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Review - Human and Animal Health

Antibacterial Activity of Plant Lectins: a Review

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HIGHLIGHTS

- Plant lectins are proteins that have biotechnological potential.
- The antibacterial activity of lectins can occur by immunomodulation.
- Due to their characteristics, lectins are promising targets for antibacterial activity.

Abstract: Lectins are proteins that form a heterogeneous group, capable of binding specifically and reversibly to carbohydrates. They occur in various types of organisms, having different functions, in plants they are present in almost all structures, however with greater proportion in seeds roots and rhizomes. This review aims to provide a more detailed understanding of the antibacterial action of lectins and their biotechnological potential against pathogenic bacteria in the last ten years. Several mechanisms of action are described for the antibacterial activity of these proteins among which the best known occurs due to the interaction between the binding site of the lectin and the carbohydrates exposed on the bacterial cell surface. In vivo studies demonstrate that lectins act on the cascade of cytokines and influencing the level of nitric oxide as ways to decrease bacterial infection. To date, lectins have performed a wide antibacterial activity, emphasizing that each lectin acts according to its carbohydrate specificity, in this way, it is possible to have a distinct performance according to the plant species that are extracted. Thus, being an alternative to the antibacterial resistance that occurs in response to antibiotics. Furthermore, more studies with this theme are necessary for clinical application.

Keywords: proteins; biological activity; antibiotics.

INTRODUCTION

Lectins are a group of heterogeneous proteins, able to establish specific and reversible bonds with monosaccharides and oligosaccharides, being free or bound to the cell surfaces by the specific binding sites [1,2]. The carbohydrate binding site allows lectins to behave as recognition molecules, being found in various organisms, including animals, fungi, viruses, bacteria and distributed in various plant organs and tissues [3]. Plants are considered the most accessible source of proteins, being possible to extract and isolate proteins from the entire anatomy, including seeds, barks, leaves, fruits, roots and tubers [2].

Plant lectins can be divided into two large groups according to gene expression and induction pattern, that constitutively expressed and regulated during development, and the lectins with low level of expression and activated by means of induction. Tissues that present higher levels of expression and consequently higher protein concentration such as seeds and vegetative storage tissues have always been major targets for the extraction and isolation. However, from the search for new lectins, have been extracted proteins from tissues with low levels of expression, such as leaves, roots and flowers. Resulting in the discovery of new lectins that have expression induced by biotic and abiotic stress factors [4].

Studies describe different activities related to plant lectin that have economic importance for agriculture, such as its use as bioinsecticides, binding to glycan's present in the insects and interfering in physiological processes such as: time of development, coloration, feeding, adult fecundity and mortality, demonstrating a high potential for the development of new pest control strategies [5]. The lectin also acts as an intermediary for symbiosis between the plant and nitrogen fixing bacteria [6-9].

Besides its agricultural importance, also arouses clinical interest due activities such as antinociceptive , anti-inflammatory and antihemolytic activity [10-12], healing of cutaneous wounds [13], control of the metastatic potential of tumor cells through mechanisms induces anti-angiogenic activity and apoptosis [14-16], anti-inflammatory activity due to the ability to inhibit the neutrophil migration and to reduce IL1-β and TNF-α levels [17], immunomodulatory effect, NO production [18,19], induction of mitosis [20], cytokine production in vitro and in vivo [21] and antifungal action [22-24].

In addition to the biological activities that have been cited, the lectins also have antibacterial activity, which is the focus of this article. These proteins may be listed as optimal candidates for the treatment of infections caused by bacteria [25-27], since its carbohydrate binding properties are able to establish interactions with pathogenic cells, promoting inhibition of microbial adhesion [28]. Thus, this review aims to provide a more detailed understanding of the antibacterial action of lectins and their biotechnological and pharmaceutical potential in the fight against pathogenic bacteria in the last ten years.

To reach the proposed objective, a search was carried out in the databases (ScienceDirect; PubMed; ScieLo; LILACS; Scopus; SpringerLink; PLoS and Hindawi) regarding the articles in the period from 2011 to 2020, for this purpose the descriptors were used: lectin, antibacterial, biological activity and antimicrobin.

Antimicrobial activity of plant lectins as an alternative to antibiotic resistence

Mechanism of action

A structural characteristic of the lectin is its site for binding to carbohydrates, which has a fundamental function for antimicrobial activity, considering that almost all microorganisms express carbohydrates on the cell surface, each polysaccharide is a potential binding site for lectin [29]. With this, the effectiveness of this protein in the antibacterial activity became possible. Gram-negative bacteria have lipopolysaccharides (Figure 1) on their surface and Gram-positive possess peptidoglycan, teichoic and teichuronic acids (Figure 2), the binding specificity carbohydrate with lectins is achieved through hydrogen bridges, van der Waals and hydrophobic interactions between sugar and lectin site [30]. When antibacterial activity is brought into focus, the most known mechanism of action is what involves the binding of the lectin to the carbohydrates exposed on the outer membrane or cell wall of the bacteria, forming a channel in the cell membrane and thus inducing its target to apoptosis with the exit of intracellular components [31-34]. By electron microscopy it was proven that the conformational change in the membrane may result in the formation of a pore [35], which leads to an increase in bacterial permeability, allowing the leakage of intracellular proteins. However studies with the *Moringa oleifera* seed lectin (WSMoL) presented that this effect occurred in a general way, that is, even in the bacteria that WSMoL had no antibacterial effect, cell wall integrity was lost, promoting increased permeability and, consequently, the release of intracellular proteins [36].

