TPM Vol. 32, No. S5, 2025
ISSN: 1972-6325
https://www.tpmap.org/

Open Access

APPLICATIONS OF FISH LECTINS AS A POTENTIAL ANTI-CANCER THERAPEUTIC AGENT

N. VISHWANATHAN[1], AKSHAYA VISWANATHAN[2], S.VIMAL[3]
[1]DEPARTMENT OF PATHOLOGY, SAVEETHA MEDICAL COLLEGE & HOSPITAL, THANDALAM, KANCHIPURAM-602105, TAMIL NADU, INDIA.
[2]DEPARTMENT OF PATHOLOGY, SAVEETHA MEDICAL COLLEGE & HOSPITAL, THANDALAM, KANCHIPURAM-602105, TAMIL NADU, INDIA.
[3]DEPARTMENT OF BIOCHEMISTRY, SAVEETHA MEDICAL COLLEGE & HOSPITAL, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES (SIMATS), THANDALAM, CHENNAI - 602105, TAMIL NADU, INDIA.

Abstract
Cancer remains one of the most formidable health challenges worldwide, necessitating the discovery of novel therapeutic agents with high specificity and minimal side effects. Fish-derived lectins, a diverse group of pattern recognition molecules, have emerged as promising candidates owing to their unique carbohydrate-binding specificity and ability to modulate tumor progression. These lectins, including C-type lectins, galectins, rhamnose-binding lectins, and others, exhibit anticancer activity through mechanisms such as apoptosis induction, autophagy, inhibition of angiogenesis, and suppression of metastasis. Several studies have demonstrated their effectiveness against a wide range of cancer cell lines, including breast, liver, ovarian, and lung cancers, with potential applications in both diagnosis and therapy. Furthermore, the synergistic effect of fish lectins when conjugated with other compounds enhances their therapeutic potential, positioning them as innovative tools in oncology. However, despite compelling preclinical evidence, further mechanistic insights and translational studies are needed to fully realize their role in clinical applications.
Keywords: Fish lectins; Apoptosis; Angiogenesis inhibition; Cancer therapeutics; Galectins;; Diagnostic biomarker; Oncological applications

INTRODUCTION

Cancer is the second-deadliest and most dreaded disease leading to death universally, and fighting it is a necessity for humanity. Several studies have been conducted all around the globe over decades, and numerous natural metabolites and molecules have been discovered to be capable of fighting this nagging disease. Of these, the impressive anti-tumour activity of pattern recognition molecules has attracted the attention of researchers across the world and remains a hot cake topic among them. Lectins are an important group of pattern recognition molecules that bind to the carbohydrate moieties present on the cell surfaces and have been reported widely to possess anti-cancer activity.

Anti-Cancer Activity of Fish Lectins

Lectins are ubiquitous in all living organisms [1, 2, 3], and fish lectins with a wide spectrum of anti-cancer activity have been derived from various tissues and organs of a variety of fish and shell fishes [3, 4, 5, 6, 7, 8]. They differ in their molecular weight, glycosylation, sugar binding specificity, amino acid sequences, and number of subunits, and in their biological characteristics like anticancer, antimicrobial, immune regulatory, and developmental functions [3, 7, 8], and are able to induce the mechanisms of apoptosis and autophagy, inhibiting angiogenesis [9, 10]. Fish lectins are structurally and functionally classified as C-type lectins, Galectins, Rhamnose-binding lectins, lily type, tectonin type, collectins, selectins, etc [3,8] and are non-immunogenic glycoproteins, specifically binding to the carbohydrate molecules present on the surface of cancer cells, acts as surface markers for cell adhesion, cytotoxicity, and initiate the recognition of tumor cells and apoptosis or cell death pathways and also inhibit the growth and proliferation of cancer cells [11,12] and hence are used for diagnosis and treatment tool for cancer [13] (Fig.1).

Galectins are able to bind glycoconjugates of intravasation of tumor cells into blood cells and the extracellular matrix and favor the process of metastasis [14] and further, various Carcinomas like, colon, breast and thyroid tumors, express two types of Galectins 1 & 3 , has been recommended and emphasized the application of Galectin-3 as a metastasis marker [15]. It has been reported that the action of oncogenes on -1, 6-N-Acetyl Glucosamine branched with N-Glycans is involved in the early stages of carcinogenesis [16].Rhamnose-binding lectin isolated from Chinook Salmon Roe, C-type lectins from Etroplus suratensis exhibited cytotoxicity against human breast cancer MCF-7 and Hematoma HepG2 cells [17, 6]. Similarly, Gb3 specific lectin from Catfish egg which binds specifically to globotriose, was reported to bind to the surfaces of Burkitts Lymphoma cells and initiate cell size reduction [18]. GANL is another homomultimeric glycoprotein from Big head Carp, which cause tumor-

