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Phyto Lectins-Wonder Biomolecules for the Benefit of Mankind

Shalini Saxena, Navneet Kumar Yadav

Abstract: ***The recent studies on different lectin and their agglutination activity have attained a distinct importance because of the wide range of applicability to problems of immune biology and clinical pathology. Now a days cancer is a fatal disease. It is wide occurrence in the people, especially in the labour class living in the polluted areas. The studies done on lectin shows that lectins are antitumor and anticancerous. So there may be correlation between increase or decrease in the lectin content and their hem-agglutination activity with water pollution and in turn with their biological role. There may also be difference in their subunits and difference in their physiochemical properties due to water pollution. Reliable and economical quantification of micronutrients in diets of humans is critical component of successful epidemiological studies to establish relationships between dietary constituents and chronic disease. Legumes are one of the major dietary components consumed by populations worldwide. consumption of legumes is thought to play a major role in lowering breast and prostate cancer risks. Recently, it has been suggested that consumption of soyfoods may contribute to the relatively low rates of breast colon and prostrate cancers in countries such as China and Japan. Soyabeans contain a number of anti - carcinogens, and a recent National Cancer Institute workshop recommended that the role of soyfoods in cancer prevention be investigated.***

Keywords: Immune Biology, Clinical Pathology, Anticancerous, Activity

Abbreviations:
WGA: Wheat Germ Lectin
AM: Alveolar Macrophage
PNA: Peanut Agglutinin
NK: Natural Killer
PNL: Peanut Nodule Lectin
PWM: Pokeweed Mitogen
ConA: Canavalia Ensiformes
HPA: Helix Pomatia
LEA: Lycopersicon Esculentum
STA: Solanum Tuperosum

I. INTRODUCTION

Lectins present on the surface of tumor cells are targeted for therapeutic purposes. It has been found that treatment with anti - lectin antibodies can suppress growth of tumor cells in agarose, and inhibit lung colonization in vivo [1].

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*Correspondence Author(s)
Shalini Saxena*, Lab of Cytogenetics Department of Botany, Bareilly college, Bareilly, UP, India. Email ID: 2126shalini@gmail.com
Navneet Kumar Yadav, Department of Chemistry, Bareilly college, Bareilly, UP, India. Email ID: drnavneetapaar@gmail.com

Lectins have the potential use in cancer treatment strategies due to the fact that lectins present on the surface of tumor cells are capable of binding exogenous carbohydrates – containing molecules and internalizing them by endocytosis [2].

For example, wheat germ lectin (WGA) is found to induce lectin - dependent macrophage - mediated cytotoxicity against human bladder cancer (T - 24) cells [3]. Alveolar macrophage (AM) are phagocytes, mainly present in the pulmonary alveoli, are important in the antitumour defense mechanism of the lung because they can bind to the target cell - but are unable to induce cytolysis [4]. However, studies have revealed that human AM tumoricidal activity can be induced by wheat germ lectins. Another findings is that the sensitivities of six human tumor cell lines depend on the number of receptor sites exist on the surface of WGA, Although the effector mechanism is still unknown, the binding of AM with tumor cells initiated by WGA may increase sensitivity to the cytotoxicity mediated by human AM [5].

In addition, WGA is found to enhance the cell killing ability of murine peritoneal macrophages. In vivo studies show that WG has an inhibitory effect on the growth of murine tumors [6]. The tumoricidal activity of human blood monocytes can be induced by the WGA [7]. As a result, the monocytes are able to become cytotoxic to four different human tumor cell lines : T - 24 bladder carcinoma, A - 375 melanoma, ACHN renal carcinoma, and U373MG glioblastoma. Murine system also shows a similar response. However, concanavalin a, PHA PWM and SBA are unable to produce tumoricidal monocytes [8].

ABL lectin from the edible mushroom **Agaricus bisporus** causes human colorectal and breats carcinoma cells to stop proliferating (does depend) [9]. ABL lectin, can bind sialylated Gal 1, 3 – n acetylgalactosamine, ABL inhibits incorporation of [3H], thymidine into DNA of Ht - 29 colon cancer cells by 87% m/caca - 2 colon cancer cells by 16%, MCF -7 breast cancer cells by 50% and Rama - 27 rat mammary fibroblasts by 55% Red blood cell agglutination by ABL is better inhibited by Gal - N - acetyl galactosamine bearing glycoproteins than by single sugars [10].