The specific carbohydrate for each lectin may influence its biological activity, and its antibacterial effect is linked to the result of the interaction between lectin and its specific receptors on the cell membrane. Due to interact with bacterial membrane receptors, the lectin leads to a change in cellular metabolism of the bacteria by inducing conformational changes. For example, N-acetylglucosamine is present on the cell wall of different bacteria, the lectin ApulSL has specificity for this carbohydrate, thus its antibacterial activity is attributed to its specificity of binding to the residues of the N-acetylglucosamine [37]. The structural difference between Gram-negative and Gram-positive bacteria can lead to a different antibacterial activity, because it is more complex for the lectin to cross the outer membrane and cell wall of a Gram-negative strain to finally reach the periplasmic space, in contrast the high level of peptidoglycan that is expressed by the Gram-positive bacteria, provides more sites of interaction with the lectin [38].

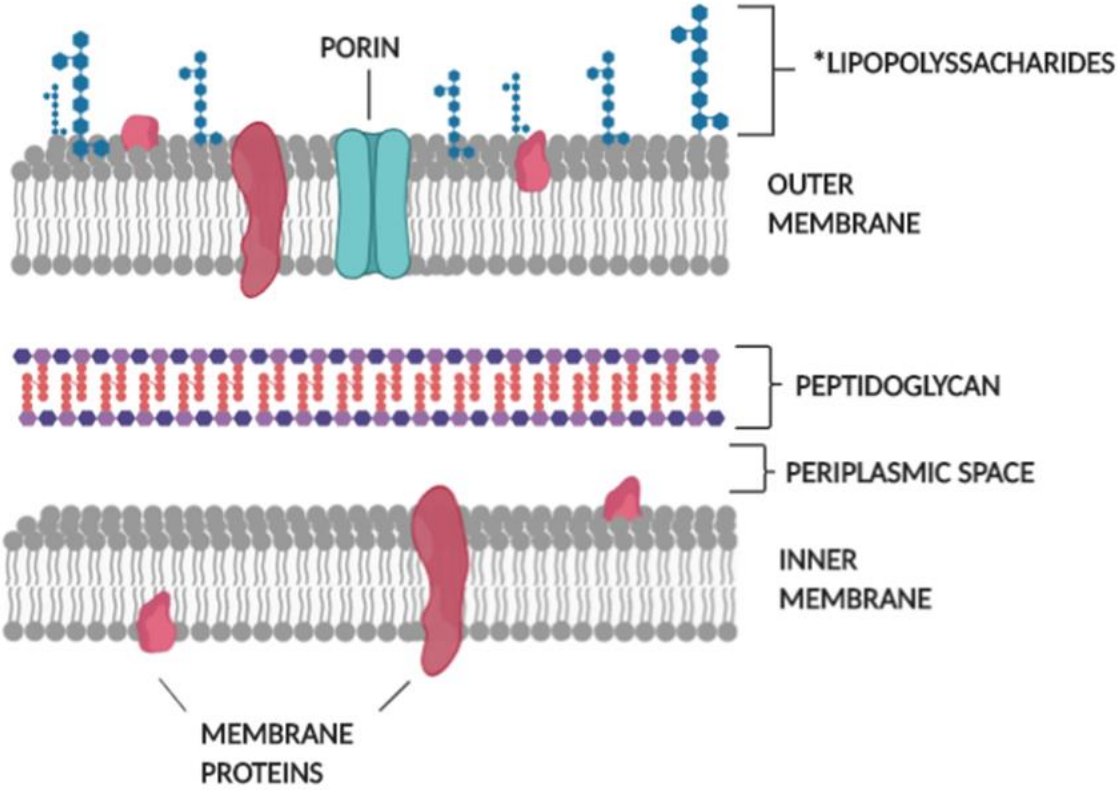

Figure 1. Scheme of a cell wall structure of Gram-negative bacteria. *The carbohydrate residues that may be the binding target of antimicrobial lectins.

