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Effect of sulfated polysaccharides from *Laminaria japonica* on vascular endothelial cells in psychological stress rats

Jing Li a,1, Shengyong Wang a,1, Xiaomei Yang a,1, Guangbao Pang b, Hua Zheng b, Bin Shen b, Guanhong Li a, Dianchun Shi a, Jienian Wang a, Liaoyun Feng a, Mulan Li a, Wuying Wei a, Wu Qin a, Lu Xie a

a Department of Physiology, Guangxi Medical University, Nanning 530021, China
b Medical Scientific Research Center, Guangxi Medical University, Nanning 530021, China

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Effect of sulfated polysaccharides from Laminaria japonica on vascular endothelial cells in psychological stress rats

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a Department of Physiology, Guangxi Medical University, Nanning 530021, China
b Medical Scientific Research Center, Guangxi Medical University, Nanning 530021, China

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A B S T R A C T
Ethnopharmacological relevance: Laminaria japonica is a popular seafood and medicinal plant in China. Laminaria japonica is used in traditional Chinese medicine to treat and prevent hypertension and edema.

Materials and methods: The vascular protective activity and mechanism of sulfated polysaccharides were studied in adrenalin-induced vascular endothelial damage in rats after psychological stress (PS). Vehicle (sham and PS groups), sulfated polysaccharide from Laminaria japonica (LP; 1 mg/kg and 5 mg/kg) and enoxaparin sodium (1 IU/kg, reference drug) were all administered for 10 days. Behavioral changes were recorded. Plasma levels of adrenalin, cortisol, monoamine oxidase (MAO), semicarbazide-sensitive amine oxidase (SSAO), formaldehyde, H2O2, nitric oxide (NO), endothelin-1 (ET-1), 6-keto-prostaglandin F1a (6-keto-PGF1a), and thromboxane B2 (TXB2) were measured. Endothelium-dependent relaxation of the thoracic aorta was measured and transmission electron microscopy of aortic vessels was performed.

Results: Adrenalin metabolites in plasma were significantly lower (P < 0.01) in rats after LP administration compared with those in the PS groups. The normalized ratios of plasma NO/ET-1 and 6-keto-PGF1a/ TXB2 were maintained and endothelium-dependent relaxation of the aorta was greatly enhanced after LP treatment (P < 0.05). Morphological alterations were observed in vascular endothelial cells (VECs) in PS rats; with a higher number of lysosomes and vague mitochondrial cristae compared with those in the sham group. However, these histopathological changes were markedly alleviated after LP treatment.

Conclusions: This study shows a protective effect of LP on VECs in PS rats. LP can regulate plasma levels of NO, ET-1, and 6-keto-PGF1a, enhance endothelium-dependent relaxation, and alleviate histopathological changes of lysosomes and mitochondria in VECs. The potential mechanism of LP on VECs in PS rats is related to its function of reducing metabolites of adrenalin.

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1. Introduction

Marine organisms are sources of numerous new compounds with multiple pharmacological properties (Arif et al., 2004; Blunt et al., 2006). They have various bioactivities depending on their composition, overall structure and physicochemical properties (Baba et al., 1990; Ellouali et al., 1993). In particular, sulfated polysaccharides extracted from seaweed are drawing increasing attention in the medical and food supplement areas because of their biological activities. Sulfated polysaccharides from brown seaweeds are generally called fucoidans because they are rich in fucose. These fucoidans are reported to have blood anticoagulant, antithrombotic, antiviral, anticoagulant, antioxidant, anti-inflammatory, and anti-proliferative agents (Almeida-Lima et al., 2010; Barroso et al., 2008; Costa et al., 2010; Cumashi et al., 2007; Dore et al., 2013). Laminaria japonica is a type of brown seaweed and is a popular seafood in China and other countries. Over the past years, Laminaria japonica has been used in traditional Chinese medicine to treat hypertension (Wang and Zhang, 1980), edema (Wang et al., 2012a), thrombosis (Zhu et al., 2010), and osteoarthritis (Myers et al., 2010; Suszko and Obminska-Mrukowicz, 2013). Moreover, the oncostatic activity of Laminaria japonica against some mouse tumors has been described (Lins et al., 2009).