ABL stimulates vascular smooth muscle and endothelial all proliferation. ABL reacts with the TF antigen and inhibits cell proliferation [11].

Peanut agglutinin (PNA) binding to breast cancer cells inhibited proliferation in culture. Not all breast cancer cell lines can bind PNA. Retionic acid, which reduces PN binding, did not reduce PNA's affection proliferation. The combination leads to an additive growth inhibitory action [12].

PNA binds Gal - B - 1, 3 - N - acetylgalactosamine and stimulates proliferation in HT

- 29 human colon cancer cells [13].

PNA agglutinin strongly binds to normal mammary epithelium and this binding strength is progressively lost with increasing malignancy [14].

PNA has high affinity for the dissacharide galactose - N - acetylgalactosamine, which is also the T - antigen. It reportedly disappears in high - grade tumors. WGA may be better correlated than PNA with poor prognosis [15].

PNA binds breast cancer cells and is associated with presence of estrogen receptors [16]. Although Retionic acid normally inhibits PNA binding, their combined effect enhances inhibition of proliferation.

Very common alteration in malignant tissues is to start to produce the PN auto antigen. widespread PNA reactive auto antigen may play a role in tumor escape from the immune system and hence tumor progression [17].

Expression of PNA receptor binding sites in ductal breast cancer cells is associated with the expression of estrogen receptors in these cells. It measures the functional differentiation of tumor cells via differential expression of glycoproteins [18].

II. REVIEW OF LITERATURE

Various studies suggested the role of plant based lectins in prevention of cancer and tumor.**Phaseolus coccineus** contains two lectins, both agglutinate all blood groups but one is mitogenic for lymphocytes [19]. **Phaseolus lunatus** is a specific agglutinator of blood type A. Ingestion of **P. lunatus** agglutinin inhibits the growth of rats [20].

Phaseolus vulgaris is a potent mitogen of human leukocytes. (Mody et al., 1995) PH lectin can :–

- help induce remission in many malignancies.
- directly kill tumor cells.
- build immunity to infection.
- make tumors more recognizable to the immune system.
- cause cells to produce cytokines.
- make cells more targetable.

HPA binds breast cancer tissue when it is near the metastatic stage. Since it is an agglutinin it probably causes these cells to clump up and may be more easily targeted by the immune system [21].

HPA binds to breast cancers, gastric cancer, colorectal cancer and prostate cancer when they're at a distant metastasis stage with poor prognosis. HPA recognizes alphalinked terminal N - acetylgalactosamine in the Tn antigen [22]. The actual binding site includes sub terminal sugars also and the arrangement of the molecules in space must also be right. lot of glycoproteins bound (determined by SDS - PAGE) breast cancer tissues but one bound specifically to breast cancer and not normal tissues, determined to be the IGA - I heavy chain (Streets et al., 1996) [23].

Galectin - 3 is expressed more with increasing dysplasia in advancing stage colon cancer compared to tissues the dysplasia originated from [24]. Galectin - 3 is also known as Mac - 2, CBP - 35, IgEBP, CBP - 30, RL - 29, hL - 31, mL - 34 and LBL. This is especially true for lymph nodes and liver metastases [25].

ML - 1 is galactose specific, ML - 2 is Galactose and N - acetyl - D - galactosamine specific and ML - 3 is N - acetyl galactosamine specific. Several studies have shown that immunological parameters of cancer patients can be changed favourbly by the application of mistletoe extracts containing ML's [26]. The dose of ML - 1 required to be toxic to breast cancer cells (10 ng/ml) is 40 X higher than the dose needed to activate lymphocytes in culture. Immunostimulatory effects could be observed after giving patients suffering from advanced breast cancer 1 ng of ML - 1 per kg body weight for 4 weeks. ML - 1 and 3 have almost identical binding characteristics, and ML - 2 is different. (Schumacher et al., 1995) [27].

