Journal of Physical Education and Sport ® (JPES),Vol 21 (Suppl. issue 4), Art 329 pp 2447 – 2452, Aug. 2021
online ISSN: 2247 - 806X; p-ISSN: 2247 – 8051; ISSN - L = 2247 - 8051 © JPES

Original Article

The preventive role of Raja banana peel (*Mussa paradisiaca sapientum*) extract as exogenous antioxidant in reducing atherosclerosis risk after exercise intervention

RIAS GESANG KINANTI[1], RAMDAN PELANA[2], MOCH. YUNUS[3], AHMAD ABDULLAH[4], ANDRE ANDARIANTO[5], SRI AGUNG FITRI KUSUMA[6], LILIANA PUSPA SARI[7], ABDURRAHMAN ABDURRAHMAN[8], YAYA RUKAYADI[9]
[1,3,4,5,]Departement of Sport Sciences, State University of Malang, INDONESIA
[2]Departement of Sport Sciences, State University of Jakarta, INDONESIA
[6]Department of Biology Pharmacy, Padjadjaran University, INDONESIA
[7]*Bina Guna Sports and Health College,* INDONESIA
[8]Departement of Physical Education Health and Recreation, Syiah Kuala University, INDONESIA
[9]Department of Food Science, Universiti Putra Malaysia, MALAYSIA

Published online: August 31, 2021
(Accepted for publication August 15, 2021)
DOI:10.7752/jpes.2021.s4329

Abstract:
Excessive exercise training can act as a trigger in the increase of free radicals, inducing oxidative damage which generate to the development of atherosclerotic plaques. Therefore, the need of exogenous antioxidants become essential to be supplemented before exercise to reduce the negative effect of ROS. It can be sourced from methanolic extract of Raja banana peel (*Musa paradisiaca sapientum*) that has been investigated in vitro for its ability to produce antioxidant defense systems. Therefore, this study was purposed to investigate the preventive role of Raja banana peel methanol extract administration in reducing the risk of atherosclerosis after exercise training with moderate and high-intensity by observing the aorta histopathology of *Rattus norvegicus* Wistar strain rats. In this study, a total of 28 male white rats were grouped and treated in different exercise intervention level: moderate and high-intensity during 60 h and administered with the extract in the same dose of 400 mg/kg, except the control group. The histopathology of aorta rats was observed using hematoxylin and eosin (HE) staining. The data were statistically interpreted with the Mann-Whitney analysis ($p < 0.05$). Our finding showed that aortic damage (100%) followed by the release of macrophages (85.71%) and intracellular lipid (71.42%) were higher obtained from the group with high-intensity exercise activity than the moderate. Statistically, this damage can be significantly reduced in the group with high exercise intensity after treating with banana peel extract (0,0142 or $p < 0,05$). The same effect of the extract also found in the group with moderate-intensity exercise, the percentage of aortic damage was lower than that of control group. Thus, it can be concluded that the methanolic extract of Raja banana peel can be promoted to be an effective exogenous antioxidant to prevent oxidation stress condition after exercise intervention.
Keywords: Raja, **Mussa paradisiaca sapientum, peel, aorta, intensity, atherosclerosis**

Introduction

Atherosclerosis is a vascular disease with morbidity risk, representing ± 31% of total deaths annually, and 44% of them are caused by atherosclerotic coronary heart disease (Herrington et al., 2016; Aengevaeren & Eijsvogels, 2020; Tabas et al., 2015). The occurrence of endothelial dysfunction in associated with the imbalance of Reactive Oxygen Species (ROS) level can be predicted as atherosclerosis conditions. The endothelium changes are caused by disturbed shear stresses that occur in the aorta, carotid, and coronary arteries (Marchio et al., 2019a; Libby & Hansson, 2015). The shear stress can activate endothelium and platelets, then attracting monocyte adhesion to the endothelium, and triggering the monocyte differentiation to develop foam cells, which responsible for exacerbates inflammatory signals to induce atherosclerotic plaques development (Chistiakov et al., 2015; Libby, 2012; Chistiakov et al., 2017; Marchio et al., 2019; Kumar et al., 2020). Endothelial cell damage related to decreased nitric oxide (NO) availability, either due to the absence of NO production or biological activity of NO. This condition is reported due to oxidative stress, marked by the rising of ROS production (Khosravi et al., 2019; Marchio et al., 2019; Powers et al., 2020).

