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Research Article
Asiatic acid Improves Physical Fatigue through Regulating Inflammatory Reaction, Oxidative Stress and Energy Metabolism in Mice

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Abstract

Background and Objective: Fatigue is a complex physiological phenomenon in daily life, which can easily evoke physical dysfunction and serious illness. Asiatic acid with multifaceted biological activities has been used in food and medicinal fields for a long period. The purpose of this study was to explore the potential anti-fatigue effect and mechanisms of asiatic acid in high-intensity exercise. **Materials and Methods:** The exercise-fatigue model was constituted via a forced swimming test. The experiment mice were continuously fed with asiatic acid for 28 days. The exhaustive time, fatigue relevant biochemical indices, inflammatory cytokines, oxidation parameters and energy metabolism indicators were detected to explore evidence of asiatic acid in high-intensity exercise. **Results:** Current researches showed that asiatic acid significantly prolonged swimming exhaustive time. In high-intensity exercise, asiatic acid dramatically alleviated fatigue relevant biochemical indices, including CK, LDH, AST, ALT, SUN and BLA to protect against organ injury. Moreover, asiatic acid relieved TNF-α and IL-6 levels to restrain inflammatory reaction. In muscle tissue, asiatic acid markedly elevated SOD, CAT and GSH-Px activities to promote antioxidant ability and observably alleviated MDA level to eliminate oxidative injury. Asiatic acid remarkably increased SDH and Na^+-K^+-ATPase activities to ameliorate energy metabolism. In addition, asiatic acid markedly activated PGC-1α, TFAM, NRF-2 and HO-1 expression to increase energy metabolism and suppress oxidative stress in excessive exercise. **Conclusion:** These results suggested asiatic acid could improve exercise-induced fatigue via inhibition of inflammatory response, prevention of oxidative stress damage and improvement of energy metabolism in mice. Asiatic acid could serve as a novel potential candidate to postpone fatigue.

Key words: Asiatic acid, fatigue, inflammatory reaction, oxidative stress, energy metabolism

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Fatigue is a common and complex phenomenon in the general population, which influences mood, causes myalgia and affects physical performance to lower the quality of life, even evoking serious illness[1]. High-intensity exercise is one of the underlying factors of physical fatigue. The pathophysiological mechanism of physical fatigue is complicated and there are some theories to illuminate the possible potential physiological process after high-intensity exercise. Firstly, extra and excessive intermediate and end metabolites, such as LA and BUN, can be produced in high-intensity exercise. These biochemical parameters were confirmed to be linked to fatigue[2]. Secondly, over-production of reactive oxygen species leads to oxidation stress in high-intensity exercise. Then, disruption of oxidative balance was involved in the pathophysiology of fatigue[3]. Thirdly, intensive muscle contraction is the cause of inflammation reaction, evidenced by accumulation of inflammatory cytokine, which has a detrimental effect on organs, such as liver and muscle[4]. Last but not least, energy is not only to maintain normal physical activity but also play a crucial role in high-intensity exercise-induced fatigue. SDH and ATPase are closely involved in the production of ATP, which are related elements of material and energy metabolism[5]. Currently, the research focus of anti-fatigue is to enhance physical performance and mitigate recovery time after exercise-induced fatigue.

Asiatic acid is one of the triterpenes, which are naturally biosynthesized by cyclization. Asiatic acid is widely cultivated in Asian and African countries and has been regarded as a vegetable, spice and herb in food and medicinal fields. Nowadays, Asiatic acid has been confirmed as a functional food and therapeutic drug that possesses plentiful pharmacological activities in tissues and organs. In addition, heart and pulmonary function play a vital position in high-intensity exercise. Previous research reported asiatic acid alleviated doxorubicin-induced heart, liver and kidney toxicities through enhancing NRF-2 protein expression[6]. Asiatic acid was also shown to ameliorate hypochlorous acid-induced pulmonary fibrosis via regulating advanced oxidation protein and TGF-β1/Smad2/3 signaling[7]. What is more, asiatic acid is involved in energy metabolism, which is closely associated with exercise-induced physical fatigue. In a hypoxia environment, asiatic acid attenuated cardiomyocytes apoptosis by miR-1290/HIF3A/HIF-1α signaling[8]. In glucose uptake, asiatic acid improved diabetic-induced glucose response and promoted glucose homeostasis by antioxidant defense[9]. In the lactate signalling cascade, asiatic acid mitigated lactate-induced apoptosis via suppression of oxidative injury[10]. This study investigated the asiatic acid exerted improvement on physical fatigue through regulating inflammatory reaction, oxidative stress and energy metabolism.

MATERIALS AND METHODS

Study area: The study was carried out at the Human Movement Science Laboratory, Hunan University of Arts and Science in May-September, 2021.

Chemicals and reagents: Asiatic acid was purchased from Sigma (St. Louis, MO, United States). The purity of asiatic acid surpassed 95% by HPLC. The assay kits of BLA, CK, LDH, BUN, AST, ALT, SOD, CAT, GPX, MDA, SDH and Na^+-K^+-ATPase were purchased from Nanjing Jiancheng Biotechnology Institute (Nanjing, China). The detection kits of TNF-α and IL-6 were purchased from BOSTER Biological Technology Co., Ltd., (Wuhan, China).