ML - 1 (VAA) has the ability to non - specifically increase immune system defense in the host. It has a dramatic anti - tumor effect, including activating Natural Killer cells (NK), enhancing monocyte and macrophage activity, stimlating secretion of cytokines (TNF - alpha and I - 6) without any toxic effects. It induces apoptosis in human myelomonocytic leukemic cells. (Mody et al., 1995) [28].

Concanavalin A. (mannose specific), WGA(N - acetylglucosamine, neuraminic acid specific), **Viscum album** lectins (galactoside - specific) and human placenta can stimulate this activity [29]. Con A had a stronger effect than WGA. Standard chemotherapy reduced the ability of neutrophils to produce superoxide when later stimulated by Con A and also reduced the effect of VAA [30]. Tumor type mayaffect the responsiveness of the neutrophileseg. Bronchial carcinoma patients expressed less super oxide when exposed to Con A., mammary carcinoma patients did not. (Timoshenko et al., 1993) [31].

Con a can agglutinate cells transformed by viruses or carcinogens more readily than it will agglutinate normal cells, but it can also be mitogenic and cytolitic to some lymph node cells, interacting with fibroblasts. (Sharon and Lis, 1972) [32].

Con A prevents Ehrlich ascites tumor cells from maintaining normal potassium content, they do not damage the cells through agglutination. Both ricin and Con A caused net K loss by stimulating K efflux. Ricin at 2 micrograms / ml is as effective as Con A at 100 micrograms / ml (Aull et al., 1976) [33].

Horse gram lectins (D. biflorus) have type specificity. D. biflorus lectin is non toxic but orally administered it inhibits the growth of rats. (Liener, 1974) [34].

Helix pomatia agglutinates blood cells. (Sharon and Lis 1972) Human placenta lectin causes super oxide release from neutrophils, decreasing free oxygen radicals in cancer patients. (Timoshenko et al., 1993) [35].

Abrin (from **A. precatorius** seed) inhibits protein synthesis similarly to recin (Leiner, 1976) type O specific agglutinin comes from the serum of the eel **(Anguilla anguilla)** (Sharon and Lis, 1972) [36].

Maclura pomifera agglutinin is a potent mitogen of human leukocytes. Osage orange (**Maclura pomifera**) is inhibited with D - galactose sugars. (Leiner, 1976) [37].

Since the turn of this century lectins were known for their cell agglutinating and carbohydrate binding property. It is now evident that lectins do perform a variety of functions in nature and the mechanisms have also been unrevealed. Suitable planning is necessary to exploit these wonder

molecules in agriculture and medicine [38]. What is needed is to mimic its role in nature. The possible application of lectins in cell targeting for drug delivery and as biopesticide may be the core areas of lectin research [39].

III. DISTRIBUTION AND BIOLOGICAL ROLE OF PHYTO LECTINS

A survey of the fresh and processed food found lectins in about 30% of the food stuff tested, including such common foods as salad, fruits, spices, dry cereals and roasted nuts. However dry heat may not completely destroy lectin activity [40]. Hemagglutinating activity is found in the processed wheat germ, peanuts and cereals. Several lectins are resistant to proteolytic digestion e.g., wheat germ agglutinin, tomato, lectin and navy bean lectin [41].

Recent studies in the field of glycoproteins have shown that they are normal constituents of green plants, fungi, algae, animal tissues and secretions. In the plant kingdom the highest percentage of glycoproteins have been found in seeds [42].

The development pattern, accumulation and disappearance of lectins in various seeds and their abundance have suggested that they may act as storage proteins. The subcellular localization of lectins in protein bodies is compatible with these roles [43]. Sexual agglutinin has been identified in chlamydomonas flagellar membrane. Phytolectins have also been identified as a single molecule of the **Azolla - Anabaena** symbiosis. Lectins are found in foods, certain foods more than others and the same food may contain varying amount of lectins depending on processing, when and where the plant was grown and species [44].

The major known potentially 'toxic' lectin containing food groups are:–

- Grains, especially wheat and wheat germ but also quinoa, rice, buckwheat, oats, rye, barley, millet and corn.
- Legumes (all dried beans, including soy and Peanuts).
- Dairy (perhaps more so when cows are fed grains instead of grass, a speculation based on research showing transference of lectins into breast milk and dairy and potentially more harmful in pasteurized, processed milk).
- Nightshade (includes potato, tomato, eggplant and pepper).

