Effects of *Sargassum horneri* and *Ulva australis* Extracts on Body Weight and Serum Glucose Levels of Sprague-Dawley Rats

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**ABSTRACT:** This study investigated the safety and functionality of a functional additive for humans and animals from *Sargassum horneri* (SH) and *Ulva australis* (UA) waste for recycling marine refuse generated in large quantities in Jeju. Sprague-Dawley rats were orally administered functional additives at 2,000 mg/kg to assess 14-day repeated dose toxicity of the two extracts. For female rats, weight gain after administration of SH was 66.2±18.8% vs. controls. Male rats administered UA showed weight gain of 92.3±8.0% vs. controls. SH and UA significantly decreased serum glucose levels in male rats compared with controls (79.8±11.10% and 76.1±9.67%, respectively). Similarly, significant decrease in serum glucose levels were shown for female rats after administration of SH and UA (79.2±1.58% and 82.8±3.21%, respectively). Furthermore, rats showed significant differences vs. controls in several serological parameters after receiving extracts, however results remained within the normal range. Thus, the SH and UA extracts were considered safe substances that may be used as functional additives to help reduce body weight and serum glucose.

**Keywords:** functional natural additive, *Sargassum horneri*, safety evaluation, serum glucose, *Ulva australis*

**INTRODUCTION**

Marine waste [e.g., from *Sargassum horneri* (SH) and *Ulva australis* (UA)] is generated in large quantities in the Jeju region, where it is recognized as an environmental pollutant and an obstacle to achieving a clean environment. Before 2013, organic waste resources were disposed of by dumping in the sea. However, such disposal has since been prohibited by the London Convention Protocol. Wastes are now disposed in landfills or eliminated by incineration. Limitations to these methods encourage the development of other options, including suppressing waste generation and developing an appropriate recycling method (Ahn et al., 2007; Kim et al., 2007; Kim et al., 2014).

SH is a yellowish-brown species of alga with thin and spatula-shaped leaves, which grows mainly during winter. SH is rich in dietary fiber, polysaccharides, amino acids, and vitamins, and is considered a delicacy in East Asia (Matsumura, 2001; Dias et al., 2020). However, the thallus of SH, which is increasing due to SH aquaculture in the waters of Zhejiang Province, China, is carried away from substrates and down prevailing currents (Preeprame et al., 2001; Liu et al., 2012; Kim, 2015). SH is now widely distributed throughout the east and south coasts of Korea and along all of the Japanese coastline. Indeed, an average of 300～9,000 tons of SH flowed into Jeju Island from 2015 to 2017. The giant seaweed grows with the help of microorganisms, provides a haven for reproduction of many marine species, and supplies nutrients to herbivorous marine life (Kim et al., 2018a). Still, the inflow of thallus causes environmental and economic problems, such as fouling fishing boat screws, impeding fishing and sailing, becoming trapped in and damaging aquaculture facilities, and causing odors due to stranding of thallus on shorelines (Byeon et al., 2019; Kim et al., 2019). Previous studies have demonstrated the ability of SH in prevention of cardiovascular disease (Cardoso et al., 2015), inhibition of atopy (Kim et al., 2020), inhibition of adipocyte production (Kwon et al., 2019), inhibition of adipocyte production (Kwon et al., 2019), inhibition of cancer cell growth (Choi et al., 2006), and anticoagulation (Kim et al., 2004).

UA is a primary cause of coastal pollution in Jeju, where it grows singly or in groups of two or three (Lin et al.,...
Materials and Methods

Extract preparation

SH and UA collected from the coast of Jeju Island were washed and dried, then pulverized with a grinder and extracted. Fifty grams of dried samples were immersed in 1 L of 80% ethanol and stirred for 24 h. The ethanol was filtered using a 0.45 μm bottle filter (Corning Bottle-Top Vacuum Filter System, Corning Inc., Corning, NY, USA), and the filtrate lyophilized after evaporating the ethanol using a vacuum concentrator to prepare a powder. The powder was stored at −20°C and used as a suspension in sterile distilled water.

