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Harnessing Lactic Acid Bacteria: A Pathway to Functional Food from Marine Seaweed

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ABSTRACT

There is a growing recognition that food form and supply affect health. This has resulted in the development of functional food that aims to improve health and reduce illnesses. Seaweeds are an important source of new bioactive compounds. However, it is difficult to prove that these compounds have defined health benefits since their effects are limited if used for a short time but significant if consumed daily with the diet. Lactic acid bacteria (LAB) represent an important category of probiotics, especially marine LAB adapted to harsh conditions, which explains their unique byproducts and ability to ferment marine biomass. Seaweed is a cost-effective source of protein. Consuming seaweed fibers regularly boosts health. They don't require arable land or freshwater, making them a suitable substrate for fermentation. Seaweed smell precludes mass manufacture. Thus, probiotics-fermented seaweed is gaining popularity since it improves shelf life, safety, nutritional value, odor, and micronutrient bioavailability and further enhances the nutritional value.

INTRODUCTION

In these modern days, the prevalence of life-threatening diseases and malnutrition on a global scale is largely attributed to the adoption of unhealthy dietary patterns and sedentary lifestyles. The growing recognition of the significant effects of food consumption and proper nutrient intake on human health, as well as their role in mitigating the risk of diseases, along with recent technological advancements, has resulted in several nutritional discoveries and product innovations. Natural bioactive compounds, in particular, which are thought to have a variety of beneficial impacts on human health, have led to the emergence of new and ongoing areas of scientific investigation and huge advances in nutritional knowledge **(Fardet & Rock, 2014)**.

On the other side, there is a rising awareness that the food form and dietary source a person consumes may impact their overall health. The importance of food and food additives as a key factor in improving health has been recognized, starting the development of a new class of food known as functional food. The functional food main concept is to improve the body's overall condition while lowering the risk of disease and illness. This implies that bioactive compounds existing naturally or added to food possess the potential to confer a diverse array of health advantages that extend beyond the food's fundamental nutritional value **(Peñalver *et al*., 2020)**.

The marine ecosystems possess a remarkable level of biodiversity, rendering them a valuable reservoir of novel nutrients and bioactive compounds, such as sterols, proteins, polyunsaturated fatty acids (PUFAs), polysaccharides, and pigments. These compounds exhibit a promising potential as functional food additives due to their beneficial physiological and pharmacological properties, including anticancer, anti-inflammatory, and anticoagulant activities **(Ghosh *et al*., 2022)**.

Marine species inhabit a complex ecosystem where they are susceptible to challenging situations. To acclimate to these distinctive environmental conditions, organisms undergo the synthesis of a diverse array of secondary metabolites and bioactive compounds that possess distinct characteristics and cannot be obtained from alternative organisms **(Ghosh *et al*., 2022)**. Moreover, the exploration of novel physiologically active compounds in the marine environment is a continuous and endless area of research, owing to its great taxonomic diversity

The marine-based functional food bioactive compounds can be derived from various sources in the marine habitat, including marine plants, sponges, and microorganisms, as each has its own set of bioactive compounds and bio-molecules. However, it is difficult to demonstrate that these natural bioactive compounds have defined beneficial health effects on the human or animal body, as the impact of bioactive compounds on the consumer body may be limited if used for a short period of time. Still, they may have a significant impact on human health if consumed on a daily basis as part of the diet throughout life **(Kim & Dewapriya, 2013)**.

Marine seaweed hold significant importance as a marine organism due to its status as a valuable reservoir of natural antimicrobial and antioxidant compounds. Additionally, they possess significant quantities of vitamins B12, A, E, D, and C, as well as niacin, pantothenic acid, riboflavin, folic acid, and minerals such as phosphorus, calcium, potassium, iodine, and sodium. Furthermore, it has been demonstrated that polysaccharides derived from seaweed possess diverse biological properties that hold considerable therapeutic implications in addition to their widely recognized role as a source of prebiotics and dietary fiber. It has been shown that consuming seaweed fibers consistently over an extended period of time increases stool volume, lowers the risk of colon cancer, and encourages the growth of beneficial gut bacteria **(Peñalver *et al*., 2020)**. Simultaneously, seaweed possesses the advantageous characteristic of not necessitating arable land or freshwater while exhibiting a substantial nutritional and bioactive content. As a result, it holds a considerable potential as a substrate for fermentation and the extraction of bioactive compounds. Consequently, there is a significant increase in the recognition of marine seaweed's significance as a valuable source of marine functional foods and new health components.

Lactic acid bacteria (LAB) are crucial in preparing functional food since they make up a very important group of probiotic bacteria, and they are already used in many probiotic food products. These probiotic bacteria are nonpathogenic, bile tolerant, acid-resistant, and they produce antimicrobial compounds, such as hydrogen peroxide, organic acids, and bacteriocins **(Kimoto-Nira *et al*., 2020)**. Therefore, there is a continuous need for new LAB strains that can be employed in manufacturing or extracting bioactive compounds and preparing fermented and marine functional foods. These new strains can be obtained from previously untapped natural biological niches that are still unexploited such as unique marine habitats.

Therefore, this review aimed to highlight the significance of LAB with probiotic traits and novel strains from the marine habitat as sources of functional ingredients and health benefits. Moreover, it emphasizes the importance of marine LAB in developing environmentally friendly processing techniques to extract bioactive compounds from seaweed through the fermentation and preparation of marine functional food. Finally, the application of the functional additives in food, feed, and nutraceutical industries.

1. Lactic acid bacteria (LAB)

1.1. Classification of LAB

LAB have been employed in the process of food fermentation over a span of approximately 4000 years, owing to their numerous advantageous properties in promoting human health. LAB exhibit a promising potential as a biotechnology option, offering unexpected health advantages in the functional food, meat, and dairy industries. At the same time, the increasing demand for functional food and its related health advantages has led to an increased interest in LAB-based probiotics, bacteriocins, and exopolysaccharides **(Hamed & Elattar, 2013; Linares *et al*., 2017)**.

LAB are common microbes that thrive in high-carbohydrate environments, such as plants, fermented foods, and human, terrestrial, and marine animal mucosal surfaces. They may be found in both human and animal bodies as part of the natural microbiota, which is an ecosystem made up of multiple bacterial species and strains that normally inhabit the gastrointestinal and urinogenital tracts **(Raj *et al*., 2021)**.

The LAB species are taxonomically classified into two distinct phyla, namely Firmicutes and Actinobacteria. Within the Firmicutes phylum, LAB are classified under the order Lactobacillales, which include the genera *Lactobacillus, Leuconostoc, Streptococcus, Pediococcus, Tetragenococcus, Symbiobacterium, Aerococcus, Alloiococcus, Carnobacterium, Weissella, Lactococcus, Enterococcus, Oenococcus* and *Vagococcus.* All of them have low guanine-cytosine (GC) content (< 50%). On the contrary, within the Actinobacteria phylum, LAB belong to the genera *Bifidobacterium* and *Atopobium* with a higher GC content **(Wedajo, 2015)**.

LAB represent a wide group of bacteria that share many common characteristics. They comprise a clade of Gram-positive, non-spore-forming, non-motile, catalase-negative, acid-tolerant rods or cocci, aerotolerant, facultative anaerobic or microaerophilic microorganisms that are linked together by their metabolic and physiological features as they all produce lactic acid as the end product of the fermentation process **(Lima *et al*., 2020)**. They grow optimally at 30– 40°C, but certain strains can thrive at temperatures as low as 5°C or as high as 45°C **(Lima *et al*., 2020)**.

This bacterial group has a remarkable ability to break down a wide range of carbohydrates and related substances. Based on the end product of carbohydrate metabolism, LAB can be classified into two groups, namely, homo-fermentative or hetero-fermentative microorganisms **(Ribeiro *et al*., 2014)**. The homo-fermentative group employs the glycolytic pathway to transform a carbon source into lactic acid, which serves as the primary or exclusive metabolic end product. In contrast, the hetero-fermentative group employs the phosphoketolase pathway to generate equimolar quantities of lactate, carbon dioxide, ethanol, or acetate from glucose. The emergence of new insights and applications for LAB has been facilitated by advancements in genetics, molecular biology, physiology, and biochemistry, alongside the discovery and publication of complete genome sequences for numerous LAB strains. Consequently, a diverse range of commercial cultures with desirable properties, including starter, functional, bio-protective, and probiotic cultures, have been successfully introduced to the market **(Bintsis, 2018)**.

