Journal of Health, Sports, and Kinesiology, 2021, 2(4), 4-9. https://doi.org/10.47544/johsk.2021.2.4.4

ORIGINAL RESEARCH

Acute Response of Blood Lipids and Lipoproteins to Different Intensities of Exercise in Obese Males

Jinkyung Park¹ & Yunsuk Koh²

¹Department of Exercise Science, Georgia College & State University, Milledgeville, GA, USA ²Department of Health, Human Performance, and Recreation, Baylor University, Waco, TX, USA

> Received 25 August 2021 | Revised 27 November 2021 | Accepted 19 December 2021 **Open Access** Available online at www.johsk.com



ABSTRACT

This study aimed to examine the response of lipid and lipoprotein levels following different intensities of exercise in obese males. Fifteen obese (body mass index > 30 kg/m²), sedentary (less than 2 days per week of physical activity) males, aged 18–30 years, participated in this randomized, cross-over study. The participants performed a single bout of cycling exercise (average energy expenditure: ~300 kcal) at two different intensities [lower-intensity: 50% of maximal heart rate and higher-intensity: 80% of maximal heart rate] in a random order. Overnight fasting blood samples were collected at baseline, immediately post-exercise (IPE), 1-hr PE, and 24-hr PE for each intensity of exercise to determine the profile of blood lipids and lipoproteins [total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C)]. A 2(intensity) × 4(time) analysis of variance with repeated measures was used to examine the main and interaction differences in intensity and time on the profile of blood lipids and lipoproteins. The blood lipids and lipoproteins were not significantly altered following either lower or higher intensity exercise. There was no significant interaction between intensity and time. The results suggest that regardless of exercise intensity, an acute bout of aerobic exercise requiring 300 kcal energy expenditure may not be enough to significantly alter blood lipids and lipoproteins in physically healthy obese males. Therefore, it is recommended that future research determine whether different intensities of chronic exercise requiring the same or higher volume of energy expenditure can positively alter the blood lipid in profiles in obese males.

Keywords: Obesity, Exercise Intensity, Lipid, Cholesterol

INTRODUCTION

With the increasing prevalence of obesity in our society, a consistent correlation between obesity and the likelihood of metabolic or cardiovascular disease has become evident (Hruby & Hu, 2015). Cardiovascular disease in particular can include high blood pressure, heart attack, stroke, heart failure, or arrhythmia. These conditions can be a byproduct of atherosclerosis—a build-up of plaque in the arteries—or blood clots in the heart or brain (Hansson, 2005; Libby, 2002). Meyers and Gokce (2007) state that increased level of body fat, as compared to the healthy recommendation, can contribute to heart disease via atrial enlargement, ventricular enlargement, and atherosclerosis (Meyers & Gokce, 2007). Given the dangers of heart disease and other conditions in an increasing obese population, combating obesity is crucial before it directly or indirectly leads to heart disease. A simple but extremely effective method to manage increased fat mass is exercise, specifically cardiovascular and metabolic conditioning (Fiuza-Luces et al., 2018). From years of study and abundant research to support this claim, it is known that physical exercise decreases blood pressure and body weight, while increasing high-density lipoprotein cholesterol (HDL-C) activity (Fiuza-Luces et al., 2018). In addition to these benefits, aerobic exercise improves circulation, while decreasing the lipid (Wang & Xu, 2017) and improving lipid profile (Nystoriak & Bhatnagar, 2018). The lipid profile test can determine the risk of plaque buildup in arteries to effectively manage diseases such as coronary artery disease. These lipid profile tests assess total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) (Goldberg et al., 2011).

