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Aurelia aurita jellyfish collagen: Recovery properties

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Abstract:
Wound and burn healing is a complex physiological process that can be facilitated by medications based on marine collagen. In this regard, biomass of the *Aurelia aurita* jellyfish is a promising alternative source of medical collagen. As the global incidence of burns and wounds continues to grow, new healing methods have become a relevant area of medical science.
This study featured acetic acid as a means of marine collagen extraction from *A. aurita* biomass. The physical and chemical properties of jellyfish collagen were determined gravimetrically and included such indicators as water solubility and water holding capacity. The molecular weight was defined by gel electrophoresis. The spectral studies relied on the method of UV spectroscopy. The regenerative experiments included such parameters as cytotoxicity, antioxidant properties, adhesion, and wound healing rate, as well as a quantitative PCR analysis.
The optimal conditions for maximal collagen yield were as follows: 0.5 M acetic acid and 48 h extraction time. However, the collagen yield was very low (≤ 0.0185%). The high water holding capacity showed good prospects for *A. aurita* collagen to be used as hemostatic sponge. The acid-soluble collagen sample had a molecular weight of 100–115 kDa, which made it possible to classify it as type I. *A. aurita* jellyfish collagen revealed no cytotoxic properties; it had no effect on adhesion, migration, and proliferation of keratinocytes, neither did it affect the expression of cell differentiation markers.
The wound healing model proved that the marine collagen had regenerative properties as it was able to increase the wound healing rate by 24.5%. Therefore, collagen extracted from the biomass of *A. aurita* jellyfish demonstrated good prospects for cosmetology and regenerative medicine.

Keywords: *Aurelia aurita*, jellyfish, marine collagen, biological activity, regenerative properties, cytotoxicity, extraction, regenerative medicine

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INTRODUCTION

Burn injuries and wounds are a major global health issue. High temperatures, accidents, surgery, and infections damage skin structure and function, which makes wound healing a complex physiological process [1].

Silver sulfadiazine and mafenide acetate are popular medications against wounds and burns. However, they are expensive and may cause severe side effects. Moreover, they are not effective against deep burn wounds and often cause scarring. As a result, novel burn-treating substances are a relevant medical issue [2].

The second half of the XX century witnessed a great progress in regenerative medicine and burn therapy. For instance, pharmacotherapy with tissue scaffolds promote the formation of new viable human issues, offering an alternative to donor tissues. Unfortunately, the use of skin substitutes is limited by immunogenicity, postoperative infections, and donor site area [3].

Collagen is a promising wound healing biomaterial. However, collagen and its derivatives are usually obtained from swine and bovine skins and bones, which means a certain risk of transmissible spongiform

encephalopathy. Religious restrictions also limit the use of biomaterials obtained from pigs and cows [4].

Fish, jellyfish, sponges, and other marine invertebrates can serve as an alternative source of collagen. Their biocompatibility is quite high, and they do not transmit diseases to humans [5]. Collagens isolated from marine organisms make excellent scaffolds with high biodegradability and low immunogenicity [6].

Jellyfish is a biomass that consists of proteins organized into a complex polymer, i.e., collagen. Fibrillar collagen is the most abundant component in most jellyfish [7]. Jellyfish tissue structure resembles that of human skin tissue, which makes marine jellyfish a popular subject of scientific research [8]. Unlike mammalian collagens, jellyfish collagen does not transmit spongiform encephalopathy. Jellyfish collagen extracts are known to stimulate the immune response *in vivo* without causing allergy [1].

In addition, jellyfish collagen peptides accelerate the healing of skin wounds. In the future, they may render new wound treatment medications [9]. Jellyfish collagen peptides are a source of bioactive compounds, polysaccharide structures, and extracts, which makes jellyfish a potential raw material in medical therapy and tissue engineering, e.g., biomaterials, new pharmaceuticals, and nutraceuticals [1].

Despite all their numerous benefits, modern medicine still possesses very limited data on collagen peptides derived from *Aurelia aurita* or their effect on wound healing. *A. aurita* is a species of *Scyphozoa* jellyfish [10]. These marine creatures have a translucent pinkish body that consists of a flat bell of up to 40 cm across and numerous short tentacles [11]. They inhabit sea waters with consistent currents and temperatures from −6 to 31°C, the optimal temperatures being 9–19°C. *A. aurita* are so common in Russia that they may affect human activities in coastal areas [12–14]. For instance, they sting tourists, thus causing harm to local tourism when their population increases as a result of climate change, eutrophication, or life cycle patterns [1]. Jellyfish are often discarded as waste in commercial fishing. Therefore, *A. aurita* biomass can become a valuable raw material for collagen without causing damage to the environment.

This study assesses the most popular method of collagen extraction from *A. aurita*, as well as the physicochemical composition and biochemical properties of collagen obtained.