1.2. Significance of LAB

LAB members are critical to the preservation and manufacture of fermented foods and drinks, as well as the enhancement of food properties such as flavor and texture **(Landete, 2017)**. These microorganisms play a significant role in the maintenance of human and animal health by collaborating with other intestinal bacteria to metabolize biogenic amines, lactose, and allergenic compounds, ultimately producing short-chain fatty acids, organic acids, and gases **(Capozzi *et al*., 2012)**.

The consumption of LAB through food products has several beneficial effects on the gastrointestinal tract of the consumer, including improved lactose malabsorption, normal insulin levels in the blood, post-operative pouchitis, relief from viral and drug-induced diarrhea and inflammatory bowel disease **(Guandalini *et al*., 2015)**. Moreover, they enhance blood pressure, improve fatty acid absorption in the intestine, and have antineoplastic effects on human cell lines **(Khalesi *et al*., 2014)**.

They boost health by the production of several compounds, such as antioxidants, vitamins, enzymes, organic acids (namely lactic and acetic acids), bacteriocins, and other antimicrobial compounds **(Mokoena *et al.*, 2016)**. All these characteristics enable intestinal LAB to function as an essential mechanism for metabolizing and detoxifying foreign chemicals that enter the body and provide them with a competitive advantage over other microbes.

The human digestive tract is a complicated ecosystem populated by bacteria from over 500 species. 20 genera among these, including LAB are dominant. It is very critical to maintain intestinal homeostasis and microbial balance between all these bacterial species **(Rajilić-Stojanović & De Vos, 2014)**. There is a rising interest in new LAB species in order to learn more about the potential health benefits they can provide **(Quinto *et al.*, 2014)**. Fig. (1) depicts the diverse applications and functional components of LAB.

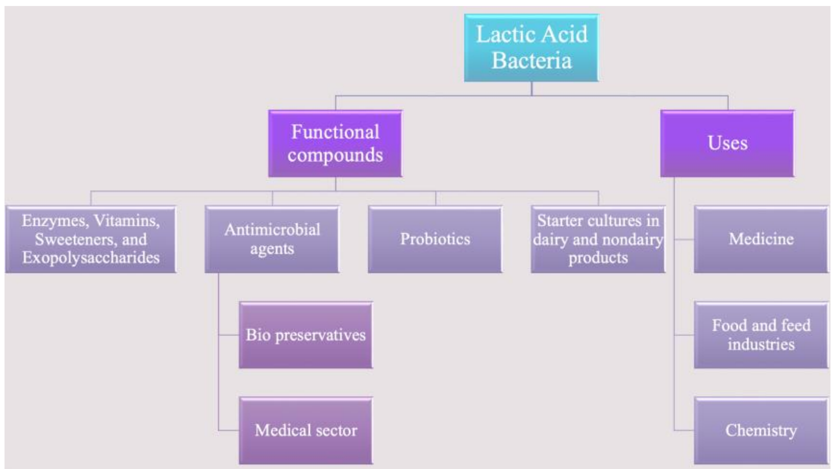

Fig. 1. Uses and functional ingredients of LAB

LAB strains are widely recognized as significant members utilized in the food and feed sectors. Moreover, LAB have been employed in the preservation of food, as well as in the modification of organoleptic attributes, including flavor and texture. Furthermore, LAB strains are present in a diverse range of dairy products, such as yogurt, fermented milk, and cheese, fermented vegetables including olives and sauerkraut, as well as fermented meats like salami, sourdough bread, and various other food products. Additionally, in the contemporary industry, LAB play a crucial role in the process of synthesizing chemicals, medications, and several other valuable compounds **(Raj *et al.*, 2021)**.

1.3. Marine LAB

Marine LAB are a very important category in the LAB world due to their numerous industrial and pharmaceutical applications and their substantial environmental function in the transformation of organic material in marine sediments. Despite their significance, only a few studies have addressed marine LAB **(Otaru *et al.*, 2021; Sakkaa *et al.*, 2022; Zaghloul & Ibrahim, 2022)**.

The fundamental distinction between marine and terrestrial LAB can be stated in marine LAB's strong endurance to extreme environmental conditions that characterize the marine environments, which may explain the unique attributes of the by-products derived from marine LAB **(Abuohashish *et al*., 2022; Zaghloul *et al*., 2023a)**. They include genera such as *Marinilactibacillus psychrotolerans*, *Halolactibacillus halophilus*, *H. miurensis*, *H. alkaliphilus* and *Alkalibacterium psychrotolerans.*

Marine LAB have demonstrated their importance in various fields, including fish and animal health, the food industry, biotechnological applications, and the development of biopolymers with unique structural and biological properties. In addition, their capability to thrive in marine physicochemical conditions enhances their competitive advantage against terrestrial LAB, at least from an industrial standpoint. For example, in lactic acid production, *H. halophilus* is preferred over commonly used LAB strains due to their ability to withstand higher levels of salt and pH values, which is expected to reduce contamination difficulties during processing **(Calabia *et al*., 2011)**.

The importance of marine LAB in the food industry cannot be overstated. The quality of the starting culture, for example, is critical to the success of the cheese-making process. *Lactococcus lactis* is an essential component of the so-called cheese mesophilic cultures. However, *Lc. lactis* development is inhibited by merely a 4% NaCl concentration in the culture media, implying that in cheeses like blue, parmesan, or cheddars with a final salt content of more than 5%, the starter cultures will stop growing **(Dorau *et al*., 2021)**. Halotolerant *Lc. lactis* subsp. lactis strains, conversely, have been isolated from marine environments (from the digestive tracts of coastal fish). These strains can thrive in a medium containing up to 6% salt **(Melgar-Lalanne *et al*., 2015)**. As a result, they can be beneficial for the development of cheese technology and other marine food products. Furthermore, promising results have been obtained regarding using marine LAB as a probiotic in fish aquaculture, which could be a way for the rapid development of the marine LAB market **(Li *et al*., 2018)**.

Aquaculture has emerged as a significant economic contributor in numerous countries. As a result, in industrial-scale production facilities where fish and shellfish are subjected to adverse conditions, the occurrence of diseases and deterioration of environmental conditions is a common phenomenon, causing large economic losses. The utilization of diverse medication has been employed in the past decade to address the prevention or the control of diseases in aquaculture. Nevertheless, researchers have explored the efficacy of antimicrobial medications as a preventive strategy, considering the substantial evidence of the emergence of antibiotic resistance in pathogenic microbes **(Fox *et al*., 2020)**.

Probiotics, or beneficial bacteria that control pathogens through various mechanisms, are increasingly being seen as an alternative to antibiotic treatment, and a demand for probiotics in the aquaculture industry for eco-friendly and sustainable aquaculture has increased dramatically in recent years. However, due to their fragility and lack of proven immunity, larval cultures should be handled with caution. The larvae's endogenous microbial community is influenced by both the egg and the ambient microbial composition. The larval digestive tract is immature when it hatches, the gall bladder has yet to form, and bile is discharged later in development. As a result, the probiotics are not required to pass through an acidic environment on their way to the gut, and, unlike the adult probiotics, they are not required to be acid and bile-tolerant. To enhance the competitive advantage of probiotics, early administration, particularly before the first meal, increases the likelihood of establishing a persistent population **(Jahangiri & Esteban, 2018)**.

All these indicate that marine LAB's future uses as a functional ingredient in food and feed are promising, thanks to their distinct characteristics. However, increasing the number of research is regarded as a significant step forward in gaining a better understanding of their significance in marine environments and improving our knowledge of their physical and biochemical characteristics **(Raj *et al*., 2021)**.

