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INVERTEBRATE LECTINS AND THEIR BIOMEDICAL APPLICATIONS

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Abstract: -

Invertebrate lectins are diverse biological functions, including "self-nonself" recognition, bacterial agglutination and lysis, metamorphosis, moulting, wound repair, regeneration, and host parasite interactions. Agglutinins/lectins are predominantly found in the hemolymph, hemocytes and hepatopancreas of crustaceans. The functioning of the agglutinins/lectins depends upon its ability to recognize and bind to specific sugars on the cell surface glyco-conjugates. Lectins can be used as tools for blood typing, diagnosing of micro-organisms, mitogenic stimulation of lymphocytes, and discrimination between normal and malignant cells, purification of glycoconjugates and as tools to examine cell surface carbohydrates. The functioning of the agglutinin depends upon its ability to recognize and bind to specific sugars on the cell surface glycoconjugates.

Keywords: - *Lectins, agglutination, glyco-conjugates, Invertebrates, tumor.*

INTRODUCTION

The capacity to mount an immune response that eliminates infection of a host by a microbial pathogen is critical for species survival and propagation[1]. Invertebrate animals, which lack adaptive immune systems, have developed other systems of biological host defense, so called innate immunity, that respond to common antigens on the cell surfaces of potential pathogens. The innate immune system is the first line of inducible host defense against bacterial, fungal and viral pathogens[2]. This defense system is essential for the survival and perpetuation of all multicellular organisms[3,4]. Invertebrates which do not possess immunoglobulins, have developed unique modalities, to detect and respond to microbial surface antigens like lipopolysaccharides (LPS), lipoteichoic acids, lipoproteins, peptidoglycans (PGN) and (1-3) □-D-glucans [5].

Defense molecules in invertebrates

Invertebrate innate immunity relies on both cellular and humoral components. Invertebrate humoral immunity involves the presence of biologically active molecules that occur naturally or that may be induced. These molecules, by their lytic or agglutinating properties are able to act on the antigens responsible for their induction; only in this respect do they resemble vertebrate antibodies. The humoral factors (native, induced) in invertebrates include LPS binding proteins, phenoloxidase system, antibacterial proteins, antifungal proteins, lysins and agglutinins. According to Iwanaga and Lee (2005)[6], the defense molecules include phenoloxidases, clotting factors, complement factors, protease inhibitors, antimicrobial peptides, toll-free receptors, lectins and other humoral factors found mainly in hemolymph plasma and cell hemocytes. Hemolymph in association with the hemocytes performs an essential role in immune defense and wound healing in insects and other invertebrates, revealing that both cellular (phagocytosis, nodule formation, encapsulation) and humoral elements (agglutinin, antibacterial proteins) are involved in the reaction to non-self[7].

Agglutinins/Lectins

Lectin from castor bean extracts were first described by Stillmark (1888)[8]. They are distributed widely in bacteria, plant and animals[9] and have been given various definitions. Lectins are a group of proteins that interact with glycoproteins and glycolipids by binding to specific carbohydrate residues[10]. Lectins (formerly found as hemagglutinin) are carbohydrate-binding proteins which recognize specific carbohydrate structures on mammalian cells[11]. Lectins are a group of sugar binding proteins that recognize a specific carbohydrate structure and agglutinate various cells by binding to cell surface glyco-conjugates[12]. Lectins are protein complexes with carbohydrate specific binding properties that have been found in viruses, bacteria, plants, invertebrates and vertebrates and may have a wide variety of functions[13].

Sialic acids

Sialic acids are a family of nine carbon acidic ketoses found predominantly at the non-reducing end of oligosaccharide chains on glycoproteins and glycolipids[14]. Sialic acids show remarkable structural diversity with the family currently comprising over 50 naturally occurring members[15]. The largest structural variations of naturally occurring sialic acids are at carbon 5, which can be substituted with an acetamino, hydroxyl acetamino or hydroxyl moiety to form 5-Nacetyl neuraminic acid (Neu5Ac), 5-N-glycolyl neuraminic acid (Neu5Gc) or Keto Deamino Neuraminic acid (KDN) respectively[16]. This diversity of structure reflects their involvement in a variety of biologically and medically important functions [17].

Importance of sialic acids

Sialic acids play an important role as ligands in cell sociology. The unique structural features of the molecule, which includes a negative charge owing to a carboxyl group, enables it to play a role in cellular functions, such as transport of positively charged compounds, cell to cell repulsion, influencing conformation of glycoprotein on cell membranes, and even masking antigenic determinants on receptor molecules[18]. The derivatives of sialic acids are very important constituents of the cell surface. The normal human tissues possess the common sialic acid, NAcetyl neuraminic acid, which gets modified to O-Ac or NeuGc on neoplastic transformation[19]. They occur as components of glycoproteins and glycosphingolipids on the cell surface and in body fluids. Sialylation of glycoprotein changes under pathological conditions as well as during developmental stages and altered sialylation often has significant implications in the physiological role of glycoproteins[20]. Lectins that recognize the linkages or modifications of sialic acids are therefore indispensable as reagents in biochemical research and diagnostic analysis.