In fact, exercise training is a proven treatment to minimize the potential of cardiovascular disease (Eijsvogels et al., 2016). Several findings have shown that exercise can increase nitric oxide synthase (eNOS) expression to elevate NO availability by regulating the vasodilator and producing the endogenous anti-oxidants (Phillips et al., 2015). Bayram et al. 2016, have also observed that the aerobic exercise enhances the capability to adapt the oxidative stress condition. However, the dose of exercise and the mechanisms underlying

Corresponding Author: RIAS GESANG KINANTI, E-mail: rias.gesang.fik@um.ac.id

cardiometabolic risk have not been well identified. Multiple recent studies have reported that the prevalence potential of coronary atherosclerosis was more serious in athletes with higher-intensity exercise (Möhlenkamp et al., 2008; Aengevaeren et al., 2020a; Merghani et al., 2017). Doing exercise in high volume and intensity can decrease vascular function (Sapp & Hagberg, 2018). Excessive exercise activity can produce excess ROS, so that the antioxidant defenses in the body will be reduced, and triggering oxidative stress (Harun et al., 2017). When oxygen consumption increases during exercise, there is a redox imbalance and increased superoxide release, which in turn results in damage to structure of mitochondria and other cells. This damage may inhibit the cells adaptation against homeostatic demands, especially during high-intensity exercise (Hostrup & Bangsbo, 2017). During exercise, ROS as a by-product is unavoidable due to increased oxidative metabolism, and their production is continuous with a greater amount of antioxidant capacity. ROS production and the clearance should be balance to optimize the cellular function (Powers et al., 2011). Antioxidants are compounds that donate electrons and reductants, which function to neutralize the free radicals. Therefore, risk factors control in exercise training is an important way to prevent major effects associated with atherosclerosis.

Targeted antioxidant administration is an approach to deal with the harmful effects of ROS during exercise. Therefore, supplements containing exogenous antioxidants should be given to athletes or physically active individuals (Finaud et al., 2006). Exogenous antioxidants can be obtained through foodstuffs, bananas are one of them. It has been studied that Raja banana peels have a fairly high nutritional content, even better than the fruit (Yani, 2017). Raja banana peel extract is a source of natural antioxidants with a fairly high flavonoid content and is easily found in abundance in Indonesia (Irtanto et al., 2017). It has been proven in vitro that administration of this banana peel methanol extract can increase superoxide dismutase (SOD) activity after high-intensity exercise (Rahmawati, 2020). Role of SOD in cardiovascular disease is indispensable for regulating vascular ROS levels, mainly superoxide anion. Nitric oxide (NO) must be able to react with superoxide anions at a very fast rate. Thus, the balance between the ambient superoxide anion levels and cellular antioxidant capacity, mostly superoxide dismutase (SOD) is important in regulating nitric oxide bioactivity (Fukai et al., 2002). However, the improve effect of the Raja Banana peel extract on the endothelial damage resulted due to the high intensity exercise, has not been reported. This is an important data to support the defense system of this extract to be a potential exogenous antioxidant because the change of endothelium is related to the increasing of free radical availability as the causative agent of oxidative stress. Therefore, the protective effect of this peel extract in reducing the risk of atherosclerosis caused by inappropriate exercise intensity was investigated.

Materials & methods

Participants

In total, 28 male rats were used with the following specifications: *Rattus norvegicus* strain Wistar, aged of 10-12 w, body weight of 125-150 g, active movement, white fur, not dull, not physically disabled, and authenticated by a health certificate. All rats were adapted for 7 d, fed with BR1-511B type of feed, and received drink at a control rate of 80 mL/d.

