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Lectins: Multifaceted Molecules

Senjam Sunil Singh[*1] and Tzi Bun Ng[*2]

[1]Laboratory of Protein Biochemistry, Biochemistry Department, Manipur University, Canchipur, Imphal-795003, India

[2]School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong, China

[*]**Corresponding Author**: Tzi Bun Ng, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong, China;

1. E-mail: sunil_senjam@rediffmail.com; Tel.: +91-986-589128 (S.S.S); Fax: +91-385-2435145 (S.S.S)

2. E-Mail: b021770@mailserv.cuhk.edu.hk; Tel.852-3943-6872 (T.B.N.); Fax: 852-6053-5123(T.B.N.)

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Lectins belong to a class of carbohydrate binding proteins of immense importance as attested to by the voluminous literature. They are a group of proteins of non-immune origin possessing at least one non-enzymatic domain that recognize and bind to carbohydrate moieties [1]. Lectins are detected in almost all forms of organisms such as viruses, bacteria, fungi, animals, and plants. They can agglutinate cells and precipitate glycoconjugates [2].

"Lectin" is derived from the Latin word "legere", which means "to select", by William Boyd in 1954. Nowadays, proteins that can agglutinate red blood cells with known sugar specificity are also referred to as "lectins". The name "hemagglutinins" is employed in the case of unknown sugar specificity. A typical lectin is multivalent, hence it can agglutinate cells by binding to the carbohydrate moieties on the surface of these cells, without altering the properties of the carbohydrates [3]. Although it seems apparent now that Weir Mitchell had already observed lectin activity in rattle snake venom before 1860, it wasn't until at least six years later, when Stillmark reported the dramatic action of ricin on red blood cells and then Helin followed it up by a similar report on abrin, that agglutinins caught the attention of the medical community [4].

These proteins display a diversity of structures, carbohydrate binding specificities, and functional properties [1]. In term of functions, lectins manifest a wide array of properties such as antifungal, antitumor, immunomodulatory, anti-insect, antiviral, anti-HIV-1 reverse transcriptase and immunomodulatory activities which may find applications in many therapeutic areas [5]. Hence, lectins have drawn the attention of many researchers and occupy an important place in agricultural and therapeutic areas of research [5, 6].

Nowadays, lectins with unique characteristics are being continuously isolated and their properties elucidated [7]. However, there are certain areas that we can still focus on in lectin research. One of the explorable areas of lectin research is on mushrooms, both from wild as well as from edible species. Mushrooms are famous for their nutritional and medicinal values and also for the diversity of bioactive compounds including lectins. Macro fungi are a large repository of lectins in which 82% of the lectins identified are from mushrooms [6]. Recently Singh et al. published an extensive review on mushroom lectins, in which more than 300 mushroom lectins were reported [8, 9]. Ng also reported that mushroom lectins are localized on the caps, stipes and the mycelia [10]. Compared to higher plants, the role of lectins in fungi seems to be more complicated [11]. For instance, in higher fungi (mushrooms), lectins play different roles in different situations such as in fungal metabolism, symbiotic or parasitic relationships with other organisms etc. [12]. Mushroom lectins may also play other crucial roles in physiological processes such as dormancy, growth, morphogenesis, morphological changes and molecular recognition during the early stages of mycorrhization [12]. So far many mushroom lectins have been reported, and in the last few years they have attracted increased attention due to their exploitable properties with a wide range of biological activities such as antiproliferative activity toward tumor cells, antitumor activity against tumors, hypotensive activity, immunomodulatory activities and inhibitory activity toward HIV-1 reverse transcriptase, mitogenic activity toward spleen cells etc.[11,13-16]. The scientific community has growing interest on these lectins due to their potential importance in cancer research. Lectins from edible mushrooms such as those of *Agaricus bisporus, Boletus satanus, Flammulina velutipes, Ganoderma lucidum, Grifola frondosa, Tricholoma mongolicum, and Volvariella volvacea* have been reported to have immunomodulatory and/or antitumor/cytotoxic/antiproliferative activities [17, 18].

Banana is the common name for both herbaceous plants of the genus Musa and for the fruit they produce. Banana Lectins (BanLec) are reported to have the potential for inhibiting HIV-1 reverse transcriptase activity, suppressing cancer cell proliferation and stimulating macrophage activities [1]. Galectins are also a phylogenetically conserved family of lectins sharing about 130 consensus amino acid residues and having the Carbohydrate Recognition Domain (CRD) responsible for β-galactoside binding [19]. Galectins play important roles in diverse physiological and pathological processes and can be important therapeutic agents for targeting many human disease conditions including inflammatory diseases, cancers etc. [20, 21]. Initially, biological researchers paid less attention to these animal lectins (galectins) compared to their plant counterparts. Kasai and Hirabayashi commented in their article that underestimation of galectins was a great mistake [22]. Nowadays, it has become a prerogative for galectins to be a biomarker for many diseases in which their expression is abnormal and as such these molecules could be the best target for development of therapeutics.