2. Role of LAB fermentation in functional food preparation

The term "functional food" was initially introduced in the 1980s in Japan during a period when the Japanese government directed its research efforts toward the study of functional food, alternatively referred to as foods for specific health uses (FOSHU). This category encompasses food products that have been enriched with specific constituents that are known to have advantageous physiological effects. The definition of functional foods has undergone subsequent modifications **(Martirosyan *et al*., 2015)**. However, according to the Functional Food Center, a workable definition could be "natural or processed foods that contain biologically active compounds that, in defined, effective, and non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers for the prevention, management, or treatment of chronic disease or its symptoms."

The process of LAB fermentation involves the metabolic pathways responsible for the production of lactic acid, ethanol, and acetic acid, along with the synthesis of bio-preservatives and the enhancement of nutritional enrichment. These products enhance the functional attributes and extend the shelf life of food items through the elimination of potentially harmful microbes and are thus used in several food sectors to produce fermented functional food. In addition, bacteriocins and exopolysaccharides derived from LAB have shown potential in the fields of medicine, pharmaceuticals, and diagnostics **(Raj *et al*., 2021)**.

One way in which the nutritional qualities of functional food are influenced is through the impact of LAB fermentation on the bioaccessibility, bioavailability, and digestibility of different nutrients. Bioaccessibility is the term used to describe the quantity of a nutrient that is released from its food source and may be absorbed by the body **(Rousseau *et al*., 2019)**. Bioavailability and digestibility are terms used to describe the degree to which a nutrient is absorbed, utilized, or stored in relation to its intake. For example, certain minerals, such as iron, zinc, calcium, phosphorus, and copper, can be present in certain food items. However, their bioavailability may be hindered due to their association with anti-nutrient complexes, which impede their absorption by the body.

The process of fermentation has the potential to facilitate the breakdown of these complexes and subsequently liberate these minerals, hence enhancing their bioaccessibility for absorption. In contrast to bioaccessibility, the bioavailability and digestibility of nutrients can also be influenced by an individual's nutritional condition. An individual who has sufficient iron levels will have reduced the absorption of dietary iron compared to an individual who is iron-deficient **(Franz *et al*., 2014)**.

Fermentation plays a crucial role in enhancing the bioavailability of minerals and facilitating digestion, especially in diets that are predominantly plant-based. The potential impact of enhanced bioavailability of grains and legumes fermented by LAB on micronutrient consumption may not be significant in high-income countries, as these nations often fortify certain foods to prevent mineral deficiencies, and nutrient imbalances are uncommon. In contrast, diets in low- and middle-income countries tend to predominantly consist of fundamental food items, exhibiting a reduced range of diversity. The dietary phytate content in certain regions may have significant implications for the occurrence of micronutrient deficiencies. Based on a comprehensive evaluation conducted in 2014 about fermented foods in Africa, it was determined that the consumption of foods rich in LAB is crucial for communities experiencing malnutrition or impacted by diarrheal diseases **(Franz *et al*., 2014)**. The focal point of their argument revolves around the possibility of conventional meals to function as probiotics through the incorporation of specific combinations of health-promoting bacteria **(Hess, 2020)**.

LAB fermentation of cereals has the potential to provide benefits for those diagnosed with celiac disease (CD). Celiac disease is a chronic autoimmune disorder characterized by the detrimental effects of gliadin, a component of gluten or wheat proteins, on the villi of the intestines. It is estimated to impact approximately 1% of the global population **(Kelly *et al*., 2015)**. In individuals with CD, the immune response triggered by gluten ingestion leads to the occurrence of inflammation and subsequent impairment of the small intestine, which serves as the primary site for nutritional absorption **(Leonard *et al*., 2017)**. Overall, nutrient absorption is hampered by CD damage **(Wierdsma *et al*., 2013)**. The sole therapeutic approach for CD at present is a gluten-free dietary regimen **(Leonard *et al*., 2017)**.

Some people who do not test positive for CD but experience considerable abdominal pain as a result of a systemic immune response to wheat may benefit from a gluten-free diet **(Rizzello *et al*., 2016)**. These individuals may have non-celiac gluten sensitivity (NCGS) **(Uhde *et al*., 2016)**.

The prevalence of both CD and NCGS has led to a rise in scientific investigations and advancements in the field of gluten-free bakery products, including bread **(Rizzello *et al*., 2016)**. The utilization of LAB fermentation has the potential to serve as a valuable technique in the development of gluten-free baked products that meet acceptable standards. Multiple studies have indicated that the process of sourdough fermentation leads to the degradation of gluten, resulting in a natural reduction in gluten levels in bread **(Gobbetti *et al*., 2018; Muir *et al*., 2019)**. Certain strains of LAB exhibit proteolytic activity, enabling them to break down gluten enzymatically. This property has the potential to aid individuals with CD and NCGS in tolerating sourdough bread. Nevertheless, it is important to note that this effect seems to be strain-specific, as it is not observed in all sourdough fermentations **(Muir *et al*., 2019)**. Moreover, the amounts of phosphorus, calcium, magnesium, potassium, iron, and zinc in fermented bread were found to be similar to or much higher than the levels observed in conventional gluten-free bread **(Rizzello *et al*., 2016)**.

The impacts of LAB fermentation on the bioavailability and digestibility of legumes exhibit resemblances to the effects observed in cereal grains. Legumes, similar to grains, possess phytate, a mineral-chelating compound that fermentation processes can enzymatically degrade. Fermentation can also have an impact on the vitamin content of legumes. Furthermore, it is worth noting that the process of bean fermentation can lead to the production of bioactive compounds, including antihypertensive peptides and antioxidants **(Hess, 2020)**.

The occurrence of metabolic illnesses has been dramatically raised in recent decades due to substantial changes in dietary macronutrient consumption and lifestyle **(Yoo & Kim, 2016)**. Scientists have discovered that changes in the composition of the gut bacteria might cause metabolic problems **(Nagatomo & Tang, 2015; Yoo & Kim, 2016)**. Nutrient absorption, mucosal barrier protection, xenobiotic metabolism, intestinal maturation, and other tasks are all performed by different bacteria in the human intestine **(Nagpal *et al*., 2012)**. The microbiota in our gut changes due to our daily food consumption, which has been related to the development of metabolic diseases **(Lai *et al*., 2018)**. The use of probiotics and prebiotics to manipulate the gut microbiota may be a potential strategy for the prevention and therapy of metabolic diseases **(Boulangé *et al*., 2016; Marchesi *et al*., 2016)**.

As a result, the favorable health advantages attributed to probiotics and prebiotics have piqued commercial interest in exploiting various uses, resulting in the "functional food" market sector's rapid growth and expansion **(Pintado *et al*., 2014)**.

3. Marine probiotic: Promising opportunity for future marine functional food

LAB hold significant importance for both humans and animals, playing crucial roles in food production, preservation, and health-related aspects. Certain members in this group exhibit probiotic characteristics, which, when consumed in adequate quantities, confer various health advantages to the host. These benefits encompass the stimulation of the immune system **(Fooladi *et al*., 2013)**, enhancement of lactose digestion **(Dhama *et al*., 2016)**, prevention of colon cancer **(Nouri *et al*., 2016)**, reduction of serum cholesterol levels **(Wang *et al*., 2018)**, and alleviation of intestinal constipation **(Ou *et al*., 2019)**. The most widely accepted definition of probiotics is "Live microbes that, when administered in adequate amounts, confer a health benefit on the host" **(Hill *et al*., 2014)**.

Although the concept of probiotics has lately gained popularity, we have been inadvertently ingesting beneficial microorganisms through traditional fermented foods since ancient times. Probiotics are mostly delivered through fermented foods. Dairy products (especially fermented milk and yogurt) are by far the most effective and extensively used among them **(Giraffa, 2012)**.

Marine LAB have adapted to survive in marine environments and are better suited for the fermentation of marine biomass and converting complex macromolecules into simple compounds **(Shobharani *et al*., 2014)**. Furthermore, using marine LAB with probiotic qualities to prepare marine functional food (Table 1) can maintain biomass while increasing its value and health benefits.