Animals and treatment: A total of 80 male ICR mice (7 weeks old, 18-22 g) were purchased from Hunan SJA Laboratory Animal Co., Ltd. (Changsha, China). Mice lived in specific pathogen-free conditions. After 7 days of acclimatization, mice were randomly assigned into 4 groups: (1) Control group (Con), (2) 1 mg kg^{-1} asiatic acid (AA-L), (3) 10 mg kg^{-1} asiatic acid (AA-M) and (4) 20 mg kg^{-1} asiatic acid (AA-H). Asiatic acid was treated by gavage for 28 successive days. The control group was given an equivalent dose of distilled water. The body weight, liver, lung, kidney and heart were weighed by scales to calculate organ index. The form of organ index is 100 g G^{-1}. All animal experiments were inspected according to the Ethics Committee of Hunan University of Arts and Science (No. HUAS-2021-TY-179).

Forced swimming test: Weight-loaded forced swimming test was used to measure exhaust time. Briefly, 30 min after the last treatment, the mouse with a lead (5% of body weight) swam individually in the pool (24-26°C, 30 cm deep). Swimming time was defined when the mouse did not return to the surface for greater than 10 sec.

Biochemical assessment: After 28 days of intervention, mice underwent a 90 min swimming test without any loads. After resting for 1 hr, mice were anaesthetized. Blood was withdrawn by removing the eyeball. Then blood was centrifuged (1500 g, 4°C, 10 min) to prepare serum. The fatigue-associated biochemical indicators of LA, CK, LDH, AST, ALT and SUN were tested to evaluate fatigue and injury of muscle, liver and kidney.

Inflammatory variables determination: The parameters of TNF-α and IL-6 as inflammatory cytokines, were analyzed by the ELISA method. In 96-well plates, the biotin-labelled anti-mouse antibody of TNF-α and IL-6 was incubated (37°C, 90 min). After washing 3 times, avidin-peroxidase was added into plates and reacted (37°C, 30 min). The plate was again washed 5 times and TMB substrate was combined (37°C, 20 min). The wavelength of absorbance was 405 nm.

Oxidant stress, energy metabolism detection: After anesthetization, muscles were immediately excised from each group, frozen by liquid nitrogen and collected at -80°C. The tissue was weighed, ground and centrifuged (4000 g, 4°C, 15 min) to detect SOD, CAT, GSH-PX and MDA. At the end of experiments, the content of SDH and Na^+-K^+-ATPase were determined in muscle to evaluate the efficiency of energy metabolism.

mRNA gene expression: RNA from muscle was extracted by TRIzol and transformed into cDNA. mRNA expression was detected with SYBR by Bio-Rad CFX real-time PCR. Primers for PGC-1α, TFAM, NRF-2, HO-1 and β-actin were designed by Sangon Biotech (Shanghai) Co., Ltd., (Table 1). Gene expression was calculated via standardization to β-actin.

Statistical analysis: All results were expressed as Mean±SD. The significance was demonstrated by a one-way ANOVA. $p<0.05$ were deemed significant.

RESULTS

Properties of AA on exhaustive exercise time: The swimming endurance was shown in Fig. 1. The exhaustive swimming time of control, AA-L, AA-M and AA-H groups were 9.22, 10.83, 15.43 and 21.08 min, respectively. Comparison to the control group, exhaustive time in AA-M and AA-H groups was markedly prolonged by 67, 129%, respectively ($p<0.01$), which demonstrated AA had prominent properties on movement and endurance in high-intensity exercise.

Properties of AA on CK, LDH, ALT, AST, SUN and BLA: The biochemical parameters were tested to evaluate the anti-fatigue efficacy of AA. Figure 2a showed CK levels of control, AA-L, AA-M and AA-H groups were 1.96, 1.87, 1.37 and 1.20 U mL^{-1}, respectively. Figure 2b showed LDH levels of control, AA-L, AA-M and AA-H groups were 1.74, 1.60, 1.27 and 1.19 U mL^{-1}, respectively. Figure 2c showed ALT levels of control, AA-L, AA-M and AA-H groups were 53.22, 50.19, 41.26 and 39.51 U L^{-1}, respectively. Figure 2d showed AST levels of control, AA-L, AA-M and AA-H groups were 79.98, 71.97, 60.76 and 55.67 U L^{-1}, respectively. Figure 2e showed SUN levels of control, AA-L, AA-M and AA-H groups were 13.55, 12.53, 9.48 and 8.30 mmol L^{-1}, respectively. Figure 2f showed BLA levels of control, AA-L, AA-M and AA-H groups were 18.68, 17.67 L, 13.48 and 11.59 mmol L^{-1}, respectively. The levels of biochemical parameters in AA-M and AA-H groups were visibly reduced compared to the control group ($p<0.01$), which demonstrated AA prevented muscle damage, liver damage and kidney damage to made positive contribution in high-intensity exercise.