Procedures

The fresh and ripe banana peel (1 Kg) was powdered using a blender and then macerated using methanol (2 L) for 4 d at room temperature. The macerated solution was filtered and evaporated using a rotary evaporator at a temperature of 70°C until the thick extract was obtained.

This study was performed with a Randomized Control Group Posttest-Only Design. The protocol study design has approved for animal research with ethic code: 302/EC/KEPK/S1/11/2019. A total of 28 rats were grouped into four treatment groups: X1, X2, Y1, and Y2. The extract with a dose of 400 mg/Kg x 0.2 Kg was dissolved using distilled water, up to 1 ml and administered orally 1 h before the rats undertaken the treadmill activity. Group X1 (control) were trained with moderate intensity exercise by running on treadmills (14-16 m/min; 65-70% VO_2max) in duration of 540-1260 s; X2 (treatment) was treated the same as group X1 and received the extract at a dose of 400 mg/kg x 0.2 kg; Y1 (control) were trained with high-intensity exercise by running on treadmills (22-25 m/min; >80% VO_2max) in duration of 360-720 s, and Y2 (treatment) was treated the same as group Y1 and received the extract at a dose of 400 mg/kg x 0.2 kg. Exercises were carried out in 3 sets or sessions with a ratio of 2:3 and the load were added every 4 d. The treatment was undertaken every day for 60 d. The rats were anesthetized with ketamine (15-20 mg/Kg), injected intraperitonially after resting for 24 h from the last treatment. The rats were dissected to acquire the aorta, then the aorta was cleaned using phosphate buffer saline and drained. After that, it was fixed in formalin solution for 48 h to maintain the tissue structure and stained with hemotoxin and eosin (HE). The observation of histopathological images of the aorta was performed using a dot slide with 400x magnification, connected to an LCD screen. These observations include several parameters of the oxidative stress occurrence, as follows: intactness, surface defects, the presence of macrophages and foam cells.

Data collection and analysis/Statistical analysis

The histopathology condition of the aorta was observed using a scoring method, as described in Table 1. The data were statistically interpreted with the Mann-Whitney analysis ($p < 0.05$).

Table 1. Assessment of Atherosclerotic Lesions

Parameters	Score
Intactness	0
Defects of the lesion surface	1
Macrophages presence	2
Foam cells presence	3
Smooth muscle intracellular lipid accumulation	4
Little extracellular smooth muscle lipid	5
Lots of extracellular smooth muscle lipids	6
Lipid core and fibrosis layer	7
Hematoma, thrombus	8

Results

Our results demonstrated that higher level of intensity exercise improved the atherosclerosis characteristic, can be seen in Figure 1. All moderate-intensity exercise for 60 d in male Wistar strain rats fed with standard diet (Group X) showed an intact histopathological profile of the aorta in four samples (57.14%) and three samples (42.85%) showed defects on the intima surface, indicated by the presence of macrophages. However, all samples did not develop any foam cells and accumulation of intracellular lipids, extracellular lipids, and calcifications. For the aortic histopathology of group X1, found that five samples (71.42%) showed an intact aorta, and only two samples (28.57%) showed a defect on the intima surface with the presence of macrophages (14.28%). However, all samples did not show the presence of foam cells, accumulation of intracellular and extracellular lipids, and calcification. As expected, the total aortic damage (100%) found in all samples with high-intensity (Group Y), with no exception for the group treated by the banana peel extract (Group Y1). However, the presence of foam cells, extracellular lipid accumulation, and calcification has not been found yet. But in group Y1, the banana peel extracts capable to reduce the percentage of macrophage presence, from 85.71% to 42.85% and decreasing intracellular lipid accumulation from 71.42% to 14.28%. The damage of aorta in all groups can be clearly differentiated from Figure 2.

Statistically, the scores of histopathology condition of those aorta demonstrated that: a) there was no significant difference in the aortic histopathological picture of the test rats in groups X and X1 with a significance value of 0.6526 or $p > 0.05$ b) The banana peel extract showed difference effect on the histopathological picture of male rats after high-intensity exercise with a significant value 0.0142 or $p < 0.05$ c) The banana peel extract showed difference effect on the aorta histopathological profile of male rats after exercise with moderate-intensity compared to the high-intensity with a significance value of 0.0115 or $p < 0.01$. Therefore, there was a significant difference in the administration of Raja banana peel extract on the histopathological profile of male rats' aorta after moderate-intensity exercise compared to high-intensity.

