Review Article

Recent Updates on Jellyfish: Applications in Agro-based Biotechnology and Pharmaceutical Interests

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Received: 19 August 2023; Revised: 3 November 2023; Accepted: 22 November 2023; Published online: 24 January 2024

Abstract
Jellyfish are gelatinous sea creatures that belong to the subphylum Medusozoa of the phylum Cnidaria and are found on many beaches worldwide. Despite being considered a nuisance, jellyfish have many uses, such as being a source of high-value molecules such as collagen, gelatin, and protein hydrolysates and a source of high-protein food. Studies related to its availability, post-harvest applications, and need-based use in biomedicine are thrust research of analysis or investigation. Therefore, this review has been designed with all the latest information with a focus on applications of jellyfish in agro-based biotechnology and pharmaceutics. The review has been systematically arranged to present on the broader search platform for future research studies and possible need-based applications.

Keywords: Bioactive peptide, Biofertilizer, Biosensor, Collagen, Jellyfish, Pharmaceuticals

1 Introduction

Jellyfish are zooplankton that belong to the phylum Cnidaria, which consists of six classes: Hydrozoa, Scyphozoa, Cubozoa, Staurozoa, Myxozoa, and Anthozoa. Among these six classes, Scyphozoa has the most important economic value. Being a natural product, jellyfish have been used for human food, aquaculture feed, and fertilizer [1]–[3]. The jellyfish fishery business is worldwide with 100 million USD production value [4]. Jellyfish are consumed as a food source in many Asian countries, delivering the multi-million USD jellyfish business for local fishermen around the globe during the catching season [5]. The global production of jellyfish from 2015–2018 was estimated at 300,000 tons/year, representing a business trend of 20–100 million USD. Edible jellyfish possess collagen, which produces anti-hypertensive through enzymatic hydrolysis [6]. Some individuals consume the medusae raw, while others follow specific techniques for preparing jellyfish's oral arm and umbrella parts before eating them.

Besides the primary use of food, the pharmaceutical and cosmetic industries constantly search for new products. Traditional Chinese medicine has utilized jellyfish-derived products in the past, but limited scientific evidence supports their effectiveness. However, jellyfish collagen has shown promise for pharmaceutical and cosmetic purposes due to its biocompatibility and non-toxicity. Some hydrating and anti-aging products from jellyfish are available in the market [7], [8]. Mucin secreted by the jellyfish, which mainly consists of glycoprotein, has been used in removing microplastics from oceans [9], which is particularly important given the uncertain future of our oceans. In addition to their aesthetic and medicinal uses, certain jellyfish are recognized for their ability to produce light through bioluminescence. While most of these species belong to the Hydrozoa, some deep-sea scyphomedusae can also provide fascinating interest in studying these biochemical properties for labeling genes and specific cell types [9]–[11].

Meanwhile, jellyfish have a positive side with many potential uses but also have a negative impact of excessive proliferation resulting in "blooms" [12]. Eutrophication or algal blooming, which supports the growth of the jellyfish, occurs due to the enrichment of the nutrients in surface water [13]. Accumulation of the surface water leads to blockage and damage to the mechanical water intake. It has been reported that jellyfish can cause damages up to 2 million USD per day in nuclear power plant station, Ontario, USA, and 205 USD million per year in Korea [14]. Hence, this review focuses on possible explorations of such species for need-based utilizations in agro-based biotechnology (food, collagen and gelatin, protein hydrolysate and bioactive peptides, and plant fertilizers), their potential use in biomedical-pharmaceutical therapy and biosensors for microplastic sequencers.

2 Applications in Agro-based Biotechnology

2.1 *Jellyfish as food*

Seafood is integral to people's diets as it provides essential and delicious nutrients. Over 1 billion people rely on seafood as their primary source of protein, and seafood yields are expected to increase by 36–74% by 2050 [15]. Due to the impact of climate change and the growing demand for food, alternative seafood products have become increasingly popular in recent years. One alternative that has gained attention is jellyfish, a sustainable marine resource in Asian countries. Edible jellyfish production has been estimated at around 300,000 tons per year from 2015 to 2018, with a value ranging from 10,000 USD per ton, depending on the product type and species [16]. Jellyfish as food, in general, has been accepted and commercially available for Asian people. The primary business of the jellyfish market as salted products involves Japan, China, South Korea, Malaysia, Thailand, and the USA.

In contrast, the major edible jellyfish species are *Lobonema smithii*, *Rhopilema hispidum*, *Rhopilema esculentum* and *Stomolophus meleagris*. Thailand exports jellyfish as salted jellyfish to Asian countries such as Japan, South Korea, China, Malaysia, and Vietnam [17]. The production of commercial salted jellyfish has been reported with slight differences in edible jellyfish species, chemicals, and processing steps used in salting [16]–[19].

Treatment with salt and alum before rehydration in water is necessary to ensure safety and achieve the desired texture. Thus, prompt treatment following collection is essential to conserve the desirable attributes. Researchers have found that jellyfish are appreciated for their texture and taste, low fat and cholesterol levels, and high vitamin and mineral content [17]. Jellyfish possess a high water content, rendering them susceptible to spoilage. Nonetheless, their protein content outstrips their lipid and carbohydrate content, as shown in Tables 1 and 2. The typical salted jellyfish production in Thailand is presented in Figure 1. Jellyfish can be enjoyed raw, cooked, or processed into ready-to-eat products. The jellyfish-based food menus have diversified from fresh cook menus to shelf-stable snacks, as seen in Figure 2.

In order to ensure all citizens have access to a sufficient amount of safe food, food safety, balanced nutrition, and preference, Thai Government has increased the implementation of the food control system. Thai Food and Drug Administration (FDA), with Provisional Public Health Offices of the Ministry of Public Health (MOPH), with support from the Department of Medicinal Sciences and Accredited Laboratories, manages food imports, processing, and legal food operations [20]. Regarding commercial jellyfish products known in the Asian market, concerning the danger of aluminum, European food researchers under the project of Go Jelly starting from Jan 1, 2018–Dec 31, 2021, have created a new type of aluminum-free jellyfish based on calcium salts as a raw material for producing jellyfish mousse, jellyfish seasoning, jellyfish meringue, jellyfish semi-finished food, and alcohol dehydrated dried jellyfish [21]. Another developed jellyfish product is fermented food using a high-salt Asian-style submerged liquid fermentation method. The process involves two stages, with the first using *Aspergillus oryzae* to create a jellyfish-based product called jellyfish paste. The second stage adds selected bacteria and yeast to produce fermented jellyfish paste, which has desirable nutritional traits and a complex enzyme profile. This marks the first establishment of safety parameters for jellyfish-based fermented food. The final product has unique sensory odor descriptors such as umami, smoked, and spices [21].

Apart from being a solid-based food product, desalted jellyfish can be produced as jellyfish protein hydrolysates (JPHs) for a soft drink-based product. Researchers investigated the volatile flavor compounds of JPHs produced by acetic acid hydrolysis from white and sand jellyfish. Six volatile flavor compound groups were found: furan, terpene, alkane, acid, ester, and ketones. The acetic acid treatment accentuated fishy flavors in some compounds, using combinations of ingredients for soft drinks could be commercially feasible [22].