Properties of AA on inflammatory response in serum: The proinflammatory cytokines, including TNF-α and IL-6, were examined to evaluate the anti-inflammatory function of AA. Figure 3a showed TNF-α levels of control, AA-L, AA-M and AA-H groups were 98.04, 92.11, 82.83 and 74.62 pg mL^{-1}, respectively. Figure 3b showed IL-6 levels of control, AA-L, AA-M and AA-H groups were 54.82, 49.98, 43.71 and 36.89 pg mL^{-1}, respectively. TNF-α and IL-6 levels in AA-M and AA-H groups were relieved compared to the control group ($p<0.05$, $p<0.01$), which demonstrated AA delayed physical fatigue by regulating inflammatory mediators in high-intensity exercise.

Properties of AA on oxidation stress in muscle: The oxidation indices, including SOD, CAT, GSH-Px and MDA, were measured to estimate the anti-oxidant function of AA. Figure 4a showed SOD activities of control, AA-L, AA-M and AA-H groups were 86.65, 95.39, 106.53 and 111.09 U mg^{-1} pro, respectively.

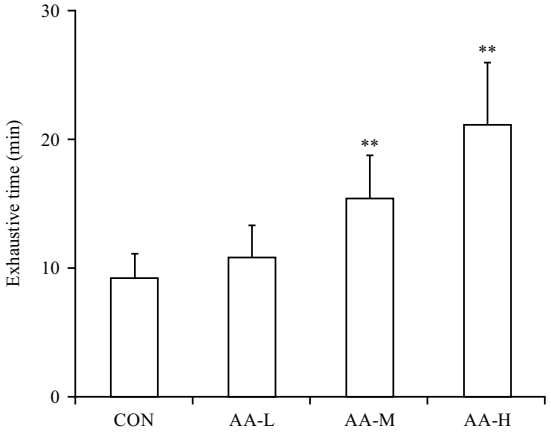

Fig. 1: Properties of AA on weight-loaded swimming time (n = 10 mice/group)
*p<0.05 and **p<0.01 versus control group

