# Insight of Lectins- A review

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**Abstract**— Lectins are the carbohydrate-binding proteins and are known for their toxic relevance. History provides various evidences for their toxicity profile and initially, it was thought that lectins are associated solely with toxic content. However, recent research shows a remarkable development in lectin science and their use in studying glycoprotein biosynthesis, investigating carbohydrates on cells/cell-organelles, mapping neuronal pathways, anti-cancer therapies and in mitogenic stimulation of lymphocytes is well documented. Even though lectins have intrigued current researchers for the investigation of their therapeutic values, not enough studies have been conducted so far and knowledge about lectins is limited to certain plants or animal sources and further research is important to identify lectins and their importance in as many sources as possible. This review is a comprehensive account of lectins starting from their initial discovery, their purification, biological role and also presents an outline of their toxic effects and therapeutic contribution. In the search for their functions, the end may not be in sight but, at last, it is conceivably around the corner. Lectins could be the next generation medicines if efficient research is contributed in their understanding.

**Index Terms**— Lectins, History, Proteins, Toxin, Purification, Future Therapeutics, Biological role of lectins, Carbohydrate specificity

## 1.0 LECTINS- AN APPRAISAL

According to the widely accepted definition by Goldstein, "A Lectin is a carbohydrate-binding protein or glycoprotein of non-immune origin which agglutinates or precipitates glyco-conjugates or both" (1). It means that the lectins are assumed to be multivalent and the specificity is largely dependent on monosaccharide termini. Some plant lectins may agglutinate various blood groups of erythrocytes and are therefore, called phytohemagglutinins (1). In brief, Lectins are carbohydrate-binding proteins that are found in most plants, particularly seeds and tubers such as cereal crops, potatoes, and beans (legumes). Current research has shown the extraction of lectins from animal sources as well (2). Traditionally, they have been used as histology and blood transfusion reagents.
Lectins may be toxic, inflammatory, resistant to cooking or digestive enzymes, and are found in much of our foods (3). Even though, lectins are associated with toxicity, their importance in terms of cancer therapeutics, immunology, antibacterial property etc. cannot be neglected. Scientific research has shown that few of the peculiar characteristics of plants and animals (anti-bacterial properties, cytotoxicity etc.) are because of the presence of lectins and the understanding of these characteristics at molecular level could only be gained by thorough investigation of their associated lectins.

## 2.0 HISTORY

Seeds of certain plants and animals being toxic to mankind have been known for a long time (4). During the latter part of 19th Century, when the science of bacteriology formed the genesis of its understanding and had a marked influence on the scientific thinking and its approach, it was believed that the toxicity of such seeds was due to bacterial toxin. However this theory was critically disproved and was widely discarded by Wander and Waddell; they investigated that the toxicity of jequirity bean, *Arbus precatorius,* resided in a 'fraction', which could be precipitated by alcohol from an aqueous extract of the bean (4). Several years later, Dixson obtained a highly toxic concentrate from extract of the Castor bean, *Ricinus Communis.* It was established that the toxic element was present in the extract of the seeds. Stillmark was the first to experimentally prove that a protein fraction of the castor bean, which he called '*Ricin'* was capable of agglutinating red blood cells and he termed it as *Phytohemagglutinnins.* The work of Stillmark intrigued the attention of Ehrlich, who decided to work with '*Ricin*' rather than the bacterial toxins, which were so popular among the bacteriologists of that time. The use of these substances led Ehrlich to the discovery of the most fundamental principles of immunology (5,6). Few years later significant work was done by Landsteiner, who stated that the relative Hemagglutinating activity of various seed extracts were quite different when tested with erythrocytes from different animals, he also compared this specificity with that of antibodies of animal blood serum (7). The specificity towards specific erythrocytes was further investigated by Boyd and Shapleigh, it was them, who coined the term 'Lectin', derived from the 'latin' word 'legere', to pick, choose, or select (8). Lectins are also referred to, in the literature, as agglutinins or phytoagglutinins (9-11). The contributions incorporated by 'Stilmark' marked the beginning of centennial on lectin identification, purification, characterization and biological properties and functions. Until 1970s, not much was known about lectins, as only few of them were isolated (mostly from plants and few invertebrates) (12).

Over the years, numerous lectins have been isolated from plants as well as from microorganisms and animals, and during the past two decades the structures of hundreds of them have been established. Concurrently, it has also been shown that lectins function as recognition molecules in cell–molecule and cell–cell interactions in a variety of biological systems (13). Table 1 presents a brief account of 100-plus years of lectin re-

search and show how these proteins have become the focus of intense interest for biologists and in particular for the glycobiologists among them.

