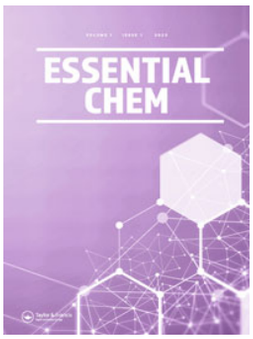

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Rare monosaccharides from marine macroalgae: occurrence, biosynthesis, and biotechnological insights

D. Yuvaraj[a], B. Bharathiraja[b], T. D. Dhanashree[c], and M. Wasiha Kowser[c]

[a]Department of Biotechnology, School of Life Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Chennai, India; [b]Department of Biotechnology, Easwari Engineering College, Chennai, India; [c]Department of Biotechnology, Vel Tech High Tech Dr.Rangarajan Dr.Sakunthala Engineering College, Chennai, India

ABSTRACT

Seaweeds are rich in bioactive compounds, and in recent years, their distinctive polysaccharide content which includes rare sugars with possible industrial uses has drawn a lot of attention. In order to shed light on the structural diversity and biotechnological significance of rare sugars, this review investigates their occurrence and biosynthesis in seaweeds. Understanding the presence of rare sugars in these marine organisms begins with a thorough analysis of the biosynthetic pathways involved in their formation. The study highlights the use of precise structural characterization in the identification and quantification of rare sugars by outlining sophisticated analytical techniques. It also addresses the difficulties in the extraction and purification procedures, emphasizing the necessity of scalable and financially feasible techniques for industrial production. Biotechnological understanding of rare sugars' possible uses extends to the food, pharmaceutical, and other industries. The review highlights the growing importance of rare sugars in applications related to health, stressing both their biological properties and possible medicinal uses. Issues including low yields, storage stability, and regulatory issues are examined, providing a thorough picture of the state of affairs at the moment. Biotechnological understanding of rare sugars' possible uses extends to the food, pharmaceutical, and other industries.

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Seaweed; bioactive compounds; rare sugars; polysaccharide; biosynthesis

1. Introduction

Marine macroalgae and other seaweeds have emerged as potential sources of valuable nutrients and chemically appealing substances, with applications ranging from food ingredients to nutritional supplements and cosmetics. Despite oceans covering over 70% of Earth's surface, relatively few marine organisms have been thoroughly studied and identified. The cell walls of seaweeds contain commercially significant polysaccharides with diverse biological functions. Marine macroalgae (seaweeds) contain diverse polysaccharides that play critical structural and storage functions within their cellular systems. These complex carbohydrates vary across different algal types: brown algae primarily feature alginates in their cell walls, providing structural support and flexibility, while also storing energy in laminarin; red algae are characterized by carrageenans and agar, sulfated polysaccharides that contribute to cell wall integrity and gel-like properties; and green algae typically utilize cellulose as a primary structural component, similar to land plants. The storage polysaccharides, such as laminarin and floridean starch, serve as energy reserves that can be metabolized when needed. Beyond their biological roles within the algae, these polysaccharides have garnered significant interest in various human applications, including food production, pharmaceutical research, biomaterial development, and potential nutraceutical innovations. The complexity and versatility of these marine macroalgal polysaccharides highlight the remarkable biochemical adaptations of these marine organisms, demonstrating how these compounds are not just passive cellular components but dynamic molecules with multiple critical functions.[1] Fucoidan, predominantly found in brown algae, exhibits variations in molecular characteristics including length, branching patterns, monomer fractions,

CONTACT D. Yuvaraj yuvarajdinakarkumar@gmail.com Department of Biotechnology, School of Life Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Chennai, Tamil Nadu, India

and sulfate levels.[2] These structurally variable fucoidans, also known as fucose-containing sulfated polysaccharides (FCSPs), demonstrate bioactive properties influenced by species, thallus age, seasons, and extraction techniques. While fucose predominates, other sugar monomers like galactose, mannose, glucose, and uronic acids are also present. In some cases, such as sulfated galactofucans, galactose ratios may be comparable to fucose.[3]

Seaweeds contain abundant bioactive compounds including vitamins, minerals, antioxidants, and rare sugars. These components demonstrate anti-inflammatory and immune-supporting properties, which are currently under investigation for potential health applications.[4] Beyond basic nutrition, seaweeds provide essential proteins, fiber, and omega-3 fatty acids that contribute to overall health and well-being when incorporated into diets.[5] The development of sustainable cultivation techniques, including offshore farming and integrated multitrophic aquaculture, is currently underway. However, challenges persist in market development, environmental impact assessment, and regulatory frameworks.[6] Addressing these challenges requires collaboration between governments, businesses, and the scientific community, along with innovative technologies and sustainable practices.[7]

Rare sugars represent a unique class of compounds distinct from common sugars like glucose and sucrose. These molecules, characterized by distinctive molecular arrangements, show promise in various applications including pharmaceutical formulations, skincare products, and wound dressings.[8] Their potential extends to biotechnological processes such as enzyme synthesis and biofuel production. Research continues to explore their chemical structures, biosynthesis pathways, and physiological roles.[9] The cultivation of seaweeds for rare sugar production aligns with sustainable practices, requiring minimal resources while offering rapid growth. Environmental impact assessments and sustainable practices are crucial for reducing ecological effects.[10] Understanding the potential of rare sugars can benefit industry stakeholders, highlighting opportunities for market expansion, product innovation, and economic development. The commercial landscape of rare sugars is experiencing a significant transformation, driven by growing market interest in biotechnological and pharmaceutical applications.[11–13] Seaweed-derived rare sugars represent an emerging field with substantial potential, as evidenced by their diverse applications across multiple industries. The manuscript highlights the increasing commercial interest in these compounds, noting their potential uses in functional foods, nutraceuticals, pharmaceuticals, and specialized chemical sectors.[6,14,15] While current commercial products remain limited, ongoing research and advances in extraction technologies suggest promising future developments.[16] The versatility of rare sugars from marine macroalgae, including their potential as low-calorie sweeteners, bioactive compounds, and precursors for various industrial applications, positions them as a strategic area of biotechnological innovation.[11,13,17] This review aims to address this critical need by providing an in-depth exploration of rare sugars from seaweeds, their occurrence, biosynthesis, and potential biotechnological applications.

2. Occurrence of rare sugars in seaweeds

These seven sugars, D-glucose, D-fructose, D-xylose, L-arabinose, D-ribose, D-mannose, and D-galactose are the most commonly employed in the carbohydrate-based refinery. With their exception, most sugars have an inherent "rarity." This includes all forms of monosaccharides and their derivatives, such as uronic acids, sugar alcohols, deoxygenated, aminated, and methylated ones, according to the International Society of Rare Sugars.[14] Small amounts of these rare sugars are found in nature, particularly in terrestrial plants, but they are always very valuable, especially in the pharmaceutical and nutraceutical sectors. Since they are generally low in calories, they are used as a sweetener in place of more common sugars like sucrose, D-glucose, and D-fructose.Rare sugars have been shown to have new physiological effects, such as prebiotics (sugar alcohols), anti-caries (sugar alcohols), anti-diabetic (D-tagatose), anti-hyperlipidemic (D-allulose), anti-atherosclerosis (D-allulose), anti-inflammatory (D-allose), and neuroprotective (D-allulose). In recent years, there has been evidence that rare sugars could be a new platform chemical in carbohydrate-based refineries for use.[18]

Enzymatic or microbiological procedures, which are always built on the basis of a systematic relationship of all potential sugar monomers in the "Izumoring" idea, are typically used to create the uncommon sugars. In this instance, the interconversion of the sugars typically entails intramolecular reduction-oxidation reactions and regio-selective epimerization/isomerization by enzymatic mechanisms[19,20]. Although it

involves multiple steps, the Izumoring method is a good way to synthesize uncommon sugars from the seven commonly used sugars indicated above. For example, an enzymatic "phosphorylation → depo-sphorylation" reaction step at 37–45°C in 12–36 hours can recover ketoses from aldoses preferentially (>90%).[21–23]

2.1. Types and distribution of rare sugars

The distribution of rare sugars in nature, including in various seaweed species, is quite diverse (Table 1). Rare sugars are not as commonly found as the more prevalent sugars like glucose and sucrose, but they play important roles in biological processes and have potential applications in various industries. The distribution of these rare sugars can vary between different species of seaweeds, and even within the same species, depending on factors such as environmental conditions, geographic location, and growth stage.[31] Understanding the distribution of rare sugars is crucial for industries that seek to harness these compounds for various applications, including food, pharmaceuticals, and cosmetics. Additionally, ongoing research in this field contributes to our understanding of the bioactive compounds present in seaweeds and their potential health benefits.

2.2. Methods for identifying and quantifying rare sugars

Identifying and quantifying rare sugars can be challenging due to their low abundance and structural complexity. Enzymatic techniques and high-performance liquid chromatography (HPLC) are widely used. Since 2004, enzymatic techniques have grown in popularity, especially in human studies.[11] HPLC is a quick and efficient method for detecting the concentration of uncommon sugars, and a simpler reverse phase HPLC method has been devised for distinguishing rare sugars like D-psicose from D-fructose. Another well-established approach for measuring uncommon sugars is to determine sugars in molasses using HPLC after solid-phase extraction.[32] However, several methods have been developed to address these challenges.

2.2.1. Chromatographic techniques

2.2.1.1. High-performance liquid chromatography (HPLC). HPLC is a widely used technique for separating and quantifying rare sugars. It involves the use of a liquid mobile phase to carry the sample through a stationary phase. The separation is based on differences in the interaction of the rare sugars with the stationary phase.[33] High-performance liquid chromatography (HPLC) is a commonly used technique in seaweed isolation for rare sugars. High performance liquid chromatography (HPLC) involves dissolving a sample containing unusual sugars in a solvent and passing it through a column filled with a stationary phase. In the stationary phase, particles are coated with a material that has a strong affinity for specific sugars. The mobile phase, which is a mixture of solvents, is pushed through the column by a high-pressure

Table 1. Sources of rare sugars and their distribution.