STUDY OBJECTS AND METHODS

Research objects. The study featured *Aurelia aurita* fished in the coastal areas of the Baltic Sea, Kaliningrad Region, Russia, where they migrate to, following seasonal patterns. Previously, vacationers and residents reported that this type of jellyfish washed on shore in masses in the third decade of August or early in September. As the weather pattern changes, mass strandings of *A. aurita* now occur in different periods. In 2020, it happened in December; in 2023, it occurred in the third decade of September.

We obtained 140 kg raw jellyfish biomass manually in the sea near the town of Pionersky (Fig. 1), using a fish net (Fig. 2). The samples were placed in sealed ten-liter containers and delivered to the laboratory within 2 h. There, we washed the jellyfish with fresh water to remove sand and foreign matter and weighed the total mass within 0.1 g. We measured the average bell size since the bell is responsible for up to 97% of biomass. We decided not to separate oral arms as this manipulation was found too labor-intensive for commercial processing. After washing, the jellyfish were frozen at –79°C in plastic containers or zip-bags.

Collagen extraction methods. ***Obtaining acid-soluble collagen from Aurelia aurita jellyfish.*** Collagen was extracted with acid following the protocol

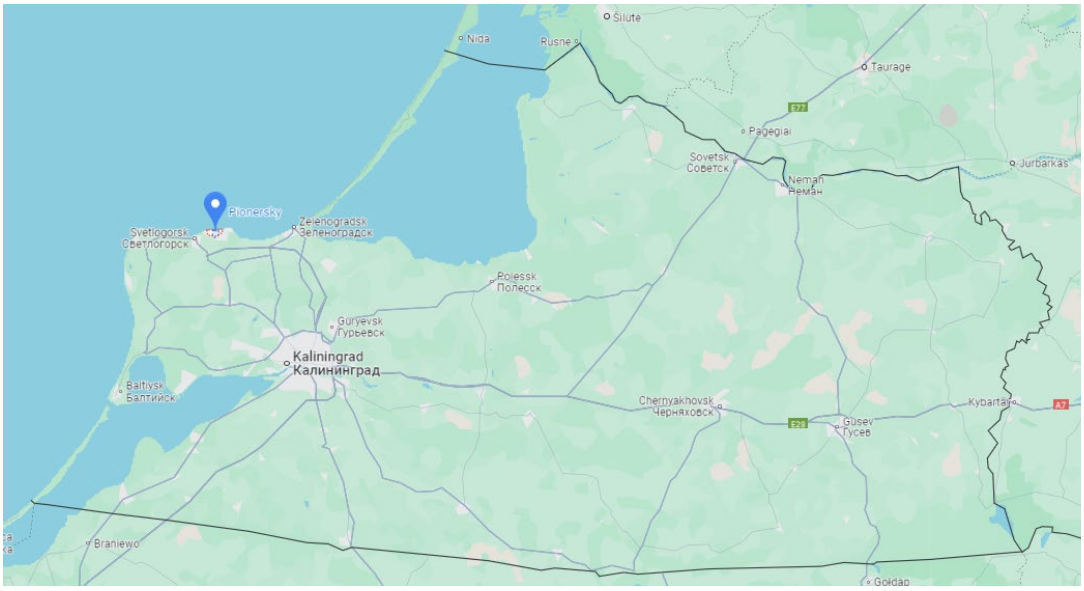


Figure 1 *Aurelia aurita* catching site on the Baltic See coast near the town of Pionersky (54.955098, 20.227932)