Animals and animal experiments

Five-week-old female and male Sprague-Dawley rats housed in specific-pathogen free conditions were purchased from KOSA BIO Inc. (Gyeonggi, Korea). After one week of quarantine and acclimatization, healthy animals were used in experiments. Animals were kept at 23±3°C, a relative humidity of 50±10%, and with 12 h of illumination per day at 150~300 Lux. Rat feed (SAMTAKO BIO KOREA, Gyeonggi, Korea) and water were provided ad libitum. This research followed the Code of Ethics for Animal Experiments at Pusan Catholic University (CUP AEC 2020-002). Rats were divided into control, SH, and UA groups. Five female and five male animals were included in each group. The daily dose of extracts was 2,000 mg/kg administered in sterile water, the maximum concentration suggested by the Organization for Economic Co-operation and Development toxicity evaluation guidelines. Rats in the control group received sterile distilled water. Oral administration was continued for 14 days using a volume of 10 mL/kg.

Clinical symptoms, body weight, and feed intake

On the first day of oral administration of each substance, rats were observed from 1 to 6 h. Throughout the study period, rats were observed for general symptomatic changes, toxic symptoms, decreased mobility, addiction, and death at designated times once daily. All laboratory rats were weighed every 2 days before and after extract administration, which measured feed intake at 3∼4-day intervals.

Necropsy and organ weight measurement

Experimental rats were fasted 12 h before necropsy, using an anesthetic comprising of a mixture of alfaxalone (Alfaxan®; Careside Co., Ltd., Gyeonggi, Korea) 25 mg/kg and xylazine (Rompun®; Bayer Korea, Seoul, Korea) 5 mg/kg. After anesthesia, blood was collected from the abdominal aorta, and gross organ abnormalities were recorded. Livers, lungs, hearts, kidneys, spleens, and thymuses were collected from all rats. In addition, ovaries and uteruses were collected from female rats, and testicles and prostates were collected from male rats. All organs were weighed after gross examination.

Analysis of blood and serum biochemistry

Blood was collected into ethylenediaminetetraacetic acid tubes (BD Caribe Ltd., Sumter, SC, USA), stirred on a roll mixer for 30 min, and analyzed using a blood analyzer (DxH500, Beckman Coulter, Inc., Brea, CA, USA). White blood cell and red blood cell count (RBC), hemoglobin (HGB), hematocrit (HCT), mean red blood cell volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and platelet (PLT) count were recorded.

Blood was collected into serum separator tube tubes (BD Caribe Ltd.) for serum biochemistry, allowed to co-
agulate at room temperature, and centrifuged at 2,500 rpm for 20 min. Serum obtained by centrifugation was analyzed using a blood biochemical analyzer BT1500 (Biotecnica Instruments SpA, Rome, Italy). Analyses included determination of total protein, albumin (ALB), aspartate aminotransferase (AST), alanine transaminase (ALT), gamma-glutamyl transferase, alkaline phosphatase (ALP), glucose (Glu), total cholesterol (CHO), triglyceride (TG), total bilirubin, high-density lipoprotein cholesterol (HDL-C), urea, and blood urea nitrogen (BUN) levels.

**Statistical analysis**

Data were analyzed using SPSS version 25 (Statistics Package for Social Sciences, Chicago, IL, USA), and expressed as mean±standard deviation (SD). Statistical analyses of body weight, feed intake, organ weight, blood, and serological values were performed using one-way ANOVA to compare multiple groups. Values with P<0.05 and P<0.01 were considered significantly different.

**RESULTS**

**General health and death observations**

After extract administration, there were no changes in clinical signs, such as salivation, reduced mobility, and toxicity, including in control rats. In addition, there were no drug-induced deaths among experimental or control rats (Table 1).