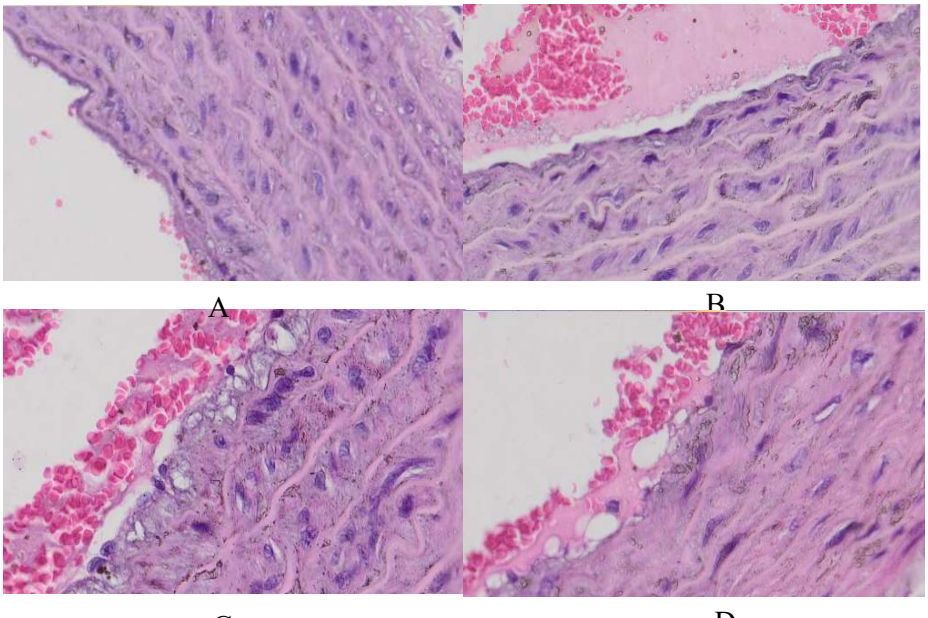

Fig. 1 Mouse aortic histopathology, cross section with HE staining, 400x magnification. (A) Control group with moderate-intensity exercise, Group X (B) group with moderate-intensity exercise and fed with the banana peel extract, Group X1 (C) Control group with high-intensity exercise, Group Y (D) group with high-intensity exercise and fed with the banana peel extract, Group Y1.

