops connect the 3 sheets and constitute about 50% of the total protein. There are 2 hydrophobic cores in the protein. The first core lies between 3 β-sheets while the second core lies in front of the curved β-sheet enclosed by the loops connecting the strands of front β-sheets. The carbohydrate binding site is located on front β-sheet with major contributions from the loops. Loops involved in carbohydrate binding are named as A, B, C and D. The legume lectins are C-type lectins as they bind to carbohydrates in a metal dependent manner. They require Ca^{2+} and Mn^{2+} ions for sugar binding. Chelated ConA fails to bind sugars; however, the carbohydrate binding is restored in the presence of metal ions (Francisco *et al* 2006).

Some of the typical lectins like ConA, pea lectin, favin with canonical structure dimerization involve alignment of anti-parallel β-sheets abreast at the interface of two monomers. Dimers further associate to form tetramer as in the case of ConA. Peanut has unusual open quaternary structure stabilised by hydrophobic interactions, hydrogen bonds and water mediated interactions. Quaternary structure of lectins is pH dependent.

Carbohydrate binding site

Advances in X-ray crystallography have shed light on lectin-ligand interactions, providing the basis for comprehension of protein interactions with natural ligands. Typically lectins exhibit fastidious specificities for di, tri and tetra saccharides with higher association constants than monosaccharides. Carbohydrate binding sites are preformed facile depressions at protein surface. Invariably in all legume lectins, irrespective of their sugar specificity, four invariant amino acids are involved in ligand interaction, an aspartic acid, an asparagine, a glycine (ConA is exception) and an aromatic amino acid or leucine. Peanut agglutinin has Asp, Gly, Asn and Tyr. Site directed mutagenesis of Asp or Asn abrogates lectin-sugar interactions. Although amino acid residues are conserved, the heterogeneity of sugar binding stems from other amino acid residues in the combining pocket. For instance ConA is specific to mannose and glucose whereas peanut agglutinin is specific to galactose. Four loops containing 4 key amino acid residues are involved in sugar

Table 1.1: Structural classes in plant lectins.

Structural class	example	Source organism
1.Legume(jelly roll fold)	Concanavalin A	*Conavalia ensiformis*
2.Hevein domain fold(cereal lectin)	Wheat germ agglutinin	*Triticum vulgaris*
3.β-trefoil fold	Ricin	*Ricinus communis*
4.β-prism fold I	Jacalin	*Artrocarpus integrifolia*
5.β-prism fold II	Snowdrop lectin	*Galanthus nivalis*
6.Cyanovirin-N homolog	CrCvNH	*Ceratopteris richardii*

binding pocket. Asp and Gly belong to loop A and B respectively, Asn and hydrophobic residues reside in loop C. Loop D imparts specificity as it is highly volatile in terms of length sequence and conformation. The Ca^{2+} and $Mn^{2+}$are juxtaposed to carbohydrate binding pocket. These divalent ions are not implicated in saccharide; rather they align amino acid residues spatially facilitating the sugar-lectin interactions. Ca^{2+} coordinates asp and asn in cisoid-peptide conformation resulting in bond formation between Asn and Ala which generally preludes Asn, imparting pertinent conformation for sugar binding. The binding interactions are predominantly hydrophobic and hydrogen bonding, with appreciable augmentation from Vanderwaal's forces as well. The spatial dislocation of hydroxyl moieties renders carbohydrates hydrophobic thereby, promoting hydrophobic interactions between lectin and sugar. Ligand-lectin reactions are mediated by water bridges (Ambrosi and Cameron 2005).

Physiological functions

Indeed lectins bind to sugars unambiguously with high specificity. This dexterity is rather evolutionarily conserved implying its significance in various biomedical applications. Lectins have been christened as plant antibodies imparting defence against pathogen invasions. Due to their sugar binding nature, legume lectins are implicated in symbiotic associations. This hypothesis however should be taken with a pinch of salt, as soyabean mutants devoid of lectins do indulge in symbiosis.