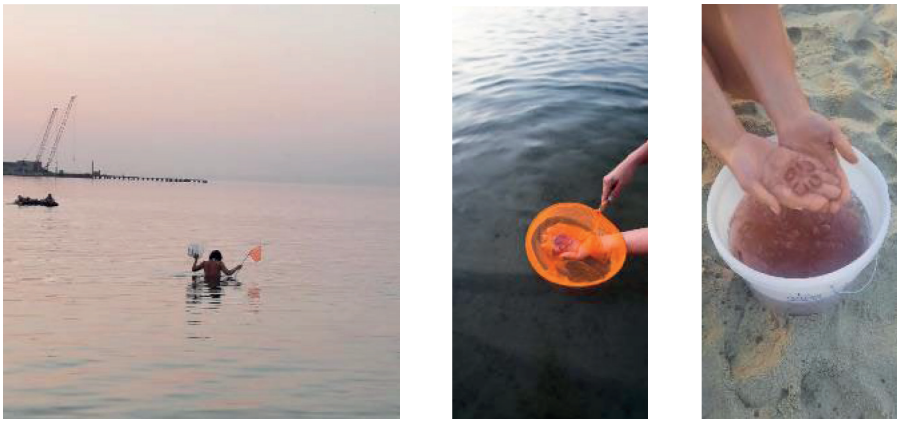


Figure 2 Fishing for *Aurelia aurita*

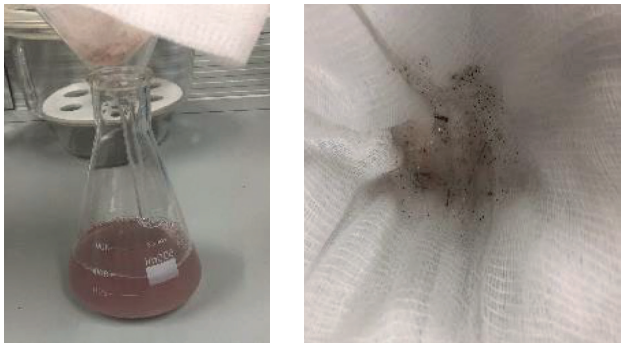
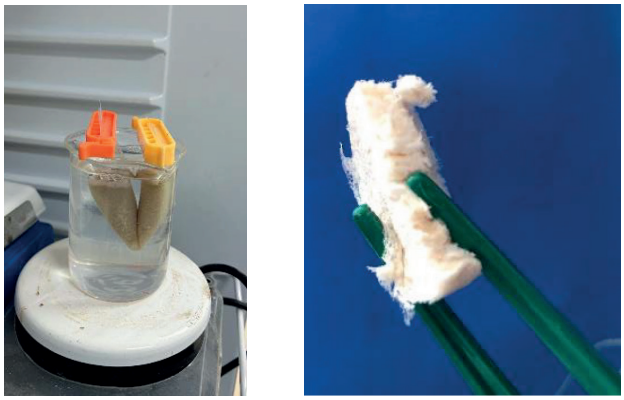


Figure 3 Filtering post-hydrolysis solution through gauze



a b

Figure 4 Dialysis of the resulting collagen against a solution of acetic acid (a) and the sponge obtained after freeze-drying (b)

described by Nagai *et al.* [15]. Crushed jellyfish biomass was placed in a flask and subjected to extraction with 0.5 M acetic acid in a ratio of 1:10 (w/v). The extraction process lasted three days at 4°C. After filtration, the insoluble residue underwent another extraction. After two extractions, we brought the filtrates (Fig. 3) to 0.9% with sodium chloride and separated precipitate by centrifugation at 3600 g for 15 min. After dissolving it in 0.5 M acetic acid, we dialyzed the obtained samples using 0.1 M acetic acid for three days, followed by dialysis with distilled water for another three days (Fig. 4a). The final solution was lyophilized to obtain acid-soluble collagen (Fig. 4b).

Assessing collagen properties. ***Solubility.*** The lyophilized collagen samples were dispersed at room temperature in such solvents as 96% ethanol, methanol, ethyl acetate, n-hexane, methylene chloride, double-distilled water, 0.5 M acetic acid, aqueous solutions of sodium hydroxide (pH 12), 37% hydrochloric acid, as well as 0.5 M acetic acid with ultrasonic treatment.

Water-holding capacity. We placed 0.05 g of lyophilized collagen in 15-mL centrifuge tubes and added 5 mL of distilled water. The resulting solution was suspended in a shaking incubator at 150 rpm for 15 min followed by a five-minute centrifugation. After removing supernatant with a dispenser, we weighed the tubes with wet collagen.

The water-holding capacity was calculated by the formula below:

$$\text{Water holding capacity} = \frac{m_{\text{wet}} - m_{\text{dry}}}{m_{\text{dry}}} \quad (1)$$

where m_{wet} is the mass of wet collagen and m_{dry} is the mass of dry collagen.

UV spectroscopy. Dry collagen was dissolved in 0.5 M acetic acid at room temperature at a concentration of 1 mg/mL. The spectral scanning involved a UV-1800 dual-beam spectrophotometer (Shimadzu, Japan) at 220–600 nm.

Molecular weight analysis. To measure the molecular weight, we dissolved 1 mL of dialyzed collagen in 0.5 M Tris-HCl buffer (pH 6.8, 1% SDS, 10% glycerol, 0.01% bromophenol blue). After denaturing the solution at 70–80°C for 5 min, we put 15 μL denatured sample and 7 μL marker with a molecular weight of 10–250 kDa into the wells at the top of the polyacrylamide gel (Protein Dual Color Standards, BioRad, USA). The polyacrylamide gel consisted of one-millimeter layers of 4% concentrating gel and 12.5% separating gel. In order to observe the separation of proteins by size, we raised the initial voltage of 15 mA (30 min) to 30 mA (1 h) after the proteins reached the separating layer. Upon separation, the gels were stained overnight with a dye solution, which consisted of 0.25% Coomassie Brilliant Blue

G-250 (JT Baker, USA), 10% acetic acid, 40% ethanol, and 50% de-ionized water. After being washed with a solution of 10% acetic acid, 40% ethanol, and 50% de-ionized water, the gels were incubated for 1 h.