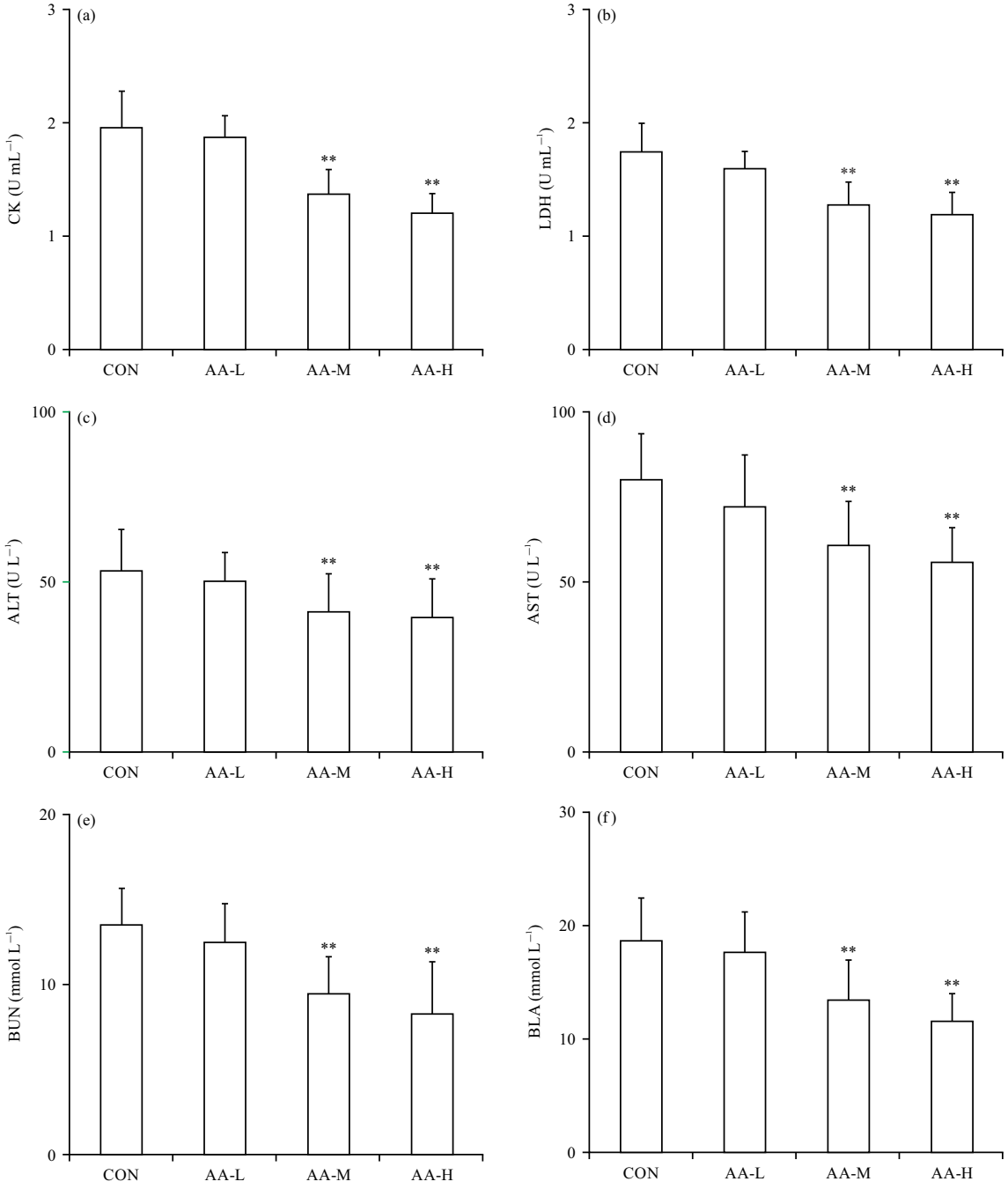

Fig. 2(a-f): Properties of AA on biochemical parameters relevant to fatigue (n = 10 mice/group), (a) Creatine kinase (CK), (b) Lactate dehydrogenase (LDH), (c) Alanine aminotransferase (ALT), (d) Aspartate aminotransferase (AST), (e) Serum urea nitrogen (SUN) and (f) Blood lactic acid (BLA)
*p<0.05 and **p<0.01 versus control group

Figure 4b showed CAT activities of control, AA-L, AA-M and AA-H groups were 26.92, 30.19, 34.14 and 36.47 U mg^{-1} pro, respectively. Figure 4c showed GSH-Px activities of control, AA-L, AA-M and AA-H groups were 41.15, 43.51, 51.79 and 55.03 U mg^{-1} pro, respectively. Figure 4d showed MDA levels of control, AA-L, AA-M and AA-H groups were 3.56, 3.31, 3.09 and 2.48 nmol mg^{-1} pro, respectively. The activities of SOD, CAT and GSH-Px in AA-M and AA-H groups were markedly elevated, while MDA levels in AA-M and AA-H groups were significantly alleviated compared to the control group

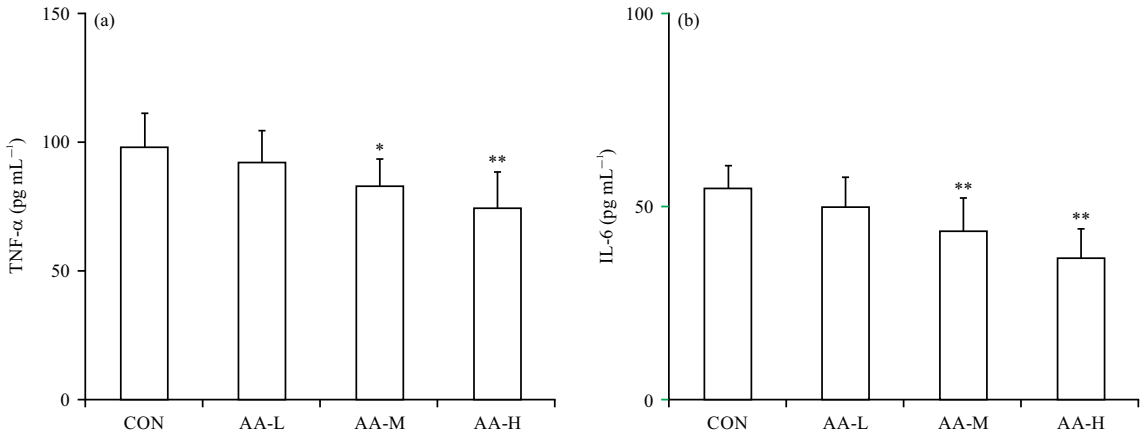

Fig. 3(a-b): Properties of AA on the inflammatory response (n = 10 mice/group), (a) Tumor necrosis factor (TNF-α) and (b) Interleukin 6 (IL-6)
*p<0.05 and **p<0.01 versus control group

Table 1: Primers were used in this study[11-13]

Gene	Accession numbers	Primer sequences
PGC-1α	NM_008904	
	Forward primer	5′-TATGGAGTGACATAGAGTGTGCT-3′
	Reverse primer	5′-CCACTTCAATCCACCCAGAAAG-3′
TFAM	NM_009360	
	Forward primer	5′-CCTGAGGAAAAGCAGGCATA-3′
	Reverse primer	5′-TCACTTCGTCCAACTTCAGC-3′
NRF-2	NM_010902	
	Forward primer	5′-TCCGCTGCCATCAGTCAGTC-3′
	Reverse primer	5′-ATTGTGCCTTCAGCGTGCTTC-3′
HO-1	NM_010442	
	Forward primer	5′-TGCAGGTGATGCTGACAGAGG-3′
	Reverse primer	5′-GGGATGAGCTAGTGCTGATCTGG-3′
β-actin	NM_007393	
	Forward primer	5′-GATTACTGCTCTGGCTCCTAGC-3′
	Reverse primer	5′-GACTCATCGTACTCCTGCTTGC-3′

(p<0.05, p<0.01). These results implied AA exerted a positive role in physical fatigue by increasing antioxidant ability and eliminating oxidative injury in high-intensity exercise.