S.no.	Names	Source	Application	Reference
1.	Rhamnose	Red and green seaweed	Antimicrobial property Skin conditioning Sweetener Flavor enhances	[24]
2.	Arabinose	Red seaweed	Cell culture media Nutraceuticals Food industry Pharmaceuticals Cosmetics	[25]
3.	D-Allulose	Brown seaweed (enzymatic conversion)	Low-calorie sweetener Anti-diabetic properties	[26]
4.	L-Rhamnulose	Red algae enzymatic processes	Pharmaceutical precursor	[27]
5.	D-Psicose	Enzymatic bioconversion from seaweed carbohydrates	Metabolic regulation	[28]
6.	D-Tagatose	Brown algae derivatives	Prebiotic Low-calorie sweetener	[29]
7.	L-Gulose	Red seaweed specific pathways	Vitamin C precursor	[30]

pump. Different interactions between the uncommon sugars in the sample and the stationary phase will occur depending on their chemical composition.[34]

The seaweed extract can be dissolved in either ethanol or methanol, which are suitable solvents. Next, any particles in the solution that might clog the HPLC column are eliminated using a filter. The filtered solution is then transferred into the HPLC apparatus. An HPLC system is composed of a pump, a column, a detector, and a data collection device. The pump forces the mobile phase through the column at a high pressure. The unusual sugars in the sample interact with the stationary phase to varying degrees. Depending on how strong their affinity is for the stationary phase, rare sugars will spend varying lengths of time on the column; those with a lower affinity will spend less time there.[35] At the end of the mobile phase, the rare sugars will elute from the column in the order that their retention durations increase. A detector locates the eluted uncommon sugars, such as a UV or refractive index detector. The detector measures the absorbance or refractive index of the rare sugars that have been eluted. Once the detector values are recorded, the data collection system creates a chromatogram. On the chromatogram, the rare sugars that were eluted are represented by the peaks. The rare sugars can be collected and used in a number of ways after purification, including additional analysis.[36]

2.2.1.2. Ion chromatography (IC). IC is suitable for the separation of ionic compounds, and it can be used for the analysis of rare sugars that form ions. It is particularly useful for sugars with acidic or basic functional groups. Ion chromatography allows for the separation and measurement of low concentrations of up to 8 or 10 distinct anions in a single chromatographic run that only takes a few minutes. This approach is also effective for cations. In aqueous samples, alkali metal ions, ammonium, magnesium, calcium, strontium, and a growing list of additional metal cations and amine cations may be easily separated and identified. Ion chromatography is cost-effective since the apparatus is generally affordable, and each chromatogram may determine multiple ions. Despite the fact that contemporary ion chromatography is just roughly 10 years old, it is already frequently utilized in an increasing number of sectors. Many scientific and environmental investigations, such as the examination of a significant number of rainwater samples, have been conducted. It would not have been possible prior to the invention of ion chromatography. Any current and effective method of separating and detecting ions is referred to as ion chromatography. The majority of materials examined by ion chromatography currently comprise inorganic or hydrophilic organic anions and cations. Ion exchange chromatography is the most frequent method of separation, with anions separated on an anion exchange column and cations separated on a cation exchange column.[37]

2.2.2. Mass spectrometry (MS)

2.2.2.1. Liquid chromatography-mass spectrometry (LC-MS). LC-MS combines the separation capabilities of liquid chromatography with the mass analysis of a mass spectrometer. It is valuable for the identification and quantification of rare sugars based on their mass-to-charge ratios[38]. The "chain of traceability" is a continuous sequence of material comparisons using proper measuring methodologies. A certified "primary reference standard" – tidy substance with verified purity and traceability to the SI unit – with a clearly described related uncertainty is situated at the top of the chain (the top/highest metrological order). Starting with this material, a primary reference measurement process (in the top position, also known as the "highest order") is used to describe a primary reference material derived from the neat standard, such as cortisol NIST SRM 921 in ethanol. A secondary reference standard (e.g., NIST SRM 921 in serum) can be produced using another (or the same) measurement process.

Following that, the chain can be extended to routine measures, which may use other measurement principles as the reference measurement processes (for example, ligand-binding tests for cortisol in serum). Mass spectrometry has traditionally been a generally recognized instrumental analytical method for small-molecule analysis due to its technical qualities, and the idea of "definitive (absolute) reference methods" was formed.[39]

2.2.2.2. Gas chromatography-mass spectrometry (GC-MS). Similar to LC-MS, GC-MS combines gas chromatography with mass spectrometry for the identification of volatile rare sugars. Gas Chromatography-Mass Spectrometry (GC-MS) is a very effective analytical method for identifying and quantifying chemical components in a sample. It combines two separate techniques, gas chromatography (GC) and mass spectrometry (MS). Separates mixture components based on volatility and interactions with a stationary phase.

The sample is vaporized and injected into a chromatograph, where an inert gas (usually helium or nitrogen) transports it through a column. Because of their chemical characteristics, various compounds flow through the column at different speeds, resulting in separation. Mass Spectrometry (MS) This technique determines the mass and structure of individual molecules in a sample.[40]

The isolated chemicals from the GC column are ionized in the mass spectrometer. The ions that arise are subsequently accelerated and sorted according to their mass-to-charge ratio (m/z). The detector generates a mass spectrum by recording the abundance of ions at various m/z values.

2.2.3. Nuclear magnetic resonance (NMR) spectroscopy

2.2.3.1. 1 H-NMR and 13C-NMR. NMR spectroscopy provides information about the structure of molecules based on their nuclear spins. It is particularly useful for determining the structure and configuration of rare sugars. Rare sugars are frequently extracted and identified using nuclear magnetic resonance (NMR) spectroscopy, more especially 1 H and 13C NMR. These methods are applied to rare sugars to characterize their chemical structure.[41] The structure of the sugar can be ascertained by the 1 H and 13C NMR spectra regarding the environments of the various hydrogen and carbon atoms in a molecule.

The identification and characterization of rare sugars using 1 H and 13C NMR is demonstrated in a number of research articles and protocols. For instance, a study that was published in Nature Protocols details the synthesis of D-glycosamine building blocks and orthogonally protected rare sugars. 1 H, 13C, and 2D NMR spectroscopy were used to thoroughly characterize these compounds. Furthermore, a study published in the Journal of Organic Chemistry describes how to use 1D FESTA to obtain pure 1 H NMR spectra of distinct reducing fluor sugar forms, such as pyranose and furanoside.[42]

Moreover, full 1 H and 13C NMR chemical shift assignments of mono- and disaccharides, including uncommon sugars, have been obtained by means of computational and experimental methods, improving the efficiency of the assignment procedure. A rare sugar called 6-deoxy-d-altrose was identified in a different study using the 1 H and 13C NMR spectra. This sugar was separated from a polysaccharide that was taken out of an edible folk medicinal mushroom. To sum up, 1 H and 13C NMR spectroscopy are useful methods for the extraction and identification of uncommon sugars. They give researchers comprehensive insight into the chemical structure of these significant molecules and allow them to characterize them.[43]

2.2.4. Enzymatic methods

2.2.4.1. Enzymatic assays. Enzymatic methods involve the use of specific enzymes that selectively react with certain sugars. The change in absorbance, fluorescence, or other properties can be measured to quantify the rare sugar.[44] The Izumoring technique is a systematic approach for producing rare sugars using enzymes.

Enzymes like keto-aldol isomerases, epimerases, and oxidoreductases are used to produce rare sugars, and their structural analysis has improved production through molecular design.[45] These enzymatic methods have facilitated the study of rare sugar properties, catalytic mechanisms, and industrial applications, making them an important tool in rare sugar research.

2.2.5. Immunoassays

2.2.5.1. Enzyme-linked immunosorbent assay (ELISA). Immunoassays use antibodies to selectively bind to specific sugars. ELISA can be adapted for rare sugar detection by using antibodies specific to the target rare sugar. ELISA techniques can identify rare sugars by utilizing particular antibodies. However, ELISA tests are typically utilized for detecting proteins, antigens, and antibodies, rather than tiny molecules such as rare sugars.

ELISA tests are widely used in medical and scientific contexts to detect various antigens, hormones, viral and bacterial antigens, and antibodies. Commercially available ELISA kits include pre-coated polystyrene plates, detecting antibodies, and reagents for ELISA tests. ELISA tests use an enzyme and an antibody or antigen to generate an antigen-antibody reaction and provide a readout.[46]

2.2.6. Chemical derivatization

2.2.6.1. Derivatization reactions. Some rare sugars may undergo chemical derivatization to enhance their detectability or improve their chromatographic behavior. Derivatization can make the analysis more sensitive and selective. Derivatization reactions are critical for the investigation of rare sugars, especially given their structural complexity and the necessity for enhanced sensitivity and selectivity in analytical procedures. Rare sugars are derivatized using the following methods are Alditol acetates, this technique generates one peak for each derivatized sugar, simplifying the analysis of complicated sugar combinations.-[47] Halide adducts, such as chloride or bromide, can be utilized to increase sensitivity and improve the distinction of positional isomers of saccharides.[48]

3. Biosynthesis of rare sugars

The enzymatic or microbial synthesis of sugars that are uncommon in nature is known as the biosynthesis of rare sugars. The food, cosmetic, and pharmaceutical industries can all benefit from the use of these uncommon sugars. Numerous microorganisms, such as yeast, fungi, and bacteria, can synthesize rare sugars. Scientists frequently locate and separate organisms that either naturally produce the desired rare sugars or can be modified to do so. The biosynthetic pathways involved in the synthesis of the rare sugar of interest are examined by researchers after a suitable source organism has been chosen. Finding the genes and enzymes in charge of the target sugar's synthesis is part of this process. Enhancing the production of rare sugars is a common application of genetic engineering techniques.[49] For the purpose of increasing the target sugar yield, this may entail altering the metabolic pathways of the source organism. With recombinant DNA technology, specific genes can be added, removed, or altered through genetic manipulation. Fermentation, in which the chosen microorganism is grown in a controlled environment, is a common step in the biosynthesis process. The fermentation medium is designed to produce the rare sugar by providing the microorganism with the nutrients and conditions it needs to thrive and produce the desired compound. Enzymatic synthesis is an additional method for creating rare sugars besides microbial fermentation. In this process, specific enzymes that can catalyze the conversion of more accessible substrates into the rare sugar are employed. The rare sugar must be extracted and purified from the fermentation broth or reaction mixture following the fermentation or enzymatic synthesis. To isolate the target compound, a variety of separation methods, including chromatography and crystallization, may be used. The isolated rare sugar is then analyzed and characterized to confirm its identity and purity. Analytical techniques such as nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry may be used for this purpose. Efforts are made to increase production for commercial purposes after the biosynthesis process has been optimized on a small scale. This includes enhancing strain performance, maximizing fermentation conditions, and guaranteeing economical production. There are several industries that use rare sugars. For instance, they could be employed in the pharmaceutical sector as building blocks for the synthesis of bioactive compounds, sweeteners, or prebiotics. In order to efficiently produce these valuable compounds, the biosynthesis of rare sugars is an interdisciplinary field that brings together genetics, biochemistry, microbiology, and bioprocess engineering. Genetic engineering and bioprocess optimization advances are still helping to create sustainable and economical processes for producing rare sugars.[50]