Mode of action of lectins

Invertebrate agglutinins are sugar-binding proteins with multiple binding sites, diverse biological roles [21]and biomedical applications. They may recognize a part of a sugar[22], a whole sugar[23], their glycosidic linkage[24]or a sequence of sugars[25]. Lectins, by acting as opsonins may mediate phagocytosis of foreign particles by hemocytes[26]. In invertebrates, which do not have an antibody based immune system [27], lectin may act as recognition molecules for defense activities such as leukocyte aggregation, heteroagglutination and opsonization [28]. Lectins play crucial roles in innate immunity and host defense both in vertebrates and invertebrates with involvement in processes such as non-self-recognition, inflammation, opsonization, cell-cell or cell-extra cellular matrix interaction, fertilization, development and regeneration, cell aggregation, wound repair, metamorphosis and transport of complex sugars [29].

Biomedical application of Lectins/Agglutinins

The availability of a number of lectins with diverse carbohydrate specificities makes these proteins a useful tool in biochemistry, immunology and cellular biology. Lectins are very sensitive to small variations in tissue epitopes and the affinity of the lectin for its binding sugars in a tissue is also affected by surrounding carbohydrate. The sialic acid binding specificity of this lectin was used to separate immature mouse thymocytes (low sialic acid content) from mature thymocytes (high sialic acid content) [30].

Typical recognition molecules, the mannose binding lectin (MBL) and ficolins, are involved in the specific recognition of carbohydrates on pathogenic micro-organism including bacteria, fungi, parasitic protozoans and viruses [31]. Ficolins and collectins play important role in host defense, non-self-recognition and opsonic activity of the neutrophil [32]. Lectins are used to identify inflammation, cancer, pregnancy and foetal development [33]. Tumor immunologists have developed murine and human monoclonal antibodies against sialyl antigens for diagnosis and immunotherapy [34]. Lectin affinity chromatography provides evidence for the alteration in the normal glycosylation of the alpha subunit of the human chorionic gonadotropic hormone in patients with pituitary tumors [35].

Lectins recognize sugars that constitute the surface components of pathogenic bacteria that invade the body cavity [36]. With a battery of immobilized lectins, mixtures of glycopeptides or oligosaccharides obtained by enzymatic or chemical cleavage of purified glycoproteins can be separated into homogenous compounds [37]. Lectins are used to characterize the structural changes on oligosaccharides in leukemias. The lectin from *M. rosenbergii* could be considered a useful tool for the diagnosis and study of T-cell acute lymphoblastic leukemia [38].

Several sialic acid specific lectins purified from plant and other sources have been employed as tools for the detection and separation of sialic-acid containing glyco-conjugates [39]. Lectins are used in cell separation, mitogenic stimulation and blood grouping [40]. Lectins could be used as drug carriers for carrying biologically active molecules and to direct those to specific molecules and cell organelles [41].

Lectins have been implicated in the attachment of a sperm to an egg, the first step in fertilization [42]. Lectins are used to study changes in the distribution of glyco-conjugates during embryonic development [43]. Forensic science laboratories use immobilized lectins for rapid typing of haptoglobin in blood stains [44]. Lysosomal storage diseases characterized by accumulation of corresponding substances could be revealed by lectin staining [45]. Lectin is used as a tracer for mapping neuronal connections in neuroanatomy [46]. Cells pre-treated with anti-lectin antibody showed decreased metastatic potential [47]. Protein-carbohydrate interaction plays a role in identifying the spread of cancer cells from the main tumor throughout the body [48].

Lectins present on various human and murine metastatic tumor cells influence the pathogenesis of cancer metastasis [49]. Lectins are specific in their reactions with human blood groups (ABO and MN) and subgroups (A_1) and have therefore been used in blood typing and in investigation of the chemical basis of blood group specificity[50]. The stimulation of lymphocytes by lectin also provide an important tool for the examination of the biochemical events involved in the conversion of a resting cell into an actively growing one [51]. Lectins (*Macrobrachium* lectin) are used in studying the process of protein glycolysation in the brain from patients with Alzheimer's disease [52].

N-acetyl-D-glucosamine specific lectin in crustacean hemocytes is used for wound healing, pathogen encapsulation, and maintenance of normal crustacean connective tissues [53]. A novel lectin (EIL) isolated from the marine hair crab *Erimuramus isenbeckii*, with high specificities for both O-acetyl sialic acid and mannose that are present in bacterial pathogens suggests that EIL may act as a defense protein against infection in this crab [54]. Romano and Alberto (2004)[55] have showed that the incorporation of the purified lectin from *Macrobrachium rosenbergii* in the food composition induced resistance of the specimen, *Litopenaeus vannamei* against the white spot disease virus.

Conclusion

Although several studies have demonstrated the presence of humoral agglutinins in several crustacean species, it can be noted that the immunological role of these lectins/agglutinins remain unknown and that the carbohydrate specificity of serum agglutinin from crustaceans have been elucidated only in a few species.

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