According to previous studies (Barfield et al., 1972; Breuer et al., 2001), a psychological stress rat model in lonely fed animals induces anxiety and depression. When a rat is invaded by an unfamiliar rat, it is more likely to become angry and aggressive. Psychological stress induces hypothalamic-pituitary-adrenal axis (HPA) and sympathetic-adrenal medullary system (SAS) activity.
accompanied by long-term emotional behavioral changes. Increased plasma cortisol levels are an important factor in the persistent emotional arousal induced by severe psychological stress (Wang et al., 2012b). With increasing social competition, the effect of psychological stress on related diseases cannot be neglected, such as cardiovascular, cerebrovascular, endocrine, and mental diseases. When humans are under chronic stress, permanent changes in their physiological responses can lead to disease through immune responses (Rief et al., 2001) and platelet activation (Kishi and Numano, 1989). Stimulation of adrenalin excretion by psychological stress can increase circulating formaldehyde levels, which may be involved in the initiation of endothelial injury, and, subsequently, angiopathy (Yu et al., 1997).

Vascular endothelial cells (VECs) play an important role in maintaining structural and functional integrity of the vasculature. VECs can synthesize and release many types of active materials, which take part in regulating the function of the cardiovascular system. Disturbance of these endothelium-derived substances is an important feature of endothelial dysfunction, as well as the basic pathogenesis of most cardiovascular diseases. Treatment for these endothelial disturbances in the cardiovascular system can effectively inhibit heart and vessel remodeling, and improve the prognosis and quality of life in hypertension, atherosclerosis, and heart failure (Lesniak et al., 2001).

People undergo psychological stress all the time in modern society. Although this psychological stress is moderate and not harmful in most cases, it would insensibly induce VECs injury under a long term impact. We had found that the antithrombotic effect in sulfated polysaccharide from *Laminaria japonica* (LP) pretreatment animals was associated with endothelial protection. In a previous study, LP also had a protective effect on exogenous adrenalin-induced VEC damage in vitro and in vivo. However, the mechanism of this protective effect on endogenous adrenalin-induced VEC damage is still unknown. Therefore, the present study aims to investigate the protective effect of LP on damaged VECs in a psychological stress rat model. LP, as a preventive drug for reducing the occurrence of cardiovascular disease risk, has potential application. Just as Aspirin, which is a common clinical drug, it is routinely used for the prevention of cardiovascular diseases.

2. Material and methods

2.1. Isolation and purification of polysaccharide

*Laminaria japonica* was harvested in June 2011 from the Beibu Gulf, and then dried and comminuted. The extractive procedure of polysaccharides was performed according to our previously reported method (Xie et al., 2011). Briefly, dry powder (50 g) was mixed with 1000 ml of distilled water with 0.02% (w/w) cellulose enzyme, 0.05% (w/w) papain, and 0.05% (w/w) neutral protein enzyme, and then incubated at 70 °C for 6 h. After incubation, the pH of the mixture was adjusted to 10.0 with 10% NaOH, and placed at room temperature for 12 h. The supernatant (A) and sediment of the mixture were separated by centrifugation at 500 g for 15 min. The sediment was transferred into 500 ml of 10% HCl and placed at room temperature for 4 h. After centrifugation (500 g, 15 min), the supernatant (B) was collected. Supernatants A and B were combined and precipitated with 80% ethanol. After centrifugation (11000 g, 15 min), the precipitate was dissolved in 100 ml of distilled water and dried. Finally, the crude extract was subjected to DEAE cellulose column chromatography (2.6 × 50 cm²) and eluted with 0.5 M NaCl. The yield of the crude polysaccharide (LP) was 6.53% of raw material. The sugar content of LP was determined to be 71.0%. The sulfate radical content was 83.28 mg/g. The monosaccharide composition consisted mainly of glucose (5.05%), mannose (25.10%), rhamnose (7.37%), galactose (8.46%), and xylose (54.02%). The molecular weight of polysaccharide was 67 kDa.