Not much is known about the functions of lectins in the organism they are formed in. There is evidence that lectins may be involved in the recognition between cells or cells and various carbohydrate - containing molecules [45]. This suggests that they may be involved in regulating physiological functions. They seem to play an important role in the defense mechanisms of plants against the attack of microorganisms, pests and insects. Fungal infection or wounding of the plant seems to increase lectins [46].

In legumes, the role of lectins in the recognition of nitrogen fixing bacteria of Rhizobium genus, which have sugar containing substances has received a special attention [47].

Binding Nitrogen fixing bacteria to legume roots is one of the important functions of the lectins.

Other functions of lectins in plants may include :

- Packaging and / or mobilization of storage materials.
- Transport of carbohydrates.
- Mitogenic stimulation.
- Cell wall extension.
- Defense mechanism.
- Storage of proteins.

Several lectins have been shown to possess agglutination properties against bacterial strains. **Staphylococcus aureas** and **mutants** have been extensively studied, these have been shown to be agglutinated by several commonly available lectins including tomato and wheat [48].

Hem agglutinating properties are not necessary for a lectin to possess mitogenic activity. Many mitogens are "lectins" only if we enlarge the category to include monovalent molecules with high carbohydrate affinity. Paradoxically, any plant polysaccharides can be thought of as "reverse lectins" i.e. their sugars bind lectin - like receptors on the cell [49]. This has been demonstrated for polysaccharides isolated from **Thuja occidentales** which show high mitogenic activity that is blocked by anti-interleukin. In antibodies, this proves that plant polysaccharides are definite biologic response modifiers. Other polysaccharides from higher plants such as **Baptisia tinctoralis** or **angefica acutiloba** and the fungi Basidiomycetes (lentinen, schizophylan, pachymaran and krestins) have also shown mitogenic and response modifying activity [50].

Con-A has been shown to reduce microtuble assembly in lymorphonuclear leukocytes. Lectins have been shown to cause early changes in cytoplasmic free Ca^{+2} and influence the lymphocyte membrane potential. Both Con-A and PHA were studied as to their effect on lymphocyte glycosyl transferase activity. The investigators found that this enzyme, associated with increased transport activity of sialic acids, galactose and NAG, was stimulated by Con-A but not by PHA. Thus the mitogenic effects of lectins on lymphocytes are not constant [51].

The Pokeweed mitogen, isolated from **Phytolacca arriericana, is the most** studied lectin in humans as regards to mitogenic effects. This lectin is one of the rare lectins, which is mitogenic for both T & B – lymphocytes [52].

A lectin isolated from chinese bitter melon **(Mornordica charantia)** has been shown to have potent immunomodulatory activity.

Injections of lentil lectin into the knee joint cavity of nonsensitized rabbits resulted in the development of arthritis, which was indistinguishable morhologically from rheumatoid [53].

No other property of lectins has attracted as much attention as their ability to agglutinate malignant cells. Josheph C. Aub discovered this by chance at Massachuselts General Hospital in 1963 [54]. aub believed that the difference between cancer cells and normal cells lay on their surfaces, and that alterations in the properties of the cell surface enabled cancer cells to multiply when normal cells would not, detach from their primary site and spread throughout the body. At the time the idea seemed quite strange, and as Nathan Sharon,in his review article on lectins In scientific American, put it : "bordered on lunancy" [55].

Aub worked with several enzymes, trying to determine whether the surface of a malignant cell was different

from that of a normal cell. Only in the case of one enzyme, a lipase from wheat germ did he observe a difference. Normal cells did not seem to be affected, but malignant cells were agglutinated. When he replaced the wheat germ lipase with a pancreatic lipase, however no agglutination took place [56].

Aub also found that heating could destroy the enzyme activity of the wheat germ, but the agglutination took place all the same. Aub and his colleagues then discovered that the wheat germ lipase contained as a contaminant a small protein that was responsible for the agglutinating activity [57].

Burger and Goldmanberg suggested that the surface of malignantly transformed cells contained a component, which was not found on the surface of normal cells. It was proposed that this component is NAG or a closely related derivative since ovomucoid, a glycoprotein rich in NAGs inhibited the agglutination at very low concentrations. A higher local density of lectin binding sites have been observed in addition to an interesting phenomenon called "capping" where lectins begin to cross link more and more surface receptors which result in more and more binding sites becoming available for cross linking [58].