dependent cell death, and these lectins are involved in the proliferation of HeLa cells, HepG2 cells and Ovarian cancer cells (SKOV3) [19]. Furthermore, Galactosidase-binding Lectins-3 (Gb3) isolated from Chum Salmon Egg (CSEL) and Catfish Silurus asutus (SAL) have antitumor activity as well as the ability to induce apoptosis and cell shrinkage [20].Anguilla japonica Lectin-1 (AJL-1) and Dicentrarchus labrax Fucose binding Lectin-1 (DIFBL-1) was reported to have activity against some of the lung cancer and liver cancer cell lines [21]. Fish lectins are effectively used as diagnostic tool and for prognosis of cancer in animal and human kidney tissues and to identify prostate cancerous cells from benign hyperplasia [22,23]. Interestingly, the functional activity of these fish lectins can be enhanced by conjugating it with other compounds and this synergistic activity has improved its application as a therapeutic agent [24,25,26].

In a nutshell, Fish lectins are a repertoire of pattern recognition molecules that are yet to be explored to reveal the mechanism behind their role in anticancer activity, programmed cell death, apoptosis, inhibition of neo-angiogenesis, and the cell cycle. Further, these molecules alone and in combination with other molecules can be applied to improve the efficiency of antitumor drugs, and their peculiar characteristics like, selectivity and cytotoxicity, make fish lectins as an ideal anticancer therapeutic agents. However, though several fish lectins are reported to have antitumor activities against various cancers, their role in oncology is yet to be explored, and hence the research addressing this knowledge gap is to be supported and further investigations in this regard should be encouraged.

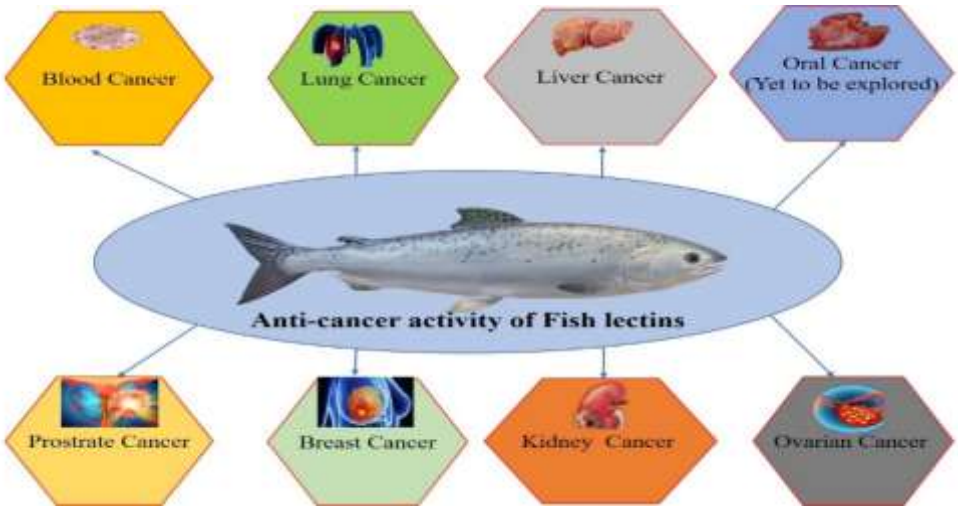

Fig. 1. Applications of Fish lectins against various cancers.

Lectin Type/Name	Source (Fish/Organ)	Cancer Cell Line/Target	Reported Activity/Mechanism	Reference
Galectin-1 & 3	Colon, breast, thyroid tumor tissues	Tumor metastasis marker	Promotes or regulates metastasis; Galectin-3 used as biomarker	[14,15]
Rhamnose-binding lectin	*Chinook Salmon* roe	Breast cancer (MCF-7), Liver cancer (HepG2)	Cytotoxicity; induces apoptosis	[6,17]
C-type lectin	*Etroplus suratensis*	Breast cancer (MCF-7), HepG2	Cytotoxicity and growth inhibition	[6,17]
Gb3-specific lectin	Catfish egg	Burkitt's Lymphoma cells	Binds globotriose; induces cell shrinkage and apoptosis	[18]
GANL (homomultimeric glycoprotein)	Bighead Carp	HeLa, HepG2, Ovarian cancer (SKOV3)	Tumor-dependent cell death	[19]
Galactosidase-binding lectins (Gb3, CSEL, SAL)	Chum Salmon egg, *Silurus asutus*	Multiple cancer cell lines	Antitumor activity, apoptosis, cell shrinkage	[20]