**Body weight and feed intake**

Body weight of both female and male rats increased from before to after extract administration. Male rats in the control group weighed 94.6±6.3 g after dosing compared with 90.8±6.8 g for rats in the SH group, and 87.3±7.5 g for rats in the UA group. Similar findings were observed for female rats: rats weighed 34.8±6.2 g, 23.0±6.6 g, and 31.0±3.6 g in the control, SH, and UA groups, respectively, after dosing (Table 2). Weight gain in male rats administered SH or UA was 96.0±7.2% and 92.3±8.0%, respectively, of control rats. Weight gain following UA

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**Table 1.** Clinical signs of Sprague-Dawley rats orally administered ethanol extracts of *Sargassum horneri* (SH) or *Ulva australis* (UA) for 14 days

| Extract | Sex   | Dose (mg/kg/d) | Signs observation |
|---------|-------|----------------|-------------------|
|         |       |                | Decrease of locomotor activity | Decreased respiration rate | Lacrimation | Salivation | Death |
| SH      | Male  | 0              | 0/5<sup>1</sup> | 0/5 | 0/5 | 0/5 | 0/5 |
|         |       | 2,000          | 0/5 | 0/5 | 0/5 | 0/5 | 0/5 |
| Female  |       | 0              | 0/5 | 0/5 | 0/5 | 0/5 | 0/5 |
|         |       | 2,000          | 0/5 | 0/5 | 0/5 | 0/5 | 0/5 |
| UA      | Male  | 0              | 0/5 | 0/5 | 0/5 | 0/5 | 0/5 |
|         |       | 2,000          | 0/5 | 0/5 | 0/5 | 0/5 | 0/5 |
| Female  |       | 0              | 0/5 | 0/5 | 0/5 | 0/5 | 0/5 |
|         |       | 2,000          | 0/5 | 0/5 | 0/5 | 0/5 | 0/5 |

<sup>1</sup>Number of animals with sign/total number of animals examined.

**Table 2.** Body weight changes of Sprague-Dawley rats orally administered ethanol extracts of *Sargassum horneri* (SH) or *Ulva australis* (UA) for 14 days

| Day after treatment | Male dose (mg/kg) | Female dose (mg/kg) |
|--------------------|-------------------|---------------------|
|                    | Control | SH     | UA    | Control | SH     | UA    |
| 0                  | 169.5±1.0 | 170.5±3.2 | 168.9±6.9 | 146.8±4.8 | 145.8±4.5 | 147.7±2.7 |
| 2                  | 190.2±4.2 | 193.7±4.9 | 190.8±7.7 | 158.2±6.2 | 151.8±4.7 | 155.7±3.8 |
| 6                  | 220.6±4.7 | 223.8±3.5 | 217.8±9.0 | 171.3±4.5 | 166.3±5.4 | 168.7±5.9 |
| 10                 | 253.2±5.3 | 254.4±4.1 | 249.3±8.4 | 182.6±4.4 | 181.4±5.3 | 183.8±2.9 |
| 14                 | 278.9±5.8 | 276.0±2.5 | 270.9±9.1 | 192.2±5.7 | 189.9±4.8 | 192.1±4.0 |
| 15                 | 264.1±6.7 | 261.3±8.2 | 256.2±10.1 | 181.6±8.5 | 168.9±7.9 | 178.7±5.9 |
| Weight gain (g)<sup>1</sup> | 94.6±6.3 | 90.8±6.8 | 87.3±7.5 | 34.8±6.2 | 23.0±6.6 * | 31.0±3.6 |
| Weight gain (%)<sup>2</sup> | 55.8±3.6 | 53.2±3.9 | 51.8±5.2 | 23.7±4.1 | 15.8±4.6 * | 20.9±2.1 |

Body weight values are expressed in grams (mean±SD). Significant difference at *P*<0.05 vs. the control group.

<sup>1</sup>Weight gain (g) differences between day 15 and day 0.