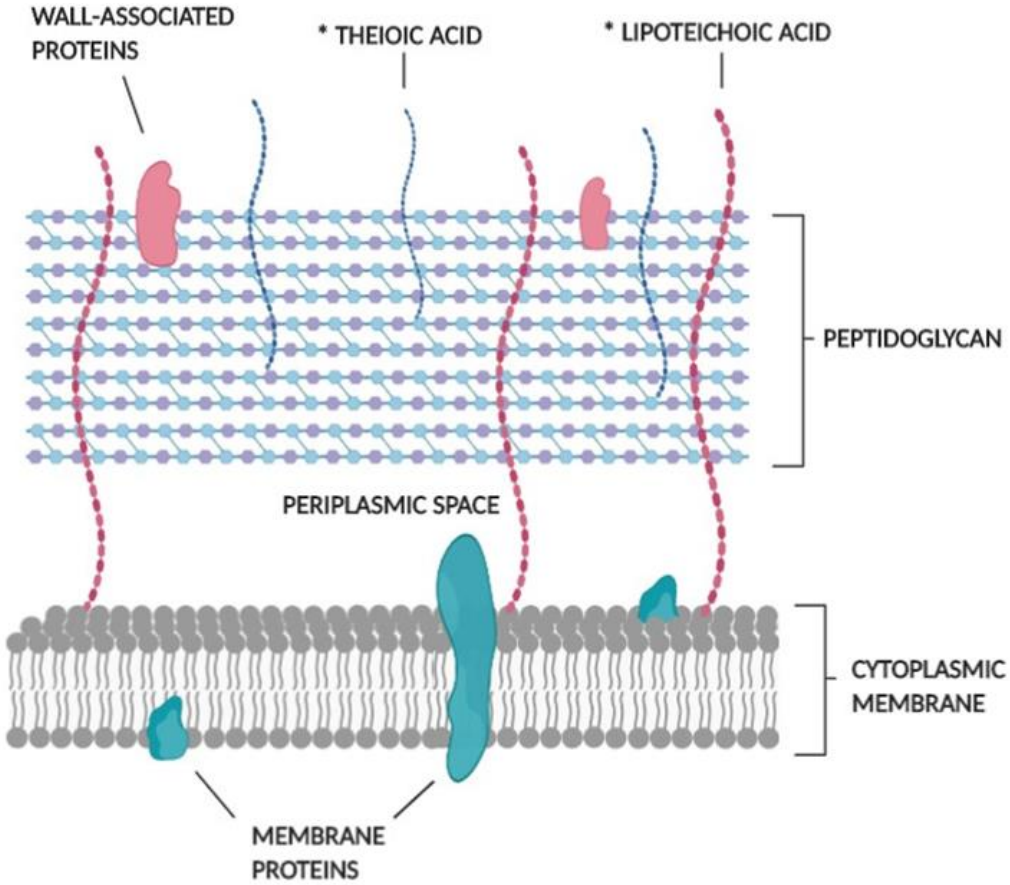

Figure 2. Scheme of a cell wall structure of Gram-positive bacteria. *The carbohydrate residues that may be the binding target of antimicrobial lectins.

Some oral pathogenic bacteria have a mechanism of adhesion on the surface of the tooth through the secretion of several extracellular polysaccharides [39]. The mechanism of action for oral bacteria has not yet been well elucidated. Although, the lectin BVL-I inhibited bacteria such as *Streptococcus mutans* and *Streptococcus sanguins*, possibly through the binding with the carbohydrate that would be used for bacterial adhesion on the surface of the tooth or in direct connection with the components of the capsule, covering the bacterial surface [39].

Another mechanism of antibacterial action associated with lectin occurs through antibiofilm activity, acting as an anti-QS molecule. The quorum-sensing (QS) process occurs in an interspecies or intraspecies manner. The bacteria produce and release chemical signaling molecules, which are called auto-inducers, the concentration of such molecules increases proportionally to the density of the cell population. When the concentration of the autoinducers reaches the appropriate level, changes occur in molecular and cellular components, such as gene expression [40]. The bacterial QS allows a certain group of cells to regulate their gene expression evenly. This process is relevant for the production of bioluminescence, formation of biolfilm, gene exchange, expression of virulence factor [41,42].

The biofilm is a sessile organization, made up of cells and a matrix, which is self-produced and formed by extracellular polymer substances [43]. Biofilms are fundamental in the research for antibacterial activity, considering that they are responsible for 80% of microbial infections and have high resistance to antibiotics [43]. To have an effect on biofilm development, one of the mechanisms adopted is the interruption of QS signaling. This and other anti-QS mechanisms have been described for lectins. An example of plant lectin with anti-QS activity is the ConM, extracted from *Canavalia maritima*, which has been able to reduce the expression of genes related to biofilm production in strains of *Streptococcus mutans,* as well as genes related to resistance to antibiotics [44].

The mechanism of action may not be directly related to the bacteria, the lectins ConBr and CFL were unable to inhibit the growth *in vitro* of the *Salmonella typhimurium* strain, however, *in vivo* tests was made daily administration of both lectins for 3 days in infected mice, and there was a survival rate of 90% for CFL and 100% for ConBr [45].