Table 1 History of Lectins

| Year | Scientist | Contribution |
|---|---|---|
| **1884** | Warden & Waddel | Toxiciy in *Abrus precatorius* seed extracts |
| **1886** | Dixson | Toxicity in *Ricinus communis* seed extracts |
| **1888** | Stillmark | Hemagglutinating activity in *Ricinus communis* seed extracts<br>Toxicity in *Croton triglium* seed extracts |
| **1890** | Power & Cambier | Toxicity in *Robinia pseudoacacia* seed extracts |
| **1890** | Erlich | Use of abrin an ricin in immunological research |
| **1891** | Hellin | Hemagglutinating activity in *Abrus precatorius* seed extracts |
| **1893** | Siegel | Hemagglutinating activity in *Jatropha curcas* seed extracts |
| **1897** | Elfstrand | Hemagglutinating activity in *Croton triglium* seed extracts |
| **1899** | Camus | Hemagglutinating activity in *Helix pomatia* |
| **1902** | Landsteiner | Reversibility of the hemagglutination by heat |
| **1902** | Kauss | Inhibition of the hemagglutinating activity by non-immune serum |
| **1903** | Noguchi | Hemagglutinating activity in horseshoe crab |
| **1907** | Landsteiner & Raubitschek | Hemagglutinating activity in non-toxic plants |
| **1908** | Wienhaus | Agglutination of leucocytes and kidney and liver cells by *Phaseolus vulgaris* |
| **1908** | Landsteiner & Raubitschek | Species specificity of plant hemagglutinatins |
| **1909** | Mendel | Hemagglutinating activity in *Robinia pseudoacacia* seed extracts |
| **1909** | Landsteiner | Inhibition of hemagglutinating activity by heat treated serum |
| **1909** | Landsteiner & Raubitschek | Inhibition of the heagglutinating activity by mucin |
| **1912** | Schneider | Hemagglutinins and germination |
| **1917** | Sumner | Isolation and crystallization of Concanavalina A (Con a) |
| **19126-7** | Marcusson-Begun/Siever | Aplicability of lectins for blood typing |
| **1935** | Sugishita | Specificity of eel serum agglutinins |
| **1936** | Sumner & Howell | Sugar specificity of Concanavalin A |
| **1947-9** | Boyd & Reguera/Renkonen | Blood group specificity of plant heagglutinins |

| | | |
|---|---|---|
| **1949** | Liener | Toxicity of *Phaseolus vulgaris* hemagglutinins |
| **1949** | Jaffe | Thermoinactivaation of *Phaseolus vulgaris* hemagglutinins |
| **1952** | Watkins & Morgan | Inhibition of lectins by simpe sugars |
| **1954** | Boyd & Sharpleigh | Introduction of the term lectin |
| **1960** | Nowell | Mitogenic stimulation of lymphocytes by *Phaseolus vulgaris* lectin |
| **1963** | Aub | Agglutination of malignant cells by lectins |
| **1964** | Muclenaere | Parallel inactivation of hemagglutinating and antinutritional activity by heat |
| **1965** | Agrawal & Goldstein | Affinity chromatography for lectin purification |
| **1966** | Boyd | Lectins in algae |
| **1970** | Apsberg *et al.* | Use of Con A for affinity purification of glycoproteins |
| **1974** | Ashwell & Morel | Role of animal lectins in endocytosis of glycoproteins |
| **1976** | Gallo | Interleukin 2 dissolved in medium of lectin stimulated lymphocytes |
| **1977** | Ofek *et al.* | Role of bacterial lectins in infection |
| **1980** | Pusztai | Interaction of *Phaseolus vulgaris* lectin with intestinal wall |
| **1981** | Reisner *et al.* | Use of lectins in bone marrow transplantation |
| **1984** | Yajko *et al.* | Combined use of lectin and enzyme in clinical identification of micro-organism |
| **1987** | Harban-Mendoza *et al.* | Control of root-knot nematodes by lectins |
| **1988** | De Oliveira *et al.* | Lectin and pancreas hyperthropy |
| **1989** | Diaz *et al.* | Root lectin as a specificity determinant in the *Rhizobium*-legume symbiosis |
| **1990** | Yamauchi & Minamikawa | Con A expression in *Escherichia coli* cells |

Until the early 1970s, although the presence of lectins was reported in numerous organisms, especially in plants, only few of them had been purified, and almost all the purification was performed by conventional techniques such as salt-induced crystallization, ethanol precipitation, ion exchange chromatography and gel filtration (13). Some of the early-purified lectins include plant lectins from soya beans, green peas, *Dolichos biflorus* seeds, wheat germ, and mushroom (*Agaricus campestris)* (12-13), and animal lectins of eel (13-14), and snail (2). These conventional methods relied on the physicochemical properties of the proteins for separation.

