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Plant Lectins with Insecticidal and Insectistatic Activities

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Abstract

Lectins are an important group of proteins which are spread in all kingdoms of life. Their most lighted characteristic is associated to their specific carbohydrate binding, although function has been not even identified. According to their carbohydrate specificity, several biological activities have been assessed, finding that lectins can be used as mitogenic agents, biomarkers, and cytotoxic and insecticide proteins. Lectins have been classified according to several features such as structure, source, and carbohydrate recognition. The Protein Research Group (PRG) has worked on Colombian seeds from the family of Fabaceae and Lamiaceae plants, isolating and characterizing their lectins, and found more than one lectin in some plants, indicating that according to its specificity, different lectins can have different biological activities. In the case of legume domain lectins, they have shown the biggest potential as insecticide or insectistatic agents due to the glycosylation pattern in insect midgut cells. This review attempts to identify the characteristics of plant legume lectin domains that determine their insecticidal and insectistatic activities.

Keywords: lectin, insecticide, insectistatic, legume

1. Introduction

Lectins are glycoproteins of nonimmune origin that recognize and bind carbohydrates. These proteins are found in a wide variety of species (viruses, bacteria, fungi, seaweed, animals, and plants). This review is mainly based on information of plant lectins that have been found as important new agents in biological control. Plant lectins have been widely studied,

and in this group, the legume lectins have been related to insecticidal and insectistatic activities. In addition, *Phaseolus vulgaris* (PHA), *Glechoma hederacea* (Glehedra), *Canavalia ensiformis* (ConA), *Griffonia simplicifolia* (GSII), and *Pisum sativum* (PSA) lectins and other legume and Lamiaceae lectins have been studied by the Protein Research Group (PRG) in Colombia. It was evidenced that plant legume lectin domains have structural features characterized by a high percentage of β -sheet structures associated with dimeric or tetrameric assembly, presenting several specific sugar recognition sites, including mannose. In addition to these features, these lectins can interact with the digestive system of insect pests and produce a decrease in intestinal absorption capacity.

2. Definition, classification, and general features of lectins

Lectins are proteins or glycoproteins of the nonimmune origin with specific binding affinity for the carbohydrate moiety of glycoconjugates [1]. Lectins comprise a structurally diverse class of proteins characterized by their ability to selectively bind carbohydrate moieties of the glycoproteins of the cell surface. Lectins may be obtained from plant, microbial, or animal sources and may be soluble or membrane bound [2]. In nature, lectins play a role in biological recognition phenomena involving cells and proteins and thereby protect plants against external pathogens such as fungi and other organisms. The ability to bind and agglutinate red blood cells is well known and used for blood typing; hence, the lectins are commonly called hemagglutinins [3].

The term lectin is derived from the Latin word *legere* meaning “to choose” or “select” and has been generalized to encompass all nonimmune carbohydrate-specific agglutinins regardless of blood type specificity or source. Lectins were initially found and described in plants, but in subsequent years, multiple lectins were isolated from microorganisms and also from animals [4]. Interestingly, plant and animal lectins show no primary structural homology, but they demonstrate similar preferential binding to carbohydrates [5]. This suggests that animal and plant lectin genes may have coevolved, thus highlighting the importance of lectin-carbohydrate interactions in living systems [6].

Based on the amino acid sequences of available lectins, it is deduced that the carbohydrate-binding property of most lectins resides in a polypeptide sequence, which is termed as “carbohydrate-recognition domain” [7]. The binding with simple or complex carbohydrate conjugates is reversible and non-covalent. The specificity of lectins toward carbohydrates can be defined on the basis of “hapten inhibition test,” in which various sugars or saccharides are tested for their capacity to inhibit the property of hemagglutination of erythrocytes [8].

Lectins have been classified according to different features such as source (animal, vegetal, fungal, viral), carbohydrate affinity (mannose, glucose, galactose, fucose, sialic acid), number, and specificity of carbohydrate recognition domains (merolectins, hololectins, chimerlectins, and superlectins) [9]. However, current classification is based on 3D structure and is related to 48 families (**Table 1**) [10].

