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An overview of lectins from freshwater and marine macroinvertebrates

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ABSTRACT

Lectins are one of several types of biological resources considered as potential medicinal importance for therapeutic agents. The present review deals with variety, sugar specificity and the medicinal importance of lectins from freshwater and marine invertebrates. The potent medicinal usage of the various types of the lectins from freshwater and marine non-chordates, which are comparatively well studied and compiled. Various literatures survey revealed that the lectin isolated in recent past from the freshwater species majorly from mollusca and arthropods (crustacean) etc. and also from marine sources of phylum porifera, cnidaria, annelida, arthropoda, mollusca and echinodermata could be rich sources of medicinal properties having remedial measures to bacterial infection, inflammatory disorders, cancer, mitogenic effect and antigen defence. The present study will be a database development to support global drug discovery researches on several types of lectins from freshwater and marine organisms for academicians, researchers and medicine manufacturers having therapeutic approaches for mankind by natural ingredients.

***Keywords*:** Bioresources, freshwater species; marine invertebrates; medicinal importance; drug development; natural therapeutic agents

1. INTRODUCTION

The biological resources as potent chemicals are prevalent in several macroinvertebrates of freshwater and marine origin (Aneiros and Garateix, 2004; Datta et al., 2015). Among these biological resources are viz. manzamines, halichondrin B, nakafuran-8 and -9, steroidal alkaloids such as plakinamine A and plakinamine B, saponins and sterol derivatives, etc. Lectins or agglutinins are known as protein or glycoprotein, which have a binding capacity onto carbohydrates expressed in different cell surfaces without catalytic activity. Lectins have tendency to bind to cells and drastic agglutination reaction. According to Marques and Barracco (2000), it was reported that characterization of lectin corresponded to agglutinins that have capacity to make reaction selectively on a specific sugar group. It was established by several researchers that different types of lectins namely limulin and carcinoscorpin, N-glycolyl neuroaminic acid-specific lectin (PAL), galactose-specific lectin, lipopolysaccharide-binding lectin, C-type lectin etc. have potent therapeutic properties and obtained from freshwater and marine biota (Barondes, 1988; Yoshizaki, 1990; Muramoto and Kamiya, 1990; Swarnakar et al., 1991; Moura et al., 2006; Chernikov et al., 2013; Denis et al., 2015). Vasta and Ahmed (2009) have also described different types of animal lectins.

The compilation of available literatures and study one of specific biological resource like lectin from freshwater and marine invertebrates and their medicinal importance are as follows:

2. LECTIN AVAILABILITY FROM FRESHWATER INVERTEBRATES

It has been documented that freshwater invertebrates have lectins in their haemolymph. There are several reports on presence of lectins and the use of endogenous and exogenous lectins in various biota (Table 1). Lectins of freshwater invertebrates and disease prevention ability, are of particular interest in the present study (Table 2). The compilation of available research works were tabulated.

Swarnakar et al., (1991) isolated N-glycolylneuroaminic acid (neuAc) specific lectin in freshwater gastropod, *Pila globosa* (apple snail) and this lectin is termed as PAL, a calcium dependent lectin.

It was reported by Vasta (1992) that a lectin isolated from the freshwater prawn *Macrobrachium rosenbergii* (crustacea: decapoda) recognizes the carbohydrates of N- and O-acetylated groups as specificity.

Denis et al. (2003) have documented that freshwater crab, *Paratelphusa jacquemontii* has potent lectin (PjLec) isolated, which is sialic acid binding in nature. In this species, the pure lectin was showed inhibition by *N*-acetylneuraminic acid whereas not by *N*-glycolylneuraminic acid.

Banerjee et al. (2004), have analysed a monomeric protein (lectin) from freshwater gastropod, *Belamyia bengalensis*. According to them, this lectin is C-type and known as BBL (Belamyia Bengalensis Lectin). The sugar specificity of BBL was found only for N-acetyl-D-glucosamine and N-acetyl-D-galactosamine when the specific lectin was found in higher concentration. It was reported that BBL has activity depends on Ca^{2+}.