The introduction of Affinity chromatography for the purification of lectins was a turning point in the field of lectinology and immensely increased the pace of purification of lectins from various sources (15-16, 30). Affinity chromatography depends on the specific interaction between the lectin and a carbohydrate structure attached to an inert matrix (30). This breakthrough discovery led the easy availability of numerous lectins for a small period of time. However, even then, plants remained the primary source for the supply of lectins. Although the occurrence of lectins in animals was noted quite early, almost in all invertebrates and in lower vertebrates, only the aforementioned three animals (eel, snail, and horseshoe crab) were actually isolated and characterised. The first lectin from the animal source, shown to be specific for a sugar (L-fucose), was from the eel (17).

Lectins are found in almost all edible plants and exposure of men and animals to lectins is inevitable. The majority of plant lectins are present in seed cotyledons, where they are found in cytoplasm or they may also be present in protein bodies (18-19). Some lectins such as 'ricin' and 'abrin' are highly toxic; the general public became aware of toxicity of ricin after the murder of 'Georgi Markov' a Bulgarian writer. Even during World War II, ricin bomb was developed and tested in British military, but was never used as bio-weapons (13).

## 3.0 Carbohydrate Specificty

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' (20). Generally, lectins are classified in five groups on the basis of their affinity for (i) Glucose / Mannose; (ii) Galactose and N-acetyl-D-galactosamine; (iii) N-acetylglucosamine; (iv) L-fucose, and (v) Sialic acid (11). Source and specificities of lectins are summarised in Table 2. The binding with simple or complex carbohydrate conjugates is reversible and non-covalent. The specificity of lectins towards 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. The binding property of many lectins can be affected by more than one carbohydrate moiety; this is because each lectin molecule possesses two or more carbohydrate-binding sites that are essential for their ability to agglutinate cells or to react with complex carbohydrates (22). Hapten inhibition test is commonly used for identification of lectin specificity in present days.

Table 2 Sources and specificity of few of the common lectins (Gal, Galactose; Fuc = fucose; Glc = glucose; GalNAc, N-acetylgalactosamine; GlcNAc, N-acetylglucosamine; Man, mannose) (21)

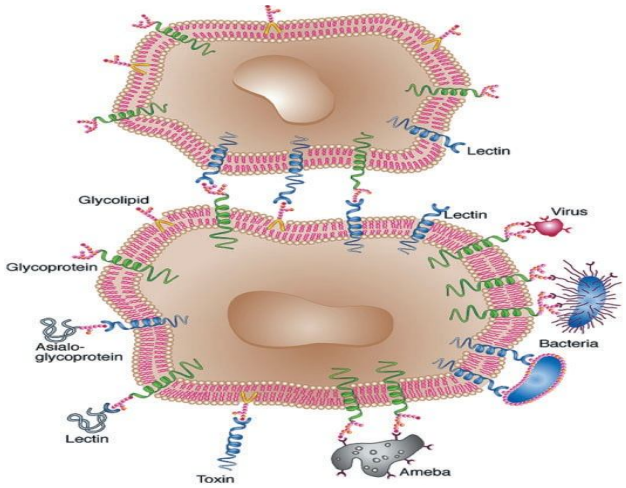
| Systemic Name of the plant source | Common Name | Preferred Abbreviation | Specifity |
|---|---|---|---|
| **Aaptos papilleta** | Sponge | AAP | GlcN Ac |
| **Abrus precatorius** | Jequirty bean | APA | Gal, GalNAc |
| **Aegapodium podagraria** | Ground elder | APP | Complex |
| **Agaricus bisporus** | Common mushroom | ABA | Complex |
| **Albizzia julibrissin** | Mimosa tree seed | ALJ | Nonspecific |
| **Allomyrina dichotoma** | Japanese beetle | AlloA | Gal, GlcAc |
| **Aloe arborescens** | Aloe plant | AAR | Nonspecific |
| **Amphicarpaea bracteata** | Hog peanut | AMB | GalNAc |
| **Anguilla Anguilla** | Eel | AAA | Fuc |
| **Aplysia depilans** | Molluse from Mediterranean sea | AGL | Galacturonic acidGal |
| **Arachis hypogaea** | Peanut | PNA | Gal, GalNH2 |
| **Artocarpus heterophullus** | Jacalin | JCA | Complex |
| **Bauhinia purpurea** | Camel's foot tree | BPA | GalNAc, Gal |
| **Bryonia diocia** | White bryony | BDA | Complex |
| **Canavalia ensiformis** | Jack Bean | Con A | Man,Glc |
| **Caragana Arborescens** | Siberian pea tree | CGA | GalN Ac |
| **Carcinoscorpius rotundacauda** | Horseshoe crab | CCN | Sialic Acid |

