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Review

Role of Fucoidan in human diseases

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Abstract: L-fucose and sulfate groups make up fucoidan, a complex polysaccharide that is extracted from brown algae and may be used as a treatment for a number of human illnesses. Through dynamic modulation of important intracellular signaling pathways, management of ROS generation, and maintenance of principal cell survival and death processes, the antioxidant and immunomodulatory actions of fucoidan contribute to their disease-preventive effectiveness. It also lessens the cachexia linked to cancer. The fucoidan is often considered an untapped profusion of druggable molecules in the current scenario, despite its vast range of therapeutic potency. One of the most important tasks to be evaluated is the isolation, screening, biological application, pre-clinical, and clinical evaluation, as well as large-scale, economical production. Thorough research is also required for the chemical synthesis of the current bioactive medication with confirmational rearrangement for improved availability and bioactivity. Therefore, in this study, we focus on the origin of fucoidan's isolation, its strategic application in disease prevention, and the mechanistic analysis of its mechanism of action in treating various illnesses that may be used to future therapeutic interventions.

Keywords: Fucoidan; therapeutics; human diseases; fucoidan targets; signaling pathways

1. Introduction

Because of its varied chemical structure and strong antioxidant activity, fucoidan has broadened its pharmacological properties to include anti-inflammatory, anticoagulant, antiangiogenic, immunomodulatory, anti-adhesive, anticancer, antidiabetic, antiviral, and anti-neurodegenerative agents. In the current situation, one of the main factors contributing to the prevalence of disease is the worldwide population growth that is accompanied by altered eating and lifestyle patterns. Numerous microorganisms linked to illnesses, diabetes, cancer, and neurological conditions including Parkinson's and Alzheimer's pose a serious threat to human life. A collection of several pathological adversities associated with unchecked cell growth, cancer has detrimental effects on individual health care. According to estimates for 2019, more than 9.6 million fatalities worldwide are attributed to more than 200 deadly cancer kinds annually. Skin and stomach cancers are the next most common causes of mortality, after lung, breast, colorectal, and prostate cancers. About 70% of recorded fatality cases occur in low- and middle-income nations[1-3]. Similar to this, diabetes also increases the risk of developing a number of illnesses, including high pressure, heart attacks, strokes, renal failure, blindness, and lower limb amputation. Over the past 40 years, the number of people with diabetes has increased from 108 million to 422 million. The prevalence of adult diabetes has risen from 4.7% throughout the anticipated period to 8.5%. An estimated 1.6 million diabetes-related deaths occur each year[4-13]. Furthermore, the death rate from Alzheimer's disease has skyrocketed to 55% in the past 20 years, accounting for almost 93,500 fatalities worldwide. Over 10 million people worldwide suffer from Parkinson's disease, another significant neurodegenerative illness[14-18]. More significantly, HIV is associated with AIDS, another serious human disease. According to studies in 2016, the expected global death rate from HIV infection was 770,000[19-25].

As medical research advances and conventional therapeutic procedures are employed, the target site may experience irreversible organ damage and an adverse environment. Furthermore, cellular tolerance to the medications utilized persists, creating additional therapeutic obstacles that render the traditional treatment ineffectual. Therefore, the development of novel therapeutic agents with negligible side effects is sought in order to adhere to these consequences that the medications possess. Natural druggable bioactive substances with a range of therapeutic potential exhibit a variety of diseases-fighting abilities. Furthermore, natural compounds or their synthetic equivalents make up the majority of therapeutic medicines[26-34]. Because of their varied chemical makeup and bioavailability, marine natural products (MNPs) have recently also been investigated for their potential as therapeutic candidates. L-fucose and sulfate groups

make up fucoidan, a polysaccharide that is often extracted from brown algae and may be used as a treatment for a number of human illnesses. Their usage as possible therapeutic agents has been supported by their pharmacological characteristics as anti-inflammatory, anticoagulant, antiangiogenic, immunomodulatory, anti-adhesive, anticancer, antidiabetic, antiviral, and anti-neurodegenerative agents. Fucoidan is a promising therapeutic pharmacological agent for clinical use due to its enormous structural diversity and robust antioxidant ability. Additionally, its high bioavailability, cheap maintenance costs, increased yield, and use as a dietary supplement make it a more sought-after medicinal substance[19, 20, 35].