Oligomerization

Legume lectins exhibit substantial variations in their oligomerization status, chiefly being dimers or tetramers. This is the yardstick for further classification as type II, XI, X2, X3 and X (Manoj and Suguna 2001). Oligomerization has natural and advantageous functional ramifications. The respective monomers of oligomers possess all indispensable features that are crucial for sugar binding. Indeed oligomerization augments lectin-ligand interactions per se. Self-association is an isochronous characteristic of a huge number of legume lectins. Each monomer houses a single sugar recognition alcove. Hence oligomerization is imperative to accomplish efficient functionality. A sizeable number of plant lectins are obligate oligomers. Native conformation is warranted by quaternary structure. Peanut lectin is little quirky in this aspect. It is an 110kDa tetramer of subunit mass of 27kDa. This tetramer dissociates into dense monomers. Nevertheless, the free subunits adopt molten globule like conformation with diminished carbohydrate binding capacity. Some plant lectins like ConA, peanut lectin, pea lectin, soy bean agglutinin, winged bean acidic lectin possess high structural stability, with amalgamated folding/oligomerization free energies of Gibb's ranging from -13 to -30$KCalmol^{-1}$ (dimer units). Exclusion to this is frutalin, with free energy of -6$KCalmol^{-1}$ (dimer units). Indeed the stability of frutalin is due to tetramer, as this oligomer forms from the unfolded free subunits. Indeed, this formation mechanism and high structural stability are not astonishing for proteins that require the oligomeric state to perform their biological activity.

Multivalency of lectins

Solution studies in garlic lectin had shown that the binding affinity of the lectin for high mannose oligosaccharide is of the order of magnitude higher than for mannose. This observation flounder the idea of multiple binding sites on a lectin molecule. Oligosaccharides of sufficient length can crosslink lectin oligomers, amplifying the protein-oligosaccharide interactions manifold, thus explaining the role of multivalency in lectins.

Lectins multitask as lipoxygenase and polyphenol oxidase in some legumes

The function of lectins in plants is still an enigma. They are crucial for seed germination, cell wall assembly and rhizobial nodulation of legume roots and in defence. Some of the lectins possess enzymatic activities and are termed leczymes. A tetrameric lectin from D.biflorus has been reported with opulent lipoxygenase activity. The LOX activity is warranted by hydrophobic binding site of tetrameric lectin, besides the presence of a Mn^{2+} ion. This was the maiden report of a protein exhibiting dual functions of hemagglutination and LOX-like activity (Roopashree and Appu Rao 2006). Both these activities are attributed to the same protein, with different loci. There is no interplay between lectin and LOX locus. LOX activity amalgamated with lectin activity reckons up a new facet to our comprehension of lectin functions.

Polyphenol oxidase (PPO) activity is observed in D.lablabII (Prakash *et al* 2018). There is a great deal of disparity in secondary structure and active site geometry of DLL II PPO activity with its canonical PPOs. Legume lectins have 2 metal binding sites *viz* A and B housing Mn^{2+} and Ca^{2+} respectively. PPO activity is reliant on Cu^{2+}, but not Ca^{2+} and the lectin activity necessitates only Ca^{2+}. A proxy mechanism of PPO reaction may be functional in DLL II, involving a mononuclear Cu^{2+} metal centre that is contrary to the binuclear Cu^{2+} metal centre observed in canonical PPOs.

Animal lectins

Animal lectins can be classified based on various parameters such as cellular localization, homogeneity of sequences, nature of their saccharide ligands and type of biological processes in which they are implicated and depends on metal ion for their carbohydrate recognition. Based on the location, lectins are classified as integral lectins of membrane and soluble lectins of intra and intercellular fluids. Based on the saccharide binding nature and structural characters, lectins are grouped as C-type lectin, S-type lectins, I-type lectins and P-type lectins. Although the overall structure of lectins differ, the carbohydrate binding property is attributed to the presence of active segment called the carbohydrate recognition domain (CRD). The above mentioned classification is based

on this feature. Galectins or S-type lectins are those that depend on the presence of thiol groups for carbohydrate binding and are specific to β-galactose. They are relatively small molecules (14-35KDa) which share a highly homologous domain called S-carbohydrate recognition domain (S-CRD) essential for the activity of galectins (Varki, Cummings 1999).

Gabius classification of animal lectins into 5 main groups is as follows.

Pentraxins

They are a superfamily of plasma proteins that are involved in innate immunity in invertebrates and vertebrates and are considered pattern-recognition receptors. They contain L-type lectin folds. The subunits are arranged in pentamers; hence name pentraxins.They may help in the assembly of a hyaluronan rich extracellular matrix, which may involve binding to the hyaluronan heavy chain-1 complex and regulation of TNF-stimulated gene-6.