| Distribution | | | | | | | | |
|---------------------|---------------------------|------------------------------|-----------------------------|--------|-------|-------|----------|-------|
| No. | Family | Fold | Assembly | Animal | Plant | Fungi | Bacteria | Virus |
| 1 | L-type | Jelly roll | Dimer | x | x | x | | |
| | L-type-like | Jelly roll | Monomer | x | x | x | | |
| 2 | Galectin | Jelly roll | Monomer, dimer | x | | x | | x |
| 3 | Pentaxim | Jelly roll | Pentamer | x | | | | |
| 4 | I-type | Ig-like β -sandwich | Linked to different domains | x | | | | |
| 5 | C-type | α/β -fold | Linked to different domains | x | | | | |
| 6 | Hyaladherin | α/β -fold | Linked to different domains | x | | | | |
| 7 | Chitinase-like | $(\beta/\alpha)_8$ -Barrel | Monomer | x | x | x | x | x |
| 8 | M-type | $(\alpha/\alpha)_7$ -Barrel | Monomer | x | x | x | x | |
| 9 | R-type | β -Trefoil | Linked to enzyme | x | x | x | x | |
| | R-type-like | β -Trefoil | Linked to different domains | | | x | x | |
| 10 | ACA-like | β -Trefoil | Dimer | | x | | | |
| 11 | Botulinum neurotoxin-like | β -Trefoil | Linked to different domains | | | | x | |
| 12 | F-box | Jelly roll | Linked to different domains | x | | | | |
| 13 | F-type | Jelly roll | Linked to different domains | x | x | x | x | |
| 14 | PA-LL-like | Jelly roll | Dimer | | | | x | |
| 15 | P-type | α/β -fold | Dimer | x | | | | |
| 16 | Ficolins | Fibrinogen-like | Trimer | x | | | | |
| 17 | Malectin | Jelly roll | Monomer | x | | | | |
| 18 | Calnexin | Jelly roll | Monomer | x | | | | |
| 19 | Tachylectin-2-like | 5-Bladed β -propeller | Monomer | x | | | | |
| 20 | Tachycitin-like | β -sheet-cysteine fold | Monomer | x | | | | |
| 21 | Hevein | Cystine-knot motif | Dimer | x | x | | | |
| 22 | Jacalin-related | β -Prism I | Tetramer | x | x | | | |
| 23 | SUEL-related | α/β -fold | Linked to different domains | x | | | | |

| Distribution | | | | | | | | |
|--------------|----------------------|-----------------------------------------------------|-----------------------------|--------|-------|-------|----------|-------|
| No. | Family | Fold | Assembly | Animal | Plant | Fungi | Bacteria | Virus |
| 24 | H-type | Six-stranded antiparallel β -sandwich | Hexamer | x | x | | | |
| 25 | Cystine-knot | Cystine-knot motif | | X | | | | |
| 26 | TgMIC4 | α/β -fold | Tandem repeat | x | | | | |
| 27 | TgMIC1 | Sialic acid binding protein | Linked to different domains | x | | | | |
| 28 | LysM | $\beta\alpha\alpha\beta$ -Motif | Triple repeat | x | x | x | x | |
| 29 | LNP-type | α/β -fold | Monomer | x | x | | x | |
| 30 | Monocot | β -Prism II | Monomer, dimer, tetramer | | x | | x | |
| 31 | ABL-like | α/β -sandwich | Dimer, tetramer | | x | x | | |
| 32 | CV-N | Three-stranded β -sheet and β -hairpins | Monomer | | x | x | x | |
| 33 | PVL-like | Seven-bladed β -propeller | Monomer | | | x | | |
| 34 | AAL-like | Six-bladed β -propeller | Monomer | | | x | x | |
| 35 | Flocculins | β -Sandwich | Monomer | | | x | x | |
| 36 | PCL-like | Jelly roll | Tandem repeat | | | x | | |
| 37 | BC2LCN | Jellyroll | Trimer | | | | x | |
| 38 | Staphylococcal toxin | β -Barrel | Monomer | | | | x | |
| 39 | AB5 toxin | α/β -fold | AB5 | | | | x | |
| 40 | PA-IIL-like | β -Sandwich | Dimer | | | | x | |
| 41 | MVL | α/β -fold | Dimer | | | | x | |
| 42 | PapG | β -Sandwich | Linked to different domains | | | | x | |
| 43 | FimH | β -Sandwich | Linked to different domains | | | | x | |
| 44 | F17-G | β -Sandwich | Linked to different domains | | | | x | |
| 45 | Hemagglutinin | Jelly roll | Trimer | | | | | x |
| 46 | RotavirusVP4 | Jelly roll | Virus capsid | | | | | x |
| 47 | Viral proteins | β -Sandwich | Virus capsid | | | | | x |
| 48 | Knob domain | Jelly roll | Virus capsid | | | | | x |

Folding, assembly, and source of each family is shown.

Table 1. Lectin families in nature.

3. Structure and biological activities of plant lectins

Lectins are mainly present in seeds of plants [4, 8, 9], but they are also identified in vegetative tissues such as bulbs, tubers, rhizomes, roots, bark, stems, fruits, and leaves [11].

As previously mentioned, based on their number domains and their characteristics, plant lectins can be divided into four classes [9]:

- **Merolectins** are lectins that possess a single carbohydrate-binding domain. As a result, the merolectins do not present agglutinating activity.
- **Hololectins** contain two or multivalent carbohydrate-binding sites.
- **Chimerolectins** possess a carbohydrate-binding domain and an additional domain that confers other biological activities.
- **Superlectins** are lectins with two or multivalent carbohydrate domains that are able to recognize structurally unrelated sugars.