This review focuses on the systematic examination of the source and mechanistic overview of regulatory pathways used by fucoidan in illness prevention, in light of the compound's possible role as a disease preventive and raising questions about its potential clinical application in the future. We have talked about the chemistry, extraction process, and sources of fucoidan in order to better understand therapeutic intervention in the context of disease prevention.

2. Source of Fucoidan: Seaweeds are used as meals and traditional medicines all over the world and are regarded as an appealing source of bioactive chemicals because of their high biodiversity. The crude extracts and partially purified polysaccharides of several seaweed-derived bioactive compounds have been evaluated for a range of therapeutic actions against a variety of human ailments. The phyto-products derived from seaweed have the ability to prevent disease because of their robust antioxidant qualities. Laminarans, alginic acids, and fucoidans are among the structurally and functionally distinct polysaccharides found in brown seaweeds. The biotechnology, pharmaceutical, and food processing industries all make substantial use of these main sulfated polysaccharides. Furthermore, the food processing industry and medicine also use low molecular metabolites such polyphenols, mannitol, free amino acids, vitamins, iodine-containing substances, and lipids. The main biologically active substance is fucoidan, which has a higher molecular weight, is heavily branched, and differs in its monosaccharide makeup. Long chains of linked sugar molecules make up the fucoidan, which is adorned with sulfate groups. Fucoidan's antioxidant capacity primarily contributes to its ability to prevent a variety of human diseases. It is well known that the fucoidan that is extracted from seaweeds has strong anticancer properties. In addition to this, they are known to be more potent against major human ailments like diabetes, Alzheimer's disease, Parkinson's disease, and AIDS. Brown algae often yield the majority of the fucoidan. Ascophyllum nodosum (Linnaeus) Le Jolis, Chorda filum (Linnaeus) Stackhouse, Adenocystis utricularis (Bory) Skottsberg, Analipus japonicas (Harvey) M.J. Wynne, Costaria costata (C. Agardh) De A. Saunders, Cladosiphon novaecaledoniae Kylin, Cladosiphon okamuranus Tokida, and others are the main sources of fucoidan[19, 20, 35, 36].

3. Role in human diseases: Fucoidan's biological action serves as an anti-inflammatory, anti-cancer, and anti-angiogenic agent. Fucoidan, which has been widely studied and extracted from a number of brown algae from different maritime habitats, has been shown to be a powerful anticancer agent against a variety of cancer cell lines by inducing apoptosis and modulating numerous cell survival pathways. For the creation of next-generation drugs, fucoidan's dynamic control of cell death pathways is therefore highly prevalent in cancer treatments and cancer precision medicine. Fucoidan functions as a novel therapeutic drug against diabetes and other metabolic syndromes (MetS) in the current therapeutic setting. By altering the GLUT 4 and AMPK signaling pathways, fucoidans can improve glucose tolerance. When used to treat diabetes, fucoidan, which was isolated from F. vesiculosus, was found to be a powerful α-glucosidase inhibitor. According to recent findings, fucoidan, which is derived from Pearsonothuria graeei, is utilized as a functional food to treat MetS.

Fucoidan inhibits VEGF signaling pathways, which reduces diabetic retinopathy. In the in vivo model, treatment with fucoidan showed less diabetic retinopathy. By inhibiting HIF-1α and VEGF activation, LMWF isolated from L. japonica showed a reduction in retinal neovascularization and retinal injury. Additionally, LMWF reduced the growth of microvascular cells or tissue brought on by excessive glucose. One of the main causes of diabetic retinopathy is hypertension. Through the activation of NO generation and improved eNOS activity, LMWF derived from L. japonica treated Goto-Kakizaki rats (glucose intolerant Wistar rats) decreased hypertension and preserved the endothelium. In obese human individuals, a daily intake of 500 mg/mL fucoidan decreased the diastolic blood pressure.