AJL-1 (Anguilla japonica lectin-1)	*Anguilla japonica*	Lung cancer, liver cancer	Apoptosis and cytotoxicity	[21]
DIFBL-1 (Fucose-binding lectin)	*Dicentrarchus labrax*	Lung cancer, liver cancer	Growth inhibition and apoptosis	[21]
Fish lectins (general)	Kidney, prostate tissues (diagnostic use)	Prostate and kidney cancers	Diagnostic biomarker for distinguishing malignant vs. benign tissues	[22,23]
Conjugated lectins	Modified/engineered forms	Broad-spectrum cancer types	Enhanced therapeutic effect via synergistic activity	[24–26]

Table 1. summarizes various fish-derived lectins, their sources, targeted cancer cell lines, and mechanisms of anticancer action. These lectins exhibit apoptosis induction, cytotoxicity, and diagnostic potential, highlighting their therapeutic value in oncology.

REFERENCES

[1]. Rubeena A.S, Abigith Abraham, K M Aarif. Microbial Lectins. In Elumalai Preetham, Sreeja Lakshmi (Eds.). *Lectins: Innate Immune defense and Therapeutics*. 2021; 131-145. Springer Publishers, Singapore. https://doi.org/10.1007/978-981-16-7462-4_7

[2]. Abigith Abraham, Rafeeq C M, Resiya Karim, K A Rubeena. Aquatic Lectins- A Paradigm. In Elumalai Preetham, Sreeja Lakshmi (Eds.). *Aquatic Lectins* 2022; 3-21. Springer Publishers, Singapore. DOI: 10.1007/978-981-19-0432-5_1

[3]. Preetham Elumalai, Abdul Salam Rubeena, Ratree Wongpanya, Matteo Cammarata, Einar Ringo, Baskaralingam Vaseeharan. The Role of Lectins in Finfish: A review. Reviews in Fisheries Science and Aquaculture 2019; 27, 152-169. https://doi.org/10.1080/23308249.2018.1520191

[4]. Elumalai Preetham, Abdul Salam Rubeena, Baskaralingam Vaseeharan, Mukesh Kumar Chaurasia, Jesu Arockiaraj, Rolf Erik Olsen. Anti-biofilm properties and immunologicalresponse of an immune molecule lectin isolated from shrimp *Metapenaeus monoceros*. Fish and Shell fish Immunology 2019; 94, 896-906. https://doi.org/10.1016/j.fsi.2019.09.032.

[5]. Rubeena A.S and Elumalai Preetham. Antimicrobial properties and phenoloxidase activation of the lectin isolated from kadal shrimp (*Metapenaeus dobsoni*). Fish and Shell fish Immunology 2019; 90, 118-125. DOI: https://doi.org/10.1016/j.fsi.2019.04.305.

[6]. Rubeena A.S, Mani Divya, Baskaralingam Vaseeharan, Sivashanmugam Karthikeyan, Einar Ringø, Elumalai Preetham. Antimicrobial and biochemicalcharacterization of a C-type lectin isolated from pearl spot (*Etroplus suratensis*). Fish and Shell fish Immunology 2019; 87, 202-211. https://doi.org/10.1016/j.fsi.2018.12.070

[7]. Nisha P, Neelima TK, Manuel Thomas, Role of Lectin in Biofilm Inhibition, Haemagglutination, Endocytosis and Phagocytosis. In Elumalai Preetham, Sreeja Lakshmi (Eds.). *Aquatic Lectins*, Springer Publishers, Singapore 2022;13. 287.

[8]. Bun, Ng T, Chi Fai Cheung R, Cheuk Wing Ng C, Fei Fang E, Ho Wong J. A review of Fish Lectins. Curr Protein Pept Sci . 2015;16(4):337–351.

[9]. Dan X, Wenlong L, Ng T. Development and applications of lectins as biological tools in biomedical research. Med Res Rev. 2015; 36. https://doi.org/10.1002/med.21363.

[10]. Brinchmann MF, Patel DM, Pinto N, Iversen MH. Functional aspects of fifish mucosal lectins—interaction with non-Self. Molecules. 2018; 23(5):1119. https://doi.org/10.3390/ molecules23051119

[11]. Catanzaro E, Cinzia Calcabrini, Anupam Bishayee, Carmela Fimognari. Antitumor Potential of Marine and Freshwater Lectins. Mar Drugs. 2020; 18(1): 11.

[12]. Zarogoulidis P, Tsakiridis K., Karapantzou C, Lampaki S, Kioumis I, Pitsiou G, Papaiwannou A, HohenforstSchmidt W, Huang H, Kesisis G, Karapantzos I, Chlapoutakis S , Korantzis I, Mpakas A , Karavasilis V, Mpoukovinas I , Li Q, Zarogoulidis K. Use of proteins as biomarkers and their role in carcinogenesis. J. Cancer.2015; 6: 9–18.