Collectins

These are collagen containing C-type lectins. C-type lectins depend on Ca^{2+} ions for ligand binding. They exhibit great diversity in their structure and function (Cambi and Figdor 2005). The large family of C-type lectins include collectins, selectins, endocytic receptors and proteoglycans. Some of these proteins are secreted and some are trans membrane. They function as adhesion and signalling receptors in many immune functions such as inflammation and immunity to tumour and virally infected cells (Rini 1995). They contribute to "innate immunity" and act before the induction of antibody-mediated response (Holmskov 1993). Amongst total of six known lectins "mannose binding lectin" (MBL) is well studied. MBL involves the association of three 32KDa polypeptides through the formation of a collagen like triple helix domain (Matsushita 1996, Wallis and Drickamer 1999). MBL recognizes carbohydrate moieties on the surface of a large number of microorganisms. Binding of MBL to microorganisms results in the activation of "Lectin-pathway" of complement system (Endo and Fujita 2000). Apart from mannose binding lectin, lung surfactant proteins A and D are key collectins of the superfamily that bind carbohydrates and glycolipids with broad specificity (Van De *et al* 2004, Kuroki and Gasa 1992). The mannose specific C-type lectin DC-SIGN is a trans membrane protein phagocytic receptor for microorganisms such as viruses, bacteria, fungi and parasites (Tsoni and Taylor 2009, Geijtenbeek). Siglecs are (Sialic acid binding immunoglobulin like lectins) that are mostly expressed by the cells of immune system. They are the major homologous subfamily of I-type lectins (O'Reilly and Paulson 2009). Siglecs from mammalian cells have been reported. They execute a battery of functions depending on lectin-ligand reactions.

Galectins

They are Ca^{2+} independent, β-galactose binding animal lectins. They were early termed as S-type lectins since they require disulphide bonds for their stability and carbohydrate binding. Even though they lack signal sequences, they are able to localize to different parts of the cells by mechanisms that remain elusive. They display jelly roll fold containing 2 antiparallel β-sheets. Galectins are specific for galactose, N-acetylgalactoseamine, lactose and N-acetyl lactose amine. Galectins regulate adaptive immune response by controlling the interaction between antigen presenting cell and T cells. They influence inflammatory response of cells by regulating the secretion of T cell cytokine (Ilarregui, Croci and Bianco *et al* 2009).

Parasite lectins

Parasites usually attach to the cell surface carbohydrates to initiate infection via adhesion to host cells. Entamoeba histolytica has a 260KDa heterodimeric lectin specific for terminal galactose/N-acetylgalactosamine on glycoproteins and glycolipids present on host cells. This adhesion is crucial for virulence (Mann 2002). Many other protozoans arbitrate function through sialic acid residues of host cells.

Bacterial lectins

Bacteria have several types of lectins. They are either located on surface or at pili. Nathon Sharon and colleagues first described bacterial surface lectins in 1970. Their primary function is to facilitate the attachment or adherence of bacteria to host cells-a prerequisite for bacterial colonisation and infection. Thus, bacterial lectins are often referred to as adhesins. Like animal lectins some microbial adhesins bind to terminal sugar residues via carbohydrate recognition domain whereas the others bind to internal sequences found in linear or branched oligosaccharide chains. The interaction

Table 1.2: Types of carbohydrate-recognition domains in animal lectins (Taylor and Drickamer 2011).

Type	structure	ligands	Function
calnexin	β-sandwich	Glc Man	Protein sorting in ER
M-Type	α-helical barrel	Man	ER associated protein degradation
L-Type	β-sandwich	Man	Protein sorting in ER
P-Type	Unique β-rich structure	Man-6-P	Protein sorting post Golgi
C-Type	Unique mixed α/β structure	Various	Cell adhesion (selectins), glycoprotein clearance, innate immunity (collectins)
Galectins	β-sandwich	β-galactosides	Glycan cross-linking at cell surfaces
I-type lectins	Immunoglobulin superfamily	Sialic acid	Cell adhesion (Siglecs)
R-Types	β-trefoil	Various	Enzyme targeting, glycoprotein hormone turnover

of adhesins with host glycans is an important determinant of the tropism of the corresponding pathogen or symbiont. Bacteria also produce soluble toxins, whose action often depends on glycan- binding subunits that allow the toxins to combine with membrane glycoconjugates to deliver the functionally active toxic subunit across the membrane. Colonisation of tissues by microorganisms is usually non-pathogenic. For example, the normal flora of the gastrointestinal tract is determined by appropriate colonisation by beneficial bacteria. Similarly, the initial formation of nitrogen—fixing nodules in leguminous root tips by species of Rhizobium involves lectins on the root tip binding to glycan-containing Nod factors produced by the bacterium (Varki 1999).