However, since 1998, five novel lectin domains have been identified in plants. At present, plant lectins are classified into 12 different families, with distinct carbohydrate-binding domains. The families are *Agaricus bisporus* agglutinin homologs, amaranthines, class V chitinase homologs, *Euonymus europaeus* agglutinin family, *Galanthus nivalis* agglutinin family, proteins with hevein domains, jacalins, proteins with legume lectin domains, LysM domain proteins, the *Nicotiana tabacum* agglutinin family, and the ricin B family [12].

In general, the three-dimensional structure of lectins is composed of a high content of β -sheets with little contribution from α -helices. The β -sheets are connected by loops forming antiparallel chains. The stability of dimers and tetramers is conferred by hydrophobic interactions, hydrogen bonds, and salt links [13]. Three regions are formed in carbohydrate-binding site [12–14]:

- The central region is constituted by a conserved core in which residues interact with metallic ions (Mg^{2+} , Mn^{2+} , and Ca^{2+}), required for carbohydrate interactions. This core provides necessary binding energy, but it is not important to the lectin's carbohydrate specificity.
- Some aromatic residues surround the core and occupy variable positions in a horseshoe shape. This region is fully involved in the lectin's monosaccharide specificity.
- Finally, residues with higher variability are located in the outer zone and are involved in interactions with larger oligosaccharide ligands.

The structural features of plant lectins are shown in **Figure 1**, which is possible to see the high content of β -sheets (**Figure 1A**) and the structure of a typical carbohydrate recognition domain (**Figure 1B**).

However, the kind of expressed lectins can have some differences according to the specific tissue or the moment in which the plant is expressing it. A lot of plant lectins are constitutively expressed in high amounts in seeds and vegetative storage tissues where

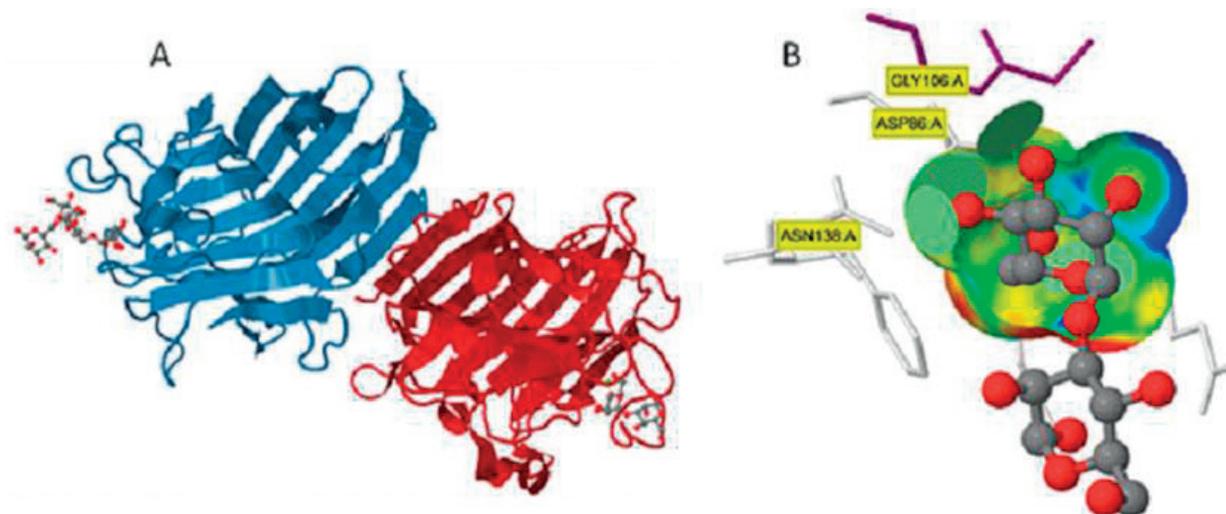


Figure 1. Structural conformation of plant lectins. (A) *Pterocarpus angolensis* homodimer lectin (PDB code (2PHF)). The β -sheet conformation is the most usual in plant lectins (β -sandwich). (B) The carbohydrate recognition domain (CRD) is highly conserved in plant lectins, according to its specificity.

they have been shown to play a role in plant defense [15]. But, plants also express minute amounts of specific lectins as particular responses toward environmental stresses and pathogen attack. In the absence of plant stress, the inducible lectins are not expressed at detectable levels [16]. According that, a central question which has often been asked but up to now not yet been answered definitively is that on the biological function(s) of plant lectins. Several functions have been mentioned, but there is not a final decision about that. However, because of its carbohydrate interactions, lectins have been tested for several biological functions, getting interesting results in some of them. Biological activities are related to immunomodulatory and antitumor [17–19], antifungal [20–23], antiparasitic [24–26], antiproliferative [27–30], healing process [31–33], drug delivery [34–36], as histochemical markers [37–39], biosensors [40, 41], insecticide [42–46], etc.