Lectins also play role in host defense against pathogens and predators by having insecticidal properties [5, 23]. This insecticidal property might be due to disruption or changes of enzymatic activity at the intestinal microvilli and induced abnormalities in the epithelial cells of insect larvae [24]. So lectins have been considered as one of the potent agents against insect pests and used in integrated pest management strategies. Lectin genes have been successfully introduced into a variety of transgenic crops like wheat, rice, tobacco, and potatoes, turning them into transgenic insecticidal and herbicide-tolerant plants. Such plants are environmentally friendly and rather improve the environment and human health because their production reduces the use of chemical insecticides and herbicides [3, 25, 26]. Some examples of lectins with insecticidal activities are lectins from *Allium sativum* (garlic) bulbs, *Arisaema intermedium, Gracilaria cornea*, etc. affecting insects like *Acyrthosiphon pisum, Bactrocera cucurbitae, Boophilus microplus* respectively. Effects of lectins on the insects may include increase in mortality, prolonged period of development, reduced body weight of female after oviposition etc. [3].

Pathogens usually utilize host cell surface glycans as either receptors or ligands to initiate adhesion and pathogenesis [27]. For example, *E. coli* interacts with host mannosides, while influenza virus binds to host sialic acids [28]. It is also quite interesting that bacteria can discriminate between two similar glycans in the host that differ only in one hydroxyl group [29]. Such host-pathogen interactions are solely dependent on lectins associated with either one of the interacting organisms, probably in the form of receptors or ligands [5].

Regarding antifungal activities of lectins, many researchers believe that despite the existence of literature of a considerable volume, only a few of the lectins manifested antifungal activity. Having said that pioneering works have been

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done in this field and some antifungal lectins are being tested by insertion of the precursor gene of stinging nettle isolectin-I into tobacco, which makes the plant resistant to infections brought about by some fungal species like *Botrytis cinerea, and Colletotrichum lindemuthianum* [30]. Thus, lectins can be the potential agents and their genes be introduced into plants and protect the transgenic plants expressing the lectin genes from fungal attack.

Lectins also have potential applications in other fields of research such as those for the detection, localization, and isolation of glycoconjugates [2]. In cancer research, many lectins are being used as therapeutic agents. Lectins interact with cancer cell membranes or their receptors, causing cytotoxicity, apoptosis, and inhibition of tumor growth. Lectins can affect the immune system by modulating the production of various interleukins, as well as by activating certain protein kinases. They can bind to cytoplasmic ribosomes and inhibit protein synthesis and thus act as Ribosome Inactivating Proteins (RIP). Lectins also modify the cell cycle, down regulate telomerase activity and inhibit angiogenesis [31]. Lectin from *Sophora FLavescens* (SFL) was demonstrated to have an anti-tumor activity against HeLa cells [32, 33]. Chinese mistletoe lectin possesses potent immunomodulatory activity as well as anti-tumor activity, [34, 35]. Similarly, *Momordica charantia* lectin was reported for the first time as having potential type II RIP activity [36].

Recently, Hu et al., [37] made comments about the drawback on using lectins as reagents for the structural characterization of glycans, especially those for sulfated glycans. This is another important area for modern lectin research. In the article they proposed for engineering lectins with novel specificity by directed evolution strategy to tailor the lectins and described a successful case screening of a lectin able to recognize a sulfated glycan. Advances in therapeutic glycopeptides are also an emerging area in biosciences which is all related to lectins. Here glycopeptides (peptides containing sugar β-amino acids) have influenced a lot in the field of chemistry research and pharmaceutical industry. Nowadays many chemotherapeutic, antiviral, antitubercular, antifungal, antiproliferative and apoptotic agents even vaccines are designed based on such glycopeptides [38]. And here we can emphasize the importance of the glycans in glycopeptides with the help of lectins.

In conclusion, this article aims to highlight the importance of lectin research in various fields of biology. As we now know, lectins are continuously isolated and investigated for their physical as well as biological properties, it is expected that the potential biomedical applications of this multifaceted molecule would be immense. However, we still feel the necessity that it is high time to coordinate among the scientific community in this field and to contribute towards the area of lectin biology covering state-of-the-art research papers and expert reviews.

Conflict of interest: The authors declare that there is no conflict of interest.

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