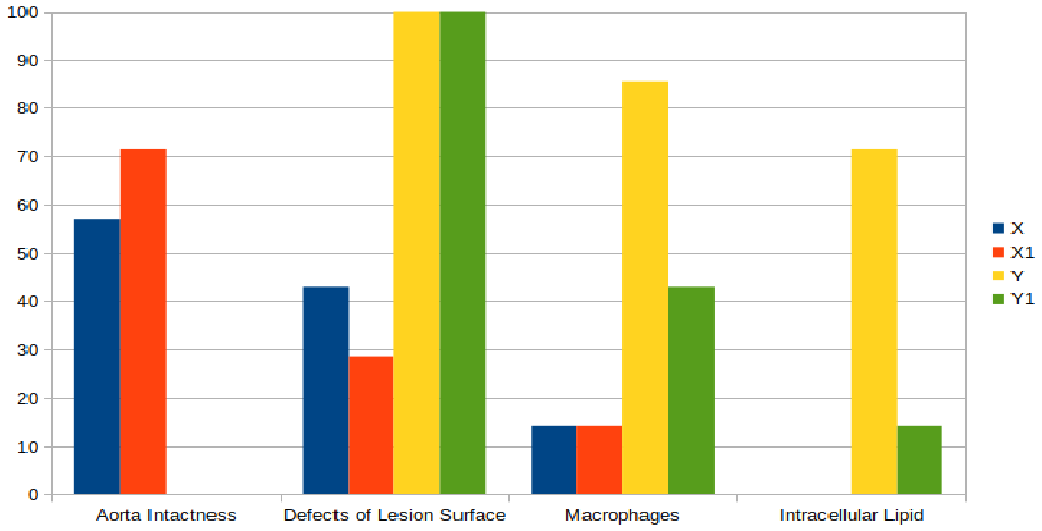

Fig. 2 The damage of aortic rat

Discussion

Several studies reported the potential advantages of exercise to treat several diseases or reduce the symptoms (Castrogiovann et al., 2019; Lavie et al., 2015; Sturgeon et al., 2014; Atkinson et al., 2016; Syahruddin et al., 2016). However, duration and intensity of the exercise showed different impacts. In particular, long-term exercise (6 w or more) can be the most effective means of treating diseases related to the cardiovascular systems. Meanwhile, short-term training (less than 6 w) may also be chosen to treat psychological disorders. However, exercise with different intensities was reported to provide an inverted phenotype. During high-intensity exercise, oxygen demand is much higher than at rest, due to the need of ATP production. Oxygen consumed 0.4%-4% will be released in the mitochondria as ROS (Sapp & Hagberg, 2018). Therefore, proper sports training protocols must be known properly to avoid unexpected results (Wang et al., 2020; Liu et al., 2013; Brusco et al., 2018; Pelana et al., 2019). In this study, the type of exercise used was treadmill training because the intensity of the exercise could be regulated by speed adjustment. So, when the rats unenthusiastic to do the movement, researchers can gently thrust their backs or giving shocked treatment using a low-level electric (Wang et al., 2020).

Exercise as a physiological stimulus can trigger the increasing of free radical production and disrupt the redox balance that supports oxidants, thereby triggering oxidative stress. Disruption of this redox balance can cause disturbances in signaling and redox control as well as molecular damage (Kawamura & Muraoka, 2018). ROS damage cells by disrupting lipid membranes through a series of lipid peroxidation reactions, causing increased membrane permeability, and impaired mitochondrial function (Kerksick & Zuhl, 2014). Targeted antioxidant administration is an approach to deal with the harmful effects of ROS during exercise. Antioxidant supplementation can support to neutralize the increased production of free radicals. This kind of banana peel methanol extract contains antioxidant flavonoids, which responsible in the inhibition of pro-oxidant enzymes or the complex formation with pro-oxidant ions such as Fe or Cu. Moreover, flavonoids provide straight effect on ROS as hydrogen atom donors. Although there is sufficient evidence of the antioxidant effects of banana peel extract in vitro, studies of their effects in vivo are lacking. However, several studies have confirmed the antioxidant activity of flavonoids in vivo (Battault et al., 2016).

From this study, we found that the administration of the extract after moderate-intensity exercise did not show any statistically significant difference in the histopathological characteristic of the aorta against the control. The X1 group with moderate intensity and given the extract showed defects on the intima surface for 28.57%, lower than that of control group. This study was consistent with our previous study, the banana peel extract reduced the malondialdehyde (MDA) levels after moderate-intensity exercise (Andarianto, 2020). So far, MDA levels can be used as a biochemical marker to diagnose atherosclerosis (Viigimaa et al., 2010). This indicates that the underlying mechanism of endothelial damage associated with exercise intensity is related to the increasing free radicals availability as the causative agent of oxidative stress. The higher level of oxidative stress is influenced by the impaired endothelial function (Marchio et al., 2019b). While the repair of surface defects after administration of antioxidants is due to several mechanisms, possibly because the capability of Circulating angiogenic cells (CACs) to repair the endothelium (Sapp et al., 2019). Beside that, endothelial progenitor cells (EPC), as a subpart of vasculogenic progenitors also give contribution in maintaining the integrity of endothelium. The EPC are responsive to exercise, and has important mechanism in the blood vessels repair and maintenance through their mobilization. Local tissue hypoxia during exercise, can increase EPC mobilization

(Montgomery et al., 2019). Improvements also occur because the beneficial effects of exercise to inhibit the atherosclerosis progression. It was reported that in Apo-E-deficient rat, the control rats produced larger plaque sizes than the trained rat after 8-16 w of exercise. In another study, it was found that development of coronary lesions was found in patients who released more than 2,200 cal/ week, equivalent to 5-6 h of exercise per week (Chacon & Fiani, 2020).