## 4.0 Biological Role

The biological role of lectins is based on conjecture rather than knowledge. The question of the possible physiological role of lectins has intrigued investigators from the beginning and the main highlight has been given to plant derived lectins, which for a long time were virtually the only ones known (23). It has been reported that feeding bruchid beetles with a diet containing 'the black bean' lectin resulted in the death of the bruchid larvae (24). On this basis, scientists concluded that the major role of lectins in legumes could be related to protection from attack by insect seed predators. In addition, it was found

that lectins may be involved in protection of plants against pathogenic microorganisms as well based on the observation that showed that WGA, PNA, and SBA inhibited the sporulation and growth of fungi such as Trichoderma viride, Penicilium notatum, and Aspergillus niger (25). Researchers found that the major carbohydrate specificity groups of about 11 lectins were all found to cause growth disruption during germination of spores of Neurospora crassa, Aspergillus amstelodami, and Botryodiplodia theobromae (26). Furthermore, it is speculated that lectins are involved in sugar transport or carbohydrate storage, because of their role in adhesion and agglutination. Lectins have also been considered to be important in both symbiotic as well as in pathogenic interaction between some microorganisms and host. They also play important role in microbial adhesion to various surfaces; they can bind to mucosal membrane and resist denaturation by acid as well as by proteolytic enzymes (27-28). Lectins are also shown responsible for the specific association between nitrogen-fixing rhizobia and leguminous plants, which provides the plant with the needed nitrogen, was advanced nearly three decades ago (29). It was based on the theory that lectin from a particular legume was bound to the surface polysaccharide or lipopolysaccharide of the corresponding rhizobial species, but not to bacteria that are symbionts of other legumes The suggestion has therefore been made that rhizobial attachment to plant roots occurs by interaction between the bacterial surface carbohydrates and lectins present in the roots of the leguminous plants. This is known as the lectin recognition hypothesis and still the subject of controversy, because of the lack of unequivocal evidence. Lectins serve as means of attachment of different kinds of cells as well as of viruses to other cells via the surface carbohydrates of the cells to be attached (28). In some cases, cell surface lectins bind to particular glycoproteins, whereas in other cases the carbohydrates of cell surface glycoproteins or glycolipids serve as sites of attachment for biologically active molecules that have specificity towards carbohydrate, for example, microorganisms, various plant toxins, galactic etc., as shown in Fig 1.

Figure 1 Specificity of cell surface carbohydrates towards various biomolecules (28)




The significance of lectins and its function in recognition or cell surface interaction occurred after 1950's, and it was demonstrated that influenza hemagglutinin is responsible for the attachment of the virus to the host cell prior to infection (13). Few years later, research showed the ability of lectins to provide innate immunity in animals. For instance, urinary tract infection in mice by mannose specific Escherichia coli can be prevented by methyl a-D-mannoside; several other lectins have also been proved to provide innate immunity. A prominent example is the mannose specific receptor present on the surface of macrophages, this receptor later binds to the infectious organism that expose mannose-containing glycans on their surface, resulting in ingestion and killing of the foreign organism (13). A recently discovered lectin of this type is dectin-1, specific for b1, 3 and/or b1, 6-glucans, present on fungi. Several lines of research have shown the importance of animal lectins as well, in marking essential biological properties, such as Calnexin, calreticulin, ERGIC-53, Collectins, Dectin-1, Galectins, Macrophage mannose receptor, Selectins to name a few (31). They have been involved in defence mechanism, lymphocytes homing and interactions of immunological cells. They also find a prominent role in cell biology i.e. in cell-cell interactions, cell growth, apoptosis, cell division and cell cycle (See Table 3).

Table 3 Functions of Lectins (31)

| Lectin | Role in |
|---|---|
| | |
| **Microorganisms** | |
| · **Amoeba** | Infection |
| · **Bacteria** | Infection |
| · **Influenza virus** | Infection |
| | |
| **Plants** | |
| · **Various** | Defense |
| · **Legumes** | Symbiosis with nitrogen-fixing bacteria |
| | |
| **Animals** | |
| · **Calnexin, calreticulin, ERGIC-53** | Control of glycoprotein biosynthesis |
| · **Collectins** | Innate immunity |
| · **Dectin-1** | Innate immunity |
| · **Galectins** | Regulation of cell growth and apoptosis; regulation of the cell cycle; modulation of cell–cell and cell–substratum interactions |
| · **Macrophage mannose receptor** | Innate immunity; clearance of sulphated glycoprotein hormones |
| · **Man-6-P receptors** | Targeting of lysosomal enzymes |
| · **L-selectin** | Lymphocyte homing |
| · **E- and P-selectins** | Leukocyte trafficking to sites of inflammation |
| · **Siglecs** | Cell-cell interactions in the immune and neural system |