[13]. Ghazarian H, Idoni B, Oppenheimer SB. A glycobiology review: carbohydrates, lectins and implications in cancer therapeutics. Acta Histochem. 2011; 113(3): 236–247.

[14]. Fortuna-Costa A, Gomes AM, Kozlowski EO, Stelling MP, Pavao MSG. Extracellular Galectin-3 in tumor progression and metastasis. Front. Oncol.2014; 4: 138

[15]. Fujii Y, Dohmae N, Takio K, Kawsar SMA, Matsumoto R, Hasan I, Koide Y, Kanaly R.A, Yasumitsu H, Ogawa Y, et al. A lectin from the mussel Mytilus galloprovincialis has a highly novel primary structure and induces glycan-mediated cytotoxicity of globotriaosylceramide-expressing lymphoma cells. J. Biol. Chem. 2012; 287: 44772–44783. doi: 10.1074/jbc.M112.418012.

[16]. Dennis J, Kosh WK, Bryce DM, Breitman ML. Oncogenes conferring metastatic potential induce

increased branching of Asn linked oligosaccharides in rat fibroblasts. Oncogene.1989; 4: 853–860.
[17]. Bah C S F, Fang E F, Ng T B, Mros S, McConnell M, Bekhit AEDA. Purification and characterization of a rhamnose-binding Chinook salmon roe lectin with anti-proliferative activity toward tumor cells and nitric oxide-inducing activity toward murine macrophages. J. Agric. Food Chem.2011;59: 5720–5728
[18]. Sugawara S, Im C, Kawano T, Tatsuta Y, Koide Y,Yamamoto DOzeki YNitta K,Hosono M. Catfish rhamnose-binding lectin induces G0/1 cell cycle arrest in Burkitt's lymphoma cells via membrane surface Gb3. Glycoconj. J. 2017; 34: 127–138.
[19]. Dutta S, Sinha B, Bhattacharya B, Chatterjee, Mazumder S. Characterization of a galactose binding serum lectin from the Indian catfish, Clarias batrachus: Possible involvement of fish lectins in differential recognition of pathogens. Comp. Biochem. Physiol. C Toxicol. Pharmacol.2005; 141: 76–84.
[20]. Yao D, Pan S, Zhou M. Structural characterization and antitumor and mitogenic activity of a lectin from the gill of bighead carp (Aristichthys nobilis). Fish Phys. Biochem. 2012; 38: 1815–1824.
[21]. Irwin M, Marin MC, Phillips AC, Seelan RS, Smith DI, Liu W, Flores ER, Tsai KY, Jacks T, Vousden KH et al. Role for the p53 homologue p73 in E2F-1-induced apoptosis. Nature. 2000;407:645–648
[22]. Hemmoranta H, Satomaa T, Blomqvist M, Heiskanen A, Aitio O, Saarinen J, Natunen J, Partanen J, Laine J, Jaatinen T .Transcriptional profiling reflects shared and unique characters for CD34 + and CD133 + cells. Stem Cells Dev. 2007;15(6):839–851.
[23]. Lima ALR, Cavalcanti CCB, Silva MCC, Paiva PMG, Coelho LCBB, Beltrão EIC, Correia MTS .Histochemical evaluation of human prostatic tissues with Cratylia mollis seed lectin. J Biomed Biotechnol 2010:179817
[24]. Preetham Elumalai, Abdul Salam Rubeena, Sreeja Lakshmi, Veerappan Anbazhagan, Jesu Arockiaraj, Mani Divya, Sekar Vijayakumar, Baskaralingam Vaseeharan. Shrimp lectin conjugated copper sulfide nanoparticles enhances immune response and gene expressionin *Etroplus suratensis* infected with *Aeromonas hydrophila.* Aquaculture International. 2021; 29, 1103-1120.
[25]. Rubeena A.S, Sreeja Lakshmi, Digi George, Siva Bala Subramaniyan, Anbazhagan Veerappan**,** Elumalai Preetham. Shrimp lectin (Md-*Lec*) conjugated copper sulfide nanoparticles enhance the elimination of aquatic pathogens in infected Nile Tilapia (*Oreochromis niloticus*). RSC Advances, 2020; 10, 44216–44224.
[26]. Nisha P, Anuj Sharma, Praveen Kumar, K A Rubeena. Synergistic Activities of Fish Lectins. In Elumalai Preetham, Sreeja Lakshmi (Eds.). *Aquatic Lectins*. 2022. 235-253. Springer Publishers, Singapore.