Enoxaparin injection, which is a sulfated polysaccharide, was used as a positive control because some studies have reported its protective effect on VECs (Iba et al., 2012; Manduteanu et al., 2002). This medicine was produced by Sanofi-Aventis Co., Ltd. (Hangzhou, China).

2.2. Animals

Male adult Sprague-Dawley rats weighing approximately 250–300 g were procured from a local animal supplier and were housed in a temperature-controlled room. The rats were acclimated for 1 week initially, and fed with a normal diet and tap water *ad libitum*. All animal treatments were conducted in accordance with the Guide for Care and Use of Animal Laboratory of Guangxi Medical University in China and were approved by the local ethics committee.

For induced psychological stress, rats were individually housed in clean cages (60 cm × 30 cm × 20 cm) and kept on a reverse 12:12 h light-dark cycle with the lights going on at midnight and off at noon. Each rat was housed in its cage for 10 days to establish home cage familiarity (Barfield et al., 1972). After 10 days, an additional male rat received in the same shipment was used as an intruder in each cage. These rats were in the same body weight range and were used only as intruder males for aggression, which can induce an emotional reaction (e.g., fear, anger, and attack) in PS rats. All aggressive activities took place between 13:30 and 15:30 h during the dark phase of the activity cycle of PS rats. Each period of aggression lasted 20 min. The PS rats did not suffer any physical injuries in addition to the psychological stress.

Animals were divided into five groups. (1) The sham control group (sham) included rats that were living in groups and were intraperitoneally injected with saline twice per day. (2) The psychological stress group (PS) included rats that were lonely fed, and intraperitoneally injected with saline twice per day. (3) The psychological stress treated with low dose LP group (PS+LP 1 mg) included rats that were lonely fed and intraperitoneally injected with LP (1 mg/kg body weight) twice per day. (4) The psychological stress treated with high dose LP group (PS+LP 5 mg) included rats that were lonely fed and intraperitoneally injected with LP (5 mg/kg body weight) twice per day. (5) The psychological stress treated with enoxaparin group (PS+Eno) included rats that were lonely fed and intraperitoneally injected with enoxaparin sodium (1 IU/kg body weight, reference drug, twice per day). All the injections were administered at 9 a.m. and 5 p.m. for 10 days.

2.3. Assessment of behavioral changes

The open field test plays a major role in coping with stress (Kaluff and Tuohimaa, 2005; Van Erp et al., 1994). The open field, constructed of black painted wood, was a 100 × 100 cm² square, divided into 25 (20 × 20 cm²) squares with white lines, and was surrounded by a 50-cm high wall. After aggression, all rats were put at the center of the open field and their emotionally reactive state was determined by recording their behavior in 3 min. Horizontal activity, expressed as the number of squares crossed, was monitored using a video tracking system. Vertical activity, expressed as the number of times of rearing, was registered by the researchers. Exploratory activity was defined as the sum of horizontal and vertical activities.
24. Blood sampling

After the experiments, rats were anaesthetized with chloral hydrate. Blood samples were taken from the common carotid artery and then mixed with 100 µl Na3EDTA, followed by centrifugation (3000g, 10 min, at 4 °C). The plasma was separated and stored at −80 °C until analysis. Plasma levels of cortisol, endothelin-1 (ET-1), 6-keto-prostaglandin F1α (6-keto-PGF1α), and thromboxane B2 (TXB2) were measured by standard radioimmunoassay. Prostacyclin (PGI2) and thromboxane A2 (TXA2) are not stable in the circulation. Therefore, 6-keto-PGF1α and TXB2, which are their products of metabolism, reflect their levels. Plasma NO levels were measured as nitrate+nitrite by a Nitrate/Nitrite Colorimetric Assay Kit (Cayman Chemical Company, USA). Plasma levels of adrenalin, monoamine oxidase (MAO), and H2O2 in plasma were measured by commercially available kits. All procedures were performed according to the manufacturer’s recommendation in the kit manuals.