<sup>2</sup>Weight gain (%) expressed as a percentage of the difference in weight between 15 and 0 days.
administration was low, but not significantly different from that of controls (Fig. 1A). However, weight gain in female rats was 66.2±18.8% and 89.2±10.3% of controls after SH and UA administration, respectively. The difference in weight gain between female rats in the SH and control was statistically significant (P<0.05) (Fig. 1B). Feed intake of female rats administered extracts tended to be lower than those of female control rat, however, feed intake did not differ significantly. Similar results were observed for male rats (Table 3). Since no differences in feed intake were seen, the algal extracts appeared to affect weight loss.

Necropsy and organ weight measurements
Necropsy of laboratory rats did not reveal any specific or abnormal findings associated with the extracts. Furthermore, there were no significant differences between control and experimental rats when all rats were grouped, or when rats were grouped by sex (Table 4).

Analysis of blood and serum biochemistry
Most hematological analyses for control and experimental rats were within normal ranges, with no significant alterations observed (Table 5). However, RBC in female rats increased from 6.32±0.77 in the control group to 7.77±0.46 and 7.48±0.46 in rats in the SH and UA groups, respectively. Furthermore, HGB levels were 13.4±1.46 in the control animals compared with 15.45±0.53 and 15.62±0.34 in rats in SH and UA groups, respectively. In addition, both RBC and HGB significantly increased following extract administration (P<0.05).

All serological analyses were within normal ranges. However, conversion of serum glucose level (%) in experimental rats to percent of controls indicated that glucose levels were significantly lower for male rats in the SH and UA groups (79.83±11.10% and 76.09±9.67% of controls, respectively; P<0.05) compared with control rats (Fig. 2A). Similarly, glucose levels were significantly lower in female rats in SH and UA groups compared with control rats (79.19±1.58% and 82.78±3.21% of controls, respectively; P<0.01) (Fig. 2B). Furthermore, ALP levels in male rats were significantly decreased in the SH and UA groups compared with the control group (332.06±27.64 and 303.06±10.31, respectively, compared with 387.96±30.90; P<0.05), and TG and BUN levels were significantly decreased in the UA group compared with

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**Table 3.** Food consumption of Sprague-Dawley rats orally administered ethanol extract of *Sargassum horneri* (SH) or *Ulva australis* (UA) for 14 days

| Extract | Sex   | Dose (mg/kg/d) | Days after treatment |
|---------|-------|----------------|---------------------|
|         |       |                | 1                   | 4       | 7       | 10      |
| SH      | Male  | 0              | 22.7±0.4            | 23.9±0.5 | 23.5±0.7 | 24.6±0.5 |
|         |       | 2,000          | 21.5±0.8            | 23.0±0.8 | 23.9±0.3 | 23.3±0.4 |
| Female  |       | 0              | 19.7±2.4            | 21.0±1.5 | 20.4±1.1 | 18.1±0.8 |
|         |       | 2,000          | 15.8±0.4            | 14.9±0.2 | 15.0±1.1 | 15.2±1.2 |
| UA      | Male  | 0              | 22.7±0.4            | 23.0±0.5 | 23.5±0.7 | 24.6±0.5 |
|         |       | 2,000          | 22.2±0.6            | 23.0±0.2 | 23.1±0.4 | 23.6±0.3 |
| Female  |       | 0              | 19.7±2.4            | 21.0±1.5 | 20.4±1.1 | 18.1±0.8 |
|         |       | 2,000          | 15.6±0.4            | 16.5±0.2 | 16.5±0.9 | 15.6±0.5 |