Table 1. Fermented marine functional food and their predominant microbial strains **(Dewapriya & Kim, 2014)**

Product	Raw material	Country/region	Microbial stains
Peda	Mackerel	Indonesia	Gram- positive cocci Lactic acid bacteria
Terasi	Planktonic shrimp	Indonesia	*Lactobacillus* sp. *Micrococcus* sp.
Ikan Tukai	Barracuda	Indonesia	*Pediococcus* sp. *Lactobacillus* sp.
Fish sauce	Anchovies Sardine Squid	Southeast Asia	*Pediococcus* sp. *Streptococcus* sp. *Staphylococcus* sp.
Jeotgal	Anchovies Shrimp	Korea	*Leuconostoc* sp.
Shiokara	Squid	Jaban	*Streptococcus* sp. *Bacillus* sp. *Micrococcus* sp.
Shottsuru	Sand fish	Jaban	*Corynebacterium* *Streptococcus* sp.
Cincaluk	Shrimp	Malaysia	*Staphylococcus*
Kung Jom	Shrimp	Thailand	*Enterococcus*
Pal som	Sneakhead fish	Thailand	*Pediococcus pentosaceus* *Lactobacillus alimentarius*
Kapi	Shrimp	Thailand	*Bacillus subtillis*
Fermented algae	Algae	Japan	*Lactobacillus rhamnosus*

The demand for health-promoting and functional food products is growing rapidly as consumers are becoming more aware of its importance to their health. Probiotic fermentation provides various health benefits to fermented foods, particularly in terms of improving gastrointestinal tract functions and boosting the immune system. At the same time, there has been an increase in demand for nondairy functional foods that contain probiotics due to lactose intolerance and elevated cholesterol caused by increased dairy product consumption **(Vella *et al.*, 2014)**. Therefore, marine functional foods fortified by probiotics are gaining popularity in various countries **(Dewapriya & Kim, 2014)**.

3.1. Probiotic selection

By adding probiotic bacteria to the food, nutraceuticals are created. The safety potential should be carefully considered when choosing imparted probiotics **(Zaghloul & Halfawy)**. The probiotic strain must not have any pathogenicity, allergenicity, or harmful effects. Additionally, the selected strain must exhibit adhering behavior to the gastric mucosa and ease about the *in vivo* gastrointestinal environment. Another crucial consideration is that the sensory qualities of the host food shouldn't be abrasively changed during preservation. Probiotics must continue to have the ability to tolerate the unfavorable environment experienced during storage and processing in order for the food to maintain the same general acceptance as fresh produce **(Parker *et al.*, 2018)**.

The careful selection of a probiotic strain is of the utmost importance, as a probiotic should not only be safe, but it should also demonstrate a positive impact on the host. The introduction of an inappropriate microorganism as a probiotic may cause adverse consequences for the host. The probiotic strain must possess stability and resilience to withstand the harsh circumstances of the digestive tract, such as its ability to endure low pH levels and resist bile salts and enzymes **(Kumar *et al.*, 2015)**. Moreover, candidate probiotics should be acquired from healthy individuals, preferably belonging to the specific target species. Additionally, it is crucial to evaluate the candidate strain and check for its capacity to produce antagonistic compounds, as well as other advantageous substances like fatty acids, digestive enzymes, and vitamins in addition to having the ability to attach to the host intestinal wall **(Pérez-Sánchez *et al.*, 2014)**. These *in vitro* investigations are crucial for establishing and enhancing the appropriate dosage and viability of the probiotic strain in order to perform the *in vivo* challenges **(Román *et al.*, 2012)**.

In order to evaluate the efficacy of probiotic strains in controlling or preventing outbreaks, it is necessary to conduct *in vivo* testing. However, it is crucial to first examine the outcomes of *in vitro* experiments to ascertain the suitability of the candidate strain for *in vivo* examination **(Sorroza *et al.*, 2012)**. The candidate strain's origin is also crucial; Hence, it is advised to take into account isolates from the same target host since they are more likely to survive and possibly be more effective than isolates from different origins **(Sun *et al.*, 2013)**.

As a result, potential probiotic microbes must be harmless. They must be capable of colonizing the gastrointestinal system, metabolically active, able to elicit an effect, suitable for commercial production, and able to tolerate industrial processing. Additionally, they must continue to be alive while the food product is being stored **(Kiron & Technology, 2012)**.

The investigation of probiotics has traditionally included culture-based methodologies, which depend on the isolation, cultivation, and identification of microorganisms in a laboratory setting by standard morphological and biochemical assessments. However, these methodologies possess various limitations and often yield outcomes that are either falsely positive or falsely negative. The utilization of contemporary molecular techniques, such as the amplification of nucleic acid and subsequent broad-range sequencing of 16S ribosomal RNA, has facilitated the identification and categorization of microbes through the analysis of their evolutionary divergence **(Donelli *et al*., 2013)**. The utilization of such tools is crucial for the identification of probiotic species, hence facilitating the process of selecting bacteria that are safe for the host **(Pérez-Sánchez *et al*., 2014)**.

3.2. Mechanism of action of probiotics

Probiotic bacteria are known to strengthen the gastrointestinal tract's defenses through a number of different mechanisms, including antimicrobial effects, competitive exclusion, barrier function maintenance, enhancement of a balanced microbial flora, immunomodulation of innate or adaptive immunity, and modulation of signal transduction **(La Fata *et al*., 2018)**.

Simple classification divided the probiotics' modes of action into three categories. In the first one, the immune-modulating ability of probiotics is used to modify both the host's innate and acquired immunity. The second one involves the direct interaction, or conflict, of probiotics with pathogenic competitors. The final mode of this fundamental classification deals with the inactivation and detoxification of toxic dietary ingredients, risky bacterial metabolites, and host-produced digestive products **(Leghari *et al*., 2021)**.

The direct interaction encompasses the competitive process of adhesion site acquisition, indicating that probiotics engage in competition for cellular attachments. In order to achieve efficient colonization, numerous pathogenic organisms necessitate association with the epithelium of the GI tract. Nevertheless, several strains of bifidobacteria and lactobacilli have the ability to adhere to the epithelium and function as colonization barriers, thereby impeding the adherence of pathogens to the mucosa. This effect was observed by the utilization of *Lactobacillus rhamnosus* strain GG and *Lactobacillus plantarum* 299v. Both species exhibited the capacity to inhibit the adhesion of *E. coli* to human colon cells **(Khalighi *et al*., 2016)**.

Another proposed mechanism involves the modification of microbial flora through the synthesis of antimicrobial compounds. Numerous species belonging to the *Lactobacilli* and *Bifidobacteria* genera have the capacity to synthesize bacteriocins and various other antimicrobial compounds. Bacteriocins are defined as "bacterially generated compounds with a biologically active protein moiety and bactericidal action". Hydrogen peroxide, diacetyl, and short-chain fatty acids represent a subset of the biologically active compounds that are synthesized by LAB. The probiotic organisms' release of these compounds induces a favorable alteration in the microbiota **(Khalighi *et al*., 2016)**.

Probiotics have demonstrated the ability to enhance the immunological response. The immunological response can manifest as increased secretion of immunoglobulin-A (IgA), elevated quantities of natural killer cells, or enhanced phagocytic activity of macrophages. Elevated secretion of IgA has the potential to mitigate the presence of harmful microbes within the gastrointestinal tract, hence enhancing the overall composition of the gut microbiota. Due to their immunomodulatory properties, probiotics are hypothesized by some researchers to have potential benefits in combating intestinal and urogenital pathogens, as well as in addressing conditions including inflammatory bowel disease (IBD), food allergy, and serving as an adjuvant in vaccinations. Probiotics may also compete for nutrients that pathogens would otherwise utilize. This is the case with *Clostridium difficile*, an organism with potential pathogenicity exhibits dependency on monosaccharides as a growth substrate. A sufficient quantity of probiotic microorganisms has the ability to metabolize the majority of the accessible monosaccharides, hence impeding the growth of *C. difficile* **(Khalighi *et al*., 2016)**.

In recent decades, the term “postbiotics” has been introduced. Postbiotics are bioactive molecules created by the metabolism of probiotics, primarily LAB **(Shaikh & Sreeja, 2017; Singh *et al*., 2018)**. They are also called pharmacobiotics **(Aguilar-Toalá *et al*., 2018)**, or heat-killed probiotics **(Hasan *et al*., 2019)**. Certain probiotic compounds that are released into the environment prior to death are referred to as postbiotics. These metabolic byproducts encompass a variety of substances such as organic acids, vitamins, short-chain fatty acids (SCFA), enzymes, polysaccharides, cell surface proteins, and lipids **(Aguilar-Toalá *et al*., 2018)**.