This discovery began a new era in lectin research. Soon it was found that Con-A also agglutinated malignant cells. Recently the Weizmann Institute of Science in Israel found that soyabean agglutinin also has the same property. As a rule malignant cells are agglutinated by very low concentrations of a particular lectin and normal cells are not agglutinated unless the concentration is many times higher [59].

Lectin has been suggested as a stimulator of plant embryonic cells and also has been found to stimulate pollen germination in **Lillium longifloroum.**

The symbiotic interaction between legumes and rhizobia provide a convenient model system for the study of plant morphogesis and plant microbe iinteraction. The role of lectins in plant symbiont attachment has been proposed on the basis of interaction of **Rhizobium trifolii** and white clover. Trifoliin, the lectin, serves as a bridge between common or similar carbohydrate structures present on the surface of root tips and bacteria [60].

Rhizobia have several ‘nodes’ genes essential for nodulation. Transfer of nod genes from one Rhizobium strain to another allowed the recipient strain to inject the particular legume host of the donor Rhizobium strain.

In **Rhizobium phaseol** and **Phaseolus vulgaris** interaction, it was found that the difference in symbiotic association capacity in different varieties of **P. vulgaris** was due to the difference in their lectin structure. A recent study on Peanut nodule lectin (PNL) revealed lack of evidence about the association between this galactose specific lectin and Brady rhizobium in any symbiotic relationship. The glucose specific Peanut root lectin PRA-II may be involved in recognition of **Rhizobium** by Peanut roots.

There is molecular biochemical, cellular, physiological and evolutionary evidence that indicate that lectins have a role in plant defense. Normally plant lectins are associated with those parts of the plant that are most susceptible to attack by foreign organisms.

Plant lectins have been found to be toxic to viruses, bacteria, fungi, insects and higher animals. Interaction of bacteria with various organisms is being dealt with individually.

A phytolectin, Type 2RIP, has an inhibitory activity against viruses. It may be noted that several plant lectins are potent inhibitors of animal and human viruses which have glycoproteins in their virious.

Chitin-binding lectins have a role in plants' defense against fungi. It has been observed that WGA inhibits spore germination and hyphal growth of **Trichoderma viridae.**

The WGA lectins bind specifically to the sugar N-acetyl glucosamine (Glc Nac), its oligomers and Chitin, a polymer of GlcNac. Chitin binding proteins affect the growth of organisms that contain Chitin (fungi and insects).

Lectins from wheat germ potato tuber and seeds of Peanut, Thorn apple and **Osage orange** have an inhibitory effect on the development of larvae of the **Cowpea weevil.**

Lectins from **Robinia pseudoaccacia** and **Sambucus nigra** bark cause severe toxicity symptoms of PHA. WGA and other N-acetyl glucosamine-specific lectins bind to the intestinal mucosa of rats and some cause enlargement of the pancreas, lesions and abnormal development of microvilli.

Boyd and Shapleigh found lectins to be blood group specific. A and B blood group specificity has been found in lectins of **Sophora Japonica, Calpurnea aurea and Dolichos Biflorus.** Lectins from the edible mushroom agglutinates human RBC irrespective of blood group.

At present hundreds of lectins are well characterized and the number is growing fast. The lists of mitogenic lectin include pokeweed mitogen (PWM), lectins from **Canavalia ensiformes** (ConA), **Wisteria floribunda,** Lima bean, Jack bean, Soya bean, Faba bean, Jack fruit and mushrooms. Recently, mitogenic lectin from the seeds of **Erythrina veluntina** has been discovered.

Lectins like PNA, SBA, Jacalin and WGA were used to differentiate cell lines of high and low metastatic potential. Out of these WGA was capable of reacting with the sialyl groups of the malignant cell.

The antitumor activity of PNA, SBA and WGA in Dalton’s lymphona in mice was studied. SBA was found to exert maximum antitumor effect without any side effect in the animal. The potential use of tomato lectin in the selective drug delivery system is also being worked out. Galectin I, a human lectin, has been shown to be important in apoptosis and tumor regression.