25. Fluorescence spectrophotometry for semicarbazide-sensitive amine oxidase (SSAO)

Plasma SSAO activity was detected by a Fluoro SSAO detection kit. Samples were read on a fluorescence spectrophotometer using an excitation of 530 nm and fluorescence was measured at 590 nm.

26. High pressure liquid chromatographic determination for formaldehyde

Plasma formaldehyde levels were determined using high pressure liquid chromatographic (HPLC) analysis as previously described (Luo et al., 2001). The HPLC column was a Supelcosil TM LC-18, 5 μm, 250 mm × 4.6 mm column (USA). The column temperature was set at 30 °C and the sample injection volume was set at 10 μl. The excitation and emission wavelengths of the fluorescence detector were set at 346 nm and 422 nm, respectively. The mobile phase was acetonitrile–water (5:95) with a flow-rate of 1 ml/min. The peak area was used for quantitative calculation.

27. Ultrastructure of VECs

After the rats were sacrificed, the thoracic arteries were immediately removed from the thoracic cavity. Pieces of selected regions of the arteries were separated and immediately placed in 2.5% glutaraldehyde for transmission electron microscopy.

28. Endothelium-dependent relaxation of the thoracic aorta

According to previous studies (Nakamura et al., 2002; Nishimatsu et al., 2001), aortic endothelial function was determined by isolated aortic vessel rings. The isolated thoracic aorta was immediately immersed in Krebs–Ringer HCO3 solution (composition in mM: 154.7 NaCl, 5.4 KCl, 2.5 CaCl2, 6.0 Tris, and 11 glucose), which was aerated with 95% O2–5% CO2 (pH=7.4; PO2=580 mmHg). The thoracic aorta was trimmed with care to prevent any damage to VECs, and cut into rings 2–3 mm in length. The aortic rings were carefully mounted on two specimen holders and placed in a glass organ chamber containing 15 ml of aerated Krebs–Ringer HCO3 solution at 37 °C. One holder was stationary, whereas the other holder was connected to an isometric force–displacement transducer (Model FT102; ADInstruments, Australia) coupled to a polygraph (Model ML785; ADInstruments). The aortic ring was incubated for 90 min at a tension of 1500 mg, during which time the organ chamber was rinsed every 15 min with aerated Krebs–Ringer HCO3 buffer. After 90 min, the base line of the tension (Tb) was recorded and aortic rings were pre-contracted with 10−6 M phenylephrine (PE). When the pre-contraction reached a steady state (TPE), increasing concentrations of acetylcholine (ACh; Sigma, USA) were added cumulatively from 10−8 to 10−4 M with 3 min interval. The tension of relaxation in each ACh concentration (TAC) was recorded. Relaxation (%) was expressed as the percentages of the level of pre-contraction. Relaxation (%)=(((TPE−TAC)/(TPE−Tb))×100%.

29. Statistical analysis

The experiment was set up with a completely randomized design. Results are presented as mean ± SD. Statistical analysis was performed using the SSPS 11.0 software package. Statistical significance was evaluated by one-way analysis of variation. Differences were considered significant if P < 0.05.
3. Results

3.1. Evaluation of the psychological stress rat model

Behavior, including vertical, horizontal, and exploratory activities, was significantly increased in rats after psychological stress compared with that in the sham group ($P < 0.01$; Fig. 1A). This finding indicated that the behavior of rats was affected by psychological stress. Furthermore, plasma levels of cortisol and adrenalin in the PS group were significantly higher than those in the sham group ($P < 0.01$; Fig. 1B and C). However, in PS rats treated with LP or enoxaparin, plasma levels of cortisol and adrenalin were not different from those in PS rats without treatment. These findings suggested that the pathway of the HPA axis and SAS was not affected by LP or enoxaparin.