4. Fabaceae (legume) and Lamiaceae (mint) lectins

The specific carbohydrate recognition shown by lectins makes them important tools in glycobiology, and, although their physiological role remains unknown, they appear to mediate protein-cell and cell-cell interactions. Lectins are widespread in nature, and most of them have been isolated and characterized from Fabaceae, Gramineae, and Lamiaceae families, among others [47, 48]. Those lectins have been related to insect defense mechanisms, storage proteins, carbohydrate transport, mechanisms of physiological regulation, and mitogenic stimulation processes [49–55]. The ability of the nitrogen-fixing bacteria rhizobia to form a symbiotic relationship with legumes, in which plant root lectins are involved, is well known. The plant-associated bacteria have important effects on plant health and productivity [56–59]. Thus biofilm formation on plants is associated with symbiotic and pathogenic responses, and some root lectins promote this process [60]. The lectins could be a good biotechnological alternative in the control of bacterial biofilms for different purposes, for example, clinical

applications [61]. In general, plant lectins have been widely used for studying carbohydrates on cell surface, for typing blood groups, isolating glycoconjugates, and detecting changes in normal oligosaccharide synthesis in tumoral disorders and other pathologies [62–66].

Lectins from Fabaceae have been extensively studied and have a broad specificity for any carbohydrate moieties regardless of having highly conserved amino acid sequences between different species. These proteins have been for a long time a paradigm in the research of interaction protein-carbohydrate and their relationship structure-function [67, 68]. Available sequences (RCSB PDB, UniProtKB/Swiss-Prot) show 20% similarity and 20% of identical amino acids, and conserved amino acids are in the “binding site” and coordinate metal ions [9]. These proteins generally have two or four identical subunits with a molecular weight around 25 kDa; each one contains a binding site for metal ions. A typical example of dimeric lectins belongs to the Viceae tribe. The tetrameric lectins are present in species of the tribe Diocleae, specific by glucose/mannose. In these tribes, many lectins have been isolated and characterized with some biochemical differences and molecular similarities [47]. Recently, subtribe Diocleinae in the Millettoid legumes have been taxonomically tangled together with the large heterogeneous tribe Phaseoleae; however, a comprehensive molecular phylogenetic analysis based on nuclear and chloroplast markers includes all genera ever referred to Diocleae except for the monospecific Philippine *Luzonia*, resolving several key generic relationships within the Millettoid legumes and considered classification of Diocleinae subtribe as a tribe with three main clades: *Canavalia*, *Dioclea*, and *Galactia*. *Canavalia* clade has species gender *Canavalia*; *Dioclea* clade includes *Dioclea*, *Cymbosema*, *Cleobulia* and *Macropsyчанthus*; and *Galactia* clade gender has *Galactia*, *Neorudolphia*, *Rhodopsis*, *Bionia*, *Cratyliа*, *Lackeya*, *Camptosema*, and *Collaea* [69].

This tribe is widely distributed throughout the neotropics, and several species from the genus *Dioclea* have been shown to possess a lectin closely related to ConA (lectin type I). The better characterized lectins have been those from *D. grandiflora* [70, 71], *D. lehmanni* Diels [72], and *D. sericea* Kunth [73], among others, all of them belong to the Man/Glc group; their physicochemical properties and structural features are very similar [74].

Studies carried out in the PRG have allowed us to find other lectins having distinct structural and functional properties (named lectin type II) from *Diocleae lehmanni* (DLL), *Dioclea sericea* (DSL), *Dioclea grandiflora* (DGL), *Canavalia ensiformis* (CEL), and *Galactia lindenii* (GLL) [73, 75–77]. These lectins are localized in the same cellular compartment as happens in *D. lehmanni* seeds [78] and have different physicochemical properties; this allow us to question about the physiological role of these proteins. Lectin type II has high affinity toward H type 2 blood group (α -L-Fuc (1–2)- β -D-Gal (1–4)- β -D-GlcNAc-O-R), and the N-terminal region presents a unique sequence hitherto found in some Diocleinae lectins and suggests a functional similarity among this type of lectin which possesses distinctive characteristics differentiating them from “classical” mannose/glucose (Man/Glc) lectins. Taking subunit MW into account, it has been demonstrated that tetrameric forms prevailed in type I lectins, being in fast equilibrium with dimers and monomers whose amount depended upon pH or solution ionic strength [79], while some lectins from type II prevalence dimeric forms (**Table 2**). Despite their high similarity, these ConA-like (type II) lectins could induce different responses in biological assays; for example, when tested for stimulation of human lymphocyte proliferation in vitro, ConBr had a higher proliferation index than ConA, possibly due to minor changes in binding specificities [80].