Although jellyfish is not a traditional food in Western countries and Europe, there is increasing interest in its use as food [17]. Introducing jellyfish-based products into Western markets will require food innovation. However, with the search for sustainable food sources and the emergence of edible jellyfish species, there may be an increase in consumption in European and Western societies.

Safety concerns for human health must be addressed before novel foods can be authorized by the EU Commission [30]. The investigation of the microbiological profile of Catostylus tagi jellyfish found no evidence of pathogenic markers or contamination by viruses or fungal biota [30]. These results align with European Commission Regulations on food safety. Therefore, the use of jellyfish as food is well-accepted by Asian people and will become familiar with non-Asian people as a novel food category.

2.2 *Jellyfish as a source of collagen and gelatin*

Collagens are abundant structural proteins in connective tissues such as bone, tooth, skin, blood vessels, intestines, and cartilage. They make up about 30% of

Table 1: Chemical composition of different species of edible jellyfish

Species	Portion	Concentration					Reference
		Moisture	Protein	Fat	Carbohydrate	Ash	
Stomolophus meleagris							[23]
Fresh	Umbrella	96	2.92	<0.01	No report	1.25	
Ready to eat	Umbrella	95.04	4.69	<0.01		0.33	
desalted jellyfish	Oral arm	94.08	5.60	<0.01		0.34	
Rhopilema hispidum	Umbrella	97.80 (13.57)	0.50 (19.95)	(0.46)	18.20	1.56 (57.15)	[24]
	Oral arm	96.14 (13.03)	2.01 (43.80)	(1.37)	10.65	1.35 (35.78)	
Desalted *Rhopilema hispidum*	Umbrella	95.54	3.06	1.56	No report	0.33	[25]
	Oral arm	95.16	2.68	0.98		2.68	
Desalted *Lobonema smithii*	Umbrella	95.78	3.17	0.84	No report	0.21	[25]
	Oral arm	95.49	2.34	1.16		2.34	
Rhopilema esculentum	Umbrella	96.02 (17.40)	1.58 (38.12)	(0.61)	8.87	1.30 (33.22)	[24]
	Oral arm	95.54 (20.73)	2.75 (53.87)	(1.79)	7.70	0.89 (15.90)	
Fresh *Acromitus flagellatus*	Umbrella	98.40 (12.17)	0.84 (21.38)	(0.38)	(17.66)	1.32 (48.42)	[24]
	Oral arm	97.93 (15.93)	1.26 (33.69)	(1.08)	(6.02)	1.30 (31.10)	
Stomolophus meleagris	Umbrella	96.10	2.92	<0.01*	No Report	1.25	[23]
Cyanea capillata	Whole body	95.8	16.5	0.50*	0.88	76.8	[26]
Catostylus tagi	Umbrella	-	0.18	0.02*	-	1.88	[27]
Acromitus hardenbergi	Oral arms	97.93	21.38	0.38*	17.66	48.42	[28]
Chrysaora pacifica	Whole body	-	7.53	0.72*	22.71	69.05	[29]

Remark: Numbers in parenthesis are reported on a dry-weight basis
Asterisk indicates lipid percentage

Table 2: Fatty acid composition in major commercial edible jellyfish

Species	Portion	Concentration (%)			Omega 3	Omega 6	Omega 3/ Omega 6	Reference
		Total Saturated Fatty Acid	Total Mono Unsaturated Fatty Acid	Total Poly-Unsaturated Fatty Acid				
Rhizostoma pulmo	Whole body	68.2	7	24.8	13.5	11.3	0.8	[31]
Stomolophus meleagris	Whole body	23	6.8	59.9	39.7	20.2	0.5	[32]
	Umbrella Oral arm	36.8 35.6	6.4 4.5	56.8 59.9	38.2 38.1	18.4 21.3	0.5 0.6	[33]
Rhopilema hispidum	Umbrella Oral arm	71.47 75.13	11.94 9.58	2.26 1.64	0.58 0.23	1.68 0.61	0.71 0.37	[22]
Lobonema smithii	Umbrella Oral arm	79.12 79.98	11.76 9.84	1.07 1.44	0 0	1.07 1.44	0 0	[22]
Aurelia sp1	Whole body	69.5	4.7	25.8	19	0.36	-	[31]
Cotylorhiza tuberculata	Whole body	54.8	15.2	30.0	16.4	13.6	-	[31]
Aurelia aurita (Linnaeus, 1758)	Whole body	26.57	7.48	65.95	-	-	-	[34]
Rhopilema esculentum (Kishinouye, 1891)	Whole body	31.75	9.46	58.79	-	-	-	[34]
P. noctiluca SPnL (CAEP-IIP)	Whole body	71.1	17.1	5.0				[35]
P. noctiluca SPnL (CAEP-IIIP)	Whole body	62.6	17.3	4.7	-	-	-	[35]

the total protein [36], [37]. Collagen is widely used for cosmetic and medical applications, and the global collagen market size is projected to reach ~6.63 billion USD by 2025 [38]. Commercial collagen is usually isolated from mammal by-products, such as the skins and bones of calves and pigs. However, frequent bovine spongiform encephalopathy (BSE) and foot and mouth diseases have been problems for human health. Thus, an alternative source of collagen from marine organisms, including fish, jellyfish, sponges, and other invertebrates, has received much attention as a significant source of collagen. They are metabolically compatible and not restricted by religious beliefs or animal pathogens [36], [37].

Jellyfish are considered an up-and-coming option among these marine organisms as they are safe for all religions and have not been linked to fatal infectious diseases. Collagen found in the body can be divided into 8 groups, that are, film forming collagen, basement membrane collagens, microfibrillar collagens, hexagonal network-forming collagens, fibril-associated collagens, transmembrane collagens, anchor fibrils, and multiplexins. Within these groups, at least 28 collagen proteins presented in different tissues are characterized [37]. The collagen molecules have a triple helix structure where three polypeptide chains of α or β chains are coiled around one another. The molecular weight of β chain is 200–210 kDa, and those of α1 and α2 are 100–120 kDa [36]. The quantity and type of collagen extracted from different species of edible jellyfish are summarized in Table 3.

The basic chemistry of collagen is amino acids, while glycine is collagen's primary amino acid content. However, jellyfish collagen is considered a low-quality protein due to the need for the essential amino acid of tryptophan. The amino acid content reported in different edible jellyfish species differs in quantity, as shown in Table 4. Marine collagen, mainly jellyfish collagen, is in great demand for cosmetic and skin care products due to the high collagen content in jellyfish protein [39]. A group of researchers recently delved into the moisturizing properties of collagen extract from jellyfish. They conducted measurements on products, including caspase 14 expression, filaggrin, hyaluronan synthase-3 (HAS-3), aquaporin-3 (AQP-3), and desmocollin (DSC). The results showed that the collagen extract had a similar effect on caspase 14 mRNA expression as retinoic acid (RA), which served as a reference control. In addition, the jellyfish collagen extract showed substantial inhibition of

Figure 1: Production of salted jellyfish *Lobonema smithii* in Thailand. (a) Fresh jellyfish; (b) The transport of caught jellyfish to the land; (c) Jellyfish Lobonema smithii; (d) The cutting and removing of the oral arm and umbrella; (e) The salting process of the umbrella portion; (f)–(g) The continuing salting process of umbrella porting; (h) The semi-dried salted umbrella portion; (i) Oral arm of Lobonema smithii; (j) The semi-dried salted oral arm portion; (k) Cleaning of semi-dried salted umbrella portion; and (l) By-product of salted jellyfish.