3.2. Effects of LP on metabolites of adrenalin

There were no significant changes in plasma MAO and SSAO activities between the sham and PS groups. Plasma MAO and SSAO activities in PS rats treated with LP or enoxaparin were not significantly different compared with that in the PS group (Fig. 2; $P > 0.05$). In PS rats, plasma levels of formaldehyde and H$_2$O$_2$ were higher than those in the sham group (Fig. 3; $P < 0.01$). LP at the 5 mg/kg resulted in lower plasma levels of formaldehyde.
and H2O2 compared with those in the PS group (Fig. 3A and B; P < 0.01). PS rats treated with LP 1 mg/kg and enoxaparin showed reduced plasma level of formaldehyde compared with that in the PS group (Fig. 3A, P < 0.05).

3.3. Effects of LP on endothelium-derived vasodilators and vasoconstrictors

As shown in Figs. 4 and 5, the PS group had significantly lower plasma NO (17.80 ± 2.82 mmol/L; P < 0.01) and 6-keto-PGF1a levels (65.25 ± 13.54 pg/ml; P = 0.01), but plasma ET-1 levels were higher (31.11 ± 4.23 pg/ml; P < 0.01) compared with those in the sham group (NO: 25.00 ± 4.04 mmol/L; 6-keto-PGF1a: 96.68 ± 15.31 pg/ml; ET-1: 24.11 ± 2.48 pg/ml). Throughout the course of the experiment, rats treated with LP at doses of 1 mg/kg and 5 mg/kg and enoxaparin at a dose of 1 IU/kg resulted in significantly higher plasma levels of NO (21.44 ± 3.51 mmol/L, 26.26 ± 3.9 mmol/L, and 21.85 ± 4.04 mmol/L, respectively; P < 0.05) and 6-keto-PGF1a (103.09 ± 16.7 pg/ml, 114.42 ± 18.96 pg/ml, and 84.17 ± 12.27 pg/ml, respectively; P < 0.05) compared with those in the PS group. Similarly, significantly lower plasma levels of ET-1 were observed in rats treated with LP at doses of 1 mg/kg (26.30 ± 3.49 pg/ml, P < 0.05) and 5 mg/kg (23.78 ± 3.63 pg/ml, P < 0.01) and enoxaparin at a dose of 1 IU/kg (25.93 ± 4.36 pg/ml, P < 0.05) compared with those in the PS group (31.10 ± 4.22 pg/ml). However, no significant changes were observed in plasma TXB2 levels among the groups. Nevertheless, treatment with LP of two doses led to significantly increased ratios of NO/ET-1 and 6-keto-PGF1a/TXB2 compared with those in PS rats (P < 0.05).

3.4. Effects of LP on endothelium-dependent relaxation of aortic vessels

Isolated thoracic aorta of PS rats without treatment had significantly lower endothelium-dependent relaxation (Fig. 6) than did the sham group (P < 0.05) from 10-6 M to 10-4 M ACh (P < 0.05). The relaxation of PS rats with LP 5 mg pretreatment was higher than that with PS rats in 10-6 M, 10-5 and 10-4 M ACh (P < 0.05). The relaxation of PS rats with LP 1 mg and enoxaparin pretreatment were enhanced compared with those in PS rats in 10-4 M ACh (P < 0.05).