Properties of AA on energy metabolism in muscle: The SDH and Na^+-K^+-ATPase, as vital regulatory enzymes in anabolism and catabolism, were detected to estimate the ATP generation rate of AA. Figure 5a showed SDH activities of control, AA-L, AA-M and AA-H groups were 0.82, 0.85, 0.97 and 0.99 U mg^{-1} pro, respectively. Figure 5b showed Na^+-K^+-ATPase activities of control, AA-L, AA-M and AA-H groups were 0.95, 1.04, 1.13 and 1.22 U mg^{-1} pro, respectively. SDH and Na^+-K^+-ATPase activities in AA-M and AA-H groups were remarkably increased compared to the control group (p<0.05, p<0.01), which manifested AA possessed anti-fatigue properties by improving energy metabolism in high-intensity exercise.

Properties of AA on the expression of PGC-1α, TFAM, NRF-2 and HO-1 in muscle: The PGC-1α, TFAM, NRF-2 and HO-1 as crucial regulatory factors in energy metabolism and antioxidation in muscle, were detected to evaluate the anti-fatigue function of AA. Figure 6a showed PGC-1α relative expression of control, AA-L, AA-M and AA-H groups were 1, 1.09, 1.57 and 1.74, respectively. Figure 6b showed TFAM relative expression of control, AA-L, AA-M and AA-H groups were 1, 1.12, 1.34 and 1.55, respectively. Figure 6c showed NRF-2 relative expression of control, AA-L, AA-M and AA-H groups were 1, 1.12, 1.50 and 1.64, respectively. Figure 6d showed HO-1 relative expression of control, AA-L, AA-M and AA-H groups were 1, 1.11, 1.71 and 2.06, respectively. The relative expressions of PGC-1α, TFAM, NRF-2 and HO-1 in AA-M and AA-H groups were significantly activated compared to the control group (p<0.05, p<0.01), which demonstrated AA was effective in anti-fatigue by regulating energy metabolism and oxidative injury in excessive exercise.

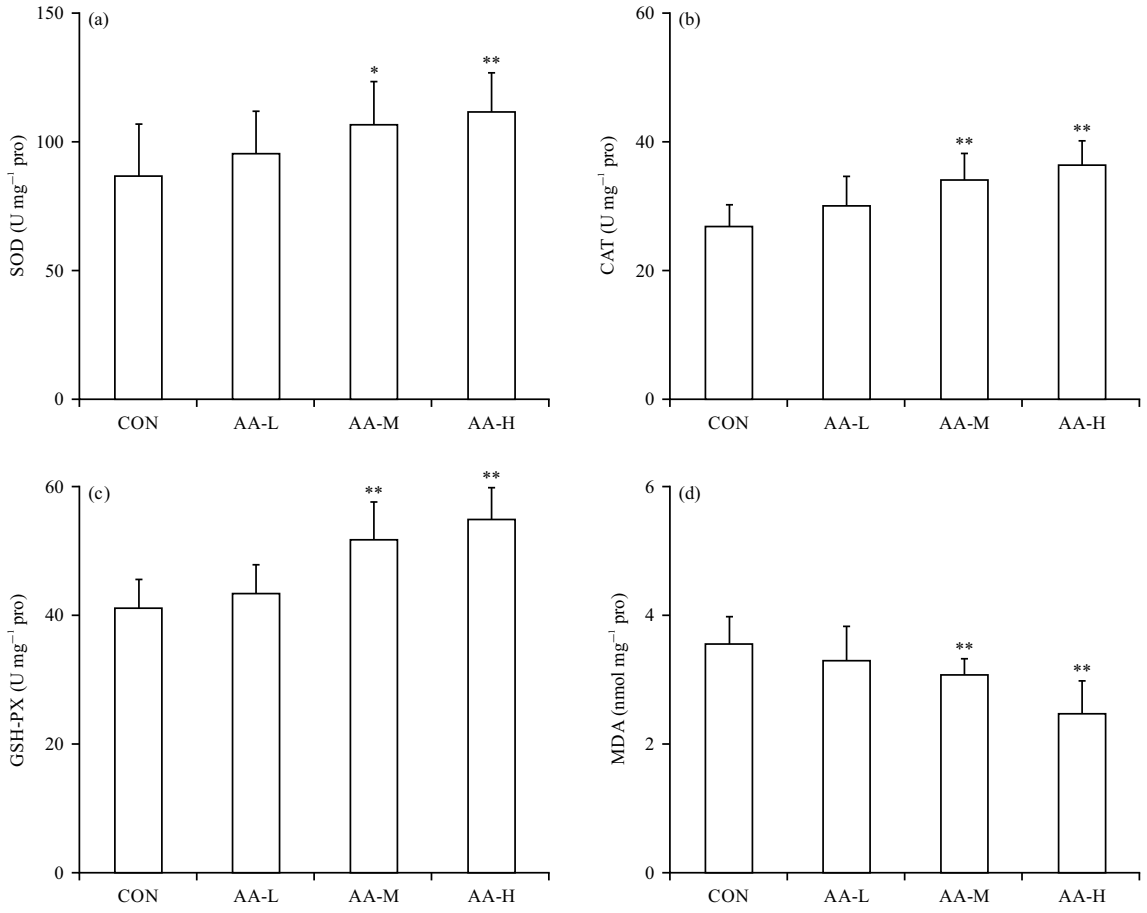

Fig. 4(a-d): Properties of AA on oxidation parameters (n = 10 mice/group), (a) Superoxide dismutase (SOD), (b) Catalase (CAT) (c) Glutathione peroxidase (GSH-Px) and (d) Malondialdehyde (MDA)