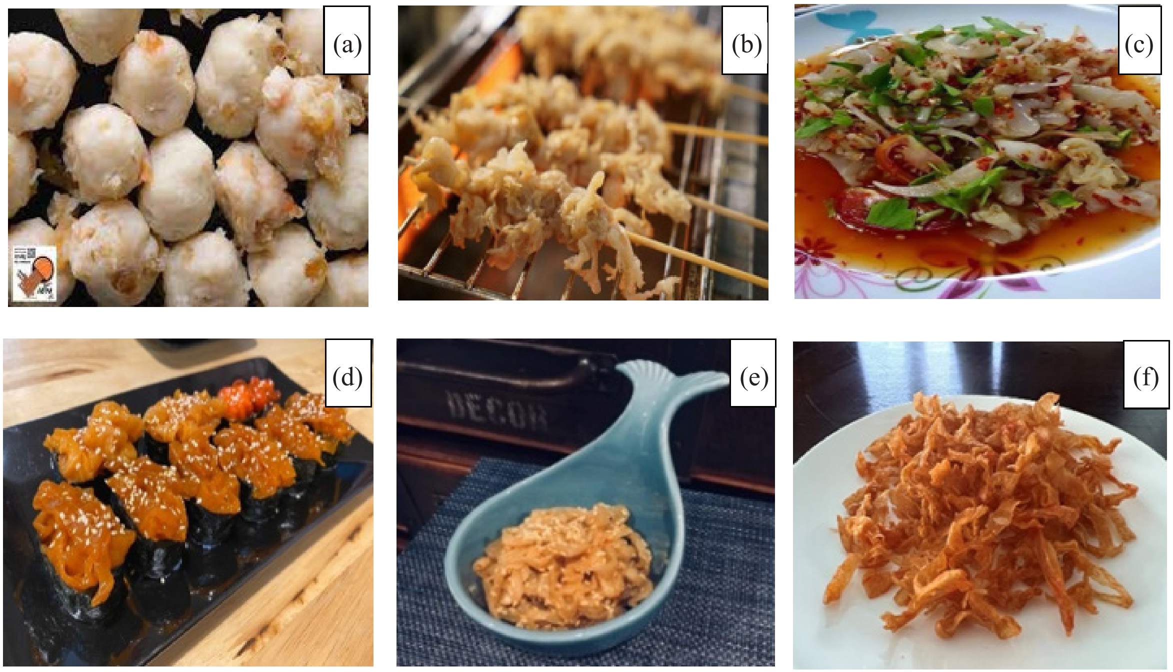

Figure 2: Jellyfish-based food menu in Thailand. (a) Fish ball mixed with jellyfish; (b) Grilled Jellyfish; (c) Jellyfish salad; (d) Sushi with seasoning jellyfish; (e) Jellyfish mixed with sesame oil; and (f) Freeze-dried jellyfish with sesame oil.

filaggrin, HAS-3, AQP-3, and DSC mRNA expression at a concentration of 2%, with reductions of 211.7%, 139.9%, 212.5%, and 116.8%, respectively. These results imply that jellyfish collagen extract has excellent potential as a moisturizing ingredient in cosmetics [7].

The limitation of being natural seasonal producing jellyfish collagen, low recovery yield of collagen, high competition of collagen from other alternative sources, and difficulties in scale-up renders the utilization of jellyfish collagen in cosmetics and skin care products. Thus, skin care products with jellyfish collagen have become less popular and are fading from the beauty market. So far, only collagen extracted from cannonball jellyfish (*Stomolophus meleagris*) mixed with peptides, amino acids, mucopolysaccharides, and minerals is sold as a food supplement for brain and memory function [7].

Gelatin, a product of heat-denatured collagen, has gained customer interest resulting in a high value of approximately 3,100 million USD by 2023, and expected to increase close to 5,400 million USD by 2033 with an average increasing rate of 6% [7]. Gelatin has long been used in the food, pharmaceutical, and cosmetic industries due to its unique functional and technological properties. To lower caloric density, food-grade gelatins are used in confections, low-fat spreads, dairy products, baked goods, and meat products. For pharmaceutical and cosmetic products, the function of gelatin is to produce capsule, thickening, or tablet coating [7]. Currently, gelatins sold in the market are produced from bovine, porcine, and marine sources. According to the constrain in religion or beliefs, and the outbreak of BSE diseases, marine gelatins gain more acceptance than land animal gelatin.

The halal and kosher certified, no genetically modified organisms, and no known allergies also increases the benefit of using marine gelatin. However, most marine gelatins give inferior gelatin gel quality [49]. Focusing on marine gelatin, fish gelatin is commercialized worldwide with a forecast market size of approximately $500 million by 2030. The diversified by-products' raw material sources for producing fish gelatin are from various fishes such as catfish, tuna, tilapia, salmon, and hake. Typically, the production of marine gelatin involves preparing the cleaned sample and multi-steps of gelatin extraction. Before extraction, the cleaned sample is suspended in an alkaline

Table 3: Type and quantity of collagen extracted from different species of edible jellyfish

Jellyfish	Body Part	Type	Quantity	Reference
Nemopilema nomurai	Mesoglea	V	2.2 (% dry basi)	[40]
Stomolophus meleagris	Mesoglea	I	46.4 (% dry basis)	[41]
Catostylus tagi	Umbrella	V/XI	2.7 (% dry basis) 4.5 (% wet basis)	[42]
Rhizostoma pulmo	Umbrella	I	0.83–3.15 (mg/g fresh jellyfish)	[43]
	Oral arm	No report	2.61–10.30 (mg/g fresh jellyfish)	
Rhizostoma pulmo	Oral arms	-	2–10 mg (mg/g wet tissue)	[31]
Rhopilema esculentum	Filaments	I	4.31 % (wet basis)	[44]
Cyanea nozakii Kishinouye	Umbrellas	-	13 % (dry basis)	[45]
Ribbon jellyfish (Chrysaora sp.)	Umbrella	II	9–19% (dry basis)	[46]
Catostylus mosaicus	Umbrella and Oral arm	I	1.46% and 2.24%, umbrella and oral arm tissues were found to be 14.61 ± 0.57 and 22.47 ± 1.25 mg/g dry weight	[47]
Acromitus hardenbergi	Bell and Oral arms	-	0.09 g and 0.16 g of lyophilized collagen was obtained from 100 g of fresh jellyfish bell and oral arms	[39]
Rhopilema hispidum (fresh)	Umbrella	I (or II)	3.68 ± 0.12 (g/100g)	[24]
	Oral arm	I (or II)	3.22 ± 0.11 (g/100g)	
Rhopilema hispidum (Salted)	Umbrella Oral arm	I (or II)	4.00 ± 0.82 (g/100g) 3.36 ± 0.32 (g/100g)	
Lobonema smihii (fresh)	Umbrella	I (or II)	2.55 ± 0.15 (g/100g)	
	Oral arm	I (or II)	2.70 ± 0.38 (g/100g)	
Lobonema smithii (Salted)	Umbrella	I (or II)	2.48 ± 1.10 (g/100g)	
	Oral arm	I (or II)	2.80 ± 0.56 (g/100g)	
Acromitus hardenbergi	Umbrella	I (or III)	693.92 (mg/g d.w)	[28], [39]
	Oral arm	I (or III)	677.78 (mg/g d.w)	
Rhopilema hispidum	Umbrella	I	122.64 (mg/g d.w)	
	Oral arm	I	396.16 (mg/g d.w)	

solution, washed until the pH is neutral, soaked in an acidic solution, rewashed, extracted with warm water, dried, and ground the gelatin [4].