According to Yang et al. (2007), it was reported that a naturally occurring lectin (namely PjLec) was isolated from haemolymph of the freshwater shrimp *Penaeus japonicas*.

This lectin was found calcium-independent and was showed inhibition by ManNAc, Neu5A and lipopolysaccharide.

Denis et al., (2015) have investigated a humoral lectin, namely Pjlec (Paratelphusa Jacquemontii Lectin) from the freshwater crab, *Paratelphusa jacquemontii* and this lectin has capacity to bind the sialic acid.

Table 1. Lectins from different biological sources.

Sl. No.	Macroinvertebrate species	Types of lectins	Sugar specificity	References
Freshwater				
1.	*Pila globosa*	Lectin (PAL)	N-glycolylneuroaminic acid (neuAc)	Swarnakar et al., 1991
2.	*Macrobrachium rosenbergii*	Lectin	N- and O-acetylated groups	Vasta, 1992; Vazquez et al., 1997
3.	*Paratelphusa jacquemontii*	Lectin	Sialic acid	Denis et al., 2003; 2015
4.	*Belamyia bengalensis*	Mucin (BBL)	*N*-acetyl-D-glucosamine and *N*-acetyl-D-galactosamine	Banerjee et al., 2004
5.	*Penaeus japonicus*	Calcium-independent lectin (PjLec)	ManNAc, Neu5A and lipopolysaccharide	Yang et al., 2007
Marine				
1.	*Tridacna maxima*	C-type (tridacin)	N-acetyl galactosamine	Baldo et al., 1978
2.	*Carcinoscorpius rotunda cauda*	Carcinoscorpin	sialic acid	Dorai et al., 1982
3.	*Balanus rostratus*	C-type (BRL)	D-galactose	Muramoto and Kamiya, 1986
4.	*Cinachyrella alloclada*	C-Lectin	galactose	Atta et al., 1989
5.	Crassostrea *virginica*	C-Lectin (CvML)	mannose	Vasta et al., 1984; Vasta et al., 1994; Jing et al., 2011
6.	*Pellina semitubulosa*	C-Lectin	D-galactose and L-arabinose	Engel et al., 1992
7.	*Axinella polypoides*	AP-I/II/III/V AP-IV	D-galactose hexuronic acid	Buck et al., 1992
8.	*Scylla serrata*	SAL	*N*-glycolylneuraminic acid (NeuGc)	Mercy and Ravindranath, 1993

9.	*Mytilus edulis*	C-Lectin	mannose	Vasta et al., 1994
10.	*Stichopus japonicus*	C-type (SPL-1); (SPL-2); (SJL-1)	uronic acid; LacNAc and others; D-galactose	Matsui et al., 1994; Himeshima et al., 1994
11.	*Limulus polyphemus*	Limulin	sialic acid	Amstrong et al., 1996
12.	*Geodia cydonium*	GCLT1	LacNAc	Wagner-Hulsmann et al., 1996
13.	*Scylla serrata*	B-Lectin (Bovine submaxillary mucin)	sialoglycoconjugates	Kongtawelert, 1998
14.	*Haliotis laevigata*	C-type (PLC)	D-galactose/D-mannose/D-glucose	Weiss et al., 2000
15.	*Aphrocallistes vastus*	C-type (LECCI)	D-galactose	Gundacker et al., 2001
16.	*Haliclona cratera*	C-Lectin	D-galactose and N-acetyl-D-galactosamine	Pajic et al., 2002
17.	*Megabalanus rosa*	C-type (BRA-1 and 2)	D-galactose	Kamiya et al., 2002
18.	*Ruditapes philippinarum*	MCL (Manila clam lectin)	N-acetyl-D-galactosamine	Bulgakov et al., 2004
19.	*Litopenaeus setiferus*	Lectin (LsL)	N-acetylated sugars (GlcNAc, GalNAc and NeuAc)	Alpuche et al., 2005
20.	*Liocarcinus depurator*	Lectin	sialic acid and O-acetyl-sialic residues	Alpuche et al., 2005
21.	*Cliona varians*	Lectin (CVL-1)	galactose	Moura et al., 2006
22.	*Pteria penguin*	PPL (Pteria Penguin Lectin)	D-galactose; D-galactose, methyl-D galactopyranoside and N-acetyl-D-lactosamine	Naganuma et al., 2006
23.	*Cucumaria echinata*	C-Lectin (CEL III)	GlcNAc (Ca+)	Yoshida et al. 2007
24.	*Aplysia kurodai*	Lectin (AKL)	D-galactose, N-acetyl-D-galactosamine and N-acetyl-D glucosamine	Kawsar et al., 2010a
25.	*Perineries nuntia*	Lectin	D-galactose, N-acetyl-D-galactosamine and N-acetyl-D glucosamine	Kawsar et al., 2010b
26.	*Holothurea grisea*	HGA	mucin O-glycan	Moura et al., 2012