*p<0.05 and **p<0.01 versus control group

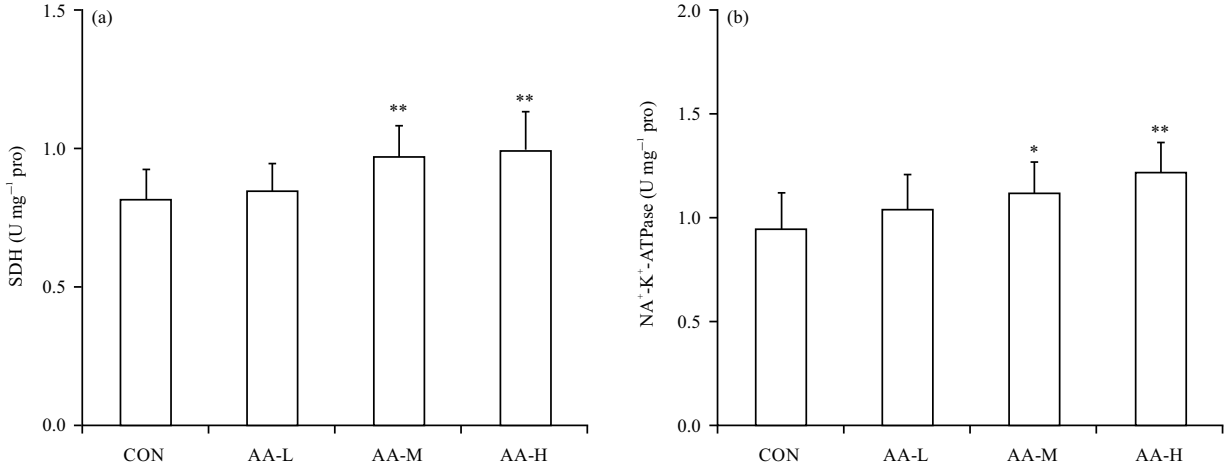

Fig. 5(a-b): Properties of AA on energy metabolism (n = 10 mice/group), (a) Saccharopine dehydrogenase (SDH) and (b) Na^+-K^+-ATPase