So far, research on jellyfish gelatin using by-products of salted jellyfish (Lobonema smithii) showed better properties of the gelatin gel than the gelatin produced from *Stomolophus meleagris* due to the remaining excess salt in the extracted sample. The recent research presents the highest gel strength of jellyfish gelatin from *Lobonema smithii* of 447 g, a viscosity of 7cP, and a melting and gelling point of 15 °C and 8 °C. The process is done by applying ultrasonication to the desalinated by-product for 80 min, hot water (80 °C) extraction time for 4 h, and drying at 60 °C for 24 h. However, jellyfish gelatin yield is relatively low at 10% [50]. The characteristics of cold temperature setting gel and the low yield of jellyfish gelatin support the application for medical purposes rather than that for food ingredients. Hence, further research is still needed, such as combining jellyfish gelatin with other hydrocolloids, which might improve gelatin quality.

2.3 *Jellyfish as a source of protein hydrolysate*

The composition of fresh jellyfish is mainly water. When the water is dried out, the protein content dominates with a quantity close to 70%, apart from carbohydrates and fat, thereby worth using as a precursor for producing protein hydrolysate. The protein can be hydrolyzed by acid, alkaline or enzymatic hydrolysis. Acid hydrolysis using hydrochloric acid or sulfuric acid is more frequently used than alkaline chemicals of sodium, calcium, or potassium hydroxide. The drawbacks of acid hydrolysis are the high sodium content and loss of essential amino acids of tryptophan.

Table 4: Amino acid content in edible jellyfish species

Amino Acid	*Rhopilema hispidum* [24]		*Lobonema smithii* [24]		*Rhopilema esculentum* [28]	*Stomolophus meleagris* [48]	*Stomolophus nomurai* [40]
	U	OR	U	OR	W	W	W
Aliphatic							
Glycine	55.45	39.70	33.79	50.13	286	309	344
Alanine	34.66	30.81	28.21	34.01	109	82	77
Isoleucine	22.09	19.30	16.09	20.28	31	22	16
Leucine	26.45	21.74	19.79	26.81	42	34	27
Valine	19.30	18.48	14.66	19.00	38	35	24
Proline	26.18	23.06	17.79	23.81	72	82	79
Hydroxy proline	17.18	19.75	12.85	16.57	No report	40	57
Aromatic							
Phenylalanine	18.81	21.06	15.24	18.88	30	10	8
Tyrosine	22.54	19.75	18.58	23.08	18	6	5
Acidic							
Aspartic acid	45.44	31.58	32.36	46.47	68	79	71
Glutamic acid	43.22	32.76	28.03	41.04	86	98	94
Basic							
Arginine	23.94	19.49	17.55	22.31	77	52	57
Lysine	15.31	16.65	11.53	11.44	51	38	24
Hydroxy lysine	No report	No report	No report	No report	No report	27	35
Hydroxylic							
Threonine	21.77	18.21	15.00	21.08	36	35	28
Serine	31.97	24.65	23.42	32.84	44	45	45
Sulfur containing							
Methionine	12.08	17.00	12.18	12.71	12	4	8
Cysteine	5.98	4.19	6.13	4.68	3	-	-
Total	445.82	378.18	323.20	425.14	1000	1000	1000

Table 5: Protein hydrolysate from jellyfish species

No.	Species	Isolation Method	Properties	Reference
1	*Lobonema smithii*	Ultrafiltration membranes (10, 3, and 1 kDa) and gel filtration chromatography	Antioxidative and tyrosinase inhibitory activity	[53]
2	*Rhopilema esculentum*	Ultrafiltrated with a hydrophilic 5000 Da cut-off membrane	Angiotensin I converting enzyme inhibitory	[54]
3	*Lobonema smithii*	Bromelain (eb-JPH) and hydrochloric acid (a-JPH) hydrolysis	foaming and emulsifying properties	[51]
4	*Rhizostoma pulmo*	Membrane filtration	Antioxidant Peptides	[55]
5	*Chiropsalmus quadrigatus*	Column chromatography reverse phase - high performance liquid chromatography (RP-HPLC)	Angiotensin I Converting Enzyme Inhibition	[56]
6	*Rhopilema esculentum Kishinouye*	Sephadex G-25 separation, chromatography, reverse-phase HPLC	Antioxidative and Angiotensin Converting Enzyme Inhibitory activity	[57]
7	*Nemopilema nomurai*	Reverse-phase HPLC	Angiotensin-converting enzyme (ACE) inhibitor	[58]

However, the reaction with alkali chemicals can cause a loss of serine and threonine and generate nonfunctional compounds [51]. Enzymatic hydrolysis is widely used in food and pharmaceutical industries due to the ease of control reaction, and it is a Generally Recognized as Safe (GRAS) method. The protease enzymes used include pepsin, bromelain, pepsin, trypsin, alcalase, neutrase and fungal protease [51]. Protein hydrolysates from different jellyfish species are shown in Table 5.

Research on the functionality of jellyfish protein hydrolysate mainly focuses on antioxidant activity. Silaprueng *et al.* [51] examined the functional properties of jellyfish (*Lobonema smithii*) protein hydrolysate (JPH) that was made through either bromelain (eb-JPH) or hydrochloric acid (a-JPH) hydrolysis. The researchers analyzed hydrolysis time's impact on the JPH's antioxidant activity. They discovered that a longer hydrolysis time led to greater degrees of hydrolysis and inhibition of the DPPH radical. The 24 h hydrolysis produced JPH with the highest hydrolysis and inhibitory effect. Other studies investigated the potential bioactivities of pepsin-hydrolyzed jellyfish protein hydrolysate (ep-JPH). They tested the effect of pepsin hydrolysis time on the antioxidant activity of ep-JPH. They found that the hydrolysis time led to higher degrees of hydrolysis and inhibition of the DPPH radical [52]. Furthermore, Mediterranean jellyfish species, such as Cotylorhiza tuberculata, *Rhizostoma pulmo*, and *Aurelia* coerulea have been found to possess significant antioxidant properties based on extracts from whole specimens [31].