Viral lectins

The first viral lectin was isolated from influenza virus. Its crystal structure was determined by Don Wiley and associates in 1981. It is specific to sialic acid. Even though the affinity of this interaction is low, like that of other lectins with their glycan ligands, the avidity is enhanced by hemagglutinin trimerization and a high density of glycan receptors present on the host cells. Rotavirus also is specific to sialic acid residues. A number of viruses, including herpes simplex virus, foot and mouth disease virus, HIV and dengue flaviviruses employ heparan sulphate proteoglycans as adhesion receptors.

Archeal lectins

Archea inhabit extreme environmental conditions like extremes of temperature and salinity. Archea run counter to bacteria in their genetic and biochemical constitution and was recognized as a province of life distinctly different from two other domains bacteria and eukaryotes (plants, animals, fungi and protists). Lectins from Archea were first reported by Vijayan (Abhinav and Vijayan 2016). They screened 165 archeal genomes of 78 different species. They identified 46 lectin domains. These lectins contain 7-bladed β-propeller, the β-trefoil, the legume lectin, β-prism I, the C-type and 5-bladed β-propeller lectin folds. Many of these lectin folds must have evolved into functional proteins before the three domains of life ramified. The single biggest group of domains identified in archea displays homology with the integrin α-XI-terminal domains of mushroom lectin from Psathyrella velutin (PVL). It assumes 7-bladed β-propeller fold. Sugar binding sites are situated in the upper part of the β-propeller, in space between consecutive blades. A hydrophobic plot, mainly made up of the aromatic amino acids interacts with each bound sugar. The saccharide is also hydrogen bonded to 2 main chain asparaginyl NH groups and tryptophan side chain.

Applications of lectins

1. Lectin research has emerged as forefront area recently. They are extensively used in drug targeting research as they provide appropriate specificity and are resistant to enzymatic degradation. Different cell types express distinct glycan arrays and particular diseased cells often express different glycans compared to their normal counterparts. Therefore lectins could be used as cargo molecules to target drugs specifically to different diseased or normal cells and tissues. Their structure and sugar specificity determine if they will be endocytosed by target cells or not. Thus, selection of appropriate lectin may allow the cellular uptake and subsequent cellular manoeuvre of such delivery systems. This approach warrants better absorption and bioavailability of poorly absorbable drugs, peptides and proteins.

2. Ribosome inactivating lectins (RIL) or ribosome inactivating proteins (RIP)-based immunotoxins: They are produced by plants and microbes against predators. They consist of lectin chain (B chain) connected by disulphide bridge with a ribosome inactivating chain (A chain). A chain can inhibit translation thereby inhibiting protein synthesis in mammalian cells. RILs can be used as immunotoxins (Juan, Recio *et al.* 2017).

Chief applications of lectins

1. Identification and separation of cells
2. Isolation and purification and structural studies of glycoproteins
3. Identification of types of carbohydrates on cells and organelles, histochemistry and cytochemistry.
4. Neuronal circuit mapping
5. Mitogenic stimulation of lymphocytes
6. Studies of glycoprotein biosynthesis
7. Blood typing
8. Aricultural applications

Lectins from sources other than plants are rarely in clinical use (Khan, Sherwani and Mehmood 2002).

Blood typing

Different blood groups are typed based on specific RBC surface sugar and lectin interactions. Lectins from Vicia cracea have been proved to be good anti A, lectin from Dolichus biflorus as anti A 1 and lectin from Griffonia simplicifolia as anti B. Basic wing bean agglutinin is specific to A and B blood group glycans while acidic winged bean agglutinin is specific to O blood group glycans.