Antioxidant activity. We applied two types of radicals, i.e., 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid (ABTS). The procedure involved a CLARIOstar microplate reader (BMG Labtech GmbH, Germany). A Trolox solution (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) of known concentration served as control. The test results were expressed in milligrams of Trolox equivalents per one gram of dry weight (mg TE/g).

To determine the antioxidant activity by the DPPH method, we mixed 20 µL of collagen solution with 300 µL of fresh 2,2-diphenyl-1-picrylhydrazyl solution (0.1 mM). The optical density was recorded at 515 nm.

To determine the antioxidant activity by the ABTS method, we added 20 µL of extract to 300 µL of ABTS· radical cation. The ABTS radical included aliquots of a 7.0 mM ABTS solution (2,2′-azino-bis(3-ethylbenzthiazolino-6-sulfonic acid) and a 2.45 mM potassium persulfate solution. The intubation occurred in the dark at room temperature and lasted for 16 h. The optical density was measured at 734 nm.

Wound healing test in vitro. The lyophilized collagen was dissolved in 0.07% acetic acid at the rate of 2 µg per 1 mL of solution. Ten minutes of ultrasonic bath at room temperature improved the solubility.

To study the collagen sorption on cultural surface, we added collagen solutions in a volume sufficient to cover 2–3 mm of the wells and incubated them at 37°C for 15 min. After draining the collagen solution, we washed the wells three times with Hanks' solution with phenol red (PanEco, Russia).

HaCaT fibroblasts and keratinocytes were cultivated in a culture medium that consisted of Dulbecco's Modified Eagle Medium (DMEM) (PanEco, Russia), 10% fetal bovine serum (Hyclon, USA), 1% Glutamax (Gibco, USA), and 1% PenStrep (Gibco, USA). The cultivation process involved a CO_2 incubator (37°C). The medium changed every 2–3 days. Cultures were removed from the surface of culture flasks with a trypsin solution and Versene solution (1:2) (PanEco, Russia) as soon as the confluent layer was reached, i.e., every 3–4 days. The cell seeding had a ratio of 1:3 or 1:5, depending on the growth rate. The experiments involved cultures of primary fibroblasts obtained at early (< 5) passages.

The scratch test was triplicated as follows: 155 000 HaCaT cells were planted in a 12-well plate with collagen. Type I collagen from rat tail tendons in 0.1% acetic acid served as positive control while empty wells served as negative control. On day 4, as the cell culture reached 100% confluence, we imitated a wound by scratching vertical lines with a Pasteur pipette in the center of each well, thus disrupting the integrity of the epithelial layer.

To assess the healing rate, we made phase contrast photographs of the cell culture immediately after scratching and on days 1, 2, and 3. We used an Olympus IX73 inverted microscope equipped with an Olympus U-TV0.63XC camera. The images were processed using Olympus cellSens Dimension, and the size of the wounds in the photographs was measured with ImageJ.

Quantitative polymerase chain reaction analysis (PCR). We applied ExtractRNA reagent (Evrogen, Russia) to isolate RNA and followed the protocol recommended by the manufacturer. The reverse transcription involved 1 µg of RNA. For the reverse transcription PCR test (RT-PCR), we used a standard qPCRmix-HS SYBR+LowROX kit (Evrogen, Russia) and a LightCycler 96 amplifier (Roche). The test pattern was triplicated as follows: 50 ten-minute cycles at 95°C; each cycle included 10 s at 95°C, 10 s at 60°C, and 20 s at 72°C. The content of products in each sample was determined by the 2-ΔΔCq method; the results were referenced to GAPDH (glyceraldehyde 3-phosphate dehydrogenase) expression (see Table 1 for primers).

Assessing cytotoxicity and adhesive properties. Primary human fibroblasts at a concentration of 66 000 cells per 1 mL were planted in a 24-well plate with collagen solution at the rate of 33 000 cells per well.

The cytotoxicity test presupposed live and dead cell counts after 48 h and involved a Luna-II counter (Logos Biosystems, South Korea) and staining with trypan blue.

After 10, 20, 30, 60 min, and 24 h, we conducted a cell count to define adhesive properties using the same Luna-II counter (Logos Biosystems, South Korea).