Apart from *in vitro* study, the *in vivo* study was conducted on mice to investigate the effects of orally administering jellyfish collagen hydrolysate (JCH) on body weight gain, inflammation, oxidative stress, and cecum microbe composition. The results showed that jellyfish collagen hydrolysate (JCH) prevented weight gain, maintained glucose, serum glucose, triglyceride, and cholesterol levels in the serum, and reduced oxidative stress and inflammation by decreasing certain gene expressions. Additionally, JCH helped recover the alteration of microbiota composition induced by a high-fat diet, suggesting it could be used to prevent and treat-induced obesity [59]. Additionally, JCH was tested for its anti-fatigue and antioxidant properties. Mice administered with JCH showed increased climbing endurance, reduced blood lactate and BUN levels, and increased hepatic and muscle glycogen. JCH also had an anti-oxidative effect on aging mice, indicating it may be a helpful ingredient in health-promoting foods [60].

In other studies, jellyfish gelatin was broken down using proteases to create antioxidative polypeptides. The best results were achieved using trypsin, and properase E. The gelatin polypeptides were obtained in three series using ultrafiltration. The polypeptide SCP3 had the most significant amount of hydrophobic amino acids, while polypeptide SCP2 exhibited the most potent antioxidant activity against hydroxyl radical and hydrogen peroxide scavenging and metal chelating abilities. On the other hand, SCP3 showed the highest reducing power, antioxidant activity in the linoleic acid emulsion system, and superoxide anion radical scavenging activity. Jellyfish gelatin could be a natural source of antioxidant polypeptides, and enzymatic hydrolysis and ultrafiltration could be future processing technologies to use jellyfish resources [61].

2.4 *Jellyfish as a plant fertilizer*

According to projections to feed a population of 9.1 billion people by 2050, food production needs to increase by 70% between 2005 and 2050. Developing countries would need to double their production [62]. Our food supply largely depends on the soil, with an estimated 95% directly or indirectly produced on Earth [63]. Soil degradation threatens food security as it reduces crop yield and may lead to farmers using harmful inputs or abandoning the land altogether [64]. Crops require an adequate supply of essential mineral elements to achieve optimal productivity. In any agricultural soil, there often needs to be more available nitrogen, phosphorus, or potassium for rapid crop growth during the early stages of development. As a result, fertilizers are commonly used in intensive and extensive agricultural systems.

Moreover, when animals or humans suffer from mineral deficiencies in certain areas, fertilizers enhance crop production and increase the concentration of necessary mineral elements in the consumable parts. Nevertheless, mineral fertilizers are associated with considerable financial and environmental expenses. Additionally, plants' nutrient absorption capabilities are constrained. Therefore, when excess nutrients enter waterways and contaminate the sea, it is because some nutrients are still present in the soil. One possible solution to this problem is to use marine organic fertilizers to transfer nutrients from the sea to the ground, especially in areas with insufficient nutrient resources. This approach could eliminate the need for additional mineral fertilizer inputs. Marine organic fertilizers could reduce water pollution by balancing nutrient levels between terrestrial and aquatic systems.

Hence, marine organic fertilizers could be a valuable local resource for enhancing ecosystem goods and services in coastal areas by providing an alternative organic nutrient for soil restoration [65] as shown in Table 6.

Marine organic fertilizers are environmentally friendly as they align with the goals of integrated management of coastal areas, known as "blue growth" for sustainable management in marine sectors [71]. This approach can contribute to achieving sustainable development goals. However, many coastal areas suffer damage from industrialization, agriculture, and urbanization, with chemical fertilizers and pesticides contaminating marine ecosystems [72]. Research has shown that chemical fertilizers can cause heavy metal contamination in soil, particularly with Cd, Pb, and As [73]. To mitigate this issue, one solution could use marine resources such as organic fertilizers. By doing so, the necessary elements for the soil can be provided while minimizing the negative impact of chemical fertilizers on both soil and marine contamination. Jellyfish blooms have increased worldwide and caused damage in coastal areas [74] but can be used as a source of organic fertilizer to enhance tree growth and improve soil properties. Research has investigated jellyfish's potential benefits for seedling growth and germination and its use as a fertilizer, weedicide, and insecticide in the agricultural industry [75].

Several researchers have reported the positive effects of using jellyfish in agricultural production. The impact of using jellyfish fertilizer on vegetable fields showed that jellyfish fertilizer had high concentrations of crucial components such as nitrogen, phosphorus, potassium, magnesium, and calcium, which positively affected vegetable growth rates [70]. Using jellyfish suspensions in cultivating crops such as pak choi, green soybeans, perilla, spinach, and cherry tomatoes positively affects growth and yield [68]. Moreover, it was observed that *Pinus thunbergii* and *Quercus palustris* seedlings showed improved growth and survival rates due to the treatment [3].

The feasibility of utilizing jellyfish blooms in Sri Lanka's coastal waters (specifically *Lychnorhiza malayensis*, *Chrysaora* sp., *Chiropsoides buitendijki*, and *Marivagia stellata*) as an organic fertilizer for the growth of *Abelmoschus esculentus*, or okra revealed that plants treated with jellyfish fertilizer began to flower within 35–40 days, while those treated with compost showed no signs of flowering during the experimental period. More investigation is necessary to explore the possibility of utilizing jellyfish as a natural fertilizer, which could be enthusiastically embraced within the community [76].

2.5 *Jellyfish as a source of green fluorescent protein*

Many marine organisms are capable of bioluminescence. Although the chemical processes involved in producing light have been studied extensively, the reasons for this phenomenon in the marine environment still need to be fully understood. It is suggested to function to attract mates or as a defense mechanism against predators [77]. Jellyfish are a renowned group of bioluminescent creatures among these organisms. There are numerous undiscovered species of jellyfish residing in deep waters. A hydromedusa Aequorea victoria, not an edible jellyfish, is the most well-known due to its green fluorescent protein (GFP). This protein was initially

Table 6: Jellyfish species as a plant fertilizer

No.	Species	Seed	Effect	Reference
1	*Aurelia aurita* and *Cyanea capillata*	Annual ryegrass (*Lolium multiflorum* L.)	Enhanced seed germination	[66]
2	*Nemopilema nomurai*	(*Phleum pratense* L.), ryegrass (*Lolium multiflorum* Lam.) and barnyardgrass (*Echinochloa crus-galli* (L.) Beauv.)	Weed inhibitory activity	[67]
3	*Aurelia aurita*	Cherry Tomato (*Lycopersicon esculentum* Mill) and tomato (*Solanum lycopersicum*)	Increased ascorbic acid, Improvement of fruit quality and taste	[68]
4	*Nemopilema nomurai, Aurelia surita*	*Pinus thunbergii*	Improvement in soil condition by enhancing moisture retention, supplying nutrients to the seedlings	[69]
5	*Aurelia aurita* and *Chrysaora melanaster*	Seedling of chingentsuai, green soybean and perilla	Improvement in the growth of vegetables	[70]

discovered by Osamu Shimomura, Martin Chalfie, and Roger Tsien in 1962, earning them a Nobel Prize in Chemistry in 2008 [11]. The discovery of GFP in jellyfish revolutionized cell biology by providing a genetically-encoded probe for labeling specific proteins inside living cells without needing exogenous synthetic or antibody-labeled fluorescent tags. Studies have demonstrated that the expression of the GFP, which originates from *A. victoria*, in *Escherichia coli* or *Caenorhabditis elegans* results in a highly fluorescent protein [78]. This fluorescence is not dependent on exogenous substrates or coenzymes [79]. Moreover, chimeric proteins were constructed by Wang and Hazelrigg (1994) using GFP that were functional and fluorescent GFP in Drosophila sp. [80].