Purification of glycoconjugates

Lectins are exploited in protein purification. Glycoproteins and glycopeptides are trapped by lectins used in affinity column chromatography. The primary lectins used are ConA, wheat germ agglutinin and Jacalin. Jacalin is generally used to isolate IgA from human serum, isolating plasma glycoproteins and for applications in histochemistry. It is used to distinguish malignant cells from benign reactive cells.

Mitogenic stimulation of lymphocytes

Certain lectins are mitogenic. Lectins bind to carbohydrate receptors on the surface of lymphocytes which contain the same sugar moieties appropriate for the specificity of the mitogenic lectins. Lectins such as phytohemagglutinins Concanavalin (ConA) and pokeweed mitogen (PWM) are mitogenic. They act as polyclonal activators of T-cells. They bind to a number of glycoproteins expressed on the plasma

membrane of T-cells. ConA is selective T-cell mitogen whereas PWM is both T and B cell mitogen (Bahadur, Sujatha *et al* 2013). Jacalin is a selective mitogen for human CD^{4+} T-cells.

Lectins in antiretroviral therapy

Lectins can be used to inhibit HIV infection. The entry of virus into the host is crucial step in infection. Lections can be used as entry inhibitors. Viral coat proteins are glycosylated. Lectins can bind to these glycans and quell the ingression of virus into the host, thereby acting as antiviral molecule. Lectins with antiretroviral nature have been identified and isolated from animals, plants and microorganisms and could aid as anti-HIV natural products. Cyanovirin-N, Microvirin, BanLec and Griffithsin are reputed anti-HIV lectins. Griffithsin is also known to mitigate hepatitis C and herpes simplex virus infection. Lectins with inhibitory activities against coronaviruses are reported (Goding 1996 Mazalovska 2018).

Lectins in agriculture

Agricultural implementation of lectins as bio pesticide against lepidopteron insects is overwhelming. Lectins are utilized in biotechnological control strategies such as gene pyramiding to combat insect inflicted crop loss. Thus, lectin genes which are related to plant defences are highly recommended (Mustafa *et al*., 2019). Incorporation of synthetic genes containing lectin domains in plants can be exploited further to cater to the alarmingly increasing food needs of the global population (Maria L *et al*., 2015). The deployment of lectins in transgenic plants has very promising result (Maria *et al*., 2015).

CONCLUSION

A thorough understanding of lectin-sugar interactions is required for biomedical applications. An in depth knowledge of the structural and energetic aspects of the interactions is thus imperative. Failure of carbohydrate therapeutics can be partly attributed to poor understanding of mechanism of action. With more emphasis on understanding of structure and mechanism, results can be highly encouraging and promising.

REFERENCES

Abhinav. K.V Vijayan. M (2014). Structural diversity and ligand specificity of lectins. The Bangalore effort. Pure and Applied Chemistry. 86(9): 1335-1355.

Abhinav. K.V, Samuel. Vijayan. M (2016). Archeal lectins: An identification through genomic research, Protein Structure Function and Bioinformatics. 84: 21-30.

Akkouh. O, Singh. S, Yin. C, Dan. X, Chan Y. S, Pan. W, Cheung. R.C. F (2015). Lections with anti-HIV activity; A Review, Molecules. 2 0: 648-668.

Ambrosi. M, Cameron. N.R, Davis. B.G (2005). Lections-Tools for the molecular understanding of the glycocode, Organic and Biomolecular Chemistry. 3: 1593-608.

Babu P, Sinha. S, Surolia. A (2007). Sugar-Quantum pot conjugates for a selective and detection of lectins, Bioconjugate chemistry. 18: 146-151.

Bhadur. B, Sujatha. M, Carels. N (2013). Jatropha challenges for new energy crop. Genetic improvement and Biotechnology volume 2 Springer.

Boyd W. C, Shapleigh. E (1954). Separation of individuals of any blood group into secretors and non-secretors by use of plant agglutinin (Lectin), Blood 9.

Cambi. A, Figdor. C.G (2005). Levels of complexity in pathogen recognition by C-type lectins, Current Opinion in Immunology. 17: 345-351.

Chandra. N.R, Prabhu. M. M, Suguna. K, Vijayan. M (2001). Structural similarity and functional diversity in proteins containing the legume lectin fold, *Protein Engineering,* Design and selection. 14: 857-866.