3.1. Mechanisms and pathways involved in the biosynthesis

The biosynthesis of rare sugars in seaweeds involves complex biochemical pathways (Figure 1). Rare sugars are monosaccharides that are not commonly found in terrestrial organisms. Seaweeds, or macroalgae, are rich sources of various bioactive compounds, including rare sugars. Seaweeds, like plants, undergo photosynthesis to convert sunlight into energy. This process involves the capture of light energy by chlorophyll, leading to the production of glucose and other simple sugars. Glucose, a common sugar, serves as the starting point for the biosynthesis of various rare sugars. Enzymes and pathways involved in primary metabolism play a crucial role in converting glucose into precursor molecules. Hexose interconversions refer to the conversion of one hexose sugar (e.g., glucose) into another.

Seaweeds may utilize enzymes such as isomerases and epimerases to convert common hexoses into rare sugars. The PPP is a metabolic pathway parallel to glycolysis that generates ribose-5-phosphate and

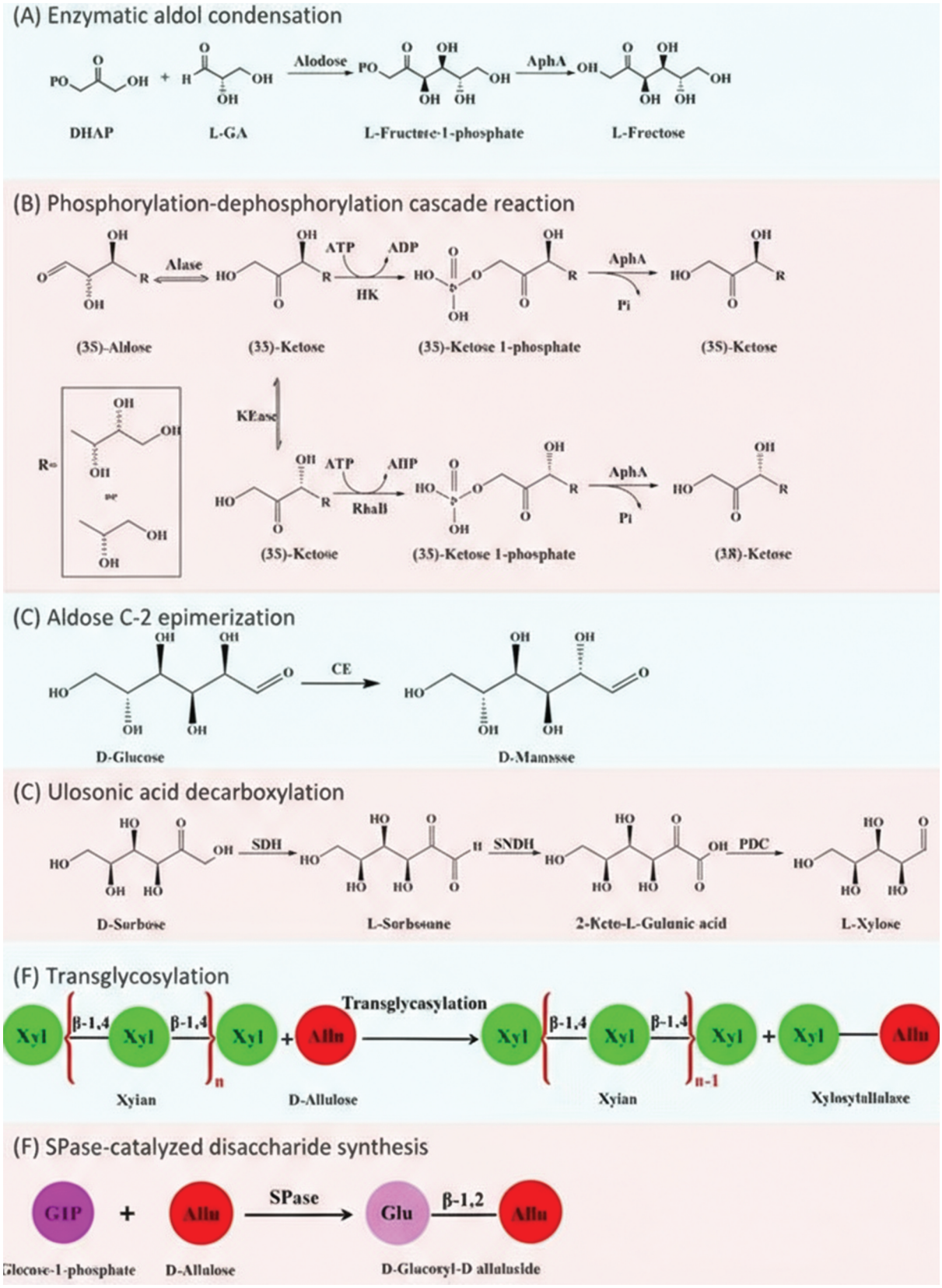

Figure 1. The metabolic and enzymatic processes involved in the conversion of common sugars to rare sugars in marine macroalgae.[51]

NADPH. Ribose-5-phosphate can be used for the synthesis of rare sugars. Some rare sugars are derived from polyols (sugar alcohols) through specific enzymatic reactions.[52] Seaweeds may have enzymes capable of converting polyols into rare sugars. Enzymes involved in epimerization and isomerization reactions are critical for the conversion of common sugars into rare sugars. These enzymes catalyze the rearrangement of functional groups, leading to the formation of rare sugar isomers. Seaweeds often contain sulfated polysaccharides, and some rare sugars may undergo sulfation. Methylation reactions can also occur, introducing methyl groups to specific positions on sugar molecules. Specific enzymes catalyze the modification of sugar molecules in seaweeds. These modifications can include glycosylation, acetylation, and other enzymatic transformations that result in the formation of rare.[15] Rare sugars are often associated with secondary metabolites in seaweeds. Enzymes involved in secondary metabolism pathways contribute to the synthesis of unique sugar derivatives with potential bioactive properties.

3.2. Enzymatic and genetic factors contributing to rare sugar production

Rare sugars are monosaccharides that are not commonly found in nature and have unique properties. Enzymatic and genetic factors play crucial roles in the production of rare sugars. Enzymatic production techniques, such as the Izumoring strategy, have been devised to synthesis rare sugars by interconverting aldose-ketose and employing particular enzymes such as aldose-ketose isomerases, aldolases, and dehydrogenases.[53] Rare sugar synthesis relies heavily on enzymatic and genetic variables. Enzymatic production techniques, such as the Izumoring strategy, have been devised to synthesis rare sugars by interconverting aldose-ketose and employing particular enzymes such as aldose-ketose isomerases, aldolases, and dehydrogenases.[54]

3.2.1. Enzymatic factors

Enzymes are highly specific catalysts that determine the type of sugar produced. Different enzymes are required for the synthesis of specific rare sugars. For example, enzymes like isomerase, epimerase, and mutase play essential roles in converting common sugars into rare sugars by rearranging their carbon skeletons. Enzymes have substrate specificity, meaning they work on specific sugar molecules. Engineering enzymes for altered substrate specificity is crucial for the production of rare sugars. Directed evolution or rational design techniques can be employed to modify enzyme specificity, allowing them to accept and convert different substrates. Through genetic engineering techniques, enzymes can be modified or engineered to enhance their catalytic efficiency, stability, and specificity for rare sugar production. Techniques such as protein engineering and directed evolution can be used to optimize enzymes for industrial applications.[55] Rare sugar biosynthesis often involves multiple enzymatic steps in a metabolic pathway. Engineering the entire pathway can improve the overall yield of rare sugars. Balancing the expression levels of different enzymes in the pathway is critical to prevent bottlenecks and ensure efficient rare sugar production.

Identifying and isolating genes responsible for encoding enzymes involved in rare sugar biosynthesis is a fundamental step. Genomic and metagenomic approaches can be employed to discover genes from organisms that naturally produce rare sugars or through heterologous expression in host organisms. Optimizing the expression of target genes is crucial for efficient rare sugar production. This involves selecting suitable promoters and regulatory elements to control gene expression. Synthetic biology techniques can be employed to design and construct genetic circuits for precise control of gene expression in host organisms. The expression of rare sugar biosynthesis genes requires careful selection of the host organism. Seldom occurring sugars can be produced by genetically modifying yeast, bacteria, and plants. Cofactors required for the enzymatic reactions, growth conditions, and the metabolic background of the host are all taken into account. Metabolic engineering includes modifying the metabolism of the host organism to redirect precursor molecules toward the production of rare sugars.[56] In order to direct pathways that compete for common precursors toward rare sugar biosynthesis, this entails manipulating those pathways. The ultimate goal of producing rare sugars in an efficient and sustainable manner is to increase the availability of these valuable compounds for a variety of uses, including the food and pharmaceutical industries. This often requires the integration of enzymatic and genetic approaches.[57]