From this study, the administration of banana peel methanol extract after high-intensity exercise can improve atherosclerotic lesion scores. The same result also correlated with the study by (Rahmawati et al., 2020), giving methanol extract after high-intensity exercise can increase levels of SOD. The increase in SOD after administration of methanol extract is beneficial for reducing oxidative stress after high-intensity exercise. Nevertheless, both intensity exercise level did not lead the formation of foam cells, even intracellular lipid accumulation was found after high-intensity exercise. This indicates that the ROS produced during exercise can be reduced by administration of Raja banana peel extract so that the foam cells that may be produced have been degraded so that they do not accumulate in macrophages, which can worsen the inflammation (Chistiakov et al., 2017). In spite of, the flavonoid content of Raja banana peel as exogenous antioxidants was not sufficient to completely neutralize free radicals both after moderate and high-intensity exercise, however, the extract exhibited play an important function as protective agent in retarding disease progression and reduced mortality due to the disease.

Conclusion

It can be summarized that the administration of Raja banana peel methanol extract can improve significantly the atherosclerotic lesion scores after high-intensity exercise. Thus, this extract can be prospected to be a potential exogenous antioxidant agent that can protect endothelium cells after moderate and high-exercise intervention by preventing the oxidative stress condition.

Conflicts of interest

There was no conflict of interest.

References

Aengevaeren, V. L., & Eijsvogels, T. M. H. (2020). Coronary atherosclerosis in middle-aged athletes: Current insights, burning questions, and future perspectives. *Clin Cardiol*, *43*(8), 863–871.

Andarianto, A. (2020). Effect of extra plantain peel (*Musa paradisiaca sapientum*) on levels of Malondialdehyde (MDA) in male rats (*Rattus norvegicus* wistar) after moderate and high intensity exercise. Thesis, Malang State University.

Atkinson, C.L., Lewis, N.C., Carter, H.H., Thijssen, D.H., Ainslie, P.N., & Green, D.J. (2016). Impact of sympathetic nervous system activity on post-exercise flow-mediated dilatation in humans. *J Physiol, 593*(23), 5145–5156.

Battault, S., Singh, F., Gayrard, S., Zoll, J., Reboul, C., & Meyer, G. (2016). Endothelial function does not improve with high-intensity continuous exercise training in SHR: implications of eNOS uncoupling. *Hypertens Res*, *39*(2), 70–78.

Bayram, M., Şam, C.T., & Demđrel, N. (2016). Effects on the antioxidant immune system of intensive training period of female athletes and female ski runners. *J Phys Educ Sport, 16(1)*, 200 – 205.

Brusco, C.M., Blazevich, A.J., Radaelli, R., Botton, C.E., Cadore, E.L., Baroni, B.M., et al. (2018). The effects of flexibility training on exercise-induced muscle damage in young men with limited hamstrings flexibility. *Scand J Med Sci Sports, 28*(6), 1671–1680.

Chacon, D., & Fiani, B. (2020). A Review of mechanisms on the beneficial effect of exercise on atherosclerosis. *Cureus*, *12*(11), 1-6.

Castrogiovanni, P., Di Rosa, M., Ravalli, S., Castorina, A., Guglielmino, C., Imbesi, R., et al. (2019). Moderate physical activity as a prevention method for knee osteoarthritis and the role of synoviocytes as biological key. *Int J Mol Sci, 20*(511), 1-18.

Chistiakov, D. A., Bobryshev, Y. V., Nikiforov, N. G., Elizova, N. V., Sobenin, I. A. & Orekhov, A. N. (2015). Macrophage phenotypic plasticity in atherosclerosis: the associated features and the peculiarities of the expression of inflammatory genes. *Int J Cardiol, 184*, 436–445.