3.5. Effects of LP on the ultrastructure of endothelial cells

Changes in ultrastructure of VECs greatly varied among all the groups as shown by transmission electron microscopy (Fig. 7). VECs in the PS group had a markedly higher number of lysosomes and vague mitochondrial cristae compared with those in the sham group. LP at a low dose (1 mg/kg) resulted in a few lysosomes and mitochondrial edema. LP exposure at a high dose (5 mg/kg) did not show any changes in lysosomes or mitochondria. Administration of the reference drug, enoxaparin, resulted in a few lysosomes and vague mitochondrial cristae in contrast with the PS group.

4. Discussion

Growing evidence demonstrates that psychological risk variables contribute to physical disease. The stress response and its correlation with chronic disorders, such as cardiovascular disease, gastrointestinal disease, autoimmune disease, metabolic syndrome, and chronic pain, have been comprehensively explored. Psychological stress has become increasingly more critical in precipitating cardiovascular events in modern society.
The mechanisms responsible for the effects of psychological stress on the endothelium have not been completely elucidated. Related regulatory mechanisms have evolved in VECs, which are in part mediated by the production of increased adrenalin levels. Adrenalin is deaminated by MAO, and then produces methylamine. Methylamine can be further deaminated by SSAO and converted into toxic formaldehyde, H$_2$O$_2$, and ammonia, which can damage VECs (Gubisne-Haberle et al., 2004; Lin et al., 2005; Zhang et al., 2010). Vascular endothelium comprises the inner lining of blood vessels, and serves as an autocrine and paracrine organ that regulates vascular function. Endothelial dysfunction is recognized as the initial step in the atherosclerotic process. Strategies capable of alleviating changes in vascular endothelium at the preclinical stage hold potential to refine cardiovascular risk. Therefore, an increasing number of researchers are currently exploring drugs that can protect VECs and prevent cardiovascular diseases induced by psychological stress.

Fig. 7. Transmission electron microscopy images of VECs in the thoracic aorta in the sham group (A), PS group (B), PS+LP 1 mg group (C), PS+LP 5 mg group (D) and PS+Eno group (E). There were a high number of lysosomes (black arrows) and vague mitochondrial cristae with high electron-density (white arrows) in the PS rat. LP exposure at a high dose (5 mg/kg) did not lead to any changes in lysosomes and mitochondria. LP at a low dose (1 mg/kg) resulted in a few lysosomes and mitochondrial edema. Administration of the reference drug, enoxaparin, led to a few lysosomes and vague mitochondrial cristae in contrast with the PS group. The scale bar is 500 nm.

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by psychological stress. Natural drugs with fewer risks are more concerned. In our study, behavior, including vertical, horizontal, and exploratory activities, was significantly greater in PS rats with or without treatment (Fig. 1) than that in sham rats. Plasma cortisol and adrenalin levels were significantly higher after psychological stress. Furthermore, MAO and SSAO, which are metabolic enzymes, did not significantly change after psychological stress or treatment (Fig. 2). Because of higher plasma adrenalin levels after psychological stress, plasma formaldehyde and H₂O₂ levels in the PS group were significantly higher than those in the sham group. Interestingly, significantly lower plasma formaldehyde and H₂O₂ levels were observed in the PS + LP 5 mg/kg group compared with those in the PS group (Fig. 3). We previously found an anti-oxidative effect of LP in UVB-radiation skin in a mouse model (Li et al., 2013). Therefore, a possible reason for low formaldehyde and H₂O₂ levels may be related to the anti-oxidative effect of LP. LP might increase formaldehyde dehydrogenase, peroxidase, and catalase activity to promote the degradation of formaldehyde and H₂O₂.