27.	*Cucumaria echinata*	C-type (CEL-I/CEL-II); (CEL-IV) Ricin-type (CEL-III)	GlcNAc; GlcNAc-Galactose D-galactose and others	Hatakeyama et al., 1994; 1995a; b; 2002

Table 2. Important lectins as therapeutic agents.

Sl. No.	Types of lectins	Therapeutic usage	References
1.	PAL	Specific H-D antigen diagnosis	Swarnakar et al., 1991
2.	C-type: SPL-I & II, SGL-I	Haemagglutination	Matsui et al., 1994
3.	Limulin	Antimicrobial and defence mechanisms	Amstrong et al., 1996
4.	B-lectin (BSM)	Carcinoembryonic antigen	Kongtawelert, (1998)
5.	LECCI	Anti-tumour	Gundacker et al., 2001
6.	C-type lectin	Cytotoxic on HeLa and FemX cells	Pajic et al., 2002
7.	BRA-1 & 2	Defence mechanism	Kamiya et al., 2002
8.	MCL	Anti-protozoan	Bulgakov et al., 2004
9.	LsL	Haemagglutination	Alpuche et al., 2005
9.	CvL	Antibacterial	Moura et al., 2006
10.	PPL	Haemagglutinating activity in presence of salts	Naganuma et al., 2006
11.	Calcium-independent lectin (PjLec)	Antibacterial	Yang et al., 2007
12.	CEL-III	Anti-malarial (Plasmodium falciparum)	Yoshida et al. 2007
13.	AKL & PnL	Antibacterial and Antifungal and also anticancer	Kawsar et al., 2009a; Kawsar et al., 2009b; Kawsar et al., 2010a; Kawsar et al., 2010b
14.	AKL	Antibacterial (only gram positive) and antifungal	Kawsar et al., 2010a
15.	HGA	Anti-inflammatory, antinociceptive and antitumour	Moura et al., 2012
16.	PjLec	Innate immune system (Opsonin)	Denis et al., 2015

3. LECTIN AVAILABILITY FROM MARINE INVERTEBRATES

It was established that marine biota have relatively new sources of lectins. There are several studies on the physiological role of these bioactive compounds as well as functions with the use of endogenous and exogenous lectins in various saltwater living systems. Lectins of marine invertebrates are of particular interest in the present study (Table 1). It was reported that lectins have been found in more than 300 species as per their carbohydrate specificity and molecular structures. The disease prevention ability was also recorded for species-specific in Table 2.

Baldo et al. (1978) have studied β-galactosyl-binding lectin (C-type) from the haemolymph of the clam, *Tridacna maxima*. According to them, tridacnin as a lectin that precipitated with several galactans, and the lectin has been documented as having anti-galactan specificity but N-acetyl galactosamine specificity.

Dorai et al. (1982) have described about the lectin from the Indian horseshoe crab *Carcinoscorpius rotunda cauda* (chelicerata: xiphosura) have potent multispecificity of carcinoscorpin, which was reported the sialic acid binding lectin by researchers. Vasta et al. (1984) have studied on two marine bivalve, *Mytilus edulis* and Eastern oyster, *Crassostrea virginica* that both the species have serum lectin (C-type) and have sugar specificity with mannose.

Muramoto and Kamiya (1986) have identified lectin (C-type) called as BRL (Balanus Rostratus Lectin) of *Balanus rostratus*, which is a similar lectin obtained from the coelomic fluid of the acorn barnacle *Megabalanus rosa* and sugar specificity is D-galactose.