How can occur activity *in vivo* and not occur *in vitro*? Before the question be elucidated it is necessary to understand that the early infection by *Salmonella* provides that the cytokine IL-12 stimulates the release of INF-γ that is derived from natural killers (NK) cells, this mechanism triggers the activation of macrophages to combat the pathogen [46,47]. But, in a bacterial septic shock occurs an overproduction of pro-inflammatory cytokines (IL – 1 e TNF – α) [47]. With this, the lectin does not act directly with the bacteria, but in the cascade of cytokines. When administered lectins in mice, a low regulation of IL-1 was observed for CFL, IL – 10 and TNF – α for ConBr, also occurred a decrease of the levels of nitric oxide (NO) [45].

The immunomodulatory lectins the release of inflammatory cytokines and nitric oxide in the immune system, this way is able to reduce the bacterial load in the affected organs and increase the survival rate [48], the importance of this mechanism of action can be viewed when it is understood, for example, that IL–10 and NO are events induced by lipopolysaccharide which is a carbohydrate present in the bacterial outer membrane. This class of protein during a bacterial infection manages to recruit leukocytes into the infectious focus and can recognize receptors in T lymphocytes induce them to mitogenic activation and differentiation in T helper lymphocyte subtypes (Th1, Th2 e Th17) [20], this event promotes maturation of macrophages and dendritic cells. Another important mechanism of immunological action that has been reported with the use of CFL and ConBr lectin was the possibility of reducing leukopenia, considering that, the *Salmonella* infection can lead the individual to a state of immunosuppression [45].

Antibacterial resistance

Antibiotics are natural or synthetic substances that are intended for use in treating infections in humans and animals, usually from bacteria. The discovery and production of antibiotics is one of the greatest achievements in medicine, which has helped to reduce the mortality rate in medical practice in hospitals around the world [49]. Currently, it can be found the indiscriminate and large-scale use of this substance to increase production in agriculture, aquaculture and livestock. It can also be used in the treatment of water or even by society in a wrong way [50,51]. This misuse of antibiotics is the primary factor in the selection and dissemination of resistant bacteria that will infect humans and animals [52]. Since antibiotics normally used for treatment against bacterial infections are no longer effective, it is necessary to resort to other options that are called 'reserve' or 'last resort', which are numerous times expensive and may have toxic preparations [53].

The cell wall of Gram-positive bacteria is fundamental for the chemical and mechanical integrity of the bacterial cell, having as its primary component the peptidoglycan, which has the biosynthesis determined by different proteins and is responsible for cell rigidity and protection. In this way the cell wall becomes a common target of many antibiotic drugs. Mechanisms of cell wall inhibition may act differently, for example the fosfomycin which inhibits the synthesis of peptidoglycan, and penicillin that prevents the cross-linking between peptides. Antibiotics such as chloramphenicol may act also inhibiting the synthesis of cytoplasmic proteins [52]. The mechanism of bacterial inhibition presented by lectins is distinguished from those presented by antibiotics [54], due to the formation of a pore in the bacterial membrane, allowing leakage of the intracellular content [55]. Because of this scenario, the search for new alternatives is of paramount importance.

Antibacterial activity of plant lectins

Over the years the plants have been used to prepare teas and extracts that are used in popular medicine for the prevention and treatment of diseases, the most reported activity is the antimicrobial action. The antimicrobial activity of plant products and the ease in obtaining its compounds has been shown to be a good source of studies to obtain new antibiotics [56]. The prospection of compounds with pharmacological applications has been gaining prominence, because of the search for more viable alternatives to treat infections. During the last eight years several authors have described antibacterial activities of lectins extracted from plant species (Table 1).

Archidendron jiringa is a leguminous that belongs to the Fabaceae family, it's found in Indonesia, Malaysia and Thailand, is used as different resources such as food flavoring, medicines, handmade wood and firewood. The antibacterial activity of the lectin present in the seeds of *A. jiringa* inhibited the straws *Staphylococcus aureus* and *Bacillus subtilis*, while the results for Gram-negative bacteria such as *Escherichia coli* and *Pseudomonas aeruginosa* were not as satisfactory, indicating a more significant inhibitory activity against Gram-positive bacteria, probably due to the binding of the lectin to the muramic acid and N-acetylmuramic acid, which are carbohydrates present mainly in the cell wall of Gram-positive bacteria. The results propose that this protein acts directly in the defense of the plant against pathogens, since the great majority of the microorganisms express surface carbohydrates and these become potential targets for the performance of the lectins. The carbohydrate binding site probably plays the role of recognition of bacteria [29].

Table 1. Bacterial activity of plant lectin in the period from 2011 to 2020.