The primary amino acid sequence encodes the chromophore in GFP and forms spontaneously through a self-catalyzed protein folding mechanism and intramolecular rearrangement. The beta-barrel structure of GFP protects the chromophore and enhances resistance to changes in pH, temperature, fixation with paraformaldehyde, and common denaturing agents. GFP has been expressed successfully in prokaryotes and various organisms to extend the analysis of protein-protein interactions, protein conformational changes, and the behavior of signaling molecules to their natural environment within intact cells [81]. GFPs have since been used extensively in biomedical research to tag cells involved in oncology and nerve cell development. Given that light production is common among scyphomedusae (such as Pelagia noctiluca), which often blooms in the Mediterranean Sea and UK waters [82], [83], GFPs may offer a promising compound that could be extracted from jellyfish by-catch.

3 Jellyfish as a Biosensor for Environmental Microplastic Quencher

Jellyfish have a natural defense system that includes the secretion of anti-microbial peptides when they face environmental changes or come into contact with other organisms [84], [85]. The research found that the mucus from *Aurelia aurita* jellyfish can bind to and reduce the toxicity of nanoplastics [9], [86], [87]. This suggests that using jellyfish to remove microplastics from water could be an effective and eco-friendly solution, especially since jellyfish blooms can be easily caught using fishing nets. Applying physical stress to the jellyfish can cause them to secrete mucus that captures the microplastics. After this, they naturally decompose in water without harmful chemicals or greenhouse gas emissions [88]. However, the seasonal nature of jellyfish blooms presents limitations to this method, and aquaculture technologies are being developed to address this issue in China. Using jellyfish as a sustainable low-carbon technology for reducing plastic pollution is in high demand worldwide [89].

Microplastics are everywhere in the ocean and almost all marine animals are affected [90], [91]. In the Atlantic Ocean alone, millions of tons of tiny plastic particles float in the top 200 m [92]. Many marine creatures swallow these microplastics with zooplankton being the main entry point into the food chain [93], [94]. Surprisingly, jellyfish have also been found to ingest these plastics in their natural habitat. Researchers have discovered plastic particles in jellyfish samples taken from labs and the field [94]–[96]. Jellyfish may take these plastics for food [9], a behavior also observed in other marine organisms [97], [98]. Although it is common knowledge that jellyfish consume a significant amount of plankton, there needs to be more understanding regarding their processing and elimination of microplastics in their natural habitat [99], [100]. To better understand this issue, researchers suggest conducting experiments under controlled conditions to investigate how microplastics affect marine biota [101].

Using jellyfish to reduce plastic pollution has its limitations. Jellyfish blooms are limited to specific seasons, making capturing them continuously in their natural state difficult. Nevertheless, China has been able to satisfy the growing demand for edible jellyfish by adopting aquaculture technology since the 1980s. As a result, reports surfaced in the 2000s of a flourishing jellyfish culture in China [102]. The mucus produced by the jellyfish species has the ability to sequester PS micoplastics. The mucus entraps the microplastic and becomes more compact which can be easily collected and removed [103]. One possible way to obtain jellyfish mucus all year round is through biochemical synthesis, which could be more cost-effective. Nonetheless, reducing microplastics with jellyfish mucus is still worth considering as it aligns with the United Nations Environment Assembly and OECD's focus on managing plastic pollution throughout its life cycle. To achieve this, minimizing the amount of plastics indirectly released into the environment is crucial, like when microplastics are discharged from laundry wastewater treatment or domestic wastewater. Bio-inspired jellyfish technology can be employed as a biomimetic and eco-friendly way to remove microplastics from water streams. Although nanoplastics pose technical challenges in identifying and characterizing them due to limited data on their occurrence and distribution, current knowledge of microplastics suggests that particle abundances increase exponentially as particle size decreases [103]–[106]. Therefore, it is likely that nanoplastics exist in extremely high numbers in the environment.

Recent studies have shown that nanoparticles can quickly enter various organisms and pass through the gut-blood and blood-brain barriers, which can have harmful health effects [107]. As more evidence surfaces about the potential hazards of nanoparticles, there is an increasing interest in developing technologies to eliminate them from water streams and prevent their release into the environment. One study found that jellyfish mucus, a hydrogel containing hydrated mucins, can capture and remove gold and quantum dot nanoparticles from water [9]. Mucus plays a critical role in moisture retention, defense against predators, anti-microbial activity, and particle removal/cleaning in jellyfish and other cnidaria [101].

4 Application in Pharmaceutical Industry

4.1 *Jellyfish-derived bioactive peptide and collagen for potential bio-medicinal research and therapy*

Bioactive peptide, a short amino acid sequence (2-20 amino acids), has received significant attention due to profound potential health benefits, such as antioxidant, anti-hypertensive, anti-cancer, anti-diabetic, anti-inflammatory, and anti-microbial activities. Not surprisingly, the market value of bioactive peptides market size is projected to increase from 48.62 billion USD by 2020 to 95.71 billion USD by 2028 at an average growth rate of 8.86%.

The successful search for natural novel marine bioactive peptides for medicinal therapy shows two marine peptides approved by the FDA, namely, ziconotide (Prialt®) and brentuximab vedotin (Adcetris®) used as an analgesic and anti-cancer drug [114]. Multiple compounds with biological properties have been discovered in various parts of scyphozoan jellyfish, such as their tentacles, oral arms, umbrellas, and mucus secretions. For example, peptides found in the tentacles of edible jellyfish *Rhopilema esculentum*, have been shown to possess both ACE inhibitory and antioxidant abilities [115], [116]. Several studies have reported the isolation and purification of peptides with potential health-beneficial effects from jellyfish, as shown in Table 7. Two peptides that inhibit angiotensin I converting enzyme (ACE) were isolated from jellyfish *Rhopilema esculentum* and purified using various chromatographic methods. The amino acid sequence of the peptides was identified, and their ACE inhibitory activity was measured. The peptides also showed anti-hypertensive effects in rats after oral administration. These findings suggest that jellyfish-derived peptides may have the potential as anti-hypertensive compounds in functional foods [117].

R. esculentum extracts possess antioxidant properties that contribute to their ability to provide photoprotection *in vivo* [118]. Peptides obtained from

Table 7: Bioactive compounds extracted from Jellyfish species

No	Species	Bioactive Compounds	Reference
1	*Cassiopea andromeda*	Beneficial fatty acids, phenolic compounds, and pigments	[108]
2	*Pelagia noctiluca, Rhizostoma pulmo, Cotylorhiza tuberculate, Caryddea marsupialis*	fatty acids and derivatives, small peptides	[109]
3	*Rhizostoma luteum*	Protein, phenols, polyunsaturated fatty acids (PUFAs), the essential fatty acid, linoleic	[110]
4	*Rhopilema esculentum*	Skin polysaccharide and monosaccharide	[111]
5	*Aurelia sp.1, Cotylorhiza tuberculata* and *Rhizostoma pulmo*	Proteins (collagen 40 %) amino acids, phenolics, and fatty acids	[31]
6	Ribbon Jellyfish (*Chrysaora* sp.)	Protein hydrolysate with a high content of hydrophobic amino acids as well as unique amino acid sequences	[112]
7	Brown cannonball jellyfish (*Stomolophus meleagris*)	Collagen and proteins with antioxidant properties	[113]

pepsin hydrolyzed proteins (which include collagen) in *Rhizostoma pulmo* are known for their remarkable antioxidant activity, which is inversely proportional to their molecular weight. These low MW peptides effectively combat oxidative stress in human epidermal keratinocyte (HEKa) cell cultures [55].