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## 5.0 Lectins- Toxins or Therapeutics

Toxic relevance of lectins is known since ages. Some lectins are resistant to the gut enzymes and do not break easily, they might bind to the wall of the gut and cause damage to the gut lining. This could be related to diseases such as colitis, Crohn's disease, Coeliac-Sprue, and IBS (3). A study by P.G Brady showed that Lectins were active in the faeces of rats and human beings, when the subjects were fed on food sources rich with these proteins. Brady and his colleagues isolated wheat germ agglutinin, a plant lectin by affinity chromatography and also isolated, purified and identified wheat germ agglutinin from faecal samples (32). Research shows that lectin derived amino acids are non-available for animals and the partially digested lectins can bind to the epithelial cell lining of the intestines (33-34). Jaffe was the first to attribute poor performance of rats after the ingestion of Phaseolus vulgaris (kidney beans lectins) (35). Years of research has shown that after the interaction of lectin with the intestine, it is edocyted and cause many disturbances in the systemic levels (35). Few similar experiments were performed by De oliveria and his colleagues, they concluded that when lectin derived from pure Phaseolus vulgaris were fed to rats, enlargement of the intestine, liver, and pancreas was observed. Apparently, this enlargement in pancreas may be responsible for the observed decrease in the insulin levels of the rats (36). It was also observed that the kidney bean lectin fed rats had thymus atrophy, it is speculated that this atrophy was developed may be because of the unusual proliferation of bacteria in the gut, as the immunological system of the rats may have been depressed due to toxic effects of lectins (36). The ingestion of kidney bean lectin also disturbs the intermediary metabolism, leading to loss of weight, inadequate development and eventually death of the experimented rats (36). Other diseases associated with lectins are insulin dependent diabetes, rheumatoid arthritis, IgA nephropathy and peptic ulcers. Lectins sensitivity could occur due to the failure of a certain type of barrier protection in the body, namely SIgA barrier protection. It could be argued that lectins are specific to certain carbohydrates and when they attach to their specific carbohydrate substrate, they may damage the cell membrane and may damage the cell (3). Although, lectins possess several toxic elements, their benefits are also documented in the literature making them a subject of therapeutic interest for several researchers

Lectins are used in various biological fields. Their contribution in Cell identification and separation (37), detection, isolation, and structural studies of glycoproteins (38), investigation of carbohydrates on cells and subcellular organelles (31, 43), mapping of neuronal pathways (39) mitogenic stimulation of lymphocytes (40), Purging of bone marrow for transplantation (41) and studies of glycoprotein biosynthesis is remarkable (42).

Certain lectins are also used as carriers for the delivery of chemotherapeutic agents; they are also used in investigating cell surface receptors in various bacteria, protozoa and fungi. Lectins can also be used in determining bacterial cell wall components and bacteriophage receptors (28, 43).

The property of lectins to bind non-covalently to simple sugars and polysaccharides is quite unique, so lectin research has attracted a wide interest in microbial taxonomy (28, 43). Lectins have a role in the clinical laboratory identification and taxonomic classification of many microorganisms. Lectins are generally monoclonal proteins and they possess a spectrum of specificities and molecular weights, due to this, they are classified as substantial tools for diagnostic microbiology applications (28, 43). One of the advantages of applying lectins in clinical microbiology is that cellular or surface receptor sites can be partially analysed by hapten inhibition studies (11, 44). Unlike the production of antisera, which requires pre-treatment of microorganisms for antigen preparation followed by injection of the microorganism and glyconjugate into animals, such as rabbits leading to the absorption of antisera to eliminate nonspecific antibody reactions (45), lectins are simple to use, when they are conjugated to a histochemical label such as fluorescein, peroxidase, or colloidal gold, lectins may be used as histochemical probes to identify and localize specific carbohydrate residues in microorganisms by light or electron microscopy, as well as by blotting methods (45).

The cell binding property of lectins elicit a wide range of biological phenomena for instance, lectins have been used to fractionate animal cells, including B and T lymphocytes and also illustrates changes in cell surface architecture following virus infection or parasite infection (11). They are very important and versatile tools and are applied as probes for fluorescence and electron microscopy as well as in gel diffusion assays. Immobilised lectins are used for affinity chromatography during the separation of glycoproteins as they have advantage over other purification techniques because elution can be pursued with a relatively inexpensive monosaccharide and the glycoprotein, which is to be purified, is not subjected to denaturation (28, 43).