RESULTS AND DISCUSSION

Optimal extraction parameters. Acetic acid with a concentration of 0.2–0.5 M proved to be the most popular means of collagen extraction from marine

Table 1 Primer sequences

Gene	Forward primer	Reverse primer
KRT1	ACTTGATTTGCTCCCTTTCTCG	TATGGTCCTGTCTGCCCTCC
KRT 5	CTCCTCGGTCCTCACCCTCT	GGCTTTCCTGTCTGCCCTCC
KRT10	AAAGAGCCACCACTGAACCC	GGAGGAGTGTCATCCCTAAGAA
KRT14	ATCTTGTACTCCTGGTTCTGCTG	GAGACCAAAGGTCGCTACTGC
FLG	CCAAACGCACTTGCTTTACAGATA	AGACATGGCAGCTATGGTAGTG
IVL	TTCCTCCTCCAGTCAATACCC	CATTCTTGCTCAGGCAGTCC
ITGA6	AAGCAGGAATCCCGAGACAT	TCTCAATCGCCCATCACAAA
ITGB4	TCCTTTGAGCAGCCTGAGTTC	CGGTAGGAGACCTGGGACTTC
GAPDH	CATCAAGAAGGTGGTGAAGCAG	TCAAAGGTGGAGGAGTGGGT

animal biomass; the most common extraction time was 24–72 h [15–19].

Table 2 shows the limits for acid concentration and treatment time.

Table 2 and Figs. 5–6 illustrate the results of acid extraction. The collagen yield grew from 143.5 ± 7.8 to 150.1 ± 5.4 mg/kg at 0.2 and 0.5 M acetic acid, respectively. A further increase in acid concentration by 0.1 M reduced the economic efficiency by 8000 rubles/g.

The maximal yield of 156.2 ± 8.8 mg collagen per 1 kg wet biomass occurred at 0.5 M acetic acid after 96 h.

The extraction time was an important variable: when it grew from 24 to 48 h, we observed a 17.4% increase in the yield. A further increase in extraction time, however, had no significant effect.

In this study, the maximal collagen yield reached 0.0156% jellyfish dry weight, which is in line with the data obtained by Addad *et al.*, who reported 0.01% collagen yield [20].

Physicochemical properties of collagen. ***Solubility.*** No solvent used in this study was able to dissolve jellyfish collagen completely. The ultrasonic treatment was the only method that transformed collagen in acetic acid into a yellow cloudy solution, which eventually produced some precipitate of collagen. The tests with acidic media demonstrated partial dissolution of collagen.

Other researchers reported similar collagen properties. Swatschek *et al.* failed to dissolve sponge collagen in any of the solutions they applied [21]. They mentioned slight dispersion in solutions with pH 8–10 and hydrolysis of collagen fragments in an acidic environment. Ahmed *et al.* tested the solubility of collagen obtained from big-eyed tuna (*Thunnus obesus*) at different pH values with the Lowry protein assay [22]. They reported the highest solubility at pH = 6.

Water holding capacity. Collagen owes its water holding capacity properties due to its porous structure, which traps moisture in the fibers. Potentially, this parameter can be used to assess the hemostatic properties of jellyfish collagen [23]. In this research, the water holding capacity of *Aurelia aurita* collagen was 4.194 g/g. This value exceeds that for medical gauze (2 g/g) but comes short of collagen sponges from *Rhopilema esculentum* [24].

UV spectroscopy. Collagen has an absorption maximum in the range of 210–240 nm because it contains manly glycine and hydroxyproline but no tryptophan. The collagen we obtained from *A. aurita* had its absorption maximum at 232 nm (Fig. 7), which is in line with other similar publications. The peak was quite homogeneous, which indicates purity.

In [25], collagen obtained from the skin of Pacific cod demonstrated its maximal absorption at 231 nm. In [26], collagen from catfish skin had it at 235 nm.

In collagen, absorption in the UV region is associated with COOH, $CONH_2$, and C=O in polypeptide chains. Tyrosine, tryptophan, and phenylalanine have their absorption maxima at 250–285 nm. The spectrum we obtained had no clear peak in this region, which indicates a low content of these amino acids.

Table 2 Extracting collagen with acid: experimental results

No.	Concentration of CH_3COOH and treatment time	Collagen yield, mg/kg wet jellyfish biomass
1	0.2 M, 48 h	143.5 ± 7.8
2	0.3 M, 48 h	144.7 ± 6.6
3	0.5 M, 48 h	150.1 ± 5.4
4	0.5 M, 24 h	127.8 ± 4.7
5	0.5 M, 72 h	153.3 ± 9.2
6	0.5 M, 96 h	156.2 ± 8.8