All of these "postbiotics" exert a functional impact on the microbiota, hence potentially influencing the overall health of the host organism **(Klemashevich *et al*., 2014)**.

4. Bioactive and functional ingredients from LAB

4.1. Bacteriocins

Bacteriocins can be defined as antimicrobial peptides synthesized by bacteria via ribosome synthesis and discharged into the surrounding environment. They can help the producing organism compete against other bacterial species **(Alvarez-Sieiro *et al*., 2016)**. Bacteriocins synthesized by LAB are particularly interesting since LAB have a long history of safe usage and are generally regarded as safe (GRAS). Furthermore, certain LAB species and their bacteriocins have the potential to be exploited in the food industry as natural preservatives **(Woraprayote *et al*., 2016)**. Databases have been built to manage the large number of bacteriocins isolated from nature **(Van Heel *et al*., 2013)**. Aside from the bacteriocins that have been disclosed, many more are hidden in the genome and have yet to be extracted. These compounds constitute an extremely promising source of novel antimicrobial agents **(Alvarez-Sieiro *et al*., 2016)**.

Bacteriocins produced by LAB, encompass a diverse range. Nevertheless, these entities can be categorized into two distinct kinds according to their structural modifications, encompassing factors such as size, thermostability, and modes of action. Class I lantibiotics are a class of small cationic peptides that possess lanthionine or ß-methyl lanthionine residues. These peptides undergo post-translational modifications and exhibit their effects primarily at the level of the cell membrane and cell wall. Nisin stands out as the most representative bacteriocin within this particular category **(Silva *et al*., 2018)**. Nisin's mode of action against Gram-positive bacteria depends on either binding to cell wall lipid II and inhibition of cell wall synthesis, or being inserted in the cell wall causing pores formation and cell death

In contrast, Class II bacteriocins, which are not classified as lantibiotics, are bacteriocins that exhibit heat stability. These bacteriocins consist of a range of 30 to 70 amino acid residues and lack the presence of lanthionine. They induce the formation of pores in the cellular membranes of the target cells. Bacteriocins induce membrane potential collapse by the formation of electrostatic bonds with the negatively charged phospholipids. After bonding, the bacteriocin's hydrophobic component is inserted into the membrane, creating pores that allow ions, primarily potassium and magnesium, to flow out. The proton motive force diminishes as a result, limiting macromolecule synthesis and energy production and ultimately leading to cell death **(Silva *et al*., 2018)**.

These bacteriocins can be divided into subclasses, with the largest subclass being IIa. Members of this subclass are known as anti-listeria, pediocin-like bacteriocins, characterized by an amino-terminal motif that contains one or two disulfide bridges. Another subclass, IIb, consists of bacteriocins that require the combined action of two peptides in order to exhibit activity, as they are unable to act individually; Subclass IIc encompasses the cyclic bacteriocins, which are characterized by the covalent linkage between the carboxy and amino terminal ends. On the other hand, subclass IId consists of a diverse collection of linear peptides that do not possess pediocin-like characteristics **(Rea *et al*., 2011)**.

The first bacteriocin produced by a LAB to be approved for use in foods is nisin. It is recognized as an effective preservative due to its ability to inhibit various Gram-positive bacteria, such as *Enterococcus*, *Staphylococcus*, *Streptococcus*, *Micrococcus*, *Lactobacillus*, *Listeria*, *Pediococcus*, and *Mycobacterium* strains. However, its inhibitory effects are limited to Gram-positive bacteria, as Gram-negative bacteria possess an outer membrane barrier that prevents nisin from exerting its antimicrobial activity. The Joint Food and Agriculture Organization/World Health Organization (FAO/WHO) evaluated this antimicrobial agent as safe for food use and designated it as GRAS **(Jung *et al*., 2018)**.

4.2. LAB Exopolysaccharides

The exopolysaccharides (EPS) synthesized by LAB exhibit a wide range of structural and functional diversity, and many criteria determine their categorization. The fundamental categorization is based on the constituent monosaccharide units of the EPS. Based on this criterion, it is possible to categorize EPS as either homopolysaccharides (HoPS) or heteropolysaccharides (HePS) **(Donot *et al*., 2012)**.

Although the comprehensive understanding of the advantageous impact of EPS synthesis on bacterial physiology remains incomplete, it is evident that LAB produce EPS as a safeguarding matrix to endure the various challenges encountered during fermentation processes, including but not limited to pH changes, temperature variations, and osmotic stress **(Donot *et al*., 2012)**. In addition, EPS play a crucial role in the synthesis of biofilm matrix and the facilitation of cell aggregation and adhesion processes on both non-living and living surfaces, such as the intestinal mucosa. EPS are of significant importance in microbial life due to their involvement in various ecological processes that facilitate bacterial colonization in both technological and gastrointestinal microenvironments, as the EPS contribute to stable cell recognition and cooperation, enabling a successful bacterial colonization. Additionally, EPS serve as a protective barrier against harmful substances such as antibiotics and toxic compounds, thereby enhancing bacterial survival **(Daba *et al*., 2021)**.

Despite the considerable number of researchers currently working on studying EPS production from LAB, there remains a lack of understanding regarding the kinetics of EPS synthesis. This information gap is crucial because differences in production yield and EPS composition might result in a total production loss, owing to the influence of various factors in production and structure. Several parameters, such as the carbon source, cultivation time, and incubation length, have the potential to influence the structure, chemical composition, and biological activity of the resulting EPS. In addition, it is important to note that the formation of EPS is strain-specific. Therefore, the implementation of appropriate techniques for screening, isolation, and purification of EPS is of the utmost significance **(Jurásková *et al*., 2022; Zaghloul & Ibrahim, 2022)**. A variety of techniques including screening, extraction, composition, and structural assessment, have recently been developed and refined for the analysis of the EPS generated by LAB. To assess the microbial ability to produce EPS, a screening method involves growing LAB in a medium enriched with various sugars, such as fructose, lactose, glucose, sucrose, or galactose. The simplest way to ascertain the generation of

EPS is to observe the phenotypic traits of the colonies, such as their ropy or slimy morphologies. Sticky colonies exhibit the slimy phenotype, whereas the ropy phenotype is illustrated by long filaments that form if the colony or pellets are lifted by the inoculation loop **(Prete *et al*., 2021)**.

The EPS produced by LAB provides many industrial and health benefits. For instance, it functions as an antioxidant, cholesterol-lowering agent, antimicrobial, immune modulator, prebiotic, and many other potential health benefits **(Prete *et al*., 2021; Zaghloul *et al*., 2023b; Zaghloul *et al*., 2024)**. For example, the EPS can induce an antioxidant state by degrading superoxide anion and H_2O_2 or inhibiting lipid peroxidation. On the other hand, the same antioxidant state may be induced by reduction of metal ion chelation activity or up-regulation of enzymatic /non-enzymatic antioxidant activities **(Kim *et al*., 2022)**. Furthermore, the EPS of LAB were associated with lowering the cholesterol. However, the exact mechanism associated with inducing this effect is unknown so far and is expected to be multifactorial. However, possible mechanisms include decreasing the amount of low-density lipoprotein cholesterol. It has also been hypothesized that LAB cells may exert a similar cholesterol-lowering effect by passively adsorbing it onto their membranes or simply assimilating cholesterol during cell growth **(Hameed *et al*., 2022)**.

The antibacterial activity of LAB-derived EPS is well documented in many studies. The activity was reported against both Gram-positive and negative pathogens. The main mode of action to counteract microbial pathogens is by inhibiting biofilm formation. Indeed, the capacity to develop a biofilm significantly augments the ecological viability and endurance of pathogenic bacteria, leading to a higher prevalence of chronic and recurring infections **(Sarikaya *et al*., 2017; Rajoka *et al*., 2018)**.