Journal of Health, Sports, & Kinesiology

ISSN 2692-9864 (online)

ISSN 2767-5874 (print)

Previous studies on the effectiveness of high-, moderate-, and low-intensity exercise on lipid levels have reported significantly variable results (Albarrati et al., 2018; Kraus et al., 2002; Yoshida et al., 2010). Kraus et al. found that high-intensity/high-volume aerobic training seemed to elicit a statistically significant change in the LDL-C and HDL-C of the sedentary overweight participants (Kraus et al., 2002). However, Yoshida et al. suggested that the moderate-intensity aerobic exercise has a significant effect on LDL levels in subjects with dyslipidemia (Yoshida et al., 2010). Although moderate-intensity exercise may improve lipid profiles, recent evidence claims that the effects of low- and moderate-intensity aerobic exercise training on LDL levels are controversial (Albarrati et al., 2018). A main limitation of previous studies is that the previous studies (Kraus et al., 2002; Yoshida et al., 2002; Yoshida et al., 2010) did not address the diet record of the participants during the study period. This is a major factor that can significantly skew the research findings if not accounted for.

Although previous studies primarily assessed the effects of exercise training on lipid profiles, these studies did not address the role of exercise intensity in the altering of lipids and lipoproteins. In this study, we sought to better describe the influence of a single bout of exercise at different intensities on blood lipids and lipoproteins. The purpose of this study was to examine the blood lipid and lipoprotein profile changes following acute lower and higher intensity exercises in sedentary college-aged obese males.

METHODS

Participants

The study recruitment yielded 15 sedentary obese males as participants (body mass index >30 kg/m², body fat percentage >25%). Participants were aged between 18 and 30 years and were physically inactive for at least 6 months prior to testing. Participants were considered physically inactive if they exercised less than twice a week. None of the participants were above the low risk of cardiovascular disease and no participant had any contraindication to exercise, as outlined by the American College of Sports Medicine exercise preparticipation health screening guidelines (Riebe et al., 2015). The study was reviewed and approved by the University Institutional Review Board for human subjects (IRB Reference No. 669721), and all subjects signed informed consent documents prior to testing. The anthropometric and body composition data of the participants are shown in Table 1.

Table 1. Anthropometric and Body Composition Data at Baseline

Variable	M ± SE
Age (years)	$21.73 \pm .47$
Height (cm)	177.09 ± 2.27
Body weight (kg)	107.88 ± 4.83
Body fat (%)	31.56 ± 1.17
Lean mass (kg)	64.62 ± 2.37
Fat mass (kg)	31.77 ± 2.50

Note: M = mean; SE = standard error; cm = centimeters; kg = kilograms; % = percent

Maximal Heart Rate Test Protocol

The maximal heart rate (HRmax) test was conducted using a Monark cycle ergometer (Medgraphics, Monark, Ergomedic, Model No. 828E, St Paul, MN, USA) based on the protocol developed by Keytel et al. (Keytel et al., 2005) to estimate each participant's HRmax. The HRmax is defined as heart rate achieved at the point of maximal exhaustion (Keytel et al., 2005). To determine HRmax, participants warmed up on bicycle with a workload of 2 W/kg for 2 minutes. After the warm-up session, participants maintained a speed of 70 revolutions per minute (rpm) with an intensity of 3.33 W/kg for 150 seconds. These are the parameters of stage 1 of the HRmax test. After completion of stage 1, workload was increased by an additional 50 W for another 150 seconds. After stage 2, the workload increased by 25 W every 150 seconds until the participants could not maintain 70 rpm or reached maximal exertion and stopped the test on their own. The heart rate of each participant was tracked using a heart rate monitor placed around their chest (Polar Electro Inc., Lake Success, NY, USA). Heart rate was measured and recorded once each minute throughout the test duration.