Values were expressed as food consumption in gram/rat/d (mean±SD).
Table 4. Absolute organ weights of Sprague-Dawley rats orally administered ethanol extracts of *Sargassum horneri* (SH) or *Ulva australis* (UA) for 14 days

| Organ          | Male dose (mg/kg) | Female dose (mg/kg) |
|----------------|------------------|---------------------|
|                | Control  | SH    | UA    | Control | SH    | UA    |
|                | 0       | 2,000 | 2,000 | 0       | 2,000 | 2,000 |
| Liver          | 9.50±0.34 | 9.45±1.16 | 8.74±0.83 | 6.69±0.47 | 7.01±1.26 | 7.18±0.84 |
| Spleen         | 0.81±0.09 | 0.78±0.13 | 0.79±0.05 | 0.58±0.12 | 0.58±0.08 | 0.57±0.04 |
| Kidney-left    | 1.18±0.10 | 1.11±0.11 | 1.08±0.10 | 0.74±0.09 | 0.75±0.04 | 0.81±0.15 |
| Kidney-right   | 1.24±0.10 | 1.21±0.10 | 1.17±0.09 | 0.77±0.11 | 0.83±0.06 | 0.83±0.18 |
| Heart          | 1.13±0.21 | 1.07±0.05 | 1.07±0.10 | 0.70±0.04 | 0.72±0.07 | 0.71±0.09 |
| Lung           | 1.46±0.04 | 1.57±0.17 | 1.45±0.08 | 1.17±0.19 | 1.14±0.04 | 1.17±0.12 |
| Thymus         | 0.67±0.03 | 0.64±0.13 | 0.56±0.10 | 0.52±0.07 | 0.53±0.11 | 0.43±0.03 |
| Testis-left    | 1.49±0.15 | 1.53±0.10 | 1.51±0.13 | —       | —     | —     |
| Testis-right   | 1.54±0.13 | 1.58±0.15 | 1.56±0.11 | —       | —     | —     |
| Prostate       | 0.94±0.19 | 0.87±0.17 | 0.95±0.08 | —       | —     | —     |
| Ovary-left     | —       | —     | —     | 0.11±0.07 | 0.08±0.01 | 0.09±0.01 |
| Ovary-right    | —       | —     | —     | 0.13±0.03 | 0.10±0.02 | 0.09±0.02 |
| Uterus         | —       | —     | —     | 0.60±0.19 | 0.61±0.28 | 0.54±0.13 |

Organ weight values were expressed in grams (mean±SD).

Table 5. Hematological parameters of Sprague-Dawley rats orally administered ethanol extracts of *Sargassum horneri* (SH) or *Ulva australis* (UA) for 14 days

| Parameter                  | Male dose (mg/kg) | Female dose (mg/kg) |
|----------------------------|------------------|---------------------|
|                            | Control  | SH    | UA    | Control | SH    | UA    |
|                            | 0       | 2,000 | 2,000 | 0       | 2,000 | 2,000 |
| WBC (×10^3/μL)             | 7.81±0.88 | 7.54±1.69 | 7.35±0.75 | 7.46±0.49 | 7.62±0.43 | 7.38±0.42 |
| RBC (×10^6/μL)             | 6.41±0.14 | 6.38±0.28 | 6.36±0.08 | 6.32±0.68 | 7.77±0.46* | 7.48±0.46* |
| HGB (g/dL)                 | 14.49±0.67 | 13.91±0.35 | 14.21±0.23 | 13.44±1.46 | 15.45±0.53* | 15.62±0.34* |
| HCT (%)                    | 40.82±0.66 | 41.90±3.45 | 40.68±0.75 | 37.08±4.21 | 39.95±3.41 | 38.12±1.47 |
| MCV (fL)                   | 63.94±0.66 | 63.86±1.31 | 63.98±0.69 | 58.66±0.78 | 58.35±0.92 | 58.37±1.17 |
| MCH (pg)                   | 22.38±0.43 | 22.08±0.84 | 22.32±0.28 | 21.28±0.31 | 19.92±0.56 | 20.96±0.83 |
| MCHC (g/dL)                | 35.02±0.77 | 34.52±1.01 | 34.96±0.64 | 36.26±0.34 | 34.13±0.54 | 35.29±1.28 |
| PLT (×10^3/μL)             | 637.68±34.33 | 699.78±31.82 | 680.28±32.84 | 672.80±31.35 | 640.65±32.36 | 672.83±27.21 |

Values were expressed as means±SD (n=5). Significant differences at *P<0.05.

WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin; HCT, hematocrit; MCV, mean red blood cell volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet.

Fig. 2. Serum glucose levels of Sprague-Dawley Rats treated with the extract for 14 days compared to the control group. (A) male experimental group, (B) female experimental group. Serum glucose levels (%) were significantly decreased in both male and female experimental groups compared to the control group. The data were calculated and expressed as the experimental group glucose level/control group glucose level×100. Data are mean±SD (n=5). *P<0.05 and **P<0.01 vs. normal control group. NC, normal control group; SH, *Sargassum horneri* administered group; UA, *Ulva australis* administered group.
Table 6. Serum biochemical parameters of Sprague-Dawley rats orally administered ethanol extracts of *Sargassum horneri* (SH) or *Ulva australis* (UA) for 14 days

| Parameter | Male dose (mg/kg) | Female dose (mg/kg) |
|-----------|-------------------|---------------------|
|           | Control | SH | UA | Control | SH | UA |
| TP (g/dL) | 5.94±0.21 | 6.22±0.22 | 5.89±0.31 | 5.51±0.29 | 5.85±0.35 | 5.80±0.28 |
| ALB (g/dL) | 3.53±0.12 | 3.69±0.15 | 3.56±0.22 | 3.32±0.20 | 3.43±0.14 | 3.44±0.12 |
| AST (U/L) | 121.26±7.55 | 128.27±7.35 | 122.66±5.70 | 108.68±17.22 | 128.25±7.44* | 108.50±7.45 |
| ALT (U/L) | 122.66±5.70 | 48.20±4.66 | 48.20±4.66 | 38.00±7.78 | 40.00±5.89 | 38.00±6.28 |
| GGT (U/L) | 2.18±0.59 | 1.37±0.81 | 1.92±0.66 | 2.35±0.66 | 2.33±0.76 | 2.19±1.16 |
| ALP (U/L) | 387.96±30.90 | 332.06±27.64* | 303.06±10.31* | 180.32±20.70 | 160.20±14.02 | 158.28±14.75 |
| GLU (mg/dL) | 118.45±16.60 | 90.73±10.75* | 90.12±12.80* | 188.46±9.22 | 148.25±2.86 ** | 156.00±6.77** |
| CHO (mg/dL) | 79.40±5.89 | 81.82±5.44 | 72.19±4.28 | 78.70±7.28 | 86.35±5.84 | 86.67±4.26 |
| TG (mg/dL) | 50.93±11.66 | 45.22±5.19 | 35.97±5.11* | 33.49±3.02 | 43.69±2.42** | 34.10±4.92 |
| HDL-C (mg/dL) | 49.61±6.89 | 54.63±5.47 | 51.56±3.54 | 57.68±7.59 | 70.43±4.80* | 62.60±4.37 |
| BUN (mg/dL) | 1.49±0.37 | 1.77±0.26 | 1.26±0.18 | 1.13±0.38 | 1.18±0.18 | 1.07±0.24 |

Values were expressed as means±SD (n=5).
Significant differences at *P*<0.05 and **P*<0.01 vs. the control group.
TP, total protein; ALB, albumin; AST, aspartate aminotransferase; ALT, alanine transaminase; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase; GLU, glucose; CHO, total cholesterol; TG, triglyceride; TB, total bilirubin; HDL-C, high-density lipoprotein cholesterol; BUN, blood urea nitrogen.

the control group (*P*<0.05). In addition, female rats treated with SH showed significantly increased AST (*P*<0.05), TG (*P*<0.01), and HDL-C (*P*<0.05) levels compared with control rats (Table 6).

**DISCUSSION**

This study was designed to support a method for efficient recycling of SH and UA waste, which cause substantial organic pollution along the Jeju coast. SH and UA extracts were orally administered to laboratory rats for 14 days, following drug toxicity testing criteria (No. 2009-116).