Plant species[a]	Family of plant species	Name of lectin	Carbohydrate ligands	Antibacterial activity	Reference
Archidendron jiringa	Fabaceae	ND	ND	*S. aureus, B. subitilis, E. coli* and *P. aeroginosa*	[29]
Schinus terebinthifolius	Anacardiaceae	SteLL	N-acetylglucosamine	*P. mirabilis, E. coli, S. aureus, K. pneumoniae, S. enteritidis* and *P. aeroginosa*	[38]
Artocarpus heterophyllus, Canavalia ensiformis, Lens culinaris and Pisum sativum	Moraceae; Fabaceae; Fabaceae; Fabaceae.	ND	ND	*B. subitilis, P. aeroginosa, E. coli* and *S. aureus*	[57]
Indigofera heterantha	Fabaceae	IHL	D-galactose, D-mannose and D-arabinose.	*K. pnuemoniae*, *S. aureus*, *E. coli* and *B. subtilis*	[55]
Cratylia floribunda	Fabaceae	CFL	ND	*S. aureus* and *S. epidermidis*	[58]
Vatairea macrocarpa; Bauhinia bauhinioides	Fabaceae	VML, BBL	ND	*S. aureus*, *S. epidermidis,* and *P. aeruginosa*	[58]
Euphorbia helioscopia	Euphorbiaceae	EHL	Fructose	*K. pneumoniae, P. aeruginosa* and *E. Coli*	[51]
Tinospora tomentosa Miers	Menispermaceae	TTML	Lactose	*V. mimicus, S. aureus, Bacillus cereus, S. typhi,* and *S. dysenteriae*	[59]
Kaempferia rotunda Linn	Zingiberaceae	KRL	ND	*S. aureus* and *E. coli*	[03]
Moringa oleifera	Moringaceae	WSMoL	ND	*Bacillus* sp., *B. pumillus*, *P. stutzeri* e *S. marcescens*	[36]
Chenopodium quinoa	Amaranthaceae	CqLec	Glucose and mannose	*E. coli, P. aeruginosa* and *S. enterica*	[60]
Broccolini (Brassica oleracea Italica x Alboglabra)	Brassicaceae	BL	D-mannose and arabinose	*H. pylori*, *S. dysenteriae*, *P. aeruginosa*, *E. coli,* and *S. aureus*	[61]
Bauhinia variegata	Fabaceae	BVL-I	Galactose and N-acetylgalactosamine (GalNAc)	*S. mutans* and *S. sanguins*	[39]
Calliandra surinamensis	Fabaceae	CasuL	Mannose and glucose	*S. saprophyticcus* and *S. aureus*	[21]

Cont. Table 1

Euphorbia antiquorum L	Euphorbiaceae	EantH	Galactose and N-acetylmuramic acid	*Staphylococcus aureus* e *Staphylococcus epidermidis, Streptococcus agalactiae, Propionibacterium acnes* and *Salmonella typhimurium.*	[62]
Artocarpus heterophyllus	Moraceae	Jacalin[b]	ND	*Methicillin resistant Staphylococcus aureus* (MRSA), *E. coli*, *Aeromonas hydrophila, Bacillus subtilis* and *S. aureus.*	[63]
Cicer arietinum L	Fabaceae	CAL	ND	*Escherichia coli*, *Bacillus subtilis*, *Serratia marcescens* and *Pseudomonas aeruginosa.*	[64]
Alpinia purpurata	Zingiberaceae	ApuL	ND	Non-resistant and oxacillin-resistant isolate of *Staphylococcus aureus* and multidrug-resistant isolate of *Pseudomonas aeruginosa.*	[65]
Portulaca elatior	Portulacaceae	PeRoL	Galactose,glucose, N-acetylglucosamine (GlcNac)	*Enterococcus faecalis, Pseudomonas aeruginosa* and *Staphylococcus aureu*	[66]
Parkia platycephala	Fabaceae	PPL[c]	ND	*Escherichia coli*	[67]
Punica granatum	Punicaceae	PgTeL	ND	Drug-resistant *Escherichia coli* isolates able to produce β-lactamases	[68]
Punica granatum	Punicaceae	PgTeL	ND	*Methicillin resistant Staphylococcus aureus* (MRSA)	[69]
Moringa oleifera	Moringaceae	WSMoL	ND	*Enterococcus faecalis, Micrococcus luteus, Klebsiella pneumoniae, Serratia sp.*	[70]

[a] Plant species from which lectins were extracted; [b] Biological activity was performed with lectin combined with copper sulfide nanoparticles; [c] Synergistic activity of lectin combined with Gentamycin; ND: There is no information in the paper