Jellyfish collagen's broad harmlessness and bioavailability make it a good candidate for replacing bovine or human collagens in selected biomedical applications [43]. Research indicated that collagen extract from *N. nomurai* has been shown to stimulate immune system function without causing allergies [119]. Moreover, collagen from jellyfish was studied for its hemostatic properties. The collagen was isolated from the mesoglea of the jellyfish and found to be type I collagen. Collagen sponges were made and tested against medical gauze for their ability to clot blood. It was found that collagen sponges had an improved hemostatic ability and were suitable for use as a hemostatic material and for wound healing applications [120]. Besides, researchers have investigated the potential of using collagens from Mediterranean jellyfish in various industries, such as food, cosmetics, and pharmaceuticals. The best yield of collagens was obtained from *Rhizostoma pulmo* oral arms using the pepsin extraction method.
Comparing the biological properties of jellyfish collagen with mammalian fibrillar collagens showed no statistical difference in cytotoxicity but a preference for fibroblast and osteoblast adhesion to jellyfish collagens [120]. The study investigated the wound-healing activity of collagen peptides derived from jellyfish. Collagen was extracted from *Rhopilema esculentum* and enzymatically broken down into collagen peptides. *In vitro* and *in vivo* studies showed that collagen peptides had a positive effect, including increased scratch closure, wound contraction, re-epithelialization, tissue regeneration, and collagen deposition. The study suggests that collagen peptides derived from jellyfish could be a potential future therapeutic product for wound clinics [61]. Researchers have studied the properties of acid-solubilized collagen from jellyfish Catostylus mosaicus (JASC) harvested from the Persian Gulf, comparing it to the industry-standard collagen used for biomedical research from rat tail tendon (RASC). JASC was found to be a type I collagen with similar molecular signatures to RASC. JASC was also shown to promote cell attachment and proliferation better than RASC on rigid substrates. Both kinds of collagen supported cell growth on blended collagen-agarose scaffolds, but RASC increased more after six days. The study suggests JASC could be an alternative to mammalian type I collagen for biomaterial applications [47].

Being essential for cell biology research, jellyfish collagen (Jellagen®) is a potential material for culturing induced pluripotent stem cell-derived cell lines (iPSCs) for modeling human diseases. It was evaluated for the growth and viability of iPSC-derived microglial-like cells (iMGL) and found comparable results to laminin-511 and better results than rat tail collagen I. The cells cultured on Jellagen® showed a more ramified cell morphology. Jellyfish-derived collagen is suitable for osteochondral engineering and enhancing vascular endothelial cell development. A recent study tested the effects of extracts from certain jellyfish species on human cancer cell lines and found that fractions from *Caryddea marsupialis* and *Cotylorhiza tuberculata* were the most active in reducing cell viability. The fractions found in jellyfish mainly consisted of fatty acids and derivatives, but *C. marsupialis* also had small peptides. According to a study, jellyfish may have the potential to be a new source of drugs that can prevent cell growth in the future.

Additionally, it could be used as a substitute for collagen taken from rat tails in microglia culture, improving the study of neural transmission and treating diseases caused by nerve network degeneration. Researchers discovered that taking from *Chiropsalmus quadrumanus* jellyfish increased neurite outgrowth length and branching junctions in human SH-SY5Y neurons without affecting cell body and viability. The extract had various low molecular mass compounds and peptides that support cytoskeleton reorganization, cell membrane expansion, and antioxidant or neuro-protective activity. This makes it a promising tool for neuronal connection recovery and potentially treating neurodegenerative diseases. A study has found that collagen from jellyfish (*Rhizostoma pulmo*) can be a safer alternative in scaffold production.

Jellyfish collagen demonstrated comparable properties to mammalian collagen and supported chondrogenesis in the presence of TGFβ1. The study suggests that jellyfish collagen could be used for osteoarthritis repair and other regenerative medicine applications [121]. In addition, there are researches conducted on the potential use of jellyfish collagen for various biomedical purposes, such as wound-healing, tissue-regenerating items, scaffolds for tissue regeneration, drug delivery, antioxidant, and melanogenesis-inhibitory properties, as well as protecting the skin from ultraviolet radiation [122], [123]. Besides, studies have examined the immunostimulatory and anti-hypertensive effects of jellyfish collagen.

4.2 *Functional jellyfish-derived bioactive compounds*

Apart from significant collagen protein, jellyfish also have beneficial bioactive compounds, including diterpenes, sesquiterpenes, terpenoids, and monoterpenoids for defense and communication [124], which have been reported to have anti-microbial properties in several studies. For example, the defensing superfamily includes aurelin, extracted from the mesoglea of the *Aurelia aurita* jellyfish. It has been found to have substantial effects against Gram-negative a nd Gram-positive bacteria [125]. Qniumucin, a glycoprotein found in *N. nomurai* jellyfish, may also have the ability to prevent cartilage degeneration in osteoarthritis [126]. Jellyfish use cnidocytes to deliver their venom, which is composed of various bioactive components that can cause harmful effects on their prey. Some jellyfish have harmless venom, while others can cause human death [127]. For instance, *Chironex fleckeri*, or box jellyfish, is one of the most venomous creatures on Earth. Its tentacles release venom that can cause extreme pain, tissue damage, and even animal death. This venom comprises proteins such as phospholipases A2, metallopeptidases, serine peptidases, CRISPs, lectins, pore-forming toxins, and protease inhibitors [128], [129]. The molecular mechanisms behind these effects have yet to be fully understood, but a recent genomic analysis sheds light on them.

The current treatment for box jellyfish envenoming is an antivenom made from sheep, but its effects are still being determined. In addition, the scientists conducted tests on 31 different substances and formulas to alleviate the sting symptoms. They determined that ammonia, barium chloride, bleach, scented ammonia, carbonated cola, lemon juice, sodium chloride, and papain caused nematocyst discharge and were, therefore not considered viable inhibitors. However, butylene glycol had a reduction effect on nematocyst discharge. Furthermore, 10% lidocaine in ethanol, 1.5% hydroxy acetophenone in distilled water and butylene glycol, as well as 3% Symsitive® in butylene glycol were all found to be effective inhibitors of nematocyst discharge [130].

Nemopilema nomurai jellyfish venom induces cytotoxicity against HepG2 cells [131]. Peptides found in *Chrysaora quinquecirrha* venom have been shown to cause cell death in alveolar epithelial carcinoma and cervical cancer cells, but do not affect normal human lymphocytes [132]. *Pelagia noctiluca* venom contains specific components that can lower nitric oxide levels and exhibit anti-inflammatory effects without compromising macrophage viability. The neurotoxins found in Gonionemus vertens jellyfish have been shown to affect macrophage adhesion. At the same time, *Pelagia noctiluca* venom and its components have demonstrated cytotoxic and antiproliferative properties, explicitly targeting tumor cells [133].