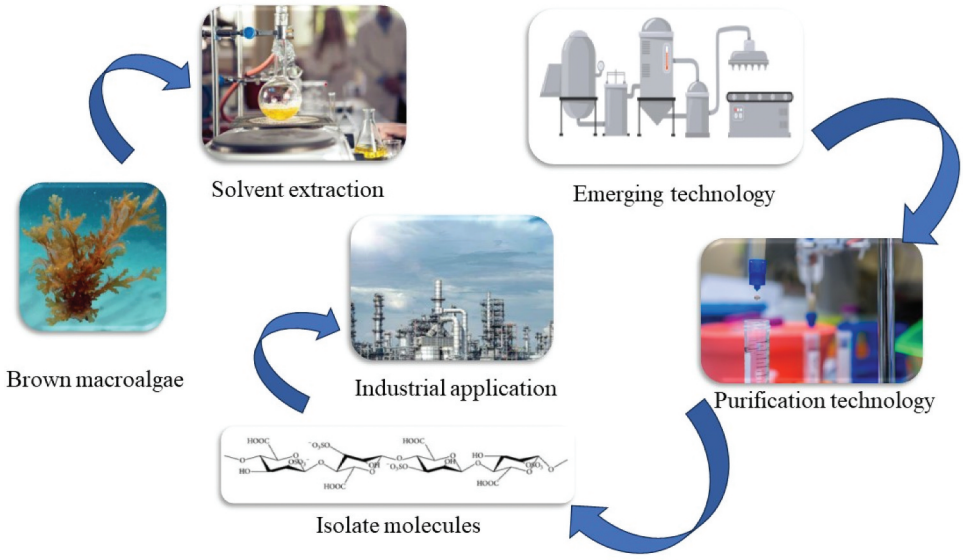

Figure 2. Methods employed for isolating rare sugars from seaweed, including modern and conventional extraction strategies.[19]

4. Extraction and purification techniques

There are a few possible phases in the extraction of macroalgal polysaccharides, which are outlined in Figure 2. In order to extract the polysaccharides of interest and test their biological activity and potential industrial uses, these extraction steps involve pre-treating the macroalgae, preparing the macroalgal biomass, extraction techniques (traditional solvent extraction versus the current innovative technologies including ultrasound, microwave, and enzyme-assisted extractions), and purification techniques.

4.1. Macroalgal biomass preparation

In order to extract polysaccharides from macroalgae, the algae must first be cleaned of sand and epiphytes using either sea water or distilled water, and then they must be dried (either by oven drying or freeze drying). After that, the dried biomass is ground to get the highest in the latter extraction processes.[18,58] Patented the exudate technique, which produces laminarin and fucoidan in industrial quantities from living macroalgal tissue, as an alternative to drying procedures. In order to extract the exudate from the live macroalgae tissue, the fresh macroalgae is chopped into pieces that are no larger than 1 cm and then placed in a dark, humid environment. Following this stage, the resulting exudates might be used to extract and purify the polysaccharides laminarin and fucoidan.

4.2. Macroalgae preparation

Pre-treatments that were most frequently carried out in the literature included washing the dried biomass with either acetone alone or a mixture of methanol, chloroform, and water (4:2:1; v/v/v).[59] A combination of acetone and ethanol has been investigated as an alternative at varying temperatures more recently[60,61] either one ethanolic pre-treatment or many ethanolic pre-treatments. These alcohol treatments were used to eliminate molecules that were heavily attached to the polysaccharides and contaminated the target compounds, such as mannitol and chlorophyll, as well as fats (defatted), proteins (deproteinated), and phenols (dephenolated).[62] Additional cutting-edge pretreatments that have been recently documented in the literature include the compressional-puffing hydrothermal process, which involves heating macroalgae to atmospheric pressure (140°C, 180°C, and 220°C) and then quickly reducing the pressure in a vessel holding

superheated water. This process enables the macroalgae's cellular structure to be altered before fucoidan is extracted.[19]

4.3. Extraction methods

4.3.1. Conventional chemical extraction

Distinct methods for extracting materials using hot or cold water, as well as acids or alkalis. Since the hydrogen bonds between polysaccharides are disrupted by hydrogen ions (H+) and hydroxyl ions (OH−), extraction is typically made easier by applying acidic or alkaline conditions.[63] Conventional extraction methods depend on the target chemicals' solubility and frequently involve pre-treatment stages in which solvents are used to remove lipids, pigments, proteins, and other contaminants.[64]

4.3.2. Ultrasound-assisted extraction (UAE)

UAE works by subjecting the biomass to high-frequency sound waves that are louder than 20 kHz. Vapor bubbles in liquids created at high pressures implode when exposed to strong ultrasonic fields. When these bubbles burst close to liquid-solid boundaries, such cell walls, the tremendous pressures acting on the solid surfaces cause the cell to break down. Low temperatures allow UAE to be used, which makes it possible to extract target molecules that are thermosensitive.[17,65]

4.3.3. Microwave assisted extraction (MAE)

With frequencies ranging from 300 MHz to 300 GHz, non-ionizing electromagnetic radiation is used by MAE to break hydrogen bonds and induce dissolved ions to migrate. This makes it possible for the solvent to permeate the cell matrix and makes it easier for the desired components to be extracted. It is possible to adjust variables like temperature, pressure, time, and the ratio of algae to water in order to maximize the production of the intended product.[66]

4.3.4. Enzyme assisted extraction (EAE)

Enzymes are used in EAE to break down the algal cell wall and release the target chemicals. To enhance the extraction outcome, critical factors such as pH, temperature, and treatment duration should be tuned for each enzyme. Target molecule extraction is typically aided by enzymes that catalyze the degradation of cell wall structural components such cellulose, β-glucan, and hemicellulose.[67]

4.3.5. Supercritical fluid extraction (SFE)

A material at a temperature and pressure above its critical point, when the distinction between the gas and liquid phases is lost, is called a supercritical fluid. The two factors can be changed to alter the fluid's solubility. Carbon dioxide is often utilized because, in comparison to compounds with greater critical points, it has a comparatively low critical point and so requires less energy input to become supercritical. Supercritical fluids have superior transport qualities than liquids because of their high diffusivity and low viscosity. Since SFE doesn't involve the use of solvents, it is regarded as an ecologically benign technique. On the other hand, compared to other extraction techniques, procurement prices are significant. For this reason, this idea is mostly used to extract extremely valuable chemicals.[19]

4.4. Purification

4.4.1. Filtration and precipitation

In many cases, precipitation is the first stage of purification. To the crude extract, a suitable precipitating agent is added, such acetone or alcohol. As a result, solid precipitate separates from the solution containing the uncommon sugars.[60] Filtration is subsequently used to remove the precipitates from the liquid; vacuum filtration and centrifugation are common techniques used for this purpose. Nanofiltration (NF) is used to separate and purify saccharides from biomass. NF has garnered a lot of attention in recent decades because of its

great selectivity, low energy consumption, and minimal environmental effect. Hybrid membrane techniques that combine NF and ultrafiltration may effectively remove undesirable solutes, resulting in greater purity saccharides.[68]

4.4.2. Crystallization

One method used to further purify rare sugars is crystallization. The formation of crystals is fostered for the rare sugars by regulating variables like concentration and temperature. After that, the crystals are extracted from the leftover solution; if desired, purity can be increased by repeating this procedure.[44] Rare sugar crystallization is a little-discussed issue in literature. However, some pertinent data may be discovered in the context of sugar purification and separation from biomass. For example, a research on the overexpression, crystallization, and preliminary X-ray crystallographic analysis of d-ribose-5-phosphate isomerase from Clostridium thermocellum was performed to identify its three-dimensional structure.[69]

4.4.3. Chromatography

Chromatographic methods are effective instruments for the separation and purification of uncommon sugars. A variety of chromatography techniques, such as affinity, size exclusion, and ion-exchange chromatography, can be used. These techniques distinguish uncommon sugars by to attributes like charge, size, or affinity for particular substances.[26]

4.4.4. Separation by membranes

Based on size exclusion, contaminants may be eliminated using membrane filtration techniques including ultrafiltration and nanofiltration. These techniques work well for eliminating undesirable materials and condensing rare sugars. Membrane filtration, particularly nanofiltration, is an appealing technology in sugar production because it may reduce the use of chemicals, create high-quality clarified juice, and limit the need for chemical pretreatment.[70]

4.4.5. Spiral agitation

Rare sugars can be separated using centrifugation methods based on density differences, such as isopycnic centrifugation. This is especially helpful for different densities of sugar fractions. Spiral agitation might be used to improve the mixing and interaction between phases during the crystallization process. For example, in the separation of glucose and fructose by freezing crystallization, spiral agitation might assist maintain a uniform distribution of the sugars and facilitate effective mass transfer between the solid and liquid phases.[31]

4.4.6. Analysis methodologies

The purity of the rare sugars is monitored and confirmed during the purification process using analytical methods such as thin-layer chromatography (TLC), high-performance liquid chromatography (HPLC), and spectroscopy (e.g., FT-IR, NMR).

The rare sugars must be purified once they have been extracted. The most popular techniques for cleaning uncommon sugars are as follows:

4.4.7. Column chromatography

Column chromatography is a refinement technique that separates mixture constituents according to how differently they mobilize in a mobile phase by using a stationary phase. Because silica gel and alumina have a great affinity for certain sugars, they are often used as the stationary phase in experiments with uncommon sugars. To elute the sugars from the stationary phase, a solvent or solvent combination is used as the mobile phase. The sugars that elute last are those that have the highest affinity for the stationary phase, while the sugars that elute first have the lowest affinity.[26] A high level of purity for the uncommon sugars may be obtained by employing a sequence of columns with various stationary phases. A more thorough description of the column chromatography procedure may be found here, either methanol or ethanol is a suitable solvent in which the seaweed extract is dissolved. After that, the solution is put into a column that has alumina or silica gel packed into it. One by one, the uncommon sugars are eluted from the column by

pumping a mobile phase across it. To ascertain the rare sugars' purity, the fractions containing the rare sugars are separated and tested. After that, the pure rare sugars can be used in different ways or utilized for additional analysis. One useful and efficient technique for removing uncommon sugars from seaweed is column chromatography. It's a rather easy and affordable technique.[71]

4.4.8. High-performance liquid chromatography (HPLC)

The method of high-performance liquid chromatography (HPLC) is frequently employed to isolate uncommon sugars from seaweed. A sample containing uncommon sugars is dissolved in a solvent and then run through a stationary phase-filled column in high performance liquid chromatography (HPLC). Particles coated in a substance that has a great affinity for certain sugars make up the stationary phase. A high-pressure pump pushes the solvent or solvent combination known as the mobile phase through the column. Depending on their chemical makeup, the uncommon sugars in the sample will interact with the stationary phase in different ways. The uncommon sugars that are more suited to the stationary phase will remain on the column for a longer period of time. Conversely, those with lower affinity levels will spend less time on the column. The uncommon sugars will ultimately elute from the column in the order that their retention durations increase during the mobile phase.[26]

