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PLANT LECTINS AS BIOLOGICAL AGENTS

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RESUMO

O estudo de lectinas de plantas tem sido há longo tempo explorado. Elas estão largamente distribuídas em várias espécies botânicas não relacionadas e encontram-se presentes em diferentes órgãos das plantas. As lectinas constituem um largo grupo de proteínas que compartilham uma propriedade em comum de reconhecer e interagir especificamente com estruturas glicanas. Suas características bioquímicas têm sido bastante investigadas e, nos últimos anos, as lectinas tornaram-se alvo de intensos estudos estruturais. Apesar do expressivo conhecimento sobre lectinas de plantas, suas funções fisiológicas ainda não estão claras. Por outro lado, as lectinas são atualmente utilizadas como ferramentas biotecnológicas na agricultura, biologia, imunologia, glicobiologia e áreas relacionadas. Considerando-se os recentes avanços na pesquisa de lectinas, é esperado que muitas delas sejam, nos próximos anos, exploradas como drogas terapêuticas em doenças de plantas e animais.

ABSTRACT

Plant lectins have been intensively studied. They are widely distributed in unrelated species and occur in different organs of the plants. They constitute a large group of proteins that share in a common feature of recognize and specificaly interact to glycan structures. Their biochemical characteristics have been largely investigated and in recent years, they became an aim of intensive structural studies. Despite the expressive information about plant lectins, their physiological functions remain unclear. On the other hand, lectins are nowadays used as biotechnological tools in agriculture, biology, immunology, glycobiology and related areas. Regarding the recent advances in lectin research it is expected that many lectins can be used, in near future, as therapeutic drug in plant and animal diseases.

INTRODUCTION

Although lectin research had its origins at the turn of the century, these cell-agglutinating and sugar-specific proteins started to attract wide attention only during the late 1960s. This was prompted largely by studies which demonstrated that lectins are extremely useful reagents for detection and isolation of glycoproteins and for the partial characterization of their carbohydrate moieties as well as following changes that occur in cell-surface sugars in such processes as development, differenciation and neoplastic transformation (Sharon, 1993). During the past few years, lectins research has grown not only in size but also in scope.

Plant lectins are a very heterogeneous class of (glyco)-proteins grouped on the basis of a single common property, namely their ability to recognize and specifically bind carbohydrate ligands (Van Damme et al., 1995a). Legume plants are the most thoroughly studied group of lectins (Moreira et al., 1991; Sharon and Lis, 1990). As a result, many legume lectins have been isolated and characterized (Van Damme et al., 1995b: Cavada et al., 1996; Kaku et al., 1990) and their biochemical and structural features determined (Bourne et al., 1990; Shanaan et al., 1991). Also from this group, it was stablished the molecular bases of the interaction lectin-sugar (Delbaere et al., 1993; Dessen et al., 1995; Bourne et al., 1994). Despite the relevant information available on lectin research, the physiological functions of these proteins are still unclear and many hypothesis have been suggested based on their location (Rudiger et al., 1993) and carbohydrate specificity (Chrispeels and Raikhel, 1991; Ayouba et al., 1991; 1992). At present, the role of defense proteins and the role of mediator in plant microbe interaction are the most speculated.

Since lectins are carbohydrate-binding proteins, they can sucessfully interact with glycoproteins, glycan receptors on cell surface and biological active carbohydrates making them eminently suitable for functioning as mediators of celullar recognition (Lis and Sharon, 1991). In fact, many biological activities have been discribed for plant lectins and in some cases it was clearly demonstrated the involvement of their carbohydrate-binding sites in these activities. In this respect lectins from different sources have been tested in heterologous system, showing to be powerful tools in agriculture and medicine research. A rapid description of some biological activities and future prospects of using lectins as biological tools is briefly discussed.