In a separate study, researchers isolated a protein called smP90 from *Stomolophus meleagris*, demonstrating high radical-scavenging superoxide anion activity with a half-scavenging concentration (EC50) of approximately 16 g/mL [134]. The venom extracted from *Chrysaora quinquecirrha*, a species of jellyfish, has shown moderate efficacy against ten different pathogens, including *Escherichia coli*, *Vibrio cholerae*, and *Klebsiella pneumoniae*. Additionally, the venom is particularly effective against *Salmonella paratyphi*, which exhibits the highest sensitivity to the venom among all tested pathogens. *Proteus mirabilis*, *Proteus vulgaris*, and *Klebsiella oxytoca* were also susceptible to the venom's effects. *Pseudomonas aeruginosa* was another pathogen that exhibited moderate sensitivity to the venom, while *Pelagia noctiluca* crude venom displayed *in vivo* analgesic effects and *in vitro* plasma antibutyrylcholinestrasic activities without inducing acute toxicity [133], [135]. *Aurelia aurita* moon jellyfish crude venom contained different peptides with potent anticoagulant activity *in vitro* [136].

Mirshamsi *et al.* [137] conducted another study, which found that the crude venom of *Cassiopea andromeda* selectively induced cytotoxicity by targeting mitochondria in cancer tissue from patients with breast adenocarcinomas through ROS mediation. Li *et al.* [138] also speculated that the metalloproteinases component of *N. nomurai* nematocyst venom (NnNV) could produce myotoxicity and trigger muscle damage during jellyfish stings. Isolated active ingredients in *Rhopilema esculentum* jellyfish venom demonstrate insecticidal activities [139]. Furthermore, *Aurelia aurita* venom displays anticoagulant effects via strong fibrinogenolytic activity cleaving Aα and Bβ chains of fibrinogen molecules [136]. Researchers have studied the potential therapeutic applications of various animal venoms and their components.

A study evaluated whether jellyfish venom has anti-cancer activity and found that *Nemopilema nomurai* jellyfish venom (NnV) strongly induced cytotoxicity of HepG2 cells through apoptotic cell death. NnV inhibited the phosphorylation of several signaling pathways associated with cancer progression and enhanced the expression of p-PTEN, a tumor suppressor gene. NnV also inactivated negative feedback loops related to Akt activation, demonstrating its highly selective cytotoxicity in HepG2 cells via dual inhibition of the Akt and mTOR signaling pathways, but not in normal cells. The study shows NnV has significant anti-cancer effects in a HepG2 xenograft mouse model without apparent toxicity [132]. To come up with a consensus based on evidence, a systematic review explores the treatment of extremity ischemia and necrosis following jellyfish envenomation. The ischemic aftermath usually takes a few days to develop and requires close medical monitoring. Surgery can be avoided by administering prostaglandin derivatives through IV infusions and intra-arterial thrombolytics, which have been shown to improve the patient's condition. More detailed information is described in Table 8.

5 Future Perspectives

Although jellyfish have long been known as one of the primitive species that can be eaten for food, studies focusing on the potential applications of jellyfish are limited. Jellyfish can benefit humans, including being consumed in eastern countries and being a source of high-value molecules and compounds for biotechnological purposes. Recently, few studies have shown that these marine creatures possess antioxidant properties, making them a healthy food option and a source of antioxidant compounds. We have also found that jellyfish contain a series of collagen, which has proven to be biocompatible with human collagen and has been used in biomedical applications such as tissue growth and regeneration. Even though some jellyfish venom causes painful stings, it has shown great potential for pharmaceutical products in numerous tests on

Table 8: Pharmacological properties of jellyfish venom proteins

Species	Pharmacological properties of jellyfish venom proteins	Reference
Rhopilema esculentum Kishinouye	The 48 h LC 50 values were 123.1 (*S. pyri*), 581.6 (*A. medicaginis*), and 716.3 (*M. persicae*) µg/mL, respectively. *R. esculentum* full proteinous venom had the most potent toxicity against S. pyri Fabriciusa, and the corrected mortality recorded at 48 h was 97.86%	[139]
Chrysaora quinquecirrha	*C. quinquecirrha* (sea nettle) nematocyst venom (SNV) peptide could induce apoptosis in HEp2 and HeLa cells	[135]
Rhopilema esculentum Kishinouye	Hemolytic activity of RFV was temperature-sensitive and when pre-incubated at temperatures over 40 °C, it was sharply reduced	[140]
Nemopilema nomurai, Rhopilema esculenta, Cyanea nozakii, Aurelia aurita	Four jellyfish venoms showed gelatinolytic, caseinolytic, and fibrinolytic properties The relative cytotoxic potency was *C. nozakii* > *N. nomurai* > *A. aurita* > *R. esculenta* The cytotoxicity in NIH 3T3 cells of jellyfish venom shows a positive correlation with its overall proteolytic activity.	[141]
Chiropsalmus quadrigatus	C. quadrigatus toxin-A, a major proteinaceous toxin from the nematocysts of *C. quadrigatus.* CqTX-A showed lethal toxicity to crayfish when administered via intraperitoneal injection (LD_{50} = 80 µg/kg)	[142]
Cassiopea xamachana, Carybdea marsupialis, Linuche unguiculata	The extract obtained from *Linuche unguiculata* was most active against the yeast *Candida albicans* and the protozoan *Giardia lamblia*. with 24 mm of inhibition zone diameter and an IC50 of 63.2 µg/mL, respectively. The results showed that only 44 mg/kg of jellyfish (*Carybdea marsupialis*) toxin were necessary to cause significant mortality in tilapias (*Oreochromis niloticus*)	[143]

various organisms, including humans. However, more information is needed, particularly on effectively utilizing such compounds derived from jellyfish, mainly in biotechnology and biomedicine.

Utilizing toxins from Cnidaria for drug development is challenging due to limited research and difficulty obtaining pure samples with sufficient quantity and specificity. Concerning bioprospecting, toxins have quite a few obstacles to overcome. They tend to have low solubility, a short half-life in serum, poor oral bioavailability, and low membrane permeability. On top of that, they can be unstable during storage and transport and may even have the potential to cause an immune response. However, advancements in techniques, technologies, and application of several in-silico or computational tools might provide a lead to explore such untouched resources for future medicinal products soon. Hence, there is considerable research potential, in post-harvest applications of jellyfish, mainly in agro-based industry or food industry, along with possible applications of such species as a biosensor to control environmental pollution on a large scale as well as the use of different bioactive compounds collected from jellyfish species for the broader applications in biotechnology and for the pharmaceutical interests.

Acknowledgments

We thank the National Research Council of Thailand for their support through the NRCT Senior Research Scholar Program (Contract No.814-2020) and the KMUTNB Postdoctoral Fellowship Program (KMUTNB-Post-66-07 and KMUTNB-Post-67-09).

Author Contributions

N. B.: investigation, data gathering and review, writing – original draft; B. T.: conceptualization; funding acquisition, writing – review & editing; V. R.: conceptualization, project administration, writing – review & editing; M. S. K.: review & editing; T. P.: supervision, writing – review & editing

Conflicts of Interest

The authors have declared no conflicts of interest for this article.

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