Either methanol or ethanol is a suitable solvent in which the seaweed extract is dissolved. After that, a filter is used to remove any particles from the solution that can clog the HPLC column. The HPLC apparatus is then filled with the filtered solution. A pump, a column, a detector, and a data gathering system make up an HPLC system. High pressure is applied by the pump to drive the mobile phase through the column. To varied degrees, the uncommon sugars present in the sample interact with the stationary phase. Rare sugars will spend different amounts of time on the column depending on how strong their affinity is for the stationary phase; those with a lower affinity will spend less time there.[27] The rare sugars will ultimately elute from the column in the order that their retention durations increase during the mobile phase. A detector, such as a UV or refractive index detector, finds the eluted uncommon sugars. The absorbance or refractive index of the eluted rare sugars is measured by the detector. A chromatogram is created by the data collection system after it has recorded the detector values. The peaks on the chromatogram represent the uncommon sugars that were eluted. Following purification, the uncommon sugars can be gathered and utilized in a variety of ways, such as further analysis.[40]

These approaches differ in terms of sustainability, scalability, and efficiency. The most effective technique is solvent extraction however it is not sustainable nor scalable. Although enzyme-assisted extraction is less effective than solvent extraction, it is more scalable. Although solvent extraction or enzyme-assisted extraction are more effective than SFE, it is still the most scalable and environmentally friendly technique. Depending on the intended use and degree of purity, the best technique for removing and purifying uncommon sugars from seaweeds will be determined. Sustainability is perhaps the most crucial factor to take into account while extracting and purifying rare sugars from seaweeds. Because seaweeds are a renewable resource, the processes needed to separate and purify their uncommon sugars shouldn't harm the ecosystem.[27]

5. Rare sugars in seaweed-based products

The following table provides a comprehensive overview of the major polysaccharides and sugars derived from red, brown, and green seaweeds, highlighting their associated bioactive applications. It summarizes the key biochemical components of each seaweed type and outlines their uses in diverse areas such as skin whitening, anti-inflammatory, anti-aging, and pharmaceutical developments (Table 2).

5.1. Product description

Seaweed extracts are seaweed hydrocolloids that act as gelling and thickening compounds in a variety of food, pharmaceutical, and biotechnological applications. Agar is extracted from the seaweed *Gracilaria* in about 80% of cases. Meanwhile, about 80% of carrageenan is derived from the seaweed species *Eucheuma*

Table 2. Review of existing seaweed-sugar based products.

Seaweed Type	Polysaccharide	Sugars	Application	Reference
Red	Agar, carrageenan, agaropectin, Cellulose, xylans, mannans	L-AHG	Skin whitening (melanin content of 23% at 100 µg mL− 1) anti-inflammatory (reduced nitrile levels by 39% at 200 µg mL- 1 in RAW264.7 cells)	[65]
		D-AHG	Skin whitening (melamin content of 50% at 100 µg mL- 1) anti-inflammatory (reduced nitrile levels by 60% at 200 µg mL- 1 in RAW264.7 cells)	
		L-Galactose	Precursor of vitamin C and Precursor of antiviral medications based on L-nucleosides	
Brown	Fucoidon, laminaran, alginates, cellulose	L-fucose (6-deoxyL-galactose)	Anti-aging (50% inhibition of elastase-type endopeptidase (MMP-2, MMP-9) at 10 µg mL− 1; 19% improvement in human skin fibroblast profile at 1 µg mL− 1) Anti-tumor (breast tumors)	[65]
		Mannitol	Low-calorie sweetener, fine chemical precursor (propanediol, mannitol hexanitrate) and also act as food additive	
		Mannuronic acid Guluronic acid	Non-steroidal anti-inflammatory drugs (NSAIDs) are used to treat arthritis and renal inflammatory disorders. polyguluronate precursor	
Green	Ulvan, starch, Xylo pyranose, cellulose, Hemicellulose, glucuronan, glucopyranose	L-rhamnose L-iduronic acid	Beneficial chemical precursors Heparin oligosaccharide precursor	[65]

and *Kapahulu's*. Agar (or agar-agar) is a gel-like substance made from the cell walls of red seaweed, specifically *Gracilaria*. Agar is a good source of iron and magnesium nutritionally. Agar's nutritional benefits include digestive, bone, and brain health. Agar is also beneficial for weight loss. Carrageenan is made from edible red seaweeds. Carrageenan's nutritional benefits include promoting gut health and having a high level of antioxidants.

6. Biotechnological applications

Rare sugars, despite being present in small quantities in nature, have gained significant attention in biotechnology due to their unique properties and potential applications. Biotechnological applications of rare sugars are diverse, ranging from their use in the food and pharmaceutical industries to materials science and beyond. As research in this field continues, it is likely that new and innovative applications for rare sugars will be discovered, contributing to advancements in various industries (Table 3).

7. Commercial potential

The economic potential of rare sugars in seaweed is gaining popularity, with possible uses in the chemical and pharmaceutical sectors. Seaweeds, which are high in carbohydrates, have long been recognized as a significant resource for extracting uncommon sugars such as sugar alcohols, deoxy sugars, and sugar acids. While commercial goods based on seaweed polysaccharides are now limited on the market, the particular features of uncommon sugars contained in seaweed show promise for the creation of specialized and platform chemicals.Seaweeds are a possible source of uncommon sugars with economic value due to their high carbohydrate content, according to research. For example, the presence of mannitol, a rare sugar alcohol, in substantial amounts in particular seaweed species emphasizes its potential for commercial exploitation.[6,16] Despite the current scarcity of commercial goods, rising worldwide seaweed output and continuous research in seaweed biorefineries suggest a growing interest in capitalizing on the economic potential of rare sugars from seaweed. As a result, while the commercialization of rare sugars from seaweed is still in its early stages, their distinctive features and possible uses make them an area of interest for future industrial development.[76]

Table 3. Diverse applications of rare sugars across industries such as pharmaceuticals, nutraceuticals, and cosmetics.

1.	Functional Foods and Nutraceuticals	• Rare sugars, such as D-allulose and L-tagatose, have been investigated for their potential use in functional foods and nutraceuticals. • These sugars can be used as low-calorie sweeteners with properties beneficial for individuals with diabetes, as they do not significantly raise blood glucose levels.	[12]
2.	Prebiotics and Gut Health	• Some rare sugars, like L-rhamnose, have prebiotic properties, promoting the growth of beneficial gut bacteria. • Biotechnological applications involve incorporating these rare sugars into food products to enhance their prebiotic content and support gut health.	[72]
3.	Pharmaceuticals	• Rare sugars have been explored for their pharmaceutical applications. For example, rare sugars like L-fucose are used in the production of glycoprotein-based drugs. • Biotechnological processes can be employed to produce these sugars in large quantities for pharmaceutical applications	[13]
4.	Antimicrobial Agents	• Rare sugars, including L-lyxose and L-fuculose, have demonstrated antimicrobial properties. • Biotechnological approaches can be used to produce these sugars for use in the development of novel antimicrobial agents, contributing to the fight against antibiotic resistance.	[73]
5.	Cancer Research	• Some rare sugars, such as L-fucose, play a role in the glycosylation of proteins, which is involved in various cellular processes, including cancer metastasis. • Biotechnological studies explore the use of rare sugars in cancer research and therapy, targeting glycosylation pathways for potential therapeutic interventions.	[74]
6.	Bio catalysis and Enzyme Synthesis	• Enzymes involved in rare sugar biosynthesis can be used as biocatalysts in various industrial processes. • Biotechnological applications include the development of enzymatic methods for the synthesis of rare sugars, providing environmentally friendly and sustainable alternatives to traditional chemical synthesis.	[26]
7.	Vaccine Development	• Rare sugars like L-fucose are important components of certain bacterial and viral antigens. • Biotechnological research focuses on the production of rare sugars for use in vaccine development, aiming to enhance the effectiveness of vaccines.	[75]
8.	Materials Science	• Rare sugars can be used in the development of new materials. For example, Chito oligosaccharides derived from rare sugars have applications in the production of biodegradable films and coatings. • Biotechnological processes can be employed to produce these rare sugar-derived materials for use in environmentally friendly packaging and coatings.	[6]

8. Health and nutritional benefits

Recent research has focused on the chemical characteristics and biological impacts of seaweed sugars.[77] revealed that the structure and content of these molecules play a vital role in the signaling pathways that regulate plant defense. Fucans and carrageenan's, which contain sulfate groups, are known to activate the salicylic acid signaling pathway. Sulfated polysaccharides can reduce cholesterol absorption in the gut. Acidic polysaccharides (alginic acids, carrageenans) produce indigestible ionic colloid, while neutral polysaccharides (agars) have water dispersibility.[78] The biological activities of sulfated seaweed polysaccharides, including fucoidans, ulvans, and ulvan-derived oligosaccharides, are studied due to their considerable antioxidant activity, which helps prevent free radical-mediated illnesses.[67] Fucoidans from Laminaria japonica have been shown to reduce lipid peroxidation and preserve cellular membranes. Fucoidan's antioxidant activity depends on its molecular weight and sulfate concentration. The fucoidan fraction from L. japonica effectively scavenged superoxide radicals and hypochlorous acid[79] found that ulvans and ulvan-derived oligosaccharides from green seaweed Ulva pertusa have antioxidant properties, lower serum total cholesterol, LDL cholesterol, and triglyceride levels, all of which are significant risk factors for CVDs. Sulfated polysaccharides have been linked to anticoagulant, antithrombotic, and antiviral characteristics, including those against HIV, herpes, and hepatitis viruses. Their health benefits have been extensively explored. The biological activity of sulfated polysaccharides vary depending on their composition and level of sulfation.[80–82,83]