Chistiakov, D. A., Melnichenko, A. A., Myasoedova, V. A., Grechko, A. V., & Orekhov, A. N. (2017). Mechanisms of foam cell formation in atherosclerosis. *J Mol Med, 95*(11), 1153–1165.

Eijsvogels, T.M., Molossi, S., Lee, D.C., Emery, M.S., & Thompson, P.D. (2016). Exercise at the extremes: the amount of exercise to reduce cardiovascular events. *J Am Coll Cardiol, 67*(3):316–329.

Finaud, J., Lac, G., & Filaire, E. (2006). Oxidative stress: Relationship with exercise and training. *Sports Med*, *36*(4), 327–358.

Fukai, T., Folz, R. J., Landmesser, U., & Harrison, D.G. (2002) Extracellular superoxide dismutase and cardiovascular disease. *Cardiovasc Res, 55*(2), 239–249.

Harun, I., Susanto, H., & Rosidi, A. (2017). Giving tempeh reduced malondialdehyde (MDA) levels and increased the activity of the superoxide dismutase (SOD) enzyme in rats with high physical activity. *Jurnal Gizi Dan Pangan*, *12*(3), 211–216.

Herrington, W., Lacey, B., Sherliker, P., Armitage, J., & Lewington, S. (2016). Epidemiology of Atherosclerosis and the Potential to Reduce the Global Burden of Atherothrombotic Disease. *Circ Res*, *118*(4), 535–546.

Hostrup, M., & Bangsbo, J. (2017). Limitations in intense exercise performance of athletes - effect of speed endurance training on ion handling and fatigue development. *J physiol*, *595*(9), 2897–2913.

Irtanto, O., Pangkahila, A., & Aman, I. (2017). Administration of plantain floret extract (*Musa x paradisiaca*) prevents decrease in superoxide dismutase (sod) levels in the liver of BALB/c Mice (*Mus musculus*) with excessive physical activity. *Jurnal Biomedik, 9*(3), 166-171.

Kawamura, T., & Muraoka, I. (2018). Exercise-induced oxidative stress and the effects of antioxidant intake from a physiological viewpoint. *Antioxidants, 7*(9), 1-19.

Kerksick, C. M., & Zuhl, M. (2014). Mechanisms of oxidative damage and their impact on contracting muscle. In *Antioxidants in Sport Nutrition.* Oca Raton (FL): CRC Press/Taylor & Francis, 1–16.

Khosravi, M., Poursaleh, A., Ghasempour, G., Farhad, S., & Najafi, M. (2019). The effects of oxidative stress on the development of atherosclerosis. *Biol Chem*, 400, 711–732.

Kumar, A., Gupta, P., Rana, M., Chandra, T., Dikshit, M., & Barthwal, M.K. (2020). Role of pyruvate kinase M2 in oxidized LDL-induced macrophage foam cell formation and inflammation. *J Lipid Res, 61*(3), 351

Lavie CJ, Arena R, Swift DL, Johannsen NM, Sui X, Lee DC, et al. (2015). Exercise and the cardiovascular system: clinical science and cardiovascular outcomes. *Circ Res, 117*(2), 207–219.

Libby, P., & Hansson, G. K. (2015). Inflammation and immunity in diseases of the arterial tree: Players and layers. *Circ Res*, *116*(2), 307–311.

Libby, P. (2012). Inflammation in atherosclerosis. *Arterioscler Thromb Vasc Biol, 32*(9), 2045– 2051.

Liu, W.Y., He, W., & Li, H. (2013). Exhaustive training increases uncoupling protein 2 expression and decreases Bcl-2/Bax ratio in rat skeletal muscle. *Oxid Med Cell Longev, 2013*, 1-7.

Marchio, P., Guerra-Ojeda, S., Vila, J. M., Aldasoro, M., Victor, V. M., & Mauricio, M. D. (2019). Targeting early atherosclerosis: A focus on oxidative stress and inflammation. *Oxid Med Cell Longev*, 2019, 1-32.