During extract administration, no rats died. Furthermore, extract administration did not induce salivation, which frequently occurs during drug oral drug delivery (Han et al., 2004; Yoon et al., 2006; Kim et al., 2012), and there were no signs of altered motility or toxicity.

Body weight gain was recorded as a gross measure of toxicity, and was lower for rats treated with SH and UA compared with control rats (Bailey et al., 2004). SH induced lower body weight gain than UA in female rats, whereas UA induced lower body weight gain than SH in male rats. Addressing gender differences has recently emerged as a priority in several medical fields, including metabolic diseases (Rich-Edwards et al., 2018). Differences in metabolism, gene expression, anatomy, behavior, stress responses, and longevity may vary between genders and may influence carbohydrate and lipid metabolism (Tower et al., 2020; Tramunt et al., 2020). Such differences affect many aspects of metabolism and related diseases, reflecting differences in male and female sex hormones (Link and Reue, 2017). Responses in female and male animals differed dependent on these factors.

Feed intake was lower in female rats administered SH and UA compared with control rats, although the differences were not significant. However, no differences were observed between control and experimental male animals. In a previous study, SH powder was added to white shrimp (*Litopenaeus vannamei*) feed; although no significant differences in feed intake were found, the growth rate of the shrimp was lower (Eom et al., 2020). The weight loss observed in the current study is likely an effect extract administration since SH exhibits anti-obesity activity (Murakami et al., 2021). Body weight of rats following UA extract administration was lower than that of control rats. These results are consistent with chronic toxicity, which has previously been reported for UA (Qi et al., 2013). Indeed, *Capsosiphon fulvescens* in the family Ulvaceae induces significant weight loss when combined with a high cholesterol diet (Kwon and Nam, 2006). Our results suggest that UA may be a functional substance to aid weight loss.

Changes in the weights of major organs are important indicators of toxicity (Bailey et al., 2004). Compared with control rats, rats administered SH and UA extracts did not exhibit any significant difference in organ weight, and the two substances appear to be non-toxic. However, organ weights tended to be higher than those recorded in historical data (Kang et al., 2001). However, in the previous study, experimental animals were seven weeks old.
when organ weights were measured, whereas in the current study organ weights were measured when rats were eight weeks of age. Therefore, higher weights were likely due to this difference in age.

Hematological examination showed that RBC and HGB levels significantly increased in female rats administered SH and UA extracts, but no significant changes were observed for MCV, MCH, and MCHC. Compared with data from the previous study values, no abnormal measurements were observed after extract administration, and all values were within normal ranges (Wolford et al., 1986).

Serological tests were conducted to confirm the presence or absence of liver and kidney abnormalities induced by SH and UA and the health statuses of the experimental rats. Results showed significantly reduced ALP and glucose levels in male rats following extract administration. In rats administered urea, TG and BUN values decreased significantly but changed remained within the normal range (Kang et al., 2004). In females, glucose were significantly decreased in both extract groups, and AST, TG, and HDL-C levels were significantly increased following administration of SH compared with control rats; however, the values remained within normal ranges.

Results of previous studies suggest that Sargassum sp. and Ulva sp. can lower serum glucose levels (Kang et al., 2012; Kim and Byun, 2018), therefore the serum glucose reducing effect shown in this study was probably induced by the experimental extracts.

Overall, rats administered algal extracts showed similar responses as rats administered distilled water as a control. However, weight gain after extract administration was low, and serum biochemistry analyses showed significantly lower blood sugar levels. However, these effects are not expected to result in notable toxicity. Therefore, algal waste may be used safely as functional additives for consumption by both animals and humans. However, additional studies are needed to explore weight loss and hypoglycemia in models of obesity and diabetes.

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AUTHOR DISCLOSURE STATEMENT

The authors declare no conflict of interest.
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