| Type | Species | Specificity | Monosaccharide inhibitor | Erythroagglutination | Native (kDa) | Subunits (kDa) | pI | References |
|------|-----------------------|-------------|-------------------------------------------------------------------------------|----------------------|--------------|--------------------------------------------------------------------------------|---------|------------|
| I | <i>D. grandiflora</i> | Man/Glc | Man, Glc, Fru | Rabbit | 100 | α :25- α :26; β :13- β :14; γ :8- γ :9 | 8.6-9 | [70, 71] |
| | <i>D. lehmanni</i> | | Man, Glc, Fru, L-sorbose, Me- α -D-Man, Me- α -D-Glc, trehalose | Rabbit, A+, O+, B+ | | α :25.3; β :14; γ :N.D | 8.0-8.4 | [72] |
| | <i>D. sericea</i> | | Man, Glc | A+, O+, B+ | 57.7 | α :29.9; β :16.5; γ : 13.4 | 6.6-6.9 | [73] |
| | <i>D. altissima</i> | | Man, Glc, Fru | Rabbit | 100 | α :26.3; β :14; γ : 9 | 8.6-9.0 | [131] |
| | <i>D. violaceae</i> | | Man, Glc, Fru, maltose | Rabbit | | α :29.5; β :15.8; γ : 11.7 | | [132] |
| | <i>D. rostrata</i> | | Man, Glc, Fru | Rabbit, O+ and B+ | | α :30.9; β :15.8; γ : 11.7 | | [67] |
| | <i>D. lasiophylla</i> | | Man, Me- α -D-Man, ovalbumin, fetuin | Rabbit | | α :25,569; β :12,998; γ : 12,588 | | [133] |
| | <i>D. sclerocarpa</i> | | Glc; Gal | Rabbit | 102 | α : 25,606; β :12,832; γ :12,752 | | [134] |
| | <i>C. ensiformis</i> | | Man, Me- α -fructofuranoside | Rabbit | 96 | α :25.5; β :14; γ :12.5 | 7.1 | [67] |
| | <i>C. mollis</i> | | Glc, Me- α -D-Man | Rabbit > A+, O+, B+ | | α :30; β :16; γ : 14 | 8.5-8.6 | [135] |
| | <i>C. roseum</i> | | Man | Rabbit | | α :30; β :18; γ : 12 | | [136] |
| | <i>G. lindenii</i> | | p-Nitrophenyl- β -D-mannopyranoside, Man | A+, O+ | 100 | 29; 60 | 6,5 | [77] |

| Type | Species | Specificity | Monosaccharide inhibitor | Erythroagglutination | Native (kDa) | Subunits (kDa) | pI | References |
|------|-----------------------|-------------|-------------------------------------|----------------------|--------------|----------------|---------|------------|
| II | <i>C. ensiformis</i> | H-Type II | Sucrose, melezitose, lactose | A+, O+, B+ | 57.5 | 29–30 | 5.2–5.4 | [76] |
| | <i>D. grandiflora</i> | | Sucrose, melezitose, lactose | A+, O+, B+ | 58.9 | 29–30 | 5.1–5.4 | [76] |
| | <i>D. lehmanni</i> | | Sucrose, melezitose, lactose | A+, O+, B+ > rabbit | 58.4 | 29–30 | 6.5–6.6 | [75] |
| | <i>D. sericea</i> | | Lactose, sucrose, melibiose | A+, O+, B+ | 57.27 | 26.58–30 | 5.3–5.7 | [73] |
| | <i>G. lindenii</i> | | GalNAc, Me-β-Gal, Lactose | B+, O+ > A+ | 104,256 | 26,064 | 8.3 | [137] |
| | <i>C. roseum</i> | | GalNAc and N-acetyl-α-D-lactosamine | Rabbit | 65 | 29 | – | [138] |
| | <i>Captosemin</i> | | N-acetyl-α-D-galactosamine | A+, O+, B+ | 104 | 26 | – | [139] |

Abbreviations: kDa, kilodalton; pI, isoelectric point; H-type II, antigen (α -L-Fuc(1-2)- β -D-Gal(1-4)- β -D-GlcNAc-O-R); Man, mannose; Glc, glucose; Me, methyl; Gal, galactose; Fru, fructose; GalNAc, N-acetyl- α -D-galactosamine.

Table 2. Physicochemical properties of lectins of Diocleae tribe.

Lamiaceae lectins have been little studied despite preliminary reports on their ability to recognize the Tn/T antigens [81], normally a cryptic structure in the peptide core of O-glycoproteins and which is widely expressed in several tumors and other disorders such as Tn syndrome and IgA nephropathy [82–85]. The importance of Thomsen-Friedenreich antigen (TF or T, galactose (Gal) β 1,3 GalNAc α -O-serine (Ser)/threonine (Thr)) as well as to its precursor, the Tn antigen, and its sialylated forms (sTn) has been reviewed recently [86–91]; according to the above, it is important to have alternatives to study these structures such as the lectins and antibodies. However, a word of caution should be given as accumulating evidence, which has shown that mAbs and lectins do not interact with Tn-containing structures in an identical manner. The observed differences have been ascribed to different Tn-density requirements for the interaction to occur [92].