Schinus terebinthifolius is a tree popularly known as Brazilian pepper, is commonly used in popular medicine for preparation of infusions to treat infections in the respiratory, digestive and urinary tract, rheumatism and oral candidiasis. The antibacterial assays performed with the lectin of *S. terebinthifolius* (SteLL) demonstrated a bactericidal activity against the strains *Proteus mirabilis, E. coli,* and *S. aureus*, and for *Klebsiella pneumoniae, Salmonella enteritidis* and *P. aeruginosa* it was obtained a bacteriostatic activity [38]. A bactericidal activity is defined by a reduction of ≥ 99.9% in viable bacterial density in an 18–24-h period while the bacteriostatic activity is characterized as a ratio of minimal bactericidal (MBC) to minimal inhibitory (MIC) of >4 [38]. The physical-chemical stability of the lectin is a fundamental characteristic for its application as an alternative to the antibiotic, since antimicrobial agents must remain active over a wide range of temperature and pH. The hemagglutinating activity of SteLL did not change in the presence of divalent cations, the lectin is structurally stable and active at temperatures and pH similar to that found in the human body (37 ºC, pH 6.5 – 7.5), suggesting its potential application in the treatment of infectious diseases [38]. Nair *and coauthors.* [57], analyzed the antibacterial activity of partially isolated lectins of the species *Artocarpus heterophyllus*, *Canavalia ensiformis*, *Lens culinaris* and *Pisum sativum* by the disk diffusion method. The lectins showed activity for *B. subtilis*, *P. aeruginosa*, *E. coli* and *S. aureus*, obtaining results similar to those presented by SteLL lectin.

Indigofera heterantha is a member of the Leguminoseae family, found in regions of the Himalayas. The lectin of *I. heterantha* is a tetramer having a molecular weight of about 70 kDa. The lectin IHL showed effective antibacterial action against four strains, *K. pneumoniae*, *S. aureus*, *E. coli* and *B. subtilis*. The physico-chemical characterization showed that IHL maintains structural stability in the range of pH 2 to 9, indicating that the amino acids which composes the protein are not easily altered by variations in pH, the thermal stability was established around 90 ºC. Indicating IHL as a source of relevant information for clinical microbiology and potential therapeutic applications [55]

Studies with CFL, VML and BBL plant lectins extracted from *Cratylia floribunda*, *Vatairea macrocarpa* and *Bauhinia bauhinioides* respectively, tested these proteins inhibition capacity against pathogenic bacteria and biofilm formation. The lectin CFL demonstrated activity in reducing the growth of bacteria *Staphylococcus epidermidis*, *S. aureus* and biomass reduction in biofilms [58].

The biofilm formation is related to a higher frequency of mutations and resistance to antibiotics, associating with more persistent bacterial infections. The antibiofilm effect presented by lectins may be related to the ability of these proteins to bind to the polysaccharides of bacterial cell walls, inhibiting cell adhesion in surfaces and among bacterial cells, and reducing bacterial cell viability, by interfering in the expression of genes related to biofilm formation, which may affect the biofilm structure [59].

Lectins with specific affinity for D-galactose (VML and BBL) showed activity against *S. aureus*, *S. epidermidis*, and *P. aeruginosa*. The ability of different types of lectins to present different biological activities is associated with their specificity, which may interact with different bacterial compounds such as teichoic and teichuronic acids, peptidoglycans and lipopolysaccharides.

The *Euphorbia helioscopia* has cosmopolitan distribution, belongs to the family Euphorbiaceae and is traditionally used in prevention and treatment of diseases such as ascites, edemas and tuberculosis. It was extracted from its leaves the lectin EHL with molecular weight of 65kDa, characterized by having fructose binding specificity, this lectin demonstrated to be capable of inhibiting bacterial growth of *K. pneumoniae, P. aeruginosa* and *E. coli* [51].

The lectin CqLec was extracted from seeds of *Chenopodium quinoa*, a pseudo cereal very nutritious used in food, by SDS-PAGE it was observed that the lectin is composed of two subunits with weights of 25 and 35 kDa, respectively, the CqLec shows specificity for glucose and mannose, in experiments performed showed inhibitory activity against Gram-negative bacteria specifically *E. coli*, *P. aeruginosa* and *Salmonella enterica.* With this it is possible to infer that the result of the bacterial inhibition is because they have in their LPS composition one or more of the sugars to which CqLec has specificity [60].

Broccolini is a hybrid from the species *Brassica oleracea Italica* and *Alboglabra* is a green vegetable similar to broccoli but with smaller florets and longer and thin stalks, from this plant was extracted the lectin BL of 27 kDa, with specificity for mannose and arabinose. The BL showed inhibition against *Helicobacter pylori*, *Shigella dysenteriae*, *P. aeruginosa*, *E. coli,* and *S. aureus*, being *H. pylori* more strongly inhibited, the result is also attributed to the specificity of the lectin for the carbohydrate mannose [61].

Using the lectin TTML, isolated from the plant *Tinospora tomentosa Miers*, that is widely used by Indian medicine as antipyretic, analgesic and anti-inflammatory, it was obtained activity against the bacteria *Vibrio mimicus*, *S. aureus*, *B. cereus*, *Salmonella typhi*, and *Shigella dysenteriae* [62].

The interaction between lectins and bacteria is confirmed by the agglutination of the bacterial cells, which occurs probably due the binding of the lectins to the carbohydrates exposed on the bacterial surface. The lectin KRL extracted from rhizomes of the plant *Kaempferia rotunda Linn,* with molecular weight of 29 kDa, demonstrated activity against *S. aureus* and *E. coli*. Two different levels of inhibition were obtained, one with a lower percentage of inhibition, presenting bacteriostatic activity and the other one with greater activity, being characterized as bactericide [3].