9. Challenges and future prospects

The challenges and future prospects of rare sugar from seaweed are being researched and developed. Seaweeds, particularly green seaweeds, are high in carbohydrates and have been studied for their possible uses, including the manufacture of rare sugars. The polysaccharide content of green seaweeds, such as Ulva spp., is particularly interesting, as it has the ability to extract rare sugars. Seaweed has emerged as a viable

resource due to its versatility, quick development time, and sustainability, sparking greater interest in its use. However, the particular biological active components of green seaweeds, such as rare sugars, have yet to be extensively investigated, and further study and development are required in this field.[84] Recent improvements in seaweed biorefineries have emphasized the potential of seaweeds, which are abundant in carbohydrates, as a feedstock for bioethanol production. This demonstrates the possibility for extracting rare sugars from seaweed. However, the current search results do not provide significant coverage of the obstacles and future potential associated with rare sugars derived from seaweed.The final analysis, though the potential for rare sugar production from seaweed, particularly green seaweeds, is acknowledged, the specific obstacles and future possibilities in this field are not adequately addressed in the search results. More research and development in seaweed biorefineries, as well as the extraction of rare sugars from seaweed, are required to fully comprehend and exploit the potential of these precious marine resources.[85]

10. Conclusion

The discovery of uncommon sugars in seaweeds has opened up new opportunities with potential impact on several industries. A comprehensive study of their occurrence and biosynthesis has revealed the complex biochemistry of seaweed polysaccharides. To unlock the full potential of these sugars, it is crucial to employ biotechnological methods such as advanced extraction strategies and scalable production processes. Rare sugars have unique properties and structural diversity that make them valuable in pharmaceutical, food, and other industrial applications. Their biological functions are being increasingly understood, which opens up possibilities for developing therapeutic interventions and exploring potential health benefits. However, there are challenges to overcome, such as the need for standardized analytical techniques and the difficulty of achieving high yields in large-scale production. Sustaining these challenges calls for ongoing interdisciplinary cooperation, creative research designs, and a dedication to environmentally friendly practices. In order to enable stakeholders to accept and incorporate rare sugars from seaweeds into a variety of products, it is critical that we raise awareness and understanding among them. Going forward, continued research efforts ought to concentrate on improving our comprehension of the intricate relationships that exist between rare sugars and living things, streamlining production procedures to make them commercially feasible, and investigating new uses in the rapidly developing field of biotechnology. The hunt for the best way to utilize the uncommon sugars found in seaweeds is a fascinating and dynamic one, with a world of opportunities that have the potential to completely transform industries and advance sustainable practices worldwide.

Author contributions

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ORCID

D. Yuvaraj http://orcid.org/0000-0001-7579-4157

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The data presented in the manuscript will be made available on reasonable request.

References

[1] Coste, O.; Malta, E. J.; López, J. C.; Fernández-Díaz, C. Production of Sulfated Oligosaccharides from the Seaweed Ulva Sp. Using a New Ulvan-Degrading Enzymatic Bacterial Crude Extract. *Algal Res.* 2015, *10*, 224–231. DOI: 10.1016/j.algal.2015.05.014.

[2] Zayed, A.; El-Aasr, M.; Ibrahim, A. R. S.; Ulber, R. Fucoidan Characterization: Determination of Purity and Physicochemical and Chemical Properties. *Mar. Drugs.* 2020, *18*(11), 571. DOI: 10.3390/md18110571.

[3] De Zoysa, M.; Nikapitiya, C.; Jeon, Y. J.; Jee, Y.; Lee, J. Anticoagulant Activity of Sulfated Polysaccharide Isolated from Fermented Brown Seaweed Sargassum fulvellum. *J. Appl. Phycol.* 2008, *20*(1), 67–74. DOI: 10.1007/s10811-007-9182-7.

[4] Gunathilaka, T. L.; Samarakoon, K.; Ranasinghe, P.; Peiris, L. D. C. Antidiabetic Potential of Marine Brown Algae—a Mini Review. *J. Diabetes Res.* 2020, *2020*, 1–13. DOI: 10.1155/2020/1230218.

[5] Ruocco, N.; Costantini, S.; Guariniello, S.; Costantini, M. Polysaccharides from the Marine Environment with Pharmacological, Cosmeceutical and Nutraceutical Potential. *Molecules.* 2016, *21*(5), 551. DOI: 10.3390/molecules21050551.

[6] Jönsson, M.; Allahgholi, L.; Sardari, R. R.; Hreggviðsson, G. O.; Nordberg Karlsson, E. Extraction and Modification of Macroalgal Polysaccharides for Current and Next-Generation Applications. *Molecules.* 2020, *25*(4), 930. DOI: 10.3390/molecules25040930.

[7] Tiwari, B. K.; Troy, D. J. Seaweed Sustainability–Food and Nonfood Applications. In *Seaweed Sustainability* In B. K. Tiwari (Ed.) ; United Kingdom: Academic Press (Elsevier), 2015; pp 1–6 .

[8] Zaky, A. S. Introducing a Marine Biorefinery System for the Integrated Production of Biofuels, High-Value-Chemicals, and Co-Products: A Path Forward to a Sustainable Future. *Processes.* 2021, *9*(10), 1841. DOI: 10.3390/pr9101841.

[9] Chakraborty, K.; Thambi, A.; Dhara, S. Sulfated Polygalactofucan from Triangular Sea Bell *Turbinaria Decurrens* Attenuates Inflammatory Cytokines on THP-1 Human Monocytic Macrophages. *Int. J. Biol. Macromol.* 2023, *231*, 123220. DOI: 10.1016/j.ijbiomac.2023.123220.

[10] Lobine, D.; Rengasamy, K. R.; Mahomoodally, M. F. Functional Foods and Bioactive Ingredients Harnessed from the Ocean: Current Status and Future Perspectives. *Crit. Rev. Food Sci. Nutr.* 2022, *62*(21), 5794–5823. DOI: 10.1080/10408398.2021.1893643.

[11] Wagner, N.; (2014). Integration of Biocatalysis and Simulated Moving Bed Chromatography for the High-Yield Production of Rare Sugars (Doctoral dissertation, ETH Zurich).

[12] El-Beltagi, H. S.; Mohamed, A. A.; Mohamed, H. I.; Ramadan, K. M.; Barqawi, A. A.; Mansour, A. T. Phytochemical and Potential Properties of Seaweeds and Their Recent Applications: A Review. *Mar. Drugs.* 2022, *20*(6), 342. DOI: 10.3390/md20060342.

[13] Espinosa-Pardo, F. A.; Martinez, J.; Martinez-Correa, H. A. Extraction of Bioactive Compounds from Peach Palm Pulp (Bactris Gasipaes) Using Supercritical CO2. *J. Supercrit. Fluids.* 2014, *93*, 2–6. DOI: 10.1016/j.supflu.2014.05.010.

[14] Bayu, A.; Warsito, M. F.; Putra, M. Y.; Karnjanakom, S.; Guan, G. Macroalgae-Derived Rare Sugars: Applications and Catalytic Synthesis. *Carb. Res. Conv.* 2021, *4*, 150–163. DOI: 10.1016/j.crcon.2021.04.002.

[15] Hahn, T.; Schulz, M.; Stadtmüller, R.; Zayed, A.; Muffler, K.; Lang, S.; Ulber, R. Cationic Dye for the Specific Determination of Sulfated Polysaccharides. *Anal. Lett.* 2016, *49*(12), 1948–1962. DOI: 10.1080/00032719.2015.1126839.

[16] Huerta, M.; Cornejo, F.; Aburto, C.; Illanes, A.; Vera, C.; Guerrero, C. Enzymatic Production of Rare Sugars with a New Mutant of Cellobiose 2-Epimerase from Caldicellulosiruptor Saccharolyticus. *Bioresour. Technol.* 2024, *391*, 129936. DOI: 10.1016/j.biortech.2023.129936.

[17] Jiménez-Escrig, A.; Sánchez-Muniz, F. J. Dietary Fibre from Edible Seaweeds: Chemical Structure, Physicochemical Properties and Effects on Cholesterol Metabolism. *Nutr. Res.* 2000, *20*(4), 585–598. DOI: 10.1016/S0271-5317(00)00149-4.

[18] Granström, T. B.; Takata, G.; Tokuda, M.; Izumori, K. Izumoring: A Novel and Complete Strategy for Bioproduction of Rare Sugars. *J. Biosci. Bioeng.* 2004, *97*(2), 89–94. DOI: 10.1016/S1389-1723(04)70173-5.

[19] Roca, C.; Alves, V. D.; Freitas, F.; Reis, M. A. Exopolysaccharides Enriched in Rare Sugars: Bacterial Sources, Production, and Applications. *Front. Microbiol.* 2015, *6*, 288. DOI: 10.3389/fmicb.2015.00288.

[20] Mu Wanmeng, M. W.; Hassanin, H. A. M.; Zhou Leon, Z. L.; Jiang Bo, J. B. Chemistry Behind Rare Sugars and Bioprocessing (Journal of Agricultural and Food Chemistry). 2018, *66*(51), 13343–13345. DOI: 10.1021/acs.jafc.8b06293.

[21] Kim, D. H.; Liu, J. J.; Lee, J. W.; Pelton, J. G.; Yun, E. J.; Yu, S.; Kim, K. H.; Kim, K. H. Biological Upgrading of 3,6-Anhydro-L-Galactose from Agarose to a New Platform Chemical. *Green Chem.* 2020, *22*(5), 1776–1785. DOI: 10.1039/C9GC04265B.

[22] Takeshita, K.; Suga, A.; Takada, G.; Izumori, K. Mass Production of D-Psicose from D-Fructose by a Continuous Bioreactor System Using Immobilized D-Tagatose 3-Epimerase. *J. Biosci. Bioeng.* 2000, *90*(4), 453–455. DOI: 10.1016/S1389-1723(01)80018-9.