*p<0.05 and **p<0.01 versus control group

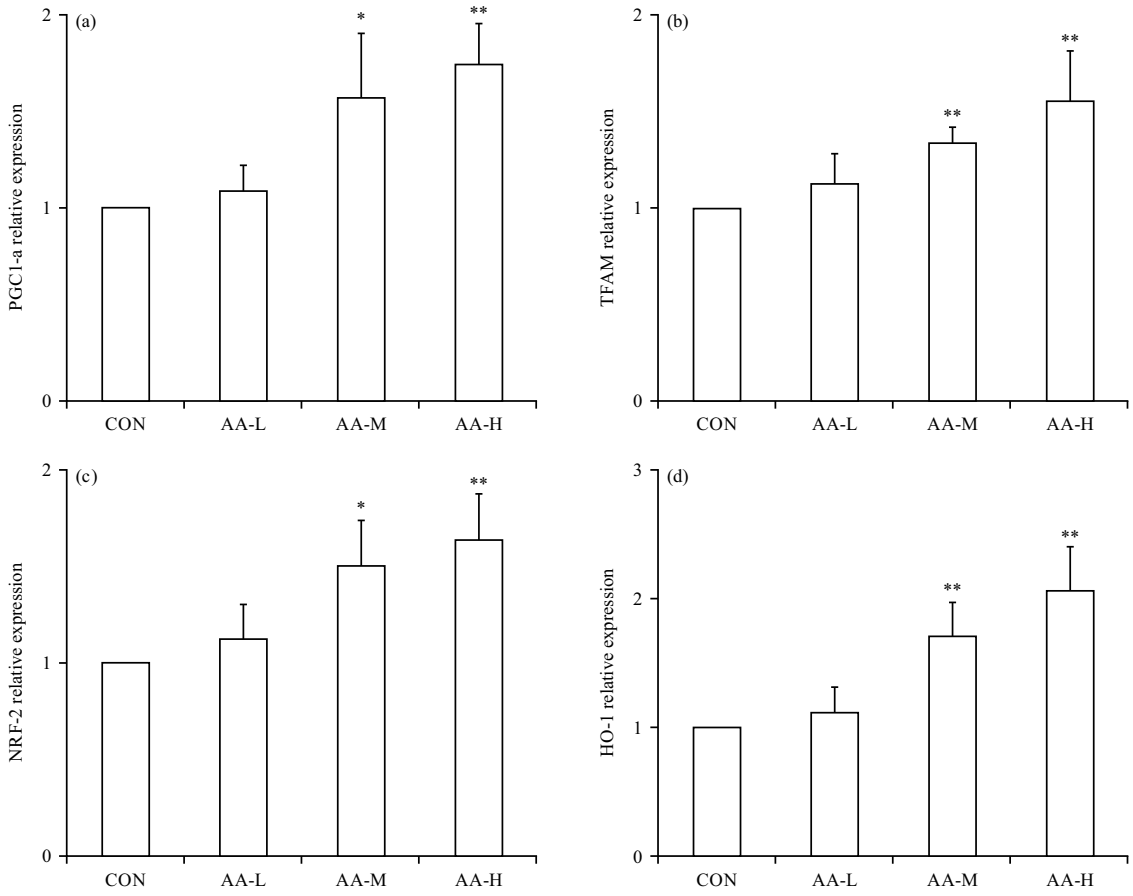

Fig. 6(a-d): Properties of AA on modulating PGC-1α, TFAM, NRF-2 and HO-1 in muscle (n = 3 mice/group), (a) Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), (b) Transcription factor A, mitochondrial (TFAM), (c) Nuclear factor (erythroid-derived 2)-like 2 (NRF-2) and (d) Heme oxygenase-1 (HO-1)
*p<0.05 and **p<0.01 versus control group

DISCUSSION

In this experiment, 1st monitored the roles of asiatic acid by forced swimming test which was approved as a well-founded animal model to assess anti-fatigue activity in present researches[14]. The indicator of exhausting time was used to manifest movement endurance and physical fatigue susceptibility. In weight-loaded forced swimming test, treatment with asiatic acid to mice over 28 days increased exhausted exercise time in dose-dependent relations. The middle and high dosages of asiatic acid concentration increased exercise capacity by 67 and 129%, respectively. These results indicated that asiatic acid was a safe and valid anti-fatigue agent.

BLA is an important indicator of fatigue. In high-intensity exercise, a large quantity of energy was generally formed via aerobic and anaerobic respiration to furnish tissues needs. In this case, lactic acid is mainly produced in skeletal muscles during the aerobic respiration process. What is more, an excess of BLA aggravates the degree of fatigue and propels fatigue development[15]. Extra lactic acid can further dissociate to manufacture hydrogen ions in the blood, which lowers pH level to affect internal environment homeostasis. More seriously, excess lactic acid derived from muscles, in turn, bring about suppression of muscle contraction and muscle damage[16,17]. Hence, bioaccumulation of BLA is a high correlation with fatigue. Moreover, treatment with asiatic acid ameliorated lactate concentration and glucose homeostasis to inhibit hyperlactatemia in malaria[18]. In this study, results demonstrated asiatic acid exerted the effect of alleviating BLA levels in high-intensity exercise.

CK and LDH, as cytosolic enzymes, principally consist in muscle tissue. CK and LDH are biomarkers of muscle injury. CK is a critical kinase and increased CK level was clinically associated with muscle-relevant diseases, such as muscular dystrophy, muscle contraction, muscle disruption, muscle

necrosis and myocardial infarction[19]. LDH is involved in eliminating BLA[20]. In a long period of train, excess and detrimental intermediate metabolites could result in myocyte damage. Then, CK and LDH are over-produced and permeate into serum[21]. Hence, excessive CK and LDH activity could play a critical role in decreasing exercise capacity and increasing the degree of movement endurance. What is more, asiatic acid was demonstrated to reduce CK vitalities and suppress apoptosis in MI/R injury[22]. In PC12 cells, asiatic acid relieved leakage and inhibit LD content in OGD/R injury[23]. In this study, results demonstrated asiatic acid ameliorated CK and LDH activities to attenuate muscle damage and physical fatigue in high-intensity exercise.

SUN is not only clinically applied to assess renal function, but also positively correlated with fatigue. SUN is a metabolite end-product that is generated in protein metabolism[24]. In strenuous exercise, energy generated from carbohydrates and fats cannot meet the requirement of the body. Then, protein as an energy substance is consumed in catabolic metabolism to supply energy. Generally, SUN is formed in the liver and excreted through the kidney. However, supernormal SUN increases the burden of renal function and a part of BUN is released into the blood. Therefore, the vitality of SUN plays a crucial role in the anti-fatigue effect. In addition, treatment with asiatic acid improved carbohydrate metabolic disorder and decreased urea level to protect renal function in diabetic rats[25]. In this study, asiatic acid was able to dramatically alleviate the bioaccumulation of SUN in high-intensity exercise, indicating that asiatic acid could strengthen movement endurance and exercise ability by reducing protein metabolism-provided energy.

AST and ALT in serum are authorized as important parameters to evaluate liver injury[26]. Under normal circumstances, the activities of AST and ALT are low. Once their activities are increased, which indicates liver injury is occurring or has occurred. Previous research proved that strenuous exercise is harmful to liver function[27,28]. Therefore, AST and ALT are biochemical parameters relevant to fatigue. In addition, asiatic acid was reported to improve liver damage by reducing the release of AST in ischemia/reperfusion rat[29]. In this study, asiatic acid notably mitigated AST and ALT activities in high-intensity exercise, indicating that the anti-fatigue effect of asiatic acid was associated with its protection on liver damage.