These EPS may function as an immune modulator. The general opinion in this regard is that the LAB-derived EPS size and charge are the main players of this immune-related effect. Specifically, the negatively charged EPS and small-size molecules stimulate the immune system, while the neutral and large-size EPS suppress the immune system. However, this topic has many contradictions as the other physicochemical characteristics of the EPS are not fully studied (for example, linkage, functional groups, monosaccharide composition,… etc.) **(Werning *et al*., 2022)**.

The different *in vitro* or *in vivo* systems used for EPS immunomodulatory studies are diverse **(Werning *et al*., 2022)**. On the other hand, the LAB-derived EPS may be used as prebiotic as they are resistant to gastrointestinal tract digestion and are easily metabolized by beneficial bacterial inhabitants of the gut. For instance, *in vivo* studies confirm that prebiotics increase the *Lactobacillus* counts while decreasing the *E. coli* counts, which implies the enhancement of beneficial bacterial growth due to the presence of EPS **(Hamdy *et al*., 2018)**. Interestingly, most EPS with prebiotic potential were found to be homo-polysaccharides, and hence are easily metabolized by gut bacteria. On the contrary, the hetero-polysaccharides are more complex in structure, which limits their prebiotic potential **(Werning *et al*., 2022)**.

5. Marine functional food

Diet is particularly vital in supporting human health, and as life expectancy rises, so will this role. This provides a dilemma for the food sector since customers want food that is not only tasty and convenient but also healthy and nutritious **(Sachdeva *et al*., 2021)**.

Pharmaceuticals are manmade substances that are employed in the treatment of illnesses. But what if we used nutrients to prevent sickness and promote good health? Pharmaceutical supplements contain high amounts of vitamins and minerals, whereas nutraceuticals are as useful as natural foods **(Kumar *et al*., 2015)**. These nutraceuticals are categorized as compounds that are part of our diet and offer a variety of health advantages. These compounds can be employed for both nutritional (since they have nutritional value) and medicinal purposes (used in the prevention of chronic diseases). Various medical conditions such as cardiovascular illnesses, cancer, hypertension, diabetes, and obesity can be effectively mitigated by the utilisation of functional foods that possess bioactive nutraceuticals (93) **(Sachdeva *et al*., 2021)**. According to a report by Precedence Research, the anticipated growth of the global functional food and beverage industry is expected to reach $309 billion by 2027, representing a significant increase from its value of $175 billion in 2020 (https://www.precedenceresearch.com/functional-food-market).

Given that the Earth's surface is predominantly covered by the ocean, exceeding 70%, there exists a diverse array of marine organisms that offer a plentiful reservoir of natural products. Consequently, the significance of marine biomass as a reservoir for novel bioactive compounds is undergoing a significant expansion **(Lindequist & therapeutics, 2016)**. The maritime environment is an important source of functional components, including essential minerals, vitamins, polysaccharides, PUFA, enzymes, bioactive peptides, and antioxidants contributing to approximately 50% of the world's biodiversity **(López-Abarrategui *et al*., 2012)**. In addition, marine organisms have been found to synthesize various substances due to the unique challenges posed by their highly demanding, the competitive and aggressive aquatic habitat, which significantly differs from terrestrial environments. Consequently, these organisms have evolved the ability to produce highly specialized and potent bioactive molecules **(Pham, 2019)**.

When compared to terrestrial ecosystems, marine ecosystems offer a greater diversity of living species, providing more nutrients for human nutrition and health. Moreover, the marine bioactive compounds appear to meet the criteria for utilization as functional food additives. They are natural compounds; their isolation is cost-effective, and they are abundant in nature with a reliable supply. Furthermore, they are functional, and their actions can influence the pathogenesis of countless diseases **(Admassu *et al*., 2015)**.

Marine secondary metabolites are produced by cyanobacteria, macroalgae, microalgae, bacteria, crustaceans, and some fish species as an adaptation to their adverse marine environment. Several forms of biomass are used to identify bioactive metabolites and functional biomolecules appropriate for cosmetic, food, and medicinal applications. Macroalgae are gaining popularity among accessible biomass due to their potential nutraceutical and health advantages, as marine macroalgae are the richest natural source of non-animal biological compounds **(Hentati *et al*., 2020; Ghosh *et al*., 2022)**. Moreover, marine algae represent an interesting option for the functional food sector. They can be regarded as the plant-based diet of the future **(Cardoso *et al*., 2015)** since they do not compete with food crops for accessible resources such as fresh water and arable land while yet providing a variety of functional and bioactive components **(Cunha & Grenha, 2016)**. At the same time, marine bioactive compounds appear to meet the criteria for utilization as functional food additives **(Admassu *et al*., 2015)**.

6. Marine algae

Marine algae are simple creatures that include chlorophyll and are made up of a single cell or a colony of cells that can work together as organisms or simple tissues. These vegetative marine algae are non-vascular organisms (unicellular or multicellular) that lack true stems and roots; they range in size from organisms as little as 3– 10m in length to massive kelps that can reach up to 70m in height. *Macrocystis*, a kelp of the order Laminariales, for example, can grow to be 60 meters long and form large underwater forests. Consequently, marine algae are divided into two categories based on their size: macroalgae and microalgae **(Bule *et al*., 2018)**.

Algae can also be classified based on their cell wall chemistry, the presence or lack of flagella, and the type of chlorophyll they produce. The most frequently utilized criterion in algae classification is the presence or lack of various pigments in addition to chlorophyll, which define the algal division to which it belongs. According to this criterion, marine macroalgae, known as seaweeds, are classified as brown algae (Phaeophyceae), red algae (Rhodophyceae), or green algae (Chlorophyceae). Because not all marine algae require the same quantity of light for photosynthesis, the existence of different pigments in them is linked to their sea habitat. Green macroalgae are generally found in coastal areas, where they are exposed to light and can absorb a lot of energy, whereas brown and red algae are more common at higher depths, where sunlight penetration is limited **(Morsilli *et al*., 2012)**.

6.1. Marine algae as functional food

The importance of marine algae as a source of new bioactive chemicals is rising rapidly, and scientists have discovered that marine algal-derived substances have a wide range of biological and medicinal properties **(Fidelis *et al*., 2014)**. For example, the red algae *Corallina elongate* gathered from the Moroccan coast demonstrated an anti-inflammatory efficacy by inhibiting elastase and phospholipase A2 with inhibition percentages greater than 95 and 70%, respectively **(Oumaskour *et al*., 2013)**. *C. elongate* methanolic extracts had an antibacterial efficacy against *Staphylococcus aureus*. Consequently, the field of research and development of marine functional food has become very interesting, and ongoing efforts should be made in that field as the consumption of this functional food could reduce the severity and prevalence of chronic diseases in the future **(Liao *et al*., 2021)**.

The key nutrients of seaweed are peptides, soluble dietary fibers, lipids, phlorotannins, and minerals **(Cardoso *et al*., 2015)**. Seaweed's high soluble fiber content (up to 50% of seaweed's dry weight) gave it a leading position ahead of fruits and vegetables **(Mišurcová *et al*., 2012)**. Furthermore, marine algae's protein, lipid, carbohydrate, metabolite, and fiber content are modified by their growth factors (light, water temperature, nutrients, and salinity). This means that, from a biotechnological perspective, marine algae can be viewed as natural bioreactors capable of producing a wide range of natural compounds in varying quantities, which is an appealing trait for the functional food industry. Macroalgae are recognized for their wide range of biologically active phytochemicals, such as phycobilin, carotenoids, fatty acids, vitamins, sterols, polysaccharides, phycocyanin, and tocopherol, among other compounds **(Santos *et al*., 2015)**. The majority of these substances have exhibited a biological activity and notable health benefits, including but not limited to anticancer, antimicrobial, antiobesity, antiallergic, anticoagulant, immunomodulatory, antifungal, antitumor, antioxidant, anti-inflammatory, hypoglycemic, and antiviral properties **(Peñalver *et al*., 2020)**.