The endothelium is the thin layer of cells lining the interior of every vessel in the circulatory system. The endothelium provides a structural barrier between the circulation and surrounding tissue, and VECs also secrete mediators that influence vascular hemodynamics in the physiological state. VECs contribute to the regulation of blood pressure and blood flow by releasing vasodilator substances, such as NO and PGI₂, as well as vasoconstrictor substances, including ET-1 and TXA₂. Endothelial dysfunction, characterized by an imbalance between endothelium-derived vasodilator and vasoconstrictor substances, induces impairment of endothelium-dependent vasodilation. Endothelial cell-derived NO, which is the most important vasoconstrictor substance in endothelium-dependent vasodilation, acts on vascular smooth muscle cells to induce vasodilation by increasing production of cyclic guanosine monophosphate. Previous studies have shown that ACh-induced vascular relaxation, which is stimulated by the release of endothelial cell-derived NO, can reflex endothelium-dependent vasodilation (Nakamura et al., 2002; Nishimatsu et al., 2001). In our study, plasma NO and 6-keto-PGF₁α levels were significantly decreased and plasma ET-1 levels were significantly increased in the PS group compared with those in the sham group. Rats pre-administered with LP at 5 mg/kg displayed significantly higher plasma NO and 6-keto-PGF₁α levels, but plasma ET-1 levels were lower compared with those in the PS group. These findings indicated that endothelium damage after psychological stress induced an imbalance between endothelial cell-derived vasodilator and vasoconstrictor substances. However, LP could regulate these substances by preventing endothelial dysfunction induced by psychological stress. Furthermore, isolated thoracic aorta in the PS group appeared to have suppressed endothelium-dependent relaxation induced by ACh (Fig. 6), but this was restored in the PS + LP 5 mg group. These results indicated that impaired endothelium induced by psychological stress could disturb endothelium-dependent vasodilation. However, LP could prevent VEC injury and maintain endothelium-dependent vasodilation, which further confirmed the protective effect of LP on VECs. Further studies are required to identify the protective mechanism of LP. Enoxaparin was used as a positive control because some studies have reported its protective effect on VECs (Iba et al., 2012; Manduteanu et al., 2002). In our study, we found that enoxaparin also attenuated endothelial damage in PS rats to some extent, but the relative mechanism needs to be further explored.

Some studies have suggested that the mitochondrion plays an important part in cell damage by stress (Sammut et al., 2001; Zhan et al., 1999). During intracellular apoptosis, lysosomes and mitochondria play an important role. Apoptotic factors may trigger lysosomal membrane permeabilization, and then increase the permeability of the mitochondrial membrane and initiate cell death. Mitochondrial membrane permeabilization can also induce lysosomal membrane permeabilization and promote cell death (Terman et al., 2006). Our results of electron microscopy (Fig. 7) showed that VECs in the PS group appeared to have a high number of lysosomes and vague mitochondrial cristae with high electron density. VECs appeared to have less lysosomes and clear mitochondrial cristae with less electron density in the PS + LP 5 mg treatment group compared with those in PS rats. These results indicated that VECs after psychological stress induced changes in lysosomes and mitochondria. However, LP reduced the number of lysosomes and the injury of mitochondria, which may be relative to avoid the apoptosis of VECs. The effect of polysaccharide on mitochondria has also been demonstrated in other studies. Gano-derma atrum polysaccharide significantly improves cell survival in cardiomyocytes through the mitochondrial pathway (Li et al., 2010). Similarly, Ulva lactuca polysaccharide stabilizes the functional status of the mitochondrial membrane through prevention of oxidative stress (Devaki et al., 2009). The reason why LP prevents ultrastructural changes of VECs may be related also to the anti-oxidative effect of LP (Liang et al., 2006; Li et al., 2013) on promoting the degradation of formaldehyde and H₂O₂, which maybe one of the mechanisms of how LP affects VECs in rats after psychological stress.

5. Conclusions

In conclusion, our study shows that LP has a potential protective effect against psychological stress-induced VEC damage. The mechanism of LP-mediated protection may be related to its ability to decrease toxic production of adrenalin in plasma. LP maintained endothelium-dependent vasodilation and reduced ultrastructural changes of VECs, which further confirmed the protective effect of LP on VECs. These observations also raise the possibility of LP being used as a prophylactic agent against endothelial injury.

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Biological activities of sulfated polysaccharides from tropical seaweeds.