Detailed studies have been carried out on a very few Lamiaceae species from the Northern hemisphere's temperate zone until now [93–97], and the lectin from *Salvia sclarea* L. seeds (SSL) was the first to be isolated and partially characterized [94]. By contrast, species from the Neotropical *Salvia* subgenus Calosphace Benth have been little explored despite their great diversity. A systematic survey has been conducted on species belonging to the Neotropical Calosphace Benth subgenus [98], and certain species naturalized in the New World have also been investigated [99], some having commercial value. Given the abundance of Lamiaceae species in Colombia and the potential biotechnological applications, our group undertook a systematic search for the identification, isolation, and characterization of lectins from selected species with the determination of their biological activities. The lectins from *S. palifolia* Kunth and *Hyptis mutabilis* (Rich.) Briq. [100] have been partially characterized, and a detailed work has been done with *S. bogotensis* Benth and *Lepechinia bullata* (Kunth) Epling [101, 102].

The importance of these proteins as tools in a variety of biological studies and detection, isolation, structural, and functional properties has been studied, and more recently, T/Tn-specific lectins have been found in the families Amaranthaceae, Fabaceae, Moraceae, and Orchidaceae, among others. The lectins themselves belong to five families of structurally and evolutionarily related proteins (amaranthines, legume lectins, jacalin-related lectins, type 2 ribosome-inactivating proteins, and GNA-related lectins) [103].

Interestingly, a lectin type I was found in *S. bogotensis* Benth. (SBoL-I) and *Lepechinia bullata* (Kunth) Epling (LBL-I) (such as those found in the tribe Diocleae type I), which recognizes mannose/glucose residues; this fact, together with the molecular properties and highly similar N-terminal regions, led us to propose that lectins type I and type II are two good differentiated groups with structural features proper of legume lectins family, particularly from Diocleae tribe, *Salvia*, and *Lepechinia* genders (**Table 3**) [104]. For these lectins, SDS-PAGE profile was similar to other mannose lectins, a band around 30 kDa with an isoelectric point near to 6.5, and they were able to agglutinate human RBCs from A, B, and O donors. This means that specificity by mannose/glucose moieties or mannose-rich glycan is not a unique feature of any family; conversely, species such as *Galanthus nivalis* (tribe Galantheae) [105] and *Centrolobium microchaete* (tribe Dalbergieae) [106], among others, even species from other families such as Moraceae have mannose/glucose lectins [107].

| Molecular properties | GLL-I ¹ | DLL-I ² | CRL-I ³ | CEL-I ⁴ | SBoL-I ⁵ | LBL-I ⁶ |
|-------------------------------------------|--------------------|------------------------------|------------------------------|------------------------------|---------------------|--------------------|
| M _r subunit (kDa) ⁷ | 29 | 25, 14 | ND | 26.5 | 30–33 | 30–34 |
| M _r protein (kDa) ⁸ | 100 | ND | ND | 106 | ND | ND |
| SDS-page (kDa) | 29, 60 | 25, 14 | 30, 18, 12 | 26, 14, 12.5 | 30, 60 | 30, 60 |
| Glycosylation | Si | ND | ND | No | Si | Si |
| Neutral Sugars (%) | ND | 1.7–1.9 | ND | ND | ND | ND |
| Isoelectric point (PI) | 6.15 | 8.0; 8.13 8.3; 8.42 | ND | 7.1 | 6.5 | 6.5 |
| Mannose inhibition (mM) | 150 | 50 | 19.5 | ND | ND | ND |
| Sequence N-terminal | ND | ADTIVAVELD SYPNTDIGDPSYPH | ADTIVAVELD SYPNTDIGDPSYPH | ADTIVAVELD TYPNTDIGDPSYPH | ADTIVAVELD | ADTIVAVELD |

¹*Galactia lindenii* lectin type -I (GLL-I) [77].

²*Dioclea lehmanni* lectin type I (DLL-I) [72].

³*Cymbosema roseum* lectin type I (CRL-I) [136].

⁴*Canavalia ensiformis* concanavalin A (CEL-I) [67].

⁵*Salvia bogotensis* lectin type I (SBoL-I) [104].

⁶*Lepechinia bullata* lectin type I (LBL-I) [104].

⁷Reduced conditions.

⁸Non-reduced conditions without heat.

ND, non-determined.

Table 3. Molecular properties of lectins type I from Fabaceae and Lamiaceae families.

5. Insecticide and insectistatic activity of plant lectins

There are several evidences for the defensive role of vegetal lectins in protecting plants against insect pests [108–110], and lectins are currently receiving a significant interest as insecticidal agents against sap-sucking insects including aphids and leaf and plant hoppers, with no effect on human metabolism [111, 112]. Lectins act on insects by binding to glycoproteins present in insect gut epithelium, eventually causing death of insect by inhibiting absorption of nutrients. It was believed that N-linked glycans in insects were exclusively of the high mannose type; therefore, there are great interests, especially in mannose-specific plant lectins, as possible insecticidal or insect-detering molecules for the new pest management strategies [113, 114]. Nevertheless, the lectins possess different sugar specificities and, considering the variety of glycan structures in the bodies of insects, have many different possible targets. Advances have been made in the knowledge related to glycan diversity and function(s) of protein glycosylation in insects, N-glycosylation, and O-glycosylation, and it postulated that the interference in insect glycosylation appears to be a promising strategy for pest insect control [115]. Therefore, it is difficult to predict the exact mode of action of each lectin and even more difficult to understand the variability in insect toxicity upon exposure to different plant lectins. The use of initial bioassays employing artificial diets has led to the most recent advances, such as plant breeding and the construction of fusion proteins, using lectins for targeting the delivery of toxins and to potentiate expected insecticide effects [116–118].