6.2. Seaweed lipid and protein contents

Seaweed often have an extremely low lipid content, constituting approximately 5% of their dry weight **(Kendel *et al*., 2015)**, In contrast, algae are known for their high levels of PUFA. The primary sterols found in seaweed include fucosterol, clionasterol, isofucosterol, and cholesterol **(Pérez *et al*., 2016)**. Sterols exhibit various beneficial qualities, including antiobesity, antitumor, anticancer, antioxidant, antiviral, and cardiovascular disease-fighting effects **(Kendel *et al*., 2015)**. The proportion of proteins, peptides, and amino acids found in seaweed exhibits a range of 5 to 47% of their dry weight (w/w). This variability is influenced by factors, such as the specific algal species, the season, and the geographic region **(Aumeerun *et al*., 2019)**.

The seaweed *Porphyra tenera* and *Palmaria palmata* have significant protein levels of 35% (w/w) and 47% (w/w), respectively. On the other hand, it is noteworthy that the green alga *Ulva pertus* has a somewhat decreased protein content of 26% (w/w) **(Harnedy & Fitzgerald, 2013)**. Chlorophyceae and Rhodophyceae often exhibit an elevated protein concentration in comparison with Pheophyceae **(Aumeerun *et al*.,**

2019). In addition, it is worth noting that seaweed proteins have a substantial presence of several amino acids, such as proline, alanine, glycine, arginine, and particularly aspartic and glutamic acids **(Hentati *et al*., 2020)**.

6.3. Seaweed vitamins and minerals content

Seaweeds possess a notable abundance of hydro- and liposoluble vitamins, hence potentially enhancing the vitamin content of both food and feed. The water-soluble vitamins include B vitamins (B1, B2, B3, B6, B12), vitamin C, pantothenic acid, niacin, folic acid, and riboflavin. Additionally, the fat-soluble vitamins include vitamin D, vitamin E, vitamin A, and carotenoids, which serve as provitamin forms of vitamin A **(Wells *et al*., 2017)**. As an example, the vitamin C concentrations reported for green, red, and brown seaweed were within a similar range (0.0347- 1.25, 0.0353- 1.61, and 0.0345- 1.85g/ 100g dry weight (DW), respectively). In contrast, the available literature presents a wider range of vitamin B12 concentrations in seaweed. Specifically, the vitamin B12 concentration in green seaweed ranges from 0.06 to 0.786g/ 100g DW, while the bed seaweed exhibits a range of 0.0961 to 1.34g/ 100g DW. The brown seaweed, on the other hand, has a narrower range of 0.0164 to 0.0431g/ 100g DW. In addition, Chlorophyceae has notable vitamin B3 concentrations ranging from 0.005 to 1.0g/ 100g DW. Similarly, the Rhodophyceae group shows values of 0.0951 to 0.10g/ 100g DW, while the Pheophyceae group displays concentrations of 0.612 to 0.90g/ 100g DW **(Gullón *et al*., 2020; Hentati *et al*., 2020)**.

Macroalgae have a notable abundance of minerals. The mineral content of these organisms varies between 7 and 40% of their dry weight (w/w), depending on the specific species of algae, the season, and the geographical location from where they are collected **(Wells *et al*., 2017)**. Seaweeds are known to possess significant concentrations of macro elements such as calcium (Ca), manganese (Mn), potassium (K), phosphorus (P), iron (Fe), sodium (Na), and magnesium (Mg) in addition to trace elements (microelements) including copper (Cu), lead (Pb), zinc (Zn), scandium (Sc), strontium (Sr), samarium (Sd), arsenic (As), and chromium (Cr) **(Gullón *et al*., 2020; Hentati *et al*., 2020)**. These minerals, particularly calcium (Ca), are found in greater amounts in seaweed than in terrestrial plants counterparts **(Balina *et al*., 2016)**. The iodine concentrations in algal biomass exhibit a considerable variation among different species, with values ranging from 0.004 to 2.66g/ kg **(Roohinejad *et al.*, 2017; Gullón *et al*., 2020; Hentati *et al*., 2020)**.

6.4. Carbohydrates content

Marine macroalgae have a significant abundance of carbohydrates, with concentrations varying between 5 and 75% (w/w, DW) based on factors such as age, species, time, and location of collection. The predominant kind of carbohydrates found in algae is mostly polysaccharides.

The marine source diversity allows for the extraction of polysaccharides obtained from seaweed, which possess unique characteristics that are entirely absent in polysaccharides produced from terrestrial plants. The diverse structural composition of algal polysaccharides offers a wide array of biological properties that exhibit potential for various therapeutic advantages and industrial uses, such as nutraceuticals, medicines, and functional foods, among others. Algae are widely acknowledged as the primary and abundant source of polysaccharides **(Hentati *et al*., 2020)**.

Seaweed polysaccharides exist in both sulfated and non-sulfated forms. Green marine seaweed is known for its high ulvan content, while brown macroalgae are characterized by the presence of alginic acids, laminarans, and fucoidans. On the other hand, the red seaweed is recognized for its carrageenans, agars, sulphated galactans, xylans, porphyran, and floridean starch. Recent research has elucidated the biological properties of seaweed polysaccharides and their derivatives, including oligosaccharides and biochemically altered polysaccharides. The effects of anti-inflammation, antidiabetic, antiobesity, antihyperlipidemia, immunomodulation, antioxidant, anticancer, antiviral, antimicrobial, and gastroprotection have been studied **(Hentati *et al*., 2020)**.

7. Sulfated polysaccharides (SP) from marine seaweed

SP have been shown to have a variety of pharmacological and physiological effects, including anticoagulant, anti-inflammatory, antiviral, and anticancer properties **(Shanthi *et al*., 2014; Wu *et al*., 2016)**. Marine algae are regarded as one of the most valuable non-animal SP sources, and the chemical composition of these polymers varies widely depending on the algal species. They are easily isolated from marine algae and occasionally from higher animals, but they are not found in bacteria or higher plants **(Cian *et al*., 2015)**. Carrageenan from the red algae, fucoidan and laminarans from the brown algae, and ulvan from the green algae are the primary SP found in marine algae **(Cunha & Grenha, 2016)**.

Because the content of these SP varies widely depending on the harvest season, climate conditions, and extraction processes, each newly isolated SP is a distinct compound with a distinct structure and function **(Gabriela *et al*., 2016)**.

Seaweed SP have recently received a lot of interest in several applications, including food, cosmetics, and pharmaceuticals **(Shanthi *et al*., 2014; Cunha & Grenha, 2016; Ruocco *et al*., 2016)**. Ulvan, for example, has numerous biological and physiochemical properties that could be useful in dietary, agricultural, medicinal, and chemical applications **(Cunha & Grenha, 2016; Ruocco *et al*., 2016)**. The red algal carrageenans are commonly employed as food additives such as stabilizers, emulsifiers, and thickeners **(Liao *et al*., 2021)**.

7.1. Extraction of the SP by LAB fermentation

It is critical to establish appropriate extraction conditions for bioactive compounds from the seaweed matrix in order to obtain homogeneous biological activity and eventual commercial uses **(Hentati *et al*., 2020)**.

Researchers used various techniques to extract marine algae bioactive compounds such as antioxidants, anticoagulants, antimicrobials, anti-inflammatory compounds, antiherpes, anti-hyperlipidemic compounds, and anticancer compounds. Hot water or solvent extraction, acid-base hydrolysis, and enzymatic digestion were among the procedures used **(Huang *et al*., 2016)**. Although these extraction methods have been proven to be efficient, there are various drawbacks to using them, including high costs, difficult procedures and toxicity. Enzymatic digestion has been used in some circumstances to boost yield. However, the pH adjustment and residual effects and the various enzyme substrate specificity are known to raise production costs significantly **(Shobharani *et al*., 2014)**.

The fermentation process using LAB has been used to produce a cost-effective way of extracting bioactive compounds, including SP with significant anticoagulant activity, from marine biomass **(Shobharani *et al*., 2014)**.

Marine LAB have adapted to live in the presence of seaweed, so they are better suited for the fermentation of marine seaweed and converting complex macromolecules into simple compounds. It has been reported that marine LAB isolates are used in the fermentation of marine seaweed to increase the anticoagulant activity **(Shobharani *et al*., 2014)**. Furthermore, the utilization of LAB with probiotic qualities in the preparation of functional food can maintain the biomass while increasing its value and health benefits **(Molina *et al*., 2012)**.