Over the past few years, Lectins have been found to have anticancer properties (46). Several researches have shown the use of Lectins to inhibit tumor growth, especially by causing cytotixicity, apoptosis and, down-regulation of telomerase activity and inhibition of angiogenesis (46). In addition, lectins have also been found to sequester the pool of available polyamines in the body; thereby help in thwarting cancer cell growth. Some lectins are potent toxins, but due to this ability they could be used as potential therapeutic agents, for instance, lectins such as 'Recin' and 'Abrin' have been coupled to specific monoclonal antibodies and are used in cancer therapy. Ricin could be used for developing specifically cytotoxic chemotherapeutic agents by linking them to cell type-specific monoclonal antibodies (47). Cancer is a deadly disease, where the aberrant behaviour of a single cell type is difficult to treat by chemotherapy (47). It is important in cancer therapy that the treatment targets only the affected cells, leaving the normal cells undisturbed, which is quite difficult, especially in chemotherapy. A promising approach is to incorporate a hybrid reagent that has selectivity towards target cells with potential cytotoxicity. Immunotoxins (ITs) conjugates in which cell reactive monoclonal antibodies are chemically joined to potent toxins are most popular manifestation of such hybrids (48). Target cell specificity is conferred by a monoclonal activity

that has been raised against the tumour cell-specific surface antigen (47). Ricin is the toxin of choice because it is well characterized and has easy purification steps and it is shown that human rarely shows prior immunity to it (49) and therefore, it is one of the most potent toxins known. Other plant lectins, relatively closer in structure and function to ricin are Abrus pecatorius seeds, Adenia digitata roots, Viscum album leaves, and Adenia volkensii roots (50). Ricin is composed of two distinct N-glycosylated polypeptides joined by disulphide bonds. One of the polypeptide chains (A chain) irreversibly inactivates 60S ribosomal subunits. Ribosomes exposed to A chain cannot bind to EF-2 and hence stops protein synthesis (47). It is stated by Olsnes and Pihl in 1982 that mammalian ribosomes are particulary sensitive to ricin than plant ribosomes. Cell surfaces bind to second polypeptide chain (B chain) of ricin by interaction with galactosyl residues of membrane glycoproteins or glycolipids. Surface-bound ricin then enters the cell by classical receptor mediated endocytosis route, which includes coated pits and vesicles and at some point of time, chain A also translocates across the membrane by Golgi cisternae (51), where it attacks ribosome substrates. Youle and Neville showed that B-chain plays a vital role in transferring toxic chain-A into the cytoplasm (52). Two main ricin based ITs are available; Chain A and B both attached to the cell-specific antibody and only Chain A attached to the cell-specific antibody. Both the forms have their pros and cons and have been widely used in In Vitro clinical applications to deplete tumour growth (47). In conclusion, these researches establish the potential role of lectins as therapeutic and diagnostic tools to combat diseases. Therefore, isolation of these lectins could be beneficial. Further line of research should involve deducing the molecular weight of the lectins. After knowing the molecular weight, amino acid sequencing of the lectin can be executed to generate the RNA coding of the protein that could eventually lead to the identification of the specific cDNA sequence. Such cDNA templets could be saved in cDNA libraries. Using these cDNA libraries, primers of the lectins can be formed to understand their properties and biological role at molecular level. Lectins of therapeutics interests can be preserved and can be used in clinical research and healthcare therapies.

## 6.0 Conclusion

Although lectins have been marketed as potential toxins, there is now extensive literature reporting the activity of lectins in a number of different tissues and processes, a diversity of reports that illustrates the widespread importance of lectins in cell biology and as a potential therapeutic agent, especially for cancer, molecular/cell biology and immunology are well documented. However, knowledge about lectins is limited to certain plants or animal sources and further research is important to identify lectins and their importance in as many sources as possible. There should be many lines of experimental investigation opening up for exploitation. In the search for their functions, the end may not be in sight but, at last, it is conceivably around the corner. Lectins could be the next generation medicines if efficient research is contributed in their understanding.