Study Design and Exercise Trials

This study followed a randomized, crossover design. Exercises of two separate intensities were used, randomly assigned, and performed at least 1 week apart to ensure that the participants fully rested and returned to basal conditions. The lower-intensity (LI) trial was aimed at 50% of HRmax, while the higher intensity (HI) trial was aimed at 80% of HRmax. The participants expended the same energy expenditure (~300 kcal) on the cycle ergometer during each trial. The participants were asked to refrain from any exercise during the study period other than that involved in the study. Energy expenditure was calculated using the following equation by Keytel et al (2005):

 $\begin{array}{l} \textit{Energy Expenditure} = \textit{gender} \times (-55.0969 + 0.6309 \times \textit{heart rate} + 0.1988 \times \textit{body weight}(\textit{kg}) + 0.2017 \times \textit{age}) + \\ (1 - \textit{gender}) \times (-20.4022 + 0.4472 \times \textit{heart rate} - 0.1263 \times \textit{body weight}(\textit{kg}) + 0.074 \times \textit{age}). \end{array}$

Dietary Intake

All participants recorded their food intake over 3 consecutive days (from 2 days prior to exercise to the day of exercise) for each exercise trial. Participants were instructed to maintain their usual caloric intake and diet composition.

Fasting Blood Sampling

Overnight fasting blood samples were collected at baseline (PRE), immediately post-exercise (IPE), 1-hour post-exercise (1-h PE), and 24-hour PE (24-h PE) for each exercise trial. Participants sat in a chair for 10 minutes before blood samples from the antecubital vein were collected into a serum separator tube. Blood samples were kept at room temperature for 20 minutes to ensure clotting, and then centrifuged for 20 minutes to separate the serum. Aliquots of serum samples were pipetted into 1.5-mL tubes and frozen at -80 °C for later analysis.

Serum Lipid Profiles Analysis

Serum samples in duplicate were assayed for TC (Kit# R85464, Cliniqa, San Marcos, CA) and TG (Kit#R84098, Cliniqa, San Marcos, CA) by an enzymatic colorimetric method. Serum lipoproteins, including LDL-C and HDL-C were analyzed by electrophoresis (Cat. # 3438 SPIFE Vis Cholesterol, Helena Laboratory, Beaumont, TX) using the SPIFE 3000 electrophoresis system (Helena Laboratory, Beaumont, TX). The lipoprotein-cholesterol analysis was performed using a commercially available kit (Cat. # 3218, Helena Laboratory, Beaumont, TX) as per the manufacturer's instructions. In brief, 80 μ L of serum samples, in duplicate, were loaded on an agarose gel, followed by 20 minutes of electrophoresis at 16 °C with 400 volts. After applying a staining reagent (Cat. #3438, Helena Laboratory, Beaumont, TX), additional electrophoresis was performed at 30 °C for 15 minutes. The gel was washed and then dried at 70 °C for 20 minutes, and the density of the stained lipoprotein-cholesterol bands were measured using a scanning densitometer (Epson Perfection V 700, Long beach, CA) using Quick Scan 2000 software (Helena Laboratory, Beaumont, TX). The coefficient of variation for each assay was: TC, 5.74%; TG, 1.04%; LDL-C, 1.86%; HDL-C 3.86%.

Statistical Analysis

All statistical analyses were performed using the IBM Statistical Package for the Social Sciences 20.0 (IBM SPSS, Armonk, USA) and reported as mean \pm standard error (SE) unless stated otherwise. A 2 × 4 (intensity x time) factorial ANOVA with repeated measures was used to test the effects of the lower and higher intensity of exercise on blood lipid and lipoprotein profiles (TC, TG, HDL-C, LDL-C) at baseline, IPE, 1-hr PE, and 24-hr PE. A p-value was set at < .05 for a statistical significance.

RESULTS

Dietary Intake

Total calories and macronutrient contents (fat, carbohydrate, and protein) between the two exercise trials were not significantly different (p > .05). Data for total calories, fat, carbohydrate, and protein content for each exercise trial are presented in Table 2.