Dam. T. K, Brewer. C.F (2010). Multivalent lectin –carbohydrate interactions. Advanced Carbohydrate Chemistry Biochemistry. 139-164.

Endo. Y, Tsurugi. (1987). RNA N-glycosidase activity of virus A-chain. Mechanism of action of the toxic lectin ricin on eukaryotic ribosomes. Journal of Biological Chemistry. 262: 8128-30.

Endo.Y, Fujita. T (2000). Complement activation through the lectin pathway. 45:671-8.

Esko. J.D, Sharon N. (2009). Microbial Lections; Hemagglutinins, Adhesins and Toxins *Essentials of glycobiology 2nd edition.*

Feizi. T (2000). Carbohydrate- mediated recognition system in innate immunity.

Francisco Corzana, Jesus. H, Busto, Gonzalo Jimenze- Oses Juan. L, Asensio, Jesus Jimenz-Barbero and Jesus. M, Perigrena, Alberto Avenoza (2006). New insights into α-Gal NAc-Ser motif: Influence of hydrogen bonding versus solvent interactions on the preferred conformations, Journal of American Chemical Society. 45: 14640-8.

Gabius. H.J, Siebert H.C andre. S, Jimenz-Barbero J, Rudiger H, (2004). Chemical Biology of sugar code, Chembiochem. 5: 740-764.

Goding. J.W (1996). Monoclonal antibodies: Principles and practice: Production and application of monoclonal antibodies in cell biology, biochemistry and immunology. Academic Press.

Gouget. A, Senchou. V, Govers. F, Sanson. A, Barre. A, Rouge. P, Pont-Lezica. R, Canut. H (2006). Lectin receptor kinases participate in protein-protein interactions to mediate plasma membrane-cell wall adhesions in *Arabidopsis*. Plant Physiology. 140: 81-90.

Hamertryck. T. W, Loris. R, Bouckaert. J, Da Thi. M. H, Strecker. G, Imberty. A, Fernandez E, Wyns. L, Etzler. M.E (1999). Carbohydrate binding site in two legume lectin oligomers from *Dolichas biflorus*. Journal of Molecular Biology. 286: 1161-1177.

Holmskov. U. (2000). Collectins and collectin receptors in innate immunity, APIMS Suppl.

Holmskov. U, Jensenius. J.C (1993). Structure and function of collectins: humoral C-type lectins collagenous regions Behring Institute of Mitt. 224-35.

Ilarregui. J.M, Croci. D.O, Bianco. G. A, Toscano. M.A, Salatino. M, Vermeuolen. M.E, Geffner. J.R, Rabinovich. G.A (2009). Tolerogenic signals delivered by dendritic cells to T-cells through a galectin-1-driven immunoregulatory circuit

involving interleukin 27 and interleukin 10. Nature Immunology. 10: 981-991.

Kaltner. H, Stierstorfor B (1998). Animal lectins as cell adhesion molecules. Cells Tissues organs. 161: 162-179.

Kaur. M, Singh. K, Rup P.J, Kamboj, S. Saxena A.K, Sharma M, Bhagat M, Sood.S. K, Singh. J (2006). A Tuber-Lectin from Arisaema jacquemontii Blume. Journal of Biochemistry Molecular Biology. 39: 432-44

Khan. F, Khan. R. H, Sherwani. A, Mohmood. S, Azfer. M.A (2002). Lectins as markers for blood grouping. Medical Science Monitor. 88: 293-300.

Kumar. K. K, Reddy. G. S, Reddy. B, Shekhar. P. C, Sumanthi. J, Chandra, P. (2012). Biological role of lectins-A review. Journal of Orofacial Sciences. 4.

Kuroki. Y, Gasa. S, Ogasawara. Y, Makita. A, Akino. T (1992). Inding of pulmonary surfactant protein A-galactosyl ceramide and asylo-GM2. Archives of Biochemistry and Biophysics. 299: 261-7.

Lavinde Juan. L, Garcia Recio. V, Jimenez Lopez. P, Girbes Juan, Cordoba-Diaz. D (2017). Pharmaceutical Applications of lectins. Journal of Drug Delivery Sciences and Technology. 42: 126-133.

Loris. R (2002). Principles of structures of animals and plant lectins. Biochemica Biophysica Acta. 1572: 198-208.