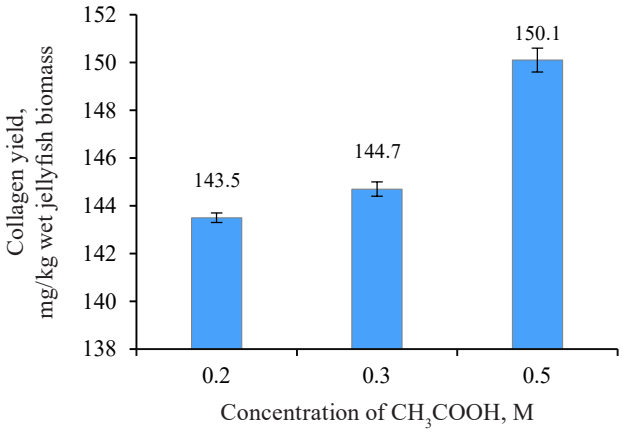


Figure 5 Collagen yield after acid extraction depending on acetic acid concentration

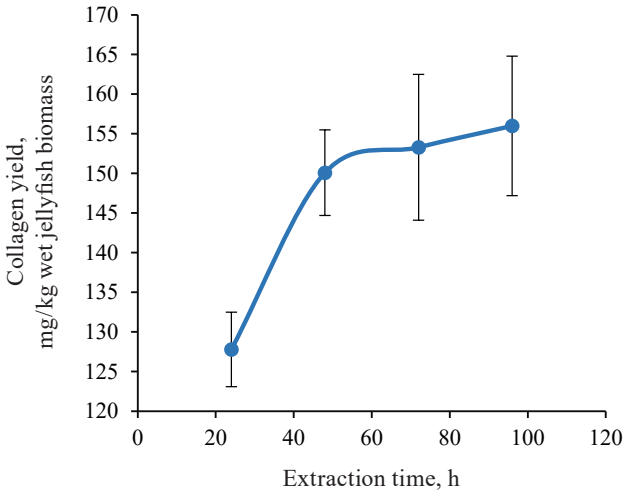


Figure 6 Collagen yield from acid extraction depending on extraction time

Molecular weight. Figure 8 illustrates the molecular weight of *A. aurita* collagen samples. For this test, we used native collagen, i.e., a sample dissolved in water, and a collagen solution obtained by sonicating a mix of collagen and 0.2 M acetic acid for 2 min.

The molecular weight of native collagen exceeded 250 kDa, which prevented the sample from advancing in the gel. The sample with acetic acid demonstrated two clear bands of 100 and 110 kDa.

To compare the proteins, we used PhotoMetrix 1.2.1, a free application that we downloaded from the Play Store

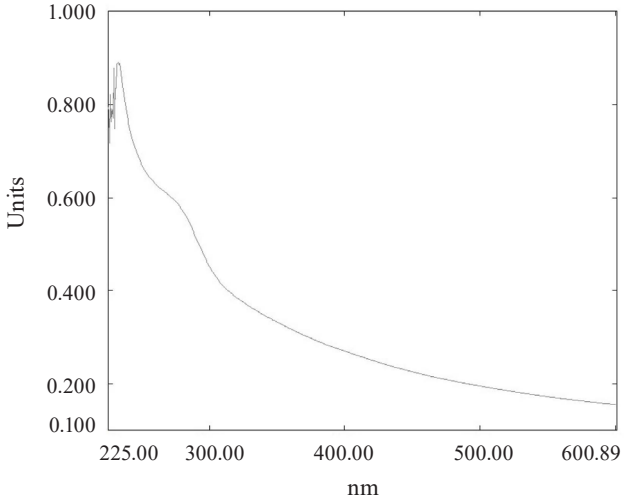


Figure 7 UV spectral profile of *Aurelia aurita* collagen

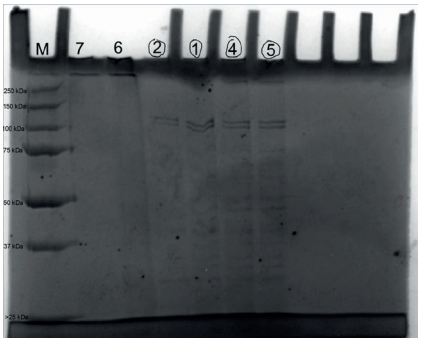


Figure 8 Electropherogram of *Aurelia aurita* collagen samples: the leftmost line is a protein marker with components of a known molecular weight (kDa); lines 7 and 6 are native collagen; lines 1–5 are *Aurelia aurita* collagen treated with ultrasound and 0.2 M acetic acid

to install on a smartphone (POCO ×3 Pro, China) [27]. The images were montaged; each band was quantified by the size of images captured from an area of 64×64 pixel. The application provided calibration curves by preentering the amount of protein at each point. A protein-free gel band was used for analytical testing. For accuracy, we scanned the same gel in Image Lab 6.0.1 (BioRad, USA) [28]. Then, we built a plot that demonstrated the effect of protein amount on band volume. The resulting linear regression produced calibration curves that made it possible to calculate the amount of protein in the sample. The calibration curves relied on albumin used at concentrations of 0–10 μg (Table 3).