One of the important applications of lectins in microbiology is direct aggregation of suspended micro-organisms. A lectin solution is mixed with a microbial suspension and examined under magnification.

A positive reaction may be used as a presumptive test for the organism. The specificity of the aggregation is illustrated by results from members of the genus **Neisseria.**

Table I. offers a limited description of some of the ways lectins have been applied to studies in microbiology. The table provides an outline of representative applications of lectin-microorganism complexes.

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Table-I: Reviews of Some Selected Lectin-Microorganism Complexes

Author	Observation
Aitchison et al	Lectins were used as probes to identify streptococcal glycoproteins on blots.
Birdsell and Doyle	Bacteriophages and Con A complete for the same site(s) on cell walls of ***Bacillus subtilis.***
Birdsell et al	Cell walls of **B.subtilis** are smooth on the inside and rough on the outside as revealed by binding of Con A.
Bonfanto-Fasolo et al	WGA-gold was used to study fibrillar wall components of fungi.
Bose et al	Lectins modify adhesion of **Chlamydia trachomatis** elementary bodies to tissue culture cells.
Corbel et al	Smooth and rough Brucella can be differentiated by lectins.
Chu and Chen	Con A inhibits DNA transformation of **Bacillus subtilis.**
Doyle et al	Use of concanavalin A-agarose to affinity purify teichoic acids.
Doyle et al	Glucosylated teichoic acid of **B. subtilis**, in dilute salts, could precipitate with Con A. In high salts, causing a random coil conformation, the teichoic acids are only slowly bound to Con A.
Ebisu et al	Studied streptococcal group polysaccharide structures with lectins.
Flemming	New methods for plotting lectin-mediated aggregations.
Fogg et al	Surface array of **Campylobacter fetus** protects against lectin binding.
Grenier et al	Membrane vesicles of **Porphyromonas gingivalis** can bind WGA.
Janzen et al	Lectins may be anti-insecticidal.
Kahane and Tully	Mycoplasma pneumoniae membrane glycoproteins were receptors for WGA, **Ricinus communis** (RCA) and Con A.
Kohler et al and selectively Wagner et al	Some lectins were able to aggregate bacteria.
Lindberg et al	Pneumococcal polysaccharide structure studies by lectins.
Maruyama	Spheroplasts of bacteria interact with Con A.
Mobley et al	Fluorescein-labeled concanavalin-A employed as probe for growth sites in bacilli.
Morioka et al	Observed binding of WGA-colloidal gold to inner and outer faces of cell walls of staphylococci.
Narasu and Gopi-nathan	Purified larvicidal protein from **Bacillus sphaericus**.
Schalla et al	Lectin aggregation patterns with bacteria formed the basis of epidemiological studies.
Stoddart et al and Karayannopoulou et al	Lectins were specific for fungi in tissue sections.
Summer and Howell	Members of the genera **Mycobacterium** and **Actinomyces** were clumped by concanavalin A.
Swanson and Kuo	**Chlamydia trachomatis** proteins were able to bind several lectins of differing specificites.
Tkacz et al	Fluorescent concanavalin A used as a probe for budding sites on yeast.

Now it is clear that lectins are able to selectively aggregate pyogenic cocci. Groups A,B,C,F and G streptococci can be readily distinguished by lectins. Ferritin-labeled Con A proved to be a good reagent for streptococcal groups A lipoteichoic acid. A Major advance in the employment of lectins as reagents in diagnostic microbiology involves use of magnetic spheres coated with the proteins. There are numerous factors which dictate how lectin and microorganism interact. These include all of the factors that combine to make any protein retain its fidelity, such as proper pH and ionic conditions, proper temperature and presence of metal ions. Many lectins (Plant, bacterial, invertebrate, vertebrate) require transition metals and/or Ca^{+2} or Mg^{+2} for activity. Interestingly, chelating agents inhibit the activity of the glucan binding lectin of **Streptococcus sobrinus.** but when the cells are washed all lectin activity returns.

Concanavalin A, in contrast, loses metals slowly by dialysis against chelating agents and in order to restore lectin activity Ca^{+2} and Mn^{+2} must be added back to the metal-depleted lectin. Factors such as receptor density, time, lectin molecular weight and presence of hydrophobic sites near the saccharide receptor influence the specificity and rate of interaction between lectins and receptors on microbial cell surfaces.