The first lectin known for insecticidal activity was *Galanthus nivalis* agglutinin, which belongs to a superfamily of alpha-D-mannose-specific plant bulb lectins [105, 119]. The mannose-binding lectins have shown strong insecticidal activity against chewing and sap-sucking insects and particularly in controlling aphids [120–124]. Lectin isolated from bulbs of *Phycella australis* presented a strong insecticidal activity against the pea aphid and green peach aphid, affecting the survival, feeding behavior, and fecundity of aphids, where *Acyrtosiphon pisum* proved to be particularly sensitive [125].

No considerable mortality effect of ASA lectins (native or recombinant lectins) was shown on larvae of potato moths (*Tecia solanivora*); however, recombinant ASAI lectin had an effect on the pupa mortality, which was bigger than the native lectin effect. The effect of lectins on the weight and fertility of adults showed that both lectins had a big effect on fertility when the lectin is used in a low concentration (lower than 0.003 mg/mL), and, in some cases, lectins produced malformations in female adults [126]. Fitches et al. found toxic effects on *Acyrtosiphon pisum* using both recombinant lectins; however, ASA II was more toxic than ASA I, at the same dose [127].

Lectins from legume family have shown insectistatic and insecticidal activity [52] (Table 4). The lectins from seeds of *Canavalia brasiliensis*, *Dioclea grandiflora*, *Dioclea rostrata*, *Cratylia floribunda*, and *Phaseolus vulgaris* have shown to protect seeds against the beetle *Callosobruchus maculatus*. In general, the plant lectins are the most potent agents against insect pests of a variety of crops including wheat, rice, tobacco, and potatoes [128]. *Canavalia* lectins exhibited a range of different toxicities toward *Artemia nauplii* and bound to a similar area in the digestive tract; differences in spatial arrangement and volume of CRD (carbohydrate recognition domain) may explain the variation of the toxicity showed by each lectin despite the high structural similarity [129]. The sensitivity of different insect species to the insecticidal effects

of lectin ingestion is variable, and the binding of a lectin to the gut does not necessarily imply toxicity. Other studies signal that lectins affect various insect hydrolytic enzymes such as glucosidases, phosphatases, and proteases which are involved in digestion, development, growth, and detoxification. To date a great number of studies have shown lectin toxicity in insects belonging to different orders, including Lepidoptera, Coleoptera, and Hemiptera. However, the exact mode of action of lectins in providing resistance against insects remains unclear. The most relevant property of lectin's anti-insect activity can be related to its interactions with different glycoproteins or glycan structures in insects, which may interfere with a number of physiological processes in these organisms. Lectins possess at least one carbohydrate-binding domain and different sugar specificities, possible targets for lectin binding are numerous, and several mechanisms can be associated (**Figure 2**).

Preliminary evidence of Gleheda's insecticidal activity against Colorado potato beetle larvae (*Leptinotarsa decemlineata*) has been obtained using a single dose of lectin [130]; it would have been very interesting to carry out dose-response experiments and to assay several insect pests to elucidate whether the lectin was insect specific. Nevertheless, Gleheda's insecticidal activity stresses the importance of this unusual lectin, begging the question of whether such activity is shared by other Lamiaceae lectins. To date Lamiaceae lectin is unique with known insecticidal activity. The importance of lectins due to their insecticidal properties, isolation of native lectins, and lectin genes could be agronomically important tools for crop plants for developing resistance against insect pests mainly for sap-sucking

| Lectin | Insect pests | Activity | References |
|---------|----------------------------------|-----------------------------|------------|
| PSA | <i>Meligethes aeneus</i> | Insecticidal, insectistatic | [140] |
| ConA | <i>Tarophagous proserpina</i> | Insectistatic | [141] |
| Gleheda | <i>Leptinotarsa decemlineata</i> | Insectistatic | [130] |
| ConA | <i>Callosobruchus maculatus</i> | Insectistatic | [142] |
| ConA | <i>Helicoverpa armigera</i> | Insectistatic | [143] |
| GS-II | <i>Callosobruchus maculatus</i> | Insectistatic | [144] |
| PHA | <i>Callosobruchus maculatus</i> | Insecticidal | [145] |
| PHA-E | <i>Empoasca fabae</i> | Insecticidal | [146] |
| Bmoll | <i>Anagasta kuehniella</i> | Insecticidal | [147] |
| | <i>Zabrotes subfasciatus</i> | | |
| | <i>Callosobruchus maculatus</i> | | |
| | <i>Callosobruchus maculatus</i> | | |
| DGL | <i>C. maculatus</i> | | [108] |
| DRL | | | |
| CFL | | | |