The molecular weight of native collagen exceeded 250 kDa (lines 6 and 7), which made it insoluble in phosphate buffer (pH = 7.4). Samples 1–5 were essentially identical but with different concentrations of collagen solution in gel pockets: Table 3 shows the difference in the intensity of collagen bands of various masses.

We also analyzed the results of *A. aurita* mesoglea collagen electrophoresis. The samples consisted of α1 and α2 chains of 110 kDa at a ratio of approximately 2:1.

Table 3 Shares of proteins with different molecular weights in *Aurelia aurita* biomass

Molecular weight, kDa	Protein share by PhotoMetrix, %	Protein share by ImageLab, %
> 250	13.75	22.7
110	14.67	19.6
100	15.16	7.5
75	7.12	5.4
70	7.1	8.7
50	7.1	9.5
43	7.1	3.9
39	7.0	3.7
35	7.0	1.1
34	7.0	5.1
31	7.0	12.8

As for β and γ chains, they were located in the high molecular weight region of ≥ 250 kDa. As a result, the collagen samples could be classified as type I. Our results confirmed those obtained by other scientists, who also reported collagen of *Rhopilema esculentum* and *Nemopilema nomurai* as type I [24, 29]. Acid-soluble collagen had a molecular weight of 100–115 kDa.

Biological activity of collagen. ***Antioxidant properties.*** Collagen owes its antioxidant activity to its amino acid composition. In this study, however, *A. aurita* collagen demonstrated no antioxidant activity, probably, because we did not use collagen hydrolysate. Li *et al.*, who studied collagen hydrolysate from Spanish mackerel skin, reported good radical scavenging properties [30]. According to Gautam *et al.*, hydrolysis increased the antioxidant activity in collagen [31].

Adhesive and cytotoxic properties of collagen on primary human fibroblasts. The cytotoxicity assay showed that fibroblasts continued to grow for three days (Fig. 9).

Table 4 presents the results of a live cell count performed on an automatic counter by the trypan blue method.

A. aurita collagen improved the survival rate of fibroblast cells by 45.6%, probably, by activating different types of cellular receptors. Besides, the interaction of collagen with cells is known to depend on various growth factors and other modulations of the cytoskeletal complex [32].

In our case, the test on adhesive properties revealed no significant difference between the two samples (Table 5).

In this study, *A. aurita* collagen had no effect on the share of free cells, compared to the control sample. However, the method was not entirely accurate. In our future research, we will need to determine the number of attached live cells.

Regenerative properties of collagen on immortalized keratinocytes of HaCaT cells. Figure 10 shows that wound healing occurred in all collagen samples.

The wound healing rate represented as an average rate of cell migration into the wound had no significant difference between the *A. aurita* collagen sample and the control sample (Table 6).

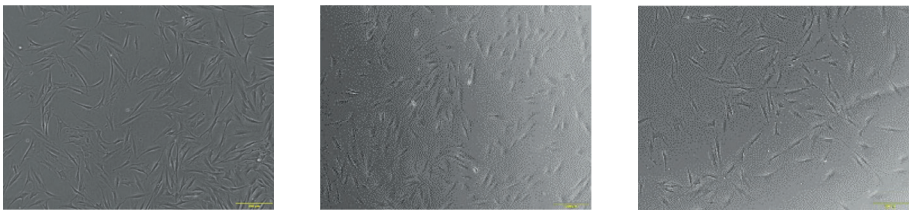


Figure 9 Fibroblasts growing on surfaces adsorbed with different collagen samples on cultivation day 3, phase contrast

Table 4 Live cell count, day 3

Sample	Live cells, %
Aurelia aurita collagen	65.87
Positive control	54.97
Negative control	45.23

Table 5 Free cell count after collagen incubation

Incubation time	*Aurelia aurita* collagen			Positive control			Negative control		
	Concentration, cells/mL×10^4	Total cells, ×10^4	% Total cells	Concentration, cells/mL×10^4	Total cells,×10^4	% Total cells	Concentration, cells/mL×10^4	Total cells, ×10^4	% Total cells
10 min	4.92	2.46	74.58	4.28	2.14	64.88	4.64	2.32	70.23
20 min	2.01	1.00	30.42	2.46	1.23	37.29	1.97	0.98	29.82
30 min	1.23	0.62	18.65	1.48	0.74	22.40	1.13	0.57	17.15
60 min	1.15	0.57	17.41	0.90	0.45	13.67	0.86	0.43	13.05
24 h	0.99	0.50	15.00	0.60	0.30	9.09	0.74	0.37	11.21