Microbial surfaces bear many of the sugar residues capable of interacting with lectins. Indeed, any surface exposed sugar is a potential lectin-binding site. The ability of lectins to react with microbial glyco-conjugates means that it is possible to employ them as sorbents for whole cells and this feature together with their extreme specificity makes them useful tools for identification of bacteria.

Lectins are attractive reagents for the clinical diagnostic laboratory because of their diverse specificity, their commercial availability, their high specific activities, their wide range of molecular weights and their stability in standard buffers, and the fact that they can be readily freeze – dried for storage, and readily labeled with fluorescent conjugates. Furthermore, lectin-based tests can be used in combination with enzyme-mediated tests.

Most lectin tests for identification of bacterial pathogens are based on selective agglutination reactions. For example, lectins such as WGA can be used in tests of this type to selectively detect species of the family Neisseriaceae, and indeed a diagnostic test specific for **Neisseria gonorrhoeae** has been developed using WGA (wheat germ agglutinin).

Lectins have been proved useful for epidemiological characterization of this pathogen. Additionally, certain non-encapsulated strains of **Neisseria meningitidis** are also agglutinated by WGA. The use of lectins in combination with conventional enzymatic tests has enabled faster testing for **Neisseria gonorrhoeae, N. meningitidis, N. lactamica** and **Moraxella catarrhalis.**

Another example of the diagnostic utility of lectins is provided by the genus Bocillus and particularly **Bacillus anthracis.** For the identification of **B. anthracis,** an agglutination procedure

using lectins from soybean (SBA) and the snail **Helix pomatia (HPA)** is included in the fourth edition of the Manual of Clinical Microbiology. SBA agglutinates **B. anthracis** and **B. mycoides** and HPA agglutinates only **B. mycoids** but not **B. anthracis.**

There have been previous studies of lectin agglutination of group-A streptococci group-B streptococci and group-C streptococci. In some instances treatment of the bacterial cells with sialidase abolished reactivity with lectins. In other instances, agglutination with lectins occurred only after enzyme treatment of the bacterial cells. With or without pretreatment, it is now clear that lectins are able to selectively agglutinate pyogenic cocci, Streptococcal group A,B,C,F and G can be readily distinguished by lectins.

A relatively wide range of lectins has been shown to agglutinate various serotypes of group-B streptococci. Group-B streptococci can be specifically agglutinated or labelled with fluorescein-conjugated lectins derived from certain plants of the Solanaceae family, like **Lycopersicon esculentum** (LEA) and **Solanum tuperosum** (STA).

A number of intestinal pathogens possess haemagglutinating properties. The conformation of terminal sialic acid on host cell glycoconjugates is important to be recognized by various bacterial lectins. In several cases, the composition and arrangement of the sialic acid terminated structures on glycoconjugates is essential for the binding process.[325] Sialic acid-specific lectins of **E.coli** and **H. pylori** bind besides glycoconjugates on host cells also to specific receptor molecules in the extracellular matrix (ECM). The binding of both S-fimbriated uropathogenic **E.coli & H. pylori** to the ECM component laminin has been shown to be sialic-acid-dependent.

Interestingly, laminin-binding by **H. pylori** was found to be mediated by specific sialic acid-binding protein in combination with lipopolysaccharide (LPS). Sialic acid-specific hemagglutinins are also shown to be involved in binding bacteria to another ECM component, i.e. Vitronectin, as shown for **H. pylori** most ECM binding proteins defined today do not show lectin-like properties but bind with high affinity by protein-protein like interaction.

The mannose-sensitive hemagglutination has been reported for a number of bacterial intestinal pathogens as well as for commensal microbes. The mannose-specific lectins are supposed to be involved in colonization of the mucus layer on cell surfaces as well as binding secretory IgA and carcinoembryonic antigens. Fucose and galactose residues have also been shown as recognition determinants for the adhesion of several pathogenic microbes.