Neurodegenerative diseases (NDDs) are expected to become a major global danger to community health due to the population's rapid expansion. Dopaminergic neurons in the substantia nigra pars compacta are damaged in Parkinson's disease (PD), a neurodegenerative illness with an unclear etiology. Generally regarded as the powerhouses of cells, mitochondria are damaged organelles found in dopaminergic neurons in patients with Parkinson's disease. Dopaminergic degeneration in Parkinson's disease has been thought to be significantly influenced by mitochondrial malfunction. Furthermore, MPTP, which in turn supports PD-related neurodegeneration, is facilitated by oxidative stress. Because of its strong antioxidant impact, fucoidan, a sulfated polysaccharide that was isolated from brown seaweeds, has been shown to exhibit a wide range of biological functions and may be a promising treatment for Parkinson's disease.

By blocking Bcl-2 translocation, lowering oxidative stress, and stopping caspase-3 activation, fucoidan therapy reduced learning and memory loss in the Aβ-infused in vivo AD (Alzheimer's disease) model through cellular protection. In the hippocampus tissue of rats given Aβ injection, fucoidan may have improved the learning and memory impairment by reducing the activity of choline acetyltransferase (ChAT), acetylcholine esterase (AchE), and the amount of acetylcholine (Ach) along with glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), and malondialdehyde (MDA).
Because of its varied physical and chemical characteristics, fucoidan has a wide range of antiviral action. Galactofucan and 1.3-α-l-fucan, two fucoidans isolated from S. cichorioides and S. japonica, had a potent antiviral activity. In Jurkat and SC-1 cells, these fucoidans demonstrated effectiveness against lentiviral transduction at low concentrations without causing any cellular damage. According to reports, fucoidan prevented Jurkat cells infected with pseudo-HIV-1 particles that shared a capsid protein with HIV-1 from being infected. When examined for anti-HIV-1 characteristics, the fucoidan fractions obtained from S. swartzii were discovered to be possible anti-HIV agents.
Fucoidan's immunomodulatory action regulates the human immune system on multiple levels and channels, and it has become a crucial avenue for drug development and next-generation therapeutic approaches. The immunomodulatory function was significantly affected by the presence of fucoidan's acetyl and sulfate groups. Fucoidan stimulates the activity of natural killer (NK), dendritic (DC), and T cells, resulting in a variety of immunomodulatory effects. Fucoidan controls the activation and proliferation of NK cells and cytotoxic T-cells (CTLs) in both in vitro and in vivo experimental paradigms. The immune-regulatory system The primary method for protecting cells by triggering host immune responses is fucoidan. In the host organism, fucoidan regulates humoral and cellular immunity. Fucoidan is thought to attach itself to Toll-like receptors (TLRs) found on monocytes, macrophages, and DCs. Along with scavenging receptor [SR] and competent receptor-3 (CR-3), fucoidan facilitates the activation of TLR4 and CD14 to stimulate the host immune response. Fucoidan, which were isolated from L. cichorioides, L. japonica, and F. evanescens, function as TLR ligands and interact with TLR2 and TLR4 to activate NF-kB through cytokine and chemokine secretion as well as MHC class I and II complex manifestation[19, 20, 35, 36].

4. Conclusions and future perspectives: The current human disease treatment system has been seen as a trustworthy source for identifying bioactive druggable compounds with a variety of therapeutic uses from marine sources. One of the main goals for the separation and use of these bioactive compounds originating from marine sources is still their bioavailability, varied chemical makeup, and non-reductant cytotoxicity. Potential lead pharmacophores for the treatment of a range of human ailments are fucoidan, which is derived from seaweed. However, the main challenges in their pharmaceutical application are their target selectivity, bioavailability, improved isolation, and purity. Additionally, their low-cost commercial production and pre-clinical and clinical applications for a variety of therapeutic interventions are important factors in their position as druggable agents.

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