LECTINS AS A MEDIATOR IN PLANT METABOLISM

The role of mediator in plant metabolism has received special attention by lectinologists. Results from Diaz et al. (1989) suggest the involvement of the lectin as a recognition molecule in early symbiosis events. The lectin seems to recognize a specific receptor produced by its ***Rhizobium*** partner and thus, assures the specificity in the legume-***Rhizobium*** nodulation. In addition, the presence of lectin in the root hair of various leguminous plants favors this hypothesis (Kijne et al., 1992).

The interaction of lectins from pea (***Pisum sativum***) and soybean (***Glycine max***) with storage proteins from their respectively seeds was recently reported by Rudiger and co-workers (Einhoff et al., 1986; Rudiger and Schecher, 1993; Barlag et al., 1993; Wenzel and Rudiger, 1995). Since these and many other lectins were showed to be accumulated in the protein bodies during seed development, the role of lectins in the structural maintainance of protein bodies became an atractive hypothesis. It is important to consider that the two refered lectins exhibit distinct monossacaride-binding specificity. Thus, if they play the same role in protein bodies, their monossacaride specificity is not a limitant factor to recognize more complex glycan structures present in the storage proteins.

In the ***Gramineae*** family, another group of plant lectins, the lectins specificaly interact with *N*-acethylglucosamine, (GlcNac), its oligomers, and chitin, a polymer of GlcNac residues. These lectins are called chitin-binding proteins and were isolated from wheat germ (WGA) from ***Triticum vulgare***, ***Secale cereale*** (rye), ***Hordeum vulgare*** (barley) and ***Oryza sativa*** (rice). Since the best inhibitor for these lectins (chitin) is not found in plants, any endogenous functions have been atributed to them. On the other hand, the proteins that bind chitin have all been found to affect the growth of organisms that contain chitin (fungi and insects). The specific accumulation of the ***Gramineae*** lectins in tissues that stablish direct contact with the environment during embryo germination and seedling growth has long been interpreted as evidence for their role in protecting the plant against fungal attack (Chrispeels and Raikhel, 1991).

PLANT LECTINS AS AN INDUCER IN ANIMAL METABOLISM

Lectins from plant seeds have long been subjected of nutritional studies. Although the complete mechanism of action of plant lectins on animal metabolism is not yet completely understood, a large amount of studies have been published showing the antinutritional effects induced by some lectins.The inclusion of raw kidney beans (***Phaseolus vulgaris***) in the diet of humans and monogastric animals has long been known to cause toxicity of varying severity depending on the actual amounts of beans consumed. There is little doubt that most of these effects are caused by the seed lectins. Undoubtedly, some lectins can reduce the efficiency of food conversion by the gut due to their direct antinutritional effects. However, their direct interference with digestion and absorption is usually not very expensive and can not fully explain the striking changes in the structure and metabolism of epithelial cells. According to recent suggestions (Oliveira et al., 1994) it is more likely that lectins may act as extraneous metabolic signal molecules which induce wasteful or harmful changes in metabolism leading to substantial losses of essential body components (see Puzstai et al., 1991; Bardocz et al., 1995).

Proteins-carbohydrate interactions occur in association with many biochemical processes. It is not surprising, therefore, that lectin-carbohydrate interactions are a common and important feature of molecular events underlying the immune response (Kilpatrick, 1995). Many plant lectins have been ivestigated in basic and applied immunological studies. The discovery of the capacity of lectins to induce mitogenicity in human lymphocytes opened a very interesting field in lectin research. Since the lectin from ***Phaseolus vulgaris*** (PHA) was showed to be mitogenic (Nowell, 1960), lectins from differents taxonomic groups were showed to possess similar activities (Barral-Netto et al., 1992; Koninkx et al., 1993). Lectins from sub-tribe ***Diocleinae*** which are glucose/mannose specific, are strong inducer of mitogenicity and g-interferon production (Barral-Netto et al., 1992). These lectins are also able to induce leukocyte immigration and rat paw edema formation (Bento et al., 1993). Histamine release induced by glucose/mannose specific lectins was also demonstrated by Gomes and co-workers (1994). Recently, the lectin isolated from the seeds of ***Canavalia brasiliensis*** showed to reduce the lesions of highly suceptible BALB/c mice infected by ***Leishmania amazonensis*** when administred *in vivo* at time of infection or maintained throughout the infection (Barral-Netto et al., 1996). From these and many other studies developed using plant lectins as a biological agents in the animal system, the utilization of these proteins as biotechnological tools have been rapidely grown. Many lectins are, today, largely used in immunological studies as mitogenic agents, as reagents to identify and/or fractionate cells of immune system (Kilpatrick, 1995).

