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REVIEW ARTICLE

Role of Lectins

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ABSTRACT

Introduction: The study of lectins began with the work of Hermann Stillmark in the year 1888. Lectins are carbohydrate-binding proteins of nonimmune origin and find application in diagnostic pathology.

Objectives: Recent research work shows a remarkable development in lectin science. This comprehensive review tries to emphasize the historical aspects, biological sources, classification, applications, and recent advances of lectins.

Materials and methods: Electronic database searches for published literature were performed. The following electronic databases with no language and publication date restrictions were searched: MEDLINE (via Ovid and PubMed), EMBASE (via Ovid), the Cochrane Oral Health Group's Trials Register, and CENTRAL.

Results: Lectins have been proven to be effective in *in vitro* trials for combating many medical conditions like cancer, autoimmune disorders, etc.

Conclusion: Lectins could be the next generation therapy if efficient research work is contributed to the understanding of their behavior.

Keywords: Carbohydrate, Drug delivery, Immunohistochemical markers, Lectins.

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INTRODUCTION

Lectin is a carbohydrate-binding protein or glycoprotein of nonimmune origin, which agglutinates or precipitates glycoconjugates or both.[1] "Lectin" hails from the Latin word "legere," which means "to select," and was coined by William Boyd in 1954.[2] Proteins that have the ability to agglutinate red blood cells with known sugar specificity are referred to as "lectins" and the term "hemagglutinins" is used when the sugar specificity is unknown[3] Lectins have the unique property of specific recognition and reversible binding with the carbohydrates and sugar-containing substances without altering the covalent structure of any glycosyl ligands.[4]

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Milestones in the History of Lectin Exploration

The study of lectins commenced with the work of Hermann Stillmark in the year 1888. He noticed that the crude extracts of castor beans (*Ricinus communis*) contained a toxic substance named ricin that agglutinated both human and some animal red blood cells. Reversibility of hemagglutination activity by heat was confirmed with the research of Landsteiner in 1902. Boyd and Sharpleigh in 1995 introduced the term "lectin" and Aub in 1963 discovered the property of agglutination of malignant cells by lectins.[1,2] In 2005, the concept of lectin microarray and lectin-based biosensors were put forth.[5,6]

Biological Sources

Lectins are widely distributed in nature in most of the edible plants and in some animals. The majority of plant lectins are present in seed cotyledons, rhizomes, and leaves. Legume seeds are rich sources of lectins. More research work has been concentrated on lectins that have been isolated from plants, particularly those extracted from members of the Leguminosae family.[1,3]

The common sources of plant lectins include the jequirty bean, common mushroom, mimosa tree seed, Japanese beetle, aloe plant, peanut, jack bean, and mango fruit seed. Animal lectin sources include eels, molluscs from Mediterranean sea and horseshoe crabs.[1,3]

Classification

- Sharon et al classified lectins based on the type of monosaccharide ligand into five groups:[5]
  1. Mannose
  2. Galactose/N-acetylgalactosamine
  3. N-acetylglucosamine
  4. Fucose
  5. N-acetylneuraminic acid
- Based on the structure, lectins are classified into:
  - *Merolectins:* These are composed of single carbohydrate-binding domain, incapable of precipitating glycol conjugates or agglutinating cells.

- *Holoectins:* These are built of two identical carbohydrate-binding domains.
- *Chimerolectins:* These are fusion of proteins that consist of two different chains, of which one has a remarkable catalytic activity (and another biological activity).
- *Superlectins:* These are built of at least two carbohydrate-binding domains that are not identical. Thus, superlectins recognize structurally different sugar.[7]

APPLICATIONS

Anticancer Activity

Plant lectins are a unique and natural source of anticancer compounds. Lectins possess anticancer properties by inhibiting tumor growth, especially by causing cytotoxicity, apoptosis, down-regulation of telomerase activity, and inhibition of angiogenesis. Cells exhibit an altered glycosylation pattern during oncogenic transformation by expressing different glycans compared to their healthy counterparts. Lectins have been used as tools for identification of aberrant glycans expressed by tumor cells.[1,6]

Ricin and Abrin lectins have been conjugated to specific monoclonal antibodies and are used in targeted cancer chemotherapy. Lectins are superior to monoclonal antibodies in the recognition of terminal or branched sugar residues, making them valuable in the study of glycosylation patterns. Lectins also possess immunomodulatory action by differentially modulating macrophage-mediated immuneresponses.[1,6]

Anti-human Immunodeficiency Virus Activity

Lectins exhibit significant activity against human immunodeficiency virus (HIV). On the viral surface, lectins can crosslink with glycans and thereby prevent interaction with co-receptors and prevent the penetration of virus. Banana-derived lectin (BanLec) has the ability to inhibit the genome integration of HIV in the target cell, and can co-inhibit viral replication. Examples of lectins that exhibit antiviral activity are Jacalin, Concanavalin A, Urtica diocia, etc.[8]

Applications in Clinical Microbiology

Lectins are multifaceted reagents that provide definitive identification and strain characterization of a particular infectious agent. They can be used for empirical testing procedures in clinical microbiology as in the identification of group A Streptococci. They can also be used for achieving diagnostic or surface structural data which is useful for characterization of microorganisms into a specific genus.[9]

Lectin Histochemistry

Lectins were utilized for the histological staining of specimens as early as in the 1980s.[6] The carbohydrate moiety may be characteristic of a particular tissue and lectin-binding profiles with the cell surface carbohydrates have diagnostic significance in the field of pathology (Damjanov 1987).[10]

Hence lectins can be used in the following pathologies as markers:

- *Epithelial dysplasia and oral Squamous cell carcinoma:* When used as immunohistochemical markers, jack fruit lectins (JFL) and peanut agglutinin have shown significant correlation in the membrane and cytoplasmic staining of all layers correlating with the histological stages of tumor progression. Peanut agglutinin and JFL may be used as histochemical probes in differentiating benign and malignant lesions of the oral mucosa.[11]
- *Odontogenic cysts and tumors:* Lectin markers Ulex Europaeus Agglutinin-I (UEA-I) and Banderirea Simplicifolia Agglutinin I (BSA-I) are useful histochemicals that aid in differentiating cystic ameloblastoma and nonneoplastic cysts.[12]

Recent Advances

- *Lectin-based bioadhesive drug delivery systems:* Lectins can be used as bioadhesive drug delivery systems. As carbohydrate-binding proteins, lectins can increase the adherence of drug delivery vehicles to the mucosal surfaces. The coupling of lectin with macromolecular drugs or particular drug carriers may lead to efficient site-specific absorption of drugs. Plant lectins are stable in low pH conditions and have the intrinsic ability to bind specifically with epithelial cells.[13]
- *Lectin functionalized particles as oral immunotherapeutic agents:* Immunotherapy is a widely acknowledged therapeutic approach for the treatment of immunologically mediated diseases, including autoimmunity, cancer, and allergic disorders. Lectins from UEA-I, Lycopersicon esculentum (tomato lectin), Canavalia ensiformis, and Aleuria aurantia lectin (AAL), have been utilized for intestinal cell targeting. Lectin-based oral formulations are useful for restoring deficient functions of the immune system.[14]

CONCLUSION

Lectins have been proven to be effective in *in vitro* trials for combating many medical conditions like cancer, autoimmune disorders etc. Lectins could be the next generation medicines if valuable research is contributed to their understanding.

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