Atta et al. (1989) have isolated lectin (C-type) from the marine sponge, *Cinachyrella alloclada*, which has D-galactose-specific binding.

Engel et al. (1992) have reported lectin (C-type) from the marine sponge, *Pellina semitubulosa*. The lectin has showed specificities on D-galactose and L-arabinose. In another research work, it was found that the marine sponge *Axinella polypoides* contained four types lectins (AP I, II, III and V) have D-galactose binding specificity while other type lectin called as lectin (AP IV), which has binding specificity for hexuronic acids (Buck et al., 1992).

Mercy and Ravindranath, (1993) have investigated lectin from the hemolymph of the marine crab *Scylla serrata*, called as sialic-acid-binding lectin (SAL) and has sugar specificity with *N*-glycolylneuraminic acid (NeuGc).

The invertebrate taxa, such as oysters (*Creassostrea virginica*) and mussel (*Mytilus edulis*) belonging to phylum mollusca, class bivalvia showed specificity for GlcNAc (Vasta et al., 1994). Matsui et al. (1994) have identified two structurally distinct C-type lectins (SPL-I and II) from holothurian *Stichopus japonicus* and these lectins have been purified from the coelomic plasma. SPL- I, II and others have uronic acid such as galacturonic acid and glucuronic acid, LacNAc, GalNAc and galactosides. In other investigation with sea cucumber, *Stichopus japonicus*, the C-type lectin called as SGL-1 has showed specificity with D-galactose (Himeshima et al., 1994). In other marine invertebrate species, *Cucumaria echinata*, the C-type lectins and also Ca^{2+} - dependent such as CEL-I, CEL-II and Cell-IV have sugar specificity with GlcNAc; GlcNAc-Galactose while other type of lectin called as ricin type (Cel-III) has sugar specificity with D-galactose and others (Hatakeyama et al., 1994).

Amstrong et al. (1996) have documented the lectin in plasma from American horseshoe crab, *Limulus Polyphemus* and this type of lectin is termed limulin, which has sugar specificity with sialic acid. In other marine sponge, *Geodia cydonium* was found lectin groups

of galectins, called as GCLT1 and the sugar specificity was obtained with LacNAc (N-acetyl-D-lactosamine) (Wagner-Hulsmann et al., 1996).

Lectins identified in other decapod crustaceans, such as in the prawn *Macrobrachium rosenbergii*, crabs viz. *Cancer antennarius* and *Liocarcinus depurator*, showed specificity for sialic acid and O-acetyl-sialic residues (Vazquez et al., 1997; 1998). Kongtawelert, (1998) has reported a B-type lectin (bovine submaxillary mucin) from Thai marine carb, *Scylla serrata*. The lectin was isolated from hemolymph and sugar specificity was known sialoglycoconjugates.

Weiss et al. (2000) have isolated a C-type lectin called perlucin from smooth Australian abalone, *Haliotis laevigata*, which has D-galactose or D-mannose or D-glucose specificity. Gundacker et al. (2001) have reported that cloud sponge, *Aphrocallistes vastus* has C-type lectin (LECCI), which has D-galactose specificity.

Pajic et al. (2002) have isolated a C-type lectin from the Adriatic sponge, *Haliclona cratera* and found independent of Ca^{2+}, Mn^{2+} and Mg^{2+} ions and D-galactose and N-acetyl-D-galactosamine specificity.

Muramoto and Kamiya, 1990 and Kamiya et al. (2002) have studied on BRA-2 and BRA-3, both are major C-type lectin found in the haemolymph and shell of the acorn barnacle *Megabalanus rosa* and sugar specificity of these lectins are D-galactose.