Ofek et al have recently reviewed the area of lectinophagocytosis, with several emphasis on the role of mannose-specific lectins on type I fimbriated enteric bacteria such as **E. coli, Klebsiellate** and **Salmonellae.** Moreover, lipopolysaccharide-binding molecules on macrophages and complement receptors have also been defined as adherence molecules on murine peritoneal macrophage. Interestingly, heparan sulphate-like molecules were recently reported as receptor moleculeson macrophages for the major human intracellular pathogens. Better knowledge of possible lectino phagocytosis is important for selection of antibiotic therapy as well as for vaccine development.

Specific pathogenicity island gene clusters were recently defined in a number of pathogens such as uropathogenic **E. coli** producing both Gal-Gal specific lectin of P-fimbriate and sialic acid-specific lectin or the S-fimbriae. During bacterial infection, the activation and regulation of virulence genes occur. Interestingly, for **B. pertussis** the activation of pertussis toxin genes is following the activation of FHA expression. Significant associations between hemagglutination activities and the production of cytotoxin by **Aeromonas spp.** have been demonstrated.

The successful development of vaccines based on K99 and other surface lectins of enterotoxigenic **E. coli** (ETEC) in veterinary medicine and soluble hem agglutinin of **B. pertussis** has stimulated research to define binding epitopes in a number of other microbial lectins also as vaccine candidates.

In most cell types, Con A binds to the endoplasmic reticulum, whereas WGA binds to the golgi apparatus, making these fluorescent lectins useful reagents for facilitating the immunolocalization of oncogene products, specific intracellular enzymes, viral proteins and components of the cytoskeleton.

Con A also binds to isolated Golgi fractions from rat liver.

Fluorescent Con A has also been used to :-

- Determine if human sperm cells have undergone the progesterone – induced acrosome reaction.
- Investigate receptor capping in leukocytes.
- Measure lateral diffusion of glycoproteins, glycolipids and viruses in membranes.
- Show the redistribution of cell-surface glycoproteins in marine fibroblasts that had been induced to migrate by exposure to an electric field.

Fluorescent lectins are also useful in microbiology applications. Fluorescent WGA conjugates stain chitin in fungal cell walls and have been reported to stain gram-positive but not gram-negative bacteria. Fluorescent WGA conjugates are utilized in Red + Bacterial Gram stain and viability kit to differentiate gram positive and gram-negative bacteria.

Lectins of known specificity recognizing sialic acid serve as valuable reagents in glyco biological research. Lectins are found in greatest quantity and are most readily purified from plant sources, especially higher plants, although relatively few sialic acid binding lectins have been identified in the plant world (including fungi), that lacks sialic acid.

There is considerable support, but little solid evidence, for the belief that lectins function primarily as recognition molecules. This function may be expressed differently in different organisms and also in different organs or tissues of the same organism.

Table-II: Roles of Lectins in Nature

Plants	Attachment of nitrogen-fixing bacteria to legumes
	Attachment of nitrogen-fixing bacteria to legumes
Animals	Endocytosis and intracellular translocation of glycoproteins.
	Endocytosis and intracellular translocation of glycoproteins.
	Recognition determinants in nonimmune phagocytosis
	Binding of bacteria to epithelial cells
Binding of Bacteria to Epithelial Cells	Attachment of bacteria and parasites (e.g. amoeba & plasmodium) to host cells
	Recognition determinants in nonimmune phagocytosis.
	Recognition determinants in cell adhesion of slime molds.

In plants, two proposed functions of lectins are currently attracting most attention : (a) as mediators of symbiosis between plants and micro-organisms and (b) in protection of plants against phytopathogens. The hypothesis that recognition of rhizobia by lectins of the plant host may account for the specificity in the initiation of nitrogenfixing symbiosis has stimulated numerous investigations at present the only lectin isolated from roots that can bind to a specific nodulating strain of Rhizobium is trifolin. The lectin has been suggested to reversibly cross-bridge receptors on the root hair cell wall with bacterial capsular polysaccharides and/or lipopolysaccharides as a prelude to nodulation.

IV. CONCLUSION

The proposal that lectins may be involved in the defense of plants against fungal, bacterial and viral pathogens during germination and early growth of the seedlings is supported primarily by two lines of evidence (a) the binding of lectins to various fungi and their ability to inhibit fungal growth and germination and (b) the presence of lectins at the potential site of invasion by the infectious agents.

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After aggregating input from all authors, I must verify the accuracy of the following information as the article's author.

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