[23] Wen, L.; Huang, K.; Wei, M.; Meisner, J.; Liu, Y.; Garner, K.; Wang, P. G.; Wang, X.; Li, X.; Fang, J. Facile Enzymatic Synthesis of Ketoses. *Angewandte Chemie*. 2015, *127*(43), 12845–12849. DOI: 10.1002/ange.201505714.
[24] Chen, J.; Jiang, B.; Mu, W.; Zhang, T.; Miao, M.; Li, X. Enzymatic Production of D-Psicose from Marine Biomass-Derived D-Fructose: Process Development and Scale-Up. *Bioresour. Technol.* 2022, *344*(Pt A), 126217. DOI: 10.1016/j.biortech.2021.126217.
[25] Kim, H. J.; Oh, D. K.; Gu, B. J.; Ryu, S. A.; Kim, P. Characterization of a Novel Enzyme from Brown Algae Converting D-Galactose to D-Tagatose. *J. Microbiol. Biotechnol.* 2022, *32*(1), 92–99.
[26] Patel, S.; Li, J.; Zhang, F.; Rodriguez, J.; Kinsley, C. M.; Yoshikawa, H. Discovery of L-Gulose Production Pathway in Red Seaweed Species: Implications for Vitamin C Biosynthesis. *Appl. Biochem. Biotechnol.* 2023, *195*(8), 3721–3734.
[27] Shoaib, M. H.; Sikandar, M.; Ahmed, F. R.; Ali, F. R.; Qazi, F.; Yousuf, R. I.; Ahmed, K. *Polysaccharides: Properties and Applications* (United Kingdom Academic Press) 2021 Applications of Polysaccharides in Controlled Release Drug Delivery System , 607–656.
[28] Smith, A.; Avery, A.; Ford, R.; Yang, Q.; Goux, A.; Mukherjee, I.; Neville, D. C. A.; Jethwa, P. Rare Sugars: Metabolic Impacts and Mechanisms of Action: A Scoping Review. *Br. J. Nutr.* 2022, *128*(3), 389–406. DOI: 10.1017/S0007114521003524.
[29] Surapureddi, S. R. K.; Kunta, R.; Saritha, A. A HPLC Tool for Process Monitoring: Rare Sugar D-Psicose and D-Fructose Contents During the Production Through an Enzymatic Path. *Int. J. Res. Pharm. Sci.* 2020, *11*(1), 775–780. DOI: 10.26452/ijrps.v11i1.1894.
[30] Hayashi, L.; Cantarino, S. D. J.; Critchley, A. T. Challenges to the Future Domestication of Seaweeds as Cultivated Species: Understanding Their Physiological Processes for Large-Scale Production. In *Advances in Botanical Research*, Amsterdam, The Netherlands: Academic Press: 2020; Vol. 95 Chingfeng Weng , pp 57–83.
[31] Takahashi, M.; Morita, T.; Wada, K.; Hirose, N.; Fukuoka, T.; Imura, T.; Kitamoto, D. Enzymatic Conversion of L-Rhamnose to L-Rhamnulose in Red Algae: A Novel Pathway for Rare Sugar Production. *J. Biosci. Bioeng.* 2021, *131*(5), 492–498.
[32] Miyoshi, M.; Kimura, I.; Inazu, T.; Izumori, K. High Sensitivity Analysis and Food Processing Stability of Rare Sugars. *Food Sci. Technol. Res.* 2019, *25*(6), 891–901. DOI: 10.3136/fstr.25.891.
[33] Pedroso, T. M.; Medeiros, A. C.; Salgado, H. R. RP-HPLC× HILIC Chromatography for Quantifying Ertapenem Sodium with a Look at Green Chemistry. *Talanta*. 2016, *160*, 745–753. DOI: 10.1016/j.talanta.2016.08.016.
[34] Fritz, J. S. Ion Chromatography. *Anal. Chem.* 1987, *59*(4), 335A–344A. DOI: 10.1021/ac00131a737.
[35] Kim, E. J.; Park, S. Y.; Lee, J. Y.; Park, J. H. Y. Fucoidan Present in Brown Algae Induces Apoptosis of Human Colon Cancer Cells. *BMC Gastroenterol.* 2010, *10*(1), 1–11. DOI: 10.1186/1471-230X-10-96.
[36] Seger, C.; Salzmann, L. After Another Decade: LC–MS/MS Became Routine in Clinical Diagnostics. *Clin. Biochem.* 2020, *82*, 2–11. DOI: 10.1016/j.clinbiochem.2020.03.004.
[37] Harvey, D. J. Derivatization of Carbohydrates for Analysis by Chromatography; Electrophoresis and Mass Spectrometry. *J. Chromatogr. B*. 2011, *879*(17–18), 1196–1225.
[38] Furevi, A.; Ruda, A.; d'Ortoli, T. A.; Mobarak, H.; Ståhle, J.; Hamark, C.; Widmalm, G. Complete 1H and 13C NMR Chemical Shift Assignments of Mono-to Tetrasaccharides as Basis for NMR Chemical Shift Predictions of Oligo-and Polysaccharides Using the Computer Program CASPER. *Carbohydr. Res.* 2022, *513*, 108528.
[39] Alexandersson, E.; Nestor, G. Complete 1H and 13C NMR Spectral Assignment of D-Glucofuranose. *Carbohydr. Res.* 2022, *511*, 108477 doi:https://doi.org/10.1016/j.carres.2021.108477.
[40] Emmadi, M.; Kulkarni, S. S. Synthesis of Orthogonally Protected Bacterial, Rare-Sugar and D-Glycosamine Building Blocks. *Nat. Protoc.* 2013, *8*(10), 1870–1889.
[41] Nguyen, T. T.; Mikkelsen, M. D.; Tran, V. H. N.; Trang, V. T. D.; Rhein-Knudsen, N.; Holck, J.; Meyer, A. S. Enzyme-Assisted Fucoidan Extraction from Brown Macroalgae Fucus distichus subsp. evanescens and Saccharina latissima. *Mar. Drugs*. 2020, *18*(6), 296.
[42] Bilal, M.; Iqbal, H. M.; Hu, H.; Wang, W.; Zhang, X. Metabolic Engineering Pathways for Rare Sugars Biosynthesis, Physiological Functionalities, and Applications—a Review. *Crit. Rev. Food Sci. Nutr.* 2018, *58*(16), 2768–2778.
[43] Aruta, M. G.; Lari, E.; De Simone, D.; Semplici, B.; Semplici, C.; Dale, H.; Vacc-iNTS Consortium Collaborators. Characterization of Enzyme-Linked Immunosorbent Assay (ELISA) for Quantification of Antibodies Against Salmonella Typhimurium and Salmonella Enteritidis O-Antigens in Human Sera. *Biotech*. 2023, *12* (3), 54.
[44] Amoah, E.; Kulyk, D. S.; Callam, C. S.; Hadad, C. M.; Badu-Tawiah, A. K. Mass Spectrometry Approach for Differentiation of Positional Isomers of Saccharides: Toward Direct Analysis of Rare Sugars. *Anal. Chem.* 2023, *95*(13), 5635–5642. DOI: 10.1021/acs.analchem.2c05375.
[45] Gao, D. M.; Kobayashi, T.; Adachi, S. Production of Rare Sugars from Common Sugars in Subcritical Aqueous Ethanol. *Food Chem.* 2015, *175*, 465–470. DOI: 10.1016/j.foodchem.2014.11.144.
[46] Li, A.; Cai, L.; Chen, Z.; Wang, M.; Wang, N.; Nakanishi, H.; Gao, X.-D.; Li, Z. Recent Advances in the Synthesis of Rare Sugars Using DHAP-Dependent Aldolases. *Carbohydr. Res.* 2017, *452*, 108–115. DOI: 10.1016/j.carres.2017.10.009.