Pisum sativum (PSA), *Canavalia ensiformis* (concanavalin A (ConA)), *Glechoma hederacea* (Gleheda), GS-II: *Griffonia simplicifolia* agglutinina, *Phaseolus vulgaris* (PHA), *Bauhinia monandra* leaf lectin (bmoll), *Dioclea grandiflora* (DGL), *D. rostrata* (DRL), *Cratylia floribunda* (CFL). Taking from Calvacante et al. [60] and modified.

Table 4. Legume lectins domain with insectistatic and insecticidal activity.

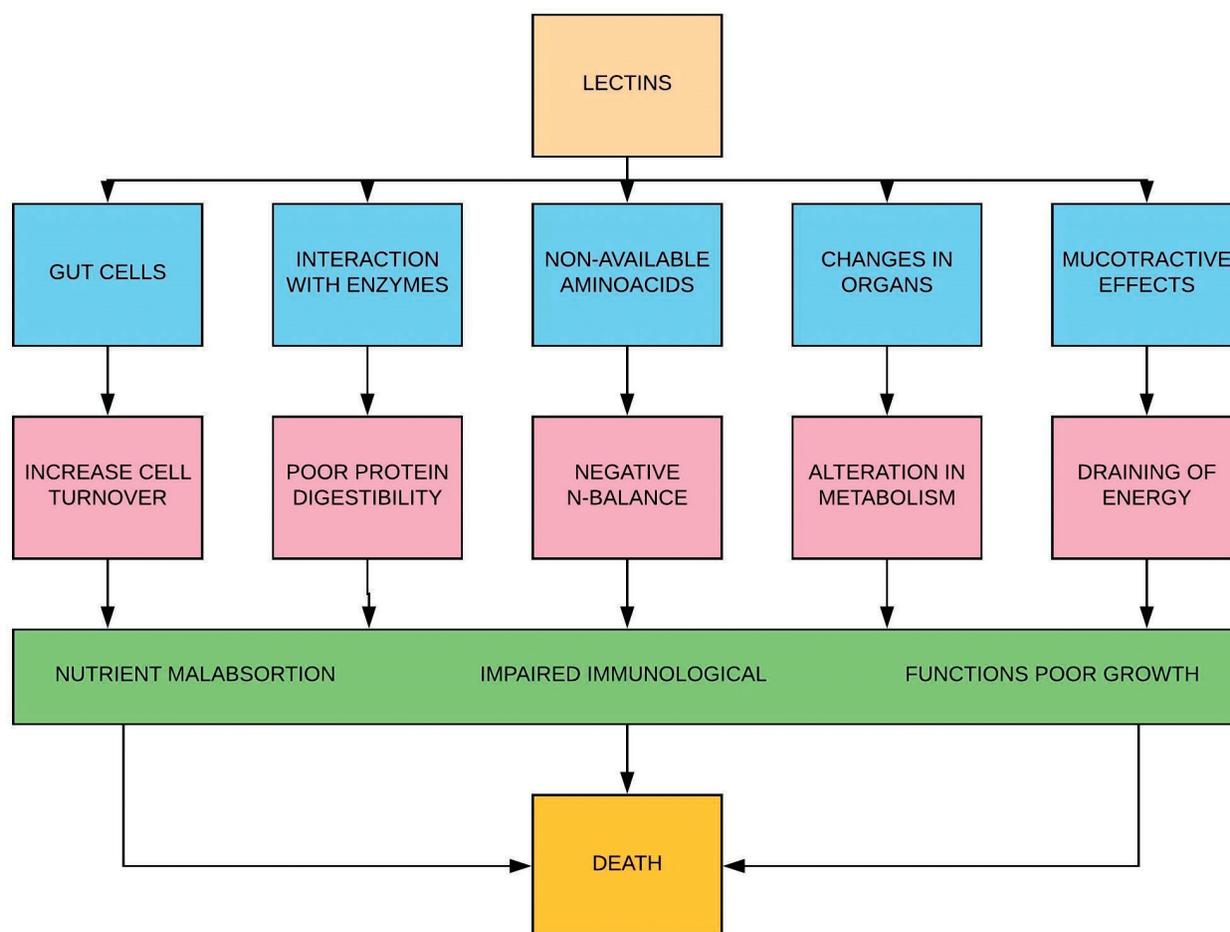


Figure 2. Possible targets and associated mechanisms of lectin anti-insect activity. Lectins have antinutritional properties by which they interact with several targets in digestive tract and other organs.

insect. These proteins are very interesting, and its molecular properties have been well described; however, there is still a long way to study and learn about the mechanisms of these molecules at a physiological and molecular level.

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