From the plant *Moringa oleifera* was isolated a lectin named WSMoL, which presents affinity with D (+) – fructose. In addition to the inhibitory activity against *Bacillus sp*., *Bacillus pumillus, Pseudomonas stutzeri* and *Serratia marcescens* the WSMoL was also able to agglutinate bacterial cells, being this phenomenon disrupted after the addition of the monosaccharide fructose. Bacterial cells that were treated with WSMoL were visualized as individual clusters of small dispersions, this result indicates that the lectin was able to interact with biofilm formation. All the bacteria tested showed leakage of proteins, even those that WSMoL did not obtain bactericidal activity, consequently, the data suggest that the lectin increasing the membrane permeability and allowing the passage of proteins, which may be due to the pores that the lectin can form in the bacterial membrane [59]. The same lectin in another study also showed bacteriostatic and bactericidal activity against *E. faecalis*, *K. pneumoniae* and *Serratia* sp., But only bacteriostatic for *M. luteus*. The Gram-negative bacteria, *K. pneumoniae* and *Serratia* sp., Incubated with WSMoL showed a significant decrease in extracellular protease activity. Bacterial proteases have a great potential to provide pathogenesis, they degrade structural and functional proteins of human tissue, as well as proteins involved in the immune system. The lectin obtained better results with Gram-negative bacteria, which raises the hypothesis that WSMoL binds to lipopolysaccharide (LPS) [63].

The lectin BVL-I was isolated from seeds of the plant *Bauhinia variegata*, it is presented as a single chain lectin specific for Galactose/N-acetylglucosamine (Gal/GalNac) with molecular weight of 32 kDa. It has been used in the inhibition of bacterial adhesion and in the healing of damaged epithelial tissue. The study of this lectin has as differential the fact that the source of the protein is limited, and then produced on a large scale through gene expression and cloning techniques, although expressed as a monomer, continued to obtain the same biological activity which was able to impair the initial adhesion of *S. mutans* and *Streptococcus sanguins*. Being an alternative for the production of a large scale isolate with biological activit [39].

The lectin ApulSL was extracted and isolated from seeds of a plant of Brazilian caatinga of the species *Apuleia leiocarpa*, this lectin is characterized as a disordered protein by having tyrosine in its structure with a highly hydrophobic nucleus. Its hemagglutinating activity proved to be resistant even after 100°C and dependent on Mg, being inhibited by N-acetylglucosamine, D (-) arabinose, and azocasein, which demonstrates affinity for these carbohydrates. The ApulSL showed inhibition of the growth of the bacteria: *Bacillus cereus*, *Bacillus subtilis*, *Enterococcus faecalis*, *Micrococcus luteus*, *Streptococcus pyogenes*, *S. aureus*, *Xanthomonas campestris pv*. *campestris*, *Xanthomonas* campestris pv. *viticola*, *Xanthomonas campestris pv. malvacearum, K. pneumoniae, E. coli, P. aerugionosa* and *Salmonella enteritidis*. The inhibition was more effective for the three species of *Xanthomonas*, for *Xanthomonas campestris pv. campestris* was obtained the lowest MIC, which reached 12.5 µg/mL [37]. As ApulSL, bracts lectin extracted from the same species (ApuL) showed bacteriostatic activity against *S. aureus* strains not resistant and oxacillin-resistant isolate, the minimum inhibitory concentration was 50 and 400 ug / ml. The lectin promoted minor damage to cell membrane of non-resistant *S. aureus*, however ApuL bacterial induced cell cycle arrest, given that some cells do not appear to have completed the cell division. On the other hand, against the lectin-resistant isolate it did not cause serious damage to the membrane, but the cells showed prominences on their surfaces without cellular morphological alteration, which demonstrates that ApuL can promote inhibition and impair the cell viability through different mechanisms. The combination of ApuL-oxaxiline showed a synergistic effect against resistant strains [64].

The lectin extracted from leaves of *Calliandra surinamensis*, was isolated and named CasuL, is characterized as an acidic protein of 48 kDa, being an oligomeric protein composed of three subunits. The degree of toxicity of CasuL was evaluated, which showed no reduction in the viability of human blood mononuclear cells, this evaluation of the cytotoxicity of lectins is fundamental, as it is known that this type of protein may be toxic to mammals, in this way, the result of CasuL indicates that it may be a potential target for studies of biological activities *in vivo*. In its antibacterial activity, it had bacteriostatic effect for

Staphylococcus saprophyticus and *S. aureus*, the antibiofilm activity was more significant than inhibition of bacterial growth, especially for *S. saprophyticus*, which shows that CasuL has a potential that needs evaluation to be used to cover surfaces [21].