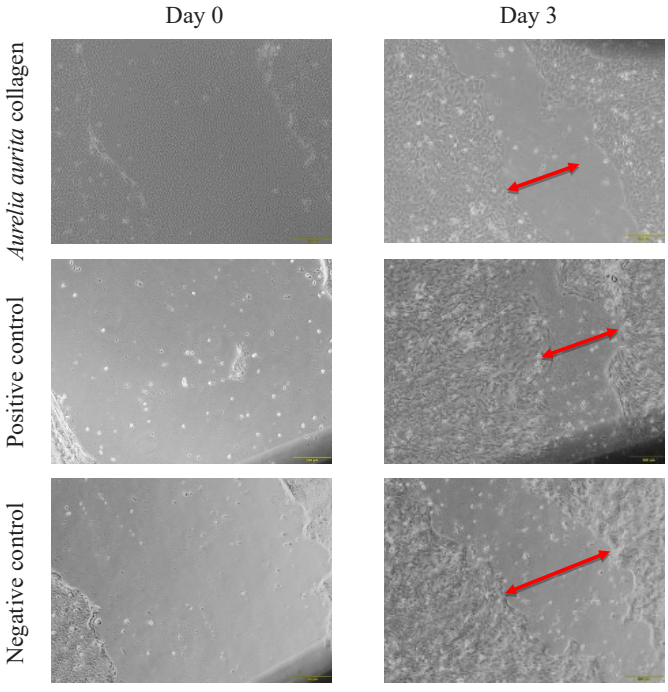


Figure 10 Wound model on HaCaT cell line *in vivo* on day 0 and day 3, phase contrast

Table 6 Wound healing assay, day 3

Aurelia aurita collagen	Healing rate, day 3		Average wound healing rate	
	µm	% from initial wound size	µm/day	% wound healing per day (from initial wound size)
Test sample	810.23	70.20	270.08	23.40
Positive control	1087.44	69.92	362.48	23.31
Negative control	712.87	56.18	237.62	18.73

Table 7 Keratinocyte differentiation markers referenced to GAPDH

Sample	KRT1	KRT10	KRT 14	KRT5	FLG	IVL	ITGA6	ITGB4
Aurelia aurita collagen	0.70	0.68	0.97	0.74	0.68	0.70	0.68	0.67
Positive control	0.78	0.75	0.97	0.79	0.76	0.75	0.73	0.73
Negative control	0.84	0.80	0.95	0.84	0.77	0.79	0.74	0.75

Differential gene expression in an immortalized keratinocyte HaCaT model after cultivation on collagen samples. The expression of KRT1, KRT10, FLG, and IVL served as markers of late differentiation while the expression of KRT5, KRT14, ITGA6, and ITGB4 served as basal differentiation. Different collagen samples showed no significant difference in these markers (Table 7), which means that *A. aurita* collagens did not affect the differentiation status of keratinocytes.

CONCLUSION

In this research, the maximal collagen extraction yield during acetic acid treatment was 185 mg/kg wet *Aurelia aurita* biomass. It was obtained in a 0.5 M solution after 48 h.

When the concentration of acetic acid increased from 0.2 to 0.5 M, the collagen yield grew from 143.5 ± 7.8 to 150.1 ± 5.4 mg/kg. A further increase in acid concentration by 0.1 M reduced the economic efficiency of the process by 8000 rubles/g.

Extraction time also had a significant effect on collagen yield: when it increased from 24 to 48 h, the yield grew by 17.4% with no effect thereafter.

The native collagen samples showed very low solubility in water and organic solvents, which is quite natural. However, it dissolved in a high-concentrated solution of acetic acid (≥ 0.5 M). This property is no disadvantage because some collagen sponges should be resistant to biological fluids.

The water holding capacity of *A. aurita* collagen was 4.194, i.e., twice as high as that of medical gauze. The UV spectroscopy showed that the collagen had a high degree of purity, as evidenced by a clear peak at 230–235 nm, i.e., in the region of glycine and hydroxyproline. The molecular weight of acid-soluble collagen was 100–115 kDa, which made it possible to classify *A. aurita* collagen as type I, typical of animal biomass.

A. aurita collagen demonstrated no cytotoxic properties. It had no effect on cell adhesion, migration, and proliferation, neither did it affect the expression of cell differentiation markers.

The wound-healing assay demonstrated regenerative properties: *A. aurita* collagen was able to increase the healing rate by 24.5%.

The high biological activity of collagen obtained from the *A. aurita* jellyfish renders it suitable for regenerative medicine. However, the product yield appeared to be very low (≤ 0.02%). As a result, *A. aurita* is a potential source of collagen but the method described in this research will be economically justified only by large-scale fishing, e.g., to increase the recreational attractiveness of a coastal area during mass stranding or to eliminate a certain negative effect of *A. aurita* mass migration on human economic activity.

CONTRIBUTION

The authors were equally involved in the research and are equally responsible for any potential plagiarism.

CONFLICT OF INTEREST

The authors declared no conflict of interests related to the publication of this article.

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