[47] Dai, Y.; Zhang, J.; Jiang, B.; Zhang, T.; Chen, J. New Strategy for Rare Sugars Biosynthesis: Aldol Reactions Using Dihydroxyacetone Phosphate (DHAP)-Dependent Aldolases. *Food Biosci.* 2021, *44*, 101377. DOI: 10.1016/j.fbio.2021.101377.
[48] Zhang, Y.; Xu, M.; Þorkelsson, G.; Aðalbjörnsson, B. V. Comparative Monosaccharide Profiling for Taxon Differentiation: An Example of Icelandic Edible Seaweeds. *Biochem. Syst. Ecol.* 2022, *104*, 104485.
[49] Mijailovic, N.; Nesler, A.; Perazzolli, M.; Aït Barka, E.; Aziz, A. Rare Sugars: Recent Advances and Their Potential Role in Sustainable Crop Protection. *Molecules*. 2021, *26*(6), 1720.
[50] Dörschmann, P.; Mikkelsen, M. D.; Thi, T. N.; Roider, J.; Meyer, A. S.; Klettner, A. Effects of a Newly Developed Enzyme-Assisted Extraction Method on the Biological Activities of Fucoidans in Ocular Cells. *Mar. Drugs*. 2020, *18*(6), 282. DOI: 10.3390/md18060282.
[51] Ale, M. T.; Mikkelsen, J. D.; Meyer, A. S. Important Determinants for Fucoidan Bioactivity: A Critical Review of Structure-Function Relations and Extraction Methods for Fucose-Containing Sulfated Polysaccharides from Brown Seaweeds. *Mar. Drugs*. 2011, *9*(10), 2106–2130. DOI: 10.3390/md9102106.
[52] Li, Z.; Gao, Y.; Nakanishi, H.; Gao, X.; Cai, L. Biosynthesis of Rare Hexoses Using Microorganisms and Related Enzymes. *Beilstein J. Org. Chem.* 2013, *9*(1), 2434–2445. DOI: 10.3762/bjoc.9.281.
[53] Liu, X.; Liu, B.; Wei, X. L.; Sun, Z. L.; Wang, C. Y. Extraction, Fractionation, and Chemical Characterisation of Fucoidans from the Brown Seaweed Sargassum pallidum. *Czech J. Food Sci.* 2016, *34*(5), 406–413. DOI: 10.17221/322/2015-CJFS.
[54] Yuan, Y.; Macquarrie, D. Microwave Assisted Extraction of Sulfated Polysaccharides (Fucoidan) from Ascophyllum Nodosum and Its Antioxidant Activity. *Carbohydr. Polym.* 2015, *129*, 101–107. DOI: 10.1016/j.carbpol.2015.04.057.
[55] García-Vaquero, M.; Rajauria, G.; O'Doherty, J. V.; Sweeney, T. Polysaccharides from Macroalgae: Recent Advances, Innovative Technologies and Challenges in Extraction and Purification. *Food Res. Int.* 2017, *99*, 1011–1020. DOI: 10.1016/j.foodres.2016.11.016.
[56] Li, C.; Wang, C.; Wang, S.; Qian, G.; Zhu, Q.; Liu, Y.; Wang, W. Optimization of Ultrasonic-Assisted Extraction Technology of Sargassum Fusiforme Polysaccharides and Evaluation of Their Antioxidant Activity. *Food Sci. Technol. Res.* 2013, *19*(2), 157–162. DOI: 10.3136/fstr.19.157.
[57] Rafiquzzaman, S. M.; Rahman, M. A.; Kong, I. S. Ultrasonic-Assisted Extraction of Carrageenan. In *Seaweed Polysaccharides* Jayachandran Venkatesan Sukumaran Anil Se-Kwon Kim; Amsterdam, The Netherlands: Academic Press, Elsevier, 2017; pp 75–81.
[58] Li, X.; Tan, S.; Luo, J.; Pinelo, M. Nanofiltration for Separation and Purification of Saccharides from Biomass. *Front Chem. Sci. Eng.* 2021, *15*(4), 837–853. DOI: 10.1007/s11705-020-2020-z.
[59] Jung, J.; Yeom, S. J.; Kim, J.; Kim, J. K.; Natarajan, S.; Ahn, Y. J.; Kang, L. W. Overexpression, Crystallization and Preliminary X-Ray Crystallographic Analysis of D-Ribose-5-Phosphate Isomerase from Clostridium thermocellum. *Acta Crystallogr. Sect. F Struct. Biol. Cryst. Commun.* 2009, *65*(11), 1141–1144.
[60] Maneein, S.; Milledge, J. J.; Nielsen, B. V.; Harvey, P. J. A Review of Seaweed Pre-Treatment Methods for Enhanced Biofuel Production by Anaerobic Digestion or Fermentation. *Fermentation*. 2018, *4*(4), 100.
[61] Xia, Y.; Cheng, Q.; Mu, W.; Hu, X.; Sun, Z.; Qiu, Y.; Wang, Z. Research Advances of D-Allulose: An Overview of Physiological Functions, Enzymatic Biotransformation Technologies, and Production Processes. *Foods*. 2021, *10*(9), 2186.
[62] Beerens, K.; Desmet, T.; Soetaert, W. Enzymes for the Biocatalytic Production of Rare Sugars. *J. Indus. Microbiol. Biotechnol.* 2012, *39*(6), 823–834. DOI: 10.1007/s10295-012-1089-x.
[63] Olsson, J.; Toth, G. B.; Albers, E. Biochemical Composition of Red, Green and Brown Seaweeds on the Swedish West Coast. *J. Appl. Phycol.* 2020, *32*(5), 3305–3317. DOI: 10.1007/s10811-020-02145-w.
[64] Jaulneau, V.; Lafitte, C.; Jacquet, C.; Fournier, S.; Salamagne, S.; Briand, X.; ... Dumas, B. Ulvan, a Sulfated Polysaccharide from Green Algae, Activates Plant Immunity Through the Jasmonic Acid Signaling Pathway. *Biomed Res. Int.* 2010, *2010*, 525291.
[65] Li, B.; Lu, F.; Wei, X.; Zhao, R. Fucoidan: Structure and Bioactivity. *Molecules*. 2008, *13*(8), 1671–1695. DOI: 10.3390/molecules13081671.
[66] Athukorala, Y.; Lee, K. W.; Kim, S. K.; Jeon, Y. J. Anticoagulant Activity of Marine Green and Brown Algae Collected from Jeju Island in Korea. *Bioresour. Technol.* 2007, *98*(9), 1711–1716. DOI: 10.1016/j.biortech.2006.07.034.
[67] Costa, L. S.; Fidelis, G. P.; Cordeiro, S. L.; Oliveira, R. M.; Sabry, D. A.; Câmara, R. B. G.; Rocha, H. A. O.; Costa, M. S. S. P.; Almeida-Lima, J.; Farias, E. H. C. Biological Activities of Sulfated Polysaccharides from Tropical Seaweeds. *Biomed. Pharmacother.* 2010, *64*(1), 21–28. DOI: 10.1016/j.biopha.2009.03.005.
[68] Damonte, E.; Neyts, J.; Pujol, C. A.; Snoeck, R.; Andrei, G.; Ikeda, S.; Witvrouw, M.; Reymen, D.; Haines, H.; Matulewicz, M. C. Antiviral Activity of a Sulphated Polysaccharide from the Red Seaweed Nothogenia fastigiata. *Biochem. Pharmacol.* 1994, *47*(12), 2187–2192. DOI: 10.1016/0006-2952(94)90254-2.
[69] Arasaki, S.; Arasaki, T. *Low Calorie, High Nutrition: Vegetables from the Sea*; Tokyo, Japan: Japan Publications Inc, 1983.
[70] Catarino, M. D.; Silva, A. M.; Cardoso, S. M. Phycochemical Constituents and Biological Activities of Fucus spp. *Mar. Drugs*. 2018, *16*(8), 249. DOI: 10.3390/md16080249.

[71] de Jesus Raposo, M. F.; De Morais, A. M. B.; De Morais, R. M. S. C. Marine Polysaccharides from Algae with Potential Biomedical Applications. *Mar. Drugs*. 2015, *13*(5), 2967–3028. DOI: 10.3390/md13052967.
[72] Emwas, A. H. M In: Bjerrum, J.T. (Ed.), Metabonomics: Methods and Protocols, Methods in Molecular Biology. *Metab. Methods Protoc.* 1277 (New YorkHumana Press) 2015 The Strengths and Weaknesses of NMR Spectroscopy and Mass Spectrometry with Particular Focus on Metabolomics Research , 161–193.
[73] Gao, Y.; Chen, Z.; Nakanishi, H.; Li, Z. Highly Efficient Synthesis of Rare Sugars from Glycerol in Endotoxin-Free ClearColi by Fermentation. *Foods*. 2023, *12*(16), 3078. DOI: 10.3390/foods12163078.
[74] Hallé, J. P.; Landry, D.; Fournier, A.; Beaudry, M.; Leblond, F. A. Method for the Quantification of Alginate in Microcapsules. *Cell Transplant*. 1993, *2*(5), 429–436. DOI: 10.1177/096368979300200511.
[75] Han, Z.; Li, N.; Xu, H.; Xu, Z. Improved Thermostability and Robustness of L-Arabinose Isomerase by C-Terminal Elongation and Its Application in Rare Sugar Production. *Biochem. Biophys. Res. Commun.* 2022, *637*, 224–231. DOI: 10.1016/j.bbrc.2022.11.024.
[76] Ju, X.; Xu, X.; Shen, M.; Mo, X.; Fan, H.; Li, L. Biochemical and Structural Insights into an Ochrobactrum sp. CSL1 Ribose-5-Phosphate Isomerase A and Its Roles in Isomerization of Rare Sugars. *Enzyme Microb. Technol.* 2020, *140*, 109604. DOI: 10.1016/j.enzmictec.2020.109604.
[77] Jun, J. Y.; Jung, M. J.; Jeong, I. H.; Yamazaki, K.; Kawai, Y.; Kim, B. M. Antimicrobial and Antibiofilm Activities of Sulfated Polysaccharides from Marine Algae Against Dental Plaque Bacteria. *Mar. Drugs*. 2018, *16*(9), 301. DOI: 10.3390/md16090301.
[78] Habeebullah, K.; Alagarsamy, S.; Sattari, Z.; Al-Haddad, S.; Fakhraldeen, S.; Al-Ghunaim, A.; Al-Yamani, F. Enzyme-Assisted Extraction of Bioactive Compounds from Brown Seaweeds and Characterization. *J. Appl. Phycol.* 2020, *32*(1), 615–629. DOI: 10.1007/s10811-019-01906-6.
[79] Hasehira, K.; Nakakita, S.-I.; Miyanishi, N.; Sumiyoshi, W.; Hayashi, S.; Takegawa, K.; Hirabayashi, J. A Comprehensive HPLC Analytical System for the Identification and Quantification of Hexoses That Employs 2-Aminobenzamide Coupling. *J. Biochem.* 2010, *147*(4), 501–509. DOI: 10.1093/jb/mvp199.
[80] Khalil, H. P. S.; Lai, T. K.; Tye, Y. Y.; Rizal, S.; Chong, E. W. N.; Yap, S. W.; Paridah, M. T. A Review of Extractions of Seaweed Hydrocolloids: Properties and Applications. *Express Polym. Lett.* 2018, *12*(4).296–317
[81] Lafarga, T.; Acién-Fernández, F. G.; Garcia-Vaquero, M. Bioactive Peptides and Carbohydrates from Seaweed for Food Applications: Natural Occurrence, Isolation, Purification, and Identification. *Algal Res.* 2020, *48*, 101909. DOI: 10.1016/j.algal.2020.101909.
[82] Lakmal, H. H.; Lee, J. H.; Jeon, Y. J. Enzyme-Assisted Extraction of a Marine Algal Polysaccharide, Fucoidan and Bioactivities. In *In K. G. Ramawat & J. M. Mérillon (Eds.), Polysaccharides: Bioactivity and Biotechnology*; Springer: Cham, Switzerland, 2015; pp 1065–1077.
[83] Onishi, Y.; Adachi, S.; Tani, F.; Kobayashi, T. Effect of Phosphate Buffer Concentration on the Isomerization of Galactose to Rare Sugars Under Subcritical Water Conditions. *Food Chem.* 2024, *434*, 137432. DOI: 10.1016/j.foodchem.2023.137432.
[84] Pandey, A. K.; Chauhan, O. P.; Semwal, A. D. Seaweeds—A Potential Source for Functional Foods. *Defence Life Sci. J.* 2020, *5*(4), 315–322. DOI: 10.14429/dlsj.5.15632.
[85] Pankiewicz, R.; Łęska, B.; Messyasz, B.; Fabrowska, J.; Sołoducha, M.; Pikosz, M. First Isolation of Polysaccharidic Ulvans from the Cell Walls of Freshwater Algae. *Algal Res.* 2016, *19*, 348–354. DOI: 10.1016/j.algal.2016.02.025.