Bulgakov et al. (2004) have studied a lectin isolated from the marine bivalve *Ruditapes philippinarum*, commonly called Manila clam. They have mentioned the name of lectin is Manila Clam Lectin (MCL), which is Ca^{2+} -dependent and sugar specificity was found with N-acetyl-D-galactosamine. According to

Alpuche et al. (2005) have isolated a lectin namely Litopenaeus setiferus Lectin (LsL) in the hemolymph of white shrimp *Litopenaeus setiferus*. The specificity was obtained on N-acetylated sugars viz. GlcNAc (N-acetylglucosamine), GalNAc (N-acetylgalactosamine) and NeuAc (neuraminic acid or sialic acid) while in harbour crab, *Liocarcinus depurator* the lectin and sugar specificity was found with sialic acid and O-acetyl-sialic residues.

According to Moura et al. (2006), it was investigated that the lectin, termed as CvL, obtained from the marine sponge *Cliona varians* and their lectin showed strong inhibition on two types of carbohydrates viz. monosaccharide D-galactose and disaccharide sucrose. It was reported that the lectin was Ca2+ dependent. Naganuma et al. (2006) have isolated a novel lectin namely PPL (Pteria Penguin Lectin), from the mantle of penguin wing oyster (*Pteria penguin*) and showed sugar specificity with D-galactose, methyl-D-galactopyranoside and N-acetyl-D-lactosamine.

Yoshida et al. (2007) have investigated C-type lectin (CEL-III) from the sea cucumber, *Cucumaria echinata* and documented GlcNAc (N-acetylglucosamine) specificity with Ca^{2+} -dependency to this particular lectin.

Kawsar et al. (2010a) have isolated a C-type lectin, namely AKL (Aplysia Kurodai Lectin) from the eggs of sea hare, *Aplysia kurodai* and it showed D-galactose specific binding lectin while in other research work with two species viz. sea hare *Aplysia kurodai* eggs and polychaete *Perineries nuntia*, it was isolated two specific lectins (AKL and PnL) from above-mentioned marine biota, which showed D-galactose-binding specificity (Kawsar et al., 2010b).

Moura et al. (2012) have documented that the lectin, namely Holothuria Grisea Agglutinin (HGA) is a dimeric lectin, isolated from the species of echinoderm, gray sea cucumber, *Holothuria Grisea* and the sugar specificity was found with mucin O-glycan.

4. THERAPEUTIC EFFICACIES ON SEVERAL DISEASES

In Table 2, several important lectins type and their medicinal importance with special reference to antimicrobial, defensive, antiinflammatory, antinociceptive and anticancer properties are tabulated from recent literatures.

According to Swarnakar et al., (1991), PAL (Pila N-glycolylneuroaminic acid-specific lectin) can be used as tool for H-D antigen diagnosis. CvL displays a cytotoxic effect on gram positive bacteria, such as *Bacillus subtilis* and *Staphylococcus aureus*.

Kamiya et al. (2002) have reported that lectins (BRA-1 and 2) is effective in defence mechanism. According to

Alpuche et al. (2005), LsL was showed haemagglutination activity. However, CvL did not affect gram negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) but it was reported that different morphological stages of the protozoan parasite *Leishmania chagasi* found agglutination by CvL.

These above findings are indicative of the physiological defence roles of CvL and its possible use in the antibiotic for bacteria and protozoa pathogenicity (Moura et al., 2006).

Yang et al. (2007) have suggested that PjLec may be an important humoral defence factor against bacterial infection showed as antibacterial activity.

The lectins namely AKL and PnL have antibacterial, antifungal and also anticancer properties (Kawsar et al., 2009a; Kawsar et al., 2009b; Kawsar et al., 2010a; Kawsar et al., 2010b) and HGA has been reported an antiinflammatory effect, antinociceptive activity and can be used as antitumour agent (Moura et al., 2012).

Denis et al., (2015) have documented that PjLec has opsonin function in the erythrocytes of rabbit by haemocytes of the crab.

5. CONCLUSION

It is concluded that lectins are very important protein present in haemolymph, mantle, shell and other body parts of different freshwater and marine invertebrate species and these lectins may be suitable components for drug development due to potent therapeutic efficacies (Kongtawelert, 1998; Denis et al., 2015). Herein, it was observed that major sources of lectins are from marine biota compared to freshwater invertebrates. This review is compiled from available literatures with special reference to diversity of important lectins and medicinal usage as ready references for the academicians, researchers, pharmaceutical manufacturers etc.

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