8. Preparation of functional fermented seaweed by marine LAB

Health-conscious consumers are driving an increased demand for functional foods that promote good health **(Vella *et al*., 2014)**. Probiotic fermentation provides various health benefits to fermented foods, particularly in terms of improving gastrointestinal tract functions and boosting the immune system. At the same time, there has been an increase in demand for nondairy functional foods that contain probiotics due to lactose intolerance and elevated cholesterol caused by increased dairy product consumption. Seaweed have been used in many dishes, including muffins, appetizers, and soups. They contain lipids, proteins, vitamins, minerals, and non-starch polysaccharides. Seaweed can be considered as one of the most affordable protein sources, beside having many biological activities with therapeutic value that have been reported for seaweed polysaccharides **(Emo & Kim, 2014)**. Furthermore, they are high in dietary fiber and prebiotics, which encourage the growth and proliferation of probiotic bacteria. All of these make seaweed a great choice for functional food industry **(Zaporozhets *et al*.,**

2014). However, the odor of seaweed limits the large-scale development of seaweed products. As a result, it is critical to develop innovative processing procedures to reduce seaweed odor in the final processed product while maintaining or improving its value and biological activities in order to attract more customers. As a result, seaweed fermented by bacteria that are generally regarded as safe are gaining a lot of attention, as fermentation is a very interesting technique used to increase the nutritional value of the final product, the bioavailability of micronutrients, and to help remove some of the undesirable compounds (Fig. 2) **(Wijesinghe & Jeon, 2012; Emo & Kim, 2014)**.

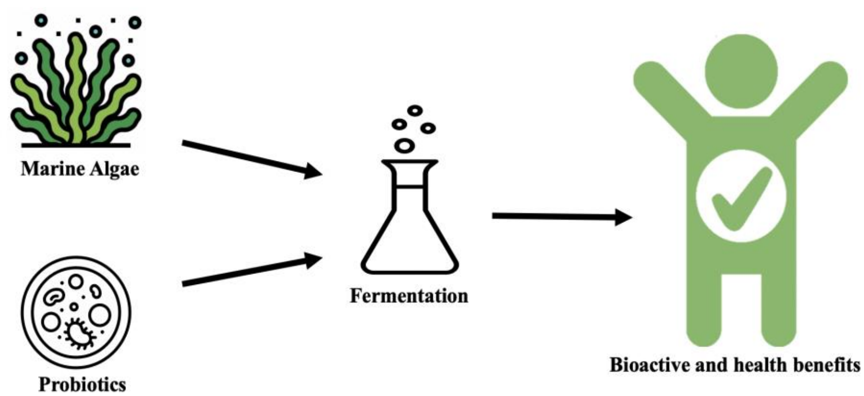

Fig. 2. Probiotics-induced algal fermentation as a source of varied health benefits

Products fermented with LAB and probiotics are gaining attention since fermentation improves the fermented product's shelf life, safety, nutritional, odor, and sensory qualities. Furthermore, some probiotic microbes create vitamins, essential amino acids, and proteins, which boost the end product's health advantages **(Monteiro *et al*., 2021)**.

9. Developmental obstacles for marine functional foods

The definition of functional food itself represents the first difficulty. Although the phrase "functional food" was coined in the 1980s, there is currently no worldwide harmonized legislation on the concept **(Domínguez *et al*., 2020)**. This scenario places countries with stricter health laws at a distinct business disadvantage and damages consumers who may be confused or misled, highlighting the necessity for regulated labeling on functional food products.

Although a formal definition is currently absent, the key factors for categorizing a food as functional include the presence of scientific evidence supporting its functionality, as well as its resemblance to a conventional food product. It is important to acknowledge that the impact of functional foods on health is contingent upon the quantity of bioactive compounds, whether naturally occurring or added, that are able to enter the systemic circulation after digestion in the gastrointestinal tract and subsequently reach organs and tissues in order to exert their biological effects.

The assessment of modifications in the health consequences of biologically active chemicals is of crucial importance, particularly in the context of gastrointestinal digestion. In order to ascertain the probability of such adjustments, it is necessary to conduct rigorous experiments that evaluate the bioaccessibility and bioavailability of these compounds.

To gather useful information on safety, modes of action, or prospective physiological effects, it is necessary to conduct preclinical research with separated compounds. However, these studies do not provide conclusive evidence for the functionality of a whole diet, as a bioactive compound can demonstrate distinct effects as an isolated compound versus as an element in a food matrix **(Lachance *et al*., 2020)**. Consequently, research on the beneficial activity of bioactive chemicals is typically conducted prior to and following their inclusion into a food product. In addition to *in vitro* models, research evidence must be validated by clinical trials involving humans **(Brown *et al*., 2018)**.

Identifying specific plasma biomarkers of the tested functional food is one of the greatest challenges in human studies **(Brown *et al*., 2018)**. On the other side, industrial processing of the final product can potentially impact the functionality of bioactive compounds. Innovative non-thermal processing techniques have been proposed to maintain the bioactive characteristics of foods and their byproducts **(Brown *et al*., 2018)**.

The unique characteristics of each substance, such as low water solubility, poor oral bioavailability, incompatibility with the food matrix, and detrimental effects on sensory attributes, often limit the application of marine lipids, carotenoids, proteins, and peptides in the food industry **(Hosseini *et al*., 2021)**. The development of a functional food that is backed by scientific evidence is a challenging process, especially for sick populations like cancer patients. For this reason, it has been proposed that experts in food science, food health, and food technology work together. Similar to medicine development, the process of creating functional food via the incorporation of bioactive substances into a food matrix is time-consuming, costly, and labor-intensive. It needs regulatory approval, human clinical trials, and preclinical testing, much like medication development **(Fuente *et al*., 2022)**.

10. Recommendations

It is recommended to assess the effectiveness of probiotic potential under various physiological situations. Maintaining the safety and efficacy of probiotics is a key problem, and worldwide criteria for the manufacture, marketing, and the use of probiotics must be standardized.

On the other hand, these wild-growing seaweeds on the coasts must be subjected to careful examination, as the detrimental effects of incorporating seaweed into the diet include the potential for an excessive intake of iodine and arsenic. Hence, it is advisable to effectively oversee the nutritional composition and harmful components of seaweed, a practice that is essential in conventional agriculture. Moreover, assessing the nutritional value and the functional ingredient in seaweed is essential before consumption, as all these parameters change with genus, species, climate, and regional variations. Some seaweed may induce allergic reactions; thus, it is recommended to choose edible seaweed before consumption. Therefore, it is also recommended to expand in the cultivation of known species of edible seaweed under controlled conditions.

Future studies should focus on long-term effects and the ideal percentage of seaweed in diets. Despite the vast number of dietary uses for marine bioactives, it is recommended to conduct more multidisciplinary research in all areas, such as chemical composition, biotechnology, extraction, bioactivity, and toxicity. Moreover, it is imperative to accurately determine the activity and composition of bioactive compounds in order to effectively apply the findings of the study in practical use.

CONCLUSION

In conclusion, there is a large variety of unexploited seaweed. The seaweed is abundant in most nutritious and bioactive substances essential for health. At the same time, in response to the increasing awareness of the importance of diet for better health, seaweed can be used as a viable alternative to synthetic pharmaceuticals used to treat chronic disease as they are rich in polyphenols, polysaccharides, all necessary amino acids, macro and micro minerals, and dietary fiber. LAB are GRAS and have a long history of usage in food fermentation, and some of them have probiotic potential with many health benefits. Marine LAB are adapted to marine habitats and produce a variety of unique bioactive compounds; they are better suited for the fermentation of marine biomass and converting complex macromolecules into simple compounds. Fermentation of seaweed and marine biomass by LAB is a relatively underdeveloped field with a lot of potential for developing novel food items that enhance these biomass's shelf life and organoleptic characteristics. The utilization of LAB with probiotic qualities in the preparation of marine functional food and extraction of bioactive compounds can maintain biomass while increasing their value and health benefits. Since seaweed does not require arable land or fresh water and has a high nutrient and bioactive content, it can be investigated further to prepare novel functional food items to cure malnutrition among low-income populations worldwide.

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