## 7.0 References

1. Goldstein, I. J., Hughes, R. C., Monsigny, M., Osawa, T. and Sharon, N. (1980) What should be called a lectin? Nature, 285, p 66.
2. Hammarstr€om, S. and Kabat, E.A. (1969). Purification and characterization of a blood-group A reactive hemagglutinin from the snail Helixpomatia and a study of its combining site. Biochemistry, 8, p2696–2705.
3. Natural therapy pages. 2012. Unknown Lectins Available. [ONLINE] Availableat: http://www.naturaltherapypages.co.uk/article/Lectins. [Accessed 01 January 12].
4. Warden, C. J. H., Waddell, L. A., (1884) Calcutta Bengal Secretarial Press, 76.
5 Ehrlich, P., (1897) Fortschr. Med. 15, p41.
6. Ehrlich, P., (1891) Deut. Med. Wochenschr. 17, p976.
7. Landsteiner, K, 1936. The Specificity of Serological Reactions. 3rd ed. Springfield: Charles C Thomas.
8. Boyd, W. C., and Shapleigh, E. (1954) Specific precipitating activity of plant agglutinins (lectins). Science 119, p419.
9. Brown, J. C., and Hunt, R. C. (1972) Lectins. Int. Rev. Cytol. 52, p277-349.
10. Cushion, M. T., DeStefano, J. A. and Walzer, P. D. (1988). Pneumocystis carinii: surface reactive carbohydrates detected by lectin probes. Exp. Parasitol. 67, p137-147.
11. Nicolson, G. L. (1974) The interactions of lectins with animal cell surfaces. Int. Rev. Cytol. 39, p89-190.
12. Moreira, R., Ainouz, I.L., Oliveira, D., and Cavada, B.S., (1991) Plant Lectins chemical and biological aspects; Mem.Inst Oswaldo Cruz, 86, p211-28.
13. Sharon, N., and Lis, H. (2004) History of lectins: from hemagglutinins to biological recognition molecules. Glycobiology. 14, p53–62.
14. Springer, G.F. and Desai, P.R. (1971) Monosaccharides as specific precipitinogens of eel anti-human blood group H (O) antibody. Biochemistry, 10, p3749–3760.
15. Goldstein, I. J., and. Hayes, C. E. (1978) The lectins: carbohydrate binding proteins of plants and animals. Carbohydr. Chem. Biochem. 35, p601-615.
16. Goldstein, I. J., Hughes, R. C., Monsigny, M., Osawa, T. and Sharon, N. (1980) What should be called a lectin? Nature, 285, p 66.
17. Watkins, W.M. and Morgan, W.T.J. (1952) Neutralization of the anti-H agglutinin in eel serum by simple sugars. Nature, 169, p825–826.
18. Mialonier, G., Privat, J.P., Monsigny, M., Kohler, G., and Durand, R. (1973) Isolement, properties, physio chemical and localization of in vivo lectins of Phaseolus vulgaris, (var. rouge). Physiol Veg 11, p519-537.
19. Youle, R.J., and Huang, A.H.C. (1976) Protein bodies from the endosperm of castor bean. Subfractionation, protein components. Lectins and changes during germination. Plant Physiol. 58, p703-709.
20. Drickamer, K. (1988) Two distinct classes of carbohydrate-recognition domains in animal lectins. J. Biol. Chem., 263,