LECTIN AS A BIOTECHNOLOGICAL TOOL

The application of lectins to human red blood cell serology is well-stablished. Most lectins are nonspecific for human blood groups, but others may be considered reagents of choise for the assignation of certain blood groups. As examples, the lectin from ***Dolichos biflorus*** seeds agglutinates specificaly A1 erytrocytes while the lectin from ***Lotus tetragonolobus*** agglutinates « O » erytrocytes. These lectins have largely been used in typing human blood groups. The lectins from ***Canavalia ensiformis*** (ConA) and ***Phaseolus vulgaris*** (PHA) are currently used as reagents to induce mitogenicity in lymphocytes to investigate the molecular basis of their activation and proliferation and their control. Mitogenic lectins as ConA and PHA may also act as immunosuppressive agents in vivo. The early animal studies on tissue grafting using these lectins has been reviewed by Nicolson (1974); these experiments demonstrated that lectins or lectin-containing extracts could prolong allograft survival over weak histocompatibility barriers (Kilpatrick, 1995).

A chemical support to affinity chromatography prepared with ConA was sucessfully used to the purification of juvenile hormone esterase from the hemolimph and the fat body of ***Lymantria dispar*** (Valaitis, 1992). Ideed, immobilized lectins have been used to isolation and characterization of glycoconjugates and glycoproteins (Allan and Crupton, 1976). Moreover, blood group-specific lectins have been applied to characterization of oligosaccharides in salivary glycoconjugates (Bals et al., 1993).

The introduction of lectins in molecular biology research is clearly growing. Since many lectins were showed to be somehow toxic to some plant predator (Gatehouse et al, 1995), a new field in lectinology was opened. On the basis of observation of the effects caused by plant lectins when incorporated in artificial diet for ***Calosobruchus maculatus***, it was suggested that the mechanism of lectin toxicity is analogous to that known to occur in rat, namely the lectin that was ingested causes disruption of the epithelial cells of the larval midgut leading to a breakdown of the transport of nutrients into these cells, and facilitating the absorption of potentially harmful substances (Gatehouse et al., 1990).

Some lectins isolated from seeds of sub-tribe ***Diocleinae*** showed to be toxic to the larvae of ***Nilaparvata lugens***. The lectin from ***Canavalia brasiliensis*** seems to induce an expressive retardement in larvae development as well as larvae death (Grangeiro., 1996). The gen coding to this lectin was isolated and had its sequence recently determined (Grangeiro, 1996). The genetic engineering of crop plants with foreign genes (lectins genes) to confer insect resistance will offer a new strategy in agriculture to control insect damage.

Concluding remarks

The literature of lectins is also very widely distributed, with research reports appearing in many unrelated specialist journals dealing with fields as diverse as , for exemple, plant morphology and cancer. The versability of lectins to recognize and interact with glycan structures independently of their origin associated to the unknown signals transduced by this specific interaction, make lectins powerful tools to be used in pratic biological, agricultural and medical problems. In this way, some lectins have been introduced as a biotechnological tool in cancer research (Schumacher, 1995), and the production of transgenic plants resistant to insect or fungi attack (Gatehouse et al., 1995). It is expected that the increasing advance in lectin research may introduce these plant proteins to the applied research.

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