Merghani, A., Maestrini, V., Rosmini, S., Cox, A.T., Dhutia, H., Bastiaenan, R., et al. (2017). Prevalence of subclinical coronary artery disease in masters endurance athletes with a low atherosclerotic risk profile. *Circ, 136*(2), 126–137.

Möhlenkamp, S., Lehmann, N., Breuckmann, F., Bröcker-Preuss, M., Nassenstein, K., Halle, M., et al. (2008). Marathon study investigators; heinz nixdorf recall study investigators. running: the risk of coronary events: prevalence and prognostic relevance of coronary atherosclerosis in marathon runners. *Eur Heart J, 29*(15), 1903–1910.

Montgomery, R., Paterson, A., Williamson, C., Florida-James, G., & Ross, M. D. (2019). Blood flow restriction exercise attenuates the exercise-induced endothelial progenitor cell response in healthy, young men. *Front Physiol*, *10*(447), 1-7.

Pelana, R., Maulana, A., Winata, B., Widiastuti, W., Sukur, A., Kuswahyudi, K., et al. (2019). Effect of contrast water therapy on blood lactate concentration after high-intensity interval training in elite futsal players. *Physiother Q, 27*(3), 12-19.

Phillips, S. A., Mahmoud, A. M., Brown, M. D., & Haus, J. M. (2015). Exercise interventions and peripheral arterial function: Implications for cardio-metabolic disease. *Prog Cardiovasc Dis*, *57*(5), 521–534.

Powers, S.K., Talbert, E.E., & Adhihetty, P.J. (2011). Reactive oxygen and nitrogen species as intracellular signals in skeletal muscle. *J Physiol, 589*(9), 2129-2138.

Powers, S. K., Deminice, R., Ozdemir, M., Yoshihara, T., Bomkamp, M. P., & Hyatt, H. (2020). Exercise-induced oxidative stress: Friend or foe? *J Sport Health Sci*, *9*(5), 415–425.

Rahmawati, A. (2020). Effect of giving methanol extract of plantain peel (*Musa paradisiaca sapientum*) on SOD (Superoxide Dismutase) activity in wistar rats (*Rattus norvegicus*) after high-intensity exercise. Thesis, Malang State University.

Sapp, R. M., Evans, W. S., Eagan, L. E., Chesney, C. A., Zietowski, E. M., Prior, S. J., et al. (2019). The effects of moderate and high-intensity exercise on circulating markers of endothelial integrity and activation in young, healthy men. *J Appl Physiol*, *127*(5), 1245–1256.

Sapp, R. M., & Hagberg, J. M. (2018). CrossTalk opposing view: Acute exercise does not elicit damage to the endothelial layer of systemic blood vessels in healthy individuals. *J Physiol*, *596*(4), 541–544.

Sturgeon, K.M., Ky, B., Libonati, J.R., & Schmitz, K.H. (2014). The effects of exercise on cardiovascular outcomes before, during, and after treatment for breast cancer. *Breast Cancer Res Treat, 143*(2), 219–226.

Syahruddin, S., Safei, I., Lungit, L., Pelana, R., & Winata, B. (2019). **Infrared Sensor Technology (IST) Test as a Tool for Assessment of Flexibility.** *Adv Rehab/Postępy Rehabilitacji*, *3,* 5–9.

Tabas, I., García-Cardeña, G., & Owens, G. K. (2015). Recent insights into the cellular biology of atherosclerosis. *J Cell Biol*, *209*(1), 13–22.

Viigimaa, M., Abina, J., Zemtsovskaya, G., Tikhaze, A., Konovalova G, Kumskova E, et al. (2010). Malondialdehyde-modified low-density lipoproteins as biomarker for atherosclerosis. *Blood Press, 19*(3),

Wang, R., Tian, H., Guo, D., Tian, Q., Yao, T., & Kong, X. (2020). Impacts of exercise intervention on various diseases in rats. *J Sport Health Sci, 9*(3), 211-227.

Yani, R. (2017). Utilization of banana peel *(Musa textilia)*. Thesis, University of Northern Sumatra.