p9557–9560.
21. Doyle, R. J., Nedjat-Haiem, Miller, F., R. D., and Keller, K. F. (1982) Interaction between plant agglutinins and Legionella species. J. Clin. Microbiol. 15, p973-975.
22. Wu, A. M., Sugii, S. and Herp, A. (1988) A guide for carbohydrate specificities of lectins. Adv. Exp. Med. Biol. 228, p819-847.
23. Etzler, M. E. (1986) Distribution and function of plant lectins, p.371-435. In I. E. Liener, N. Sharon, and I. J. Goldstein (ed.),The lectins, properties, functions, and applications in biology and medicine. Academic Press, Inc., Orlando, Fla.
24. Janzen, D.H., Juster, H.B., and Liener I.E. (1976) Insecticidal action of the phytohemagglutinin in black beans on a bruchid beetle. Science, 192, p795–796.
25. Barkai-Golan, R, Mirelman, D., and Sharon, N. (1978) Studies on growth inhibition by lectins of Penicillia and Aspergilli. Arch. Microbiol., 116, p119–121.
26. Brambl, R. and Gade, W. (1985) Plant seed lectins disrupt growth of germinating fungal spores. Physiol. Plant, 64, p402–408.
27. Etzler, M.E. (1986) Distribution and function of plant lectins. InLiener, I.E., Sharon, N., and Goldstein, I.J. (Eds.), the lectins: properties, functions and applications in biology and medicine. Academic Press, Orlando, FL, pp. 371–435.
28. Lis, H., and Sharon, N. (1986) Application of lectins, p. 293-370. In I. E. Liener, N. Sharon, and I. J. Goldstein (ed.), the lectins: properties, functions and applications in biology and medicine. Academic Press, Inc., Orlando, Fla.
29. Bohlool, B.B. and Schmidt, E.L. (1974) Lectins: a possible basis for specificity in the Rhizobium-legume root module symbiosis. Science, 188, p269–271.
30. Agrawal, B.B.I. and Goldstein, I.J. (1967) Specific binding of concanvalin A to cross-linked dextran gels. Biochem. J., 96, p23C–15C.
31. Lis, H., and Sharon, N. (1989) Lectins as molecules and tools. Annu. Rev. Biochem. 55, p35-67.
32. Brady, P. G., Vannier, A. M., and Banwell, J. G. (1978) Identification of the dietary lectin, wheat germ agglutinin, in human intestinal contents. Gastrointerol, 75, p236-239.
33. Etzler, M. E. and Branstrator, M. L., (1974) Differential localization of cell surface and secretory components in rat intestinal epithelium by use of lectins. J. Cell. Biol., 62, p329.
34. King, T. P., Pusztai, A. and Clarke, E. M.W., (1980) Immunocytochemical localization of ingested kidney bean (Phaseolus vulgaris) lectins in rat gut. Histochem. J., 12, p201-208.
35. Jaffe, W. C., (1960) Arzmeim-Forsch., 10, p1012-1016, quoted by Liener (1986).
36. Oliveira, D., Pusztai, J. T., and Grant, G., (1988) Changes in organs and tissues induce by feeding of purified kidney bean (Phaseolus vulgaris) lectins. I Nutr.Res. 8, p943.
37. Kobayshi, M., Fitz, L., Ryan, M., Hewick, R.M., Clarck, S.C., Chan, S., Loudon, R., Sherman, F., Perussiaj, I.B., and Trinchierit, G. (1989) Identification and purification of Natural Killer cell stimulatory factor (NKSF), A cytokine with multiple biologic effects on human lumphocytes. J . Exp . MED. 170 (1), p827-845.
38. Alroy, J., Orgad, U., Ucci, A.A., and Pereira, M.E. (1984) Identification of glycoprotein storage diseases by lectins: a new diagnostic method. J Histochem Cytochem. 32, p1280-1284.
39. Yoshihara, Y., Mizuno, T., Nakahira, N., Kawasaki, M., Watanabe, Y., Kagamiyama, H., Jishage, K.I., Ueda, O., Suzuki, H., Tabuchi, K.., Sawamoto, K.., Okano, H., Noda, T. and Mori, K.. (1999) A Genetic Approach to Visualization of Multisynaptic Neural Pathways Using Plant Lectin Transgene. Neuron, 22 (1), p33-41.
40.Gary, R., Gunther, J.L ., Wang, and Edelma, G.M. (1974) The Kinetics Of cellular commitment during stimulation of the lumphocytes by lectins. The Journal of Cell Biology. 62, p366-377.
41. Rhodes, E.G. (1998) Combined lectin / monoclonal antibody purging of bone marrow for use in conjunction with autologous bone marrow transplantation in the treatment of multiple myeloma. Methods in Molecular Medicine. 9, p351-61.
42. Wang, Y., Wu, S.L., and Hancock, W.S. (2006) Monitoring of glycoprotein products in cell culture lysates using lectin affinity chromatography and capillary HPLC coupled to electrospray linear ion trap-Fourier transform mass spectrometry (LTQ / FTMS). Biotechnol. Prog. 22, p873-80.
43. Sharon, N. and Lis, H. (1989). Lectins as cell recognition molecules.Science. 246 (4927), p227-224.
44. Liener, I. E., Sharon, N., and Goldstein, I.J. (ed.). 1986. The lectins: properties, functions and applications in biology and medicine. Academic Press, Inc., Orlando, Fla.
45. Slifkin, M., and Cumbie, R., (1987) Identification of group B streptococcal antigen with lectin-bound polystyrene particles. J. Clin. Microbiol. 25, p1172-1175.
46. Mody, R., Joshib, S.H.A., Chaney, W. (1995) Use of lectins as diagnostic and therapeutic tools for cancer. Journal of Pharmacological and Toxicological Methods. 33 (1), p1-10.
47. Lord, J.M. (1987) The Use of Cytotoxic Plant Lectins in Cancer Therapy. Plant Physiol. 85 (1), p1-3.
48. Pastan, I., Willingham, M. C., and FitzGerald, D. J. P. (1986) Immunotoxins. Cell, 47, p641-648.
49. Olsnes, S and Pihl, A (1982). Toxic lectins and related proteins. Amsterdam: Molecular Action of Toxins and Viruses, P. Cohen, and S. van Heyningen. P51-105.
50. Barbieri, L., Stirpe, F. (1986) Ribosome-inactivating proteins up to date. FEBS Lett 195, p1-8.
51. Van Deurs B, Tonnessen, T.I., Peterson, O.W., Sandvig, K., Olsen, S. (1986) Routing of internalized ricin and ricin conjugates to the Golgi complex. J. Cell Biol. 102 (1), p37-47.
52. Youle. R.J, Neville, D.M,. (1982) Kinetics of protein synthesis in activation by ricin-anti-Thy 1.1 monoclonal antibody hybrids. J Biol Chem, 257, p1598-1610.