EantH lectin, purified from *Euphorbia antiquorum* latex, has an affinity for galactose and N-acetylmuramic acid present in the cell walls of bacteria. This lectin has antibacterial activity for *Staphylococcus aureus* and *Staphylococcus epidermidis* (MIC of 2000 µg/ml), *Streptococcus agalactiae* (MIC of 250 µg/ml), *Propionibacterium acnes* (MIC of 125 µg/ml), *Salmonella typhimurium* (MIC of 1000 µg/ml). The results showed that the antibacterial property of lectin varies according to the constitution of the bacterial cell wall, EantH can show both bacteriostatic and bactericidal activity [65]. (Siritapetawee and coauthors).

The antibacterial activity of lectin CAL, isolated from *Cicer arietinum* L., was tested for the pathogenic strains *Escherichia coli, Bacillus subtilis, Serratia marcescens* and *Pseudomonas aeruginosa*. CAL showed antimicrobial activity with MICs in the range 80-180 µg/mL. The antimicrobial action of lectin is correlated with the peptidoglycan and/or lipopolysaccharide layer of the bacterial cell wall. Muramic acid and the binding affinity of lectin to glycogen can be directly related to antibacterial activity [66].

The development of metallic nanoparticles to fight bacterial infections has been shown to be a potential method, combining copper sulfide nanoparticles (CuS NPs) with Jacalin lectin, isolated from the seeds of *Artocarpus heterophyllus.* The action efficiency of the Jacalin-CuS NPs complex (JCuS NPs) was evaluated against clinical isolates of methicillin-resistant *Staphylococcus aureus* (MRSA). The results showed that the JCuS NPs complex promoted the inhibition of MRSA strains and reduced MIC. The mechanical study revealed that the complex exerts bactericidal activity through the recognition of glycans, generating reactive oxygen species and damage to the bacterium's membrane. The results showed that the MIC of CuS NPs after the formation of the complex with jacalin decreases from 12.5 µM to 0.78 µM. The researchers stress that the specificity of lectin by galactose plays a crucial role in the recognition of glycans, providing the site of action for CuS NPs, significantly reducing the required dose of CuS NPs nanoparticles. The antibacterial efficacy of JCuS NPs has been tested and proven in vivo in an animal model of zebrafish [67].

The results with PPL, purified lectin from *Parkia platycephala*, demonstrated that lectin was able to improve the activity of Gentamicin, an aminoglycoside antibiotic indicated for moderate to severe infections. The action of PPL decreased the MIC of Gentamicin from 32 to 20.2 µg / mL for the *E. coli* strain, corresponding to a 36.9% reduction in the amount of antibiotic needed to obtain an effective treatment. Based on these results, the researchers propose that lectin can act by two distinct mechanisms: interacting with Gentamicin in the CRD, facilitating the permeabilization of the antibiotic in the bacterial cytoplasm; or interacting with glycans present in the efflux pump, being responsible for blocking or promoting changes in the conformational structure [68].

The lectin from the roots of *Portulaca elatior (*PeRoL) has a molecular mass of 33 kDa, is composed of two subunits of 15 kDa linked by disulfide bonds. PeRoL has specificity for Galactose, glucose, mannose and N-Acetylglycosamine. The lectin did not show bactericidal activity, however, it obtained bacteriostatic activity against *Enterococcus faecalis, Pseudomonas aeruginosa* and *Staphylococcus aureus* [69].

PgTeL is a lectin extracted from the sarcotest of *Punica granatum* that showed activity for five isolates of *Escherichia coli* resistant to drugs capable of producing β-lactamases, the minimum inhibitory (MIC) and bactericidal (MBC) concentration ranged from 12.5 to 50.0 µg / mL and from 25.0 to 100.0 µg / mL, respectively. The effect of PgTel on the structure of the bacterium was evaluated by three-dimensional images, in all treatments with lectin there was a reduction in the number of cells, a serious change in shape and size was also observed. Lectin also demonstrated antibiofilm activity for all isolates. These data show the importance of PgTeL in the study of lectins with antibacterial capacity, considering that β-lactam hydrolysis is the most common mechanism for Gram-negative resistance against antibiotics. It was also found that there was a synergistic effect of the combination of PgTeL-ceftazidime for all isolates [70]. PgTeL also obtained antibiofilm, bacteriostatic and bactericidal activity for methicillin-resistant *S. aureus*, with MIC50 of 12.5 µg / mL and MBC of 50.0 µg / mL. Caused changes in the structure and cell viability, the bactericidal activity occurred through injury and death, which occurred mechanism of action against other bacterial strains, as with *E. coli* [71].

CONCLUSION

This review assembled the articles published in the last ten years about the antimicrobial activity of the lectins, describing the different mechanisms of action by which these proteins perform their action in the combat against a wide variety of both Gram-negative and Gram-positive strains. It can be observed that each the plant lectins can act on different types of bacteria with different mechanisms of action from its specificity and distinct from antibiotics. Thus, the importance of this class of proteins is reinforced as a natural alternative for antibacterial resistance. Further studies are required for the occurrence of its clinical application.

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