Strenuous exercise evokes uncoordinated activation of systemic cytokine balance. Inflammatory cytokines were unconventionally altered by heavy exertion, such as long-term endurance training, intense exercise and marathon[30]. As a secondary reaction, oxidative stress also triggers an inflammatory response in the living body[31]. What is more, the inflammatory reaction was involved in the pathophysiology of muscle damage[32]. In return, muscle injury with elevated inflammatory factors, such as TNF-α and IL-6, on physiological fatigue may induce muscle pain and efficacy deficits[33]. Hence, the inflammatory response may be a causative factor in physiological fatigue. Although physiology researchers have reported a potential connection between asiatic acid and inflammatory cytokines, little is known concerning the effect of asiatic acid on inflammatory reaction after high-intensity exercise. Therefore, inflammatory cytokines, including TNF-α and IL-6, were detected to assess the anti-fatigue properties of asiatic acid. In this study, results notarized that asiatic acid had anti-fatigue effects via suppression of inflammatory reaction.

Oxidation stress is now believed to participate in the progression of fatigue. In high-intensity exercise, the process of energy production is accompanied by large amounts of free radical, which is harmful for antioxidation and systemic redox balance. Generally, SOD, CAT and GSH-Px are vital antioxidants to exclude ROS, while MDA is a metabolite of lipid peroxidation to aggravate oxidative reaction. Previous studies have demonstrated inhibition of oxidative stress is an effective mean to enhance exercise performance and delay the degree of fatigue[34]. What is more, asiatic acid increased the activity of SOD and reduced the level of MDA to inhibit cardiac fibrosis in spontaneous hypertension rats[35]. In this study, asiatic acid observably prevented and reduced oxidative injury against fatigue by enhancing SOD, CAT and GSH-Px activities and lowering MDA content.

The mitochondrion is a crucial venue of ATP generation. ATP is regarded as direct energy in normal physiological performance, especially in high-intensity exercise[36]. Mitochondrial function is used as a vital indicator to evaluate physiological fatigue in high-intensity exercise[37]. In energy metabolism, various biological enzymes, such as SDH and Na^+-K^+-ATPase, play a regulatory role in anabolism and catabolism. SDH as a rate-limiting enzyme, participates in the TCA cycle to regulate ATP synthesis[38]. SDH can affect the electron transport chain in energy metabolism[39]. Na^+-K^+-ATPase as a degradation enzyme, performs its function via hydrolyzing ATP to replenish energy[40]. Under normal conditions, SDH and Na^+-K^+-ATPase are maintained in normal physiological standards. The previous result showed that small molecule oligopeptides as a potent anti-fatigue candidate, enhanced movement endurance and exercise capacity by increasing the activity of SDH and Na^+-K^+-ATPase[41]. What is more, Pre-treatments of asiatic acid might retain SDH and Na^+-K^+-ATPase activity in high-glucose-induced damage[42]. In

this study, asiatic acid markedly maintained SDH and Na^+-K^+-ATPase activity to improve energy metabolism and delay fatigue.

PGC-1α is known as a regulator to improve transcription in mitochondria[43]. PGC-1α is also vitally associated with energy metabolism to modulate muscle function. PGC-1α promotes mitochondrial biogenesis partly by regulating TFAM and NRF-2, which is closely associated with antioxidant capacity[44]. Previous results reported anwulignan enhanced muscle function to mitigate fatigue via enhancement expression of PGC-1α and NRF-2 in high-intensity exercise[45]. In addition, NRF-2 is an important transcription factor connected with protection against oxidative injury. NRF-2 controls antioxidant enzyme gene expression, such as HO-1, Cu, Zn-SOD and Gsr, to resistant body's oxidative response[46]. By enhancing NRF-2 expression, it exhibited cellular oxidation resistance function by augmenting SOD and GSH-Px activities and decreasing ROS and MDA contents, which was closely related to anti-fatigue[47]. In this study, asiatic acid-activated expression of PGC-1α, TFAM, NRF-2 and HO-1 in excessive exercise, which demonstrated that asiatic acid increased energy metabolism and restrained oxidative stress to protect against fatigue.

CONCLUSION

In summary, asiatic acid defended against exercise-induced fatigue in mice. The mechanism of asiatic acid on anti-fatigue efficacy is relevant to inhibition of inflammatory response, prevention of oxidative stress damage and improvement of energy metabolism. These researches affirm that asiatic acid has potential as a protection and therapy agent for exercise-induced fatigue.

SIGNIFICANCE STATEMENT

This experiment proved asiatic acid observably prolonged swimming exhaustive time. In high-intensity exercise, the fatigue relevant indicators, including CK, LDH, AST, ALT, SUN and BLA, were mitigated by treatment of asiatic acid. The anti-fatigue efficacy of asiatic acid is partly due to its effects on restraining inflammatory reaction, as represented by lower TNF-α and IL-6 levels in serum. Especially in muscle tissue, asiatic acid observably alleviated oxidative injury by enhancing SOD and CAT, GSH-Px activities and reducing MDA levels. In addition, asiatic acid remarkably ameliorated energy metabolism by increasing SDH and Na^+-K^+-ATPase activities. Lastly, asiatic acid significantly activated PGC-1α, TFAM, NRF-2 and HO-1 expression in excessive exercise. In all, results showed asiatic acid possessed anti-fatigue efficacy through regulating inflammatory reaction, oxidative stress and energy metabolism in mice. Asiatic acid can be developed as a beneficial agent to postpone fatigue.

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