Mann. B.J (2002), Structure and function of Entamoeba histolytica Gal /Gal NAc lectin. International Review of Cytology. 216: 59-80.

Manoj. N, Srinivasa. V. R, Surolia. A, Vijayan. M, Suguna. K (2000). Carbohydrate specificity and salt-bridge mediated conformational change in acidic winged bean agglutinin. Journal of Molecular Biology. 302: 1129-1137.

Manoj. N, Suguna. K (2001). Signature of quaternary structure in the sequences of legume lectins. Protein Engineering and Design Selection. 14: 735-745.

Maria Ligia. R, Caio .F.R, Carolina. T (2015). Insecticidal activity of plant lectins and potential application in crop production. Molecules. 20: 2014-2033.

Matushita. M, Fujita. T (1996). The lectin pathway. Research in immunology. 147: 115-11.

Mazaloska. M, Kouokam. J.C (2018). Lectins as promising therapeutics for the prevention and treatment of HIV and other potential confections. Biomedical Research International. 1-12.

Moulaei.T, Alexander. K.B, Shenoy. S.R, Meyerson J.R, Krumpe. L.R, Constantine. B, Wilson.J, *et al* (2015). Griffithsin tandems; flexible and potent lectins inhibitors of the human immunodeficiency virus. Retrovirology. 12: 6.

O'Reilly M.K, Paulson. J.C (2009). Siglecs as targets for therapy in immune cell-mediated disease.

Olsnes.S (2004). The history of ricin, abrin and related toxins. Toxicon. 44: 361-370.

Rini J.M, Lobsanov Y D (1999). New animal lectin structures. Current Opinion in Structural Biology. 9: 578-84.

Rini. J.M (1995). Lectin Structure. Annual Reviews of Biophysics and Biomolecular Structure. 24: 857-577.

Roopashree. S, Singh. S.A, Gowda. L. R, Appu Rao. A.G (2006). Dual-function protein in plant defence: seed lectin from *Dolichos biflorus* (horse gram) exhibits lipoxygenase activity. Biochemical Journal. 395: 629-639.

Sankaranarayanam. R, Sekar. K, Banerjee. R, Sharma. V, Surolia. A, Vijayan. M (1996). A novel made of carbohydrate recognition in Jacalin, a Moraceae plant lectin with a B-prism fold. Nature structural Biology. 3: 596-603.

Sauerborn. M.K, Wright. L.M, Reynolds. C. D, Grossmann. J.G, Rizakallah. P.J (1999). Insights into carbohydrate recognition by Narcissus Pseudonarcissus lectin. The crystal structure at 2A^{o} resolution in complex with α 1-3 mannobiose. Journal of Molecular Biology. 290: 185-199.

Sharon N, Lis. H, (2004). History of lectins-from hemagglutinins to biological recognition molecules. Glycobiology. 14: 53R-62R. (1972).

Sharon. N (2007). Lectins: Carbohydrate specific reagents and biological recognition molecules. Journal of Biological Chemistry. 282: 2753-2764.

Taylor. M.E, Drickamer. K (2011). *Introduction to Glycobiology*, Oxford University Press. Trends in Pharmacological Sciences. 30: 240-248.

Tsoni. S, V, Kerrigan. A. M, Marakalal. M.J, Srinivasan. N, Duffield. M, Stelle. C, Brown. G. D (2009). Complement C3 plays an essential role in the control of opportunistic fungal infections. Infection and Immunity. 77: 3679-3685.

Van Damme. E. J. M, Hao. Q, Chen. Y, Barre. A, Vandenbussche. F Desmyter. S, Rouge. P, Peumans W.J (2001). Ribosome -inactivating proteins; A Family of plants proteins that do more than inactivate ribosomes. Critical Reviews in Plant Sciences. 20: 395-465.

Varki. A (1999). Essentials of glycobiology, Cold Spring Harbor Laboratory Press

Varki. A, Cummings .R, Esko. J, Freeze. H, Hart. G, Marth. J (1999). S-type lectins (Galectins), Essentials of glycobiology 3rd edition chapter 27.

Vijayan. M, Chandra. N (1999). Lectins. Current Opinion in Structural Biology. 9: 707-714.

Wallis. R, Drickamer. A (1999). Molecular determinants of oligomer formation and complement fixation in mannose-binding proteins. Journal of Biological Chemistry. 274: 3580-9.