Table 2. 3-Days of Dietary Intake

Intensity	Variables	-48 Hour PRE	-24 Hour PRE	PRE
Lower-Intensity (LI)	Total calories (kcals/day) Fat (kcals/day) Carbohydrate (g/day) Protein (g/day)	$\begin{array}{rrrrr} 1,811.89 \ \pm 178.72 \\ 637.19 \ \pm 126.70 \\ 257.70 \ \pm \ 32.89 \\ 86.43 \ \pm \ 13.69 \end{array}$	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$
Higher-Intensity (HI)	Total calories (kcals/day) Fat (kcals/day) Carbohydrate (g/day) Protein (g/day)	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$

Note: All data are presented as mean ± standard error; g = grams; kcals = kilocalories; PRE = prior to exercise.

```
Journal of Health, Sports, & Kinesiology
```

Workload, Heart Rate, and Time

Each exercise trial was performed at the similar exercise volume (total energy expenditure of 300 kcal). Significant differences were found between LI and HI in workload (p = .001), heart rate (p = .001), and time (p = .001). Data for workload, heart rate, and time for each exercise trial are presented in Table 3.

Table 3. Workload, Heart Rate, and Time for Each Exercise	Trial
---	-------

Variable	LI (Lower-Intensity)	HI (Higher-Intensity)	P-value
Workload (kp)	1.51 ± 0.05	2.42 ± 0.09	.001
Heart rate (bpm)	98.80 ± 1.82	154.20 ± 2.76	.001
Time (min)	42.00 ± 1.77	19.00 ± 0.53	.001

Note: All data are presented as mean \pm standard error. kp = kilopond; min = minutes; bpm = beats per minute.

Changes in Blood Lipid Profiles

Changes in blood lipids and lipoproteins for each exercise intensity are presented in Table 4. There were no significant differences in any of blood lipids and lipoproteins between the exercise intensity or time.

Table 4. Changes in Blood Lipids and Lipoproteins

Intensity	Variable	Baseline (M ± SE)	IPE (M ± SE)	1-Hour PE (M ± SE)	24-Hour PE (M ± SE)
Lower-Intensity (LI)	TG (mg/dl) TC (mg/dl) LDL-C (mg/dl) HDL-C (mg/dl)	$\begin{array}{r} 163.08 \pm 28.84 \\ 211.70 \pm \ 9.02 \\ 146.22 \pm \ 9.06 \\ 53.51 \pm \ 2.95 \end{array}$	$\begin{array}{r} 147.35 \pm 23.52 \\ 210.48 \pm \ 7.85 \\ 144.79 \pm \ 8.50 \\ 53.46 \pm \ 2.56 \end{array}$	$\begin{array}{r} 133.04 \pm 18.00 \\ 210.67 \pm 8.35 \\ 145.53 \pm 8.07 \\ 52.68 \pm 2.45 \end{array}$	$\begin{array}{r} 139.83 \pm 21.90 \\ 208.80 \pm \ 7.89 \\ 143.27 \pm \ 8.22 \\ 54.12 \pm \ 2.00 \end{array}$
Higher-Intensity (HI)	TG (mg/dl) TC (mg/dl) LDL-C (mg/dl) HDL-C (mg/dl)	$\begin{array}{r} 128.85 \pm 28.84 \\ 216.51 \pm \ 9.02 \\ 151.09 \pm \ 9.06 \\ 55.73 \pm \ 2.95 \end{array}$	$\begin{array}{r} 126.73 \pm 23.52 \\ 217.80 \pm \ 7.85 \\ 150.35 \pm \ 8.50 \\ 54.87 \pm \ 2.56 \end{array}$	$\begin{array}{r} 129.77 \pm 18.00 \\ 213.30 \pm 8.35 \\ 152.25 \pm 8.07 \\ 53.14 \pm 2.45 \end{array}$	$135.54 \pm 21.90 209.31 \pm 7.89 147.21 \pm 8.23 54.38 \pm 2.00$

Note: TG, Triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; IPE, immediate post-exercise; PE = post-exercise; mg/dl = milligrams per deciliter; M, mean; SE, standard error.

DISCUSSION

The overall objective of this study was to examine the effectiveness of a different exercise intensity (lower vs. higher) requiring the same energy expenditure in changes in the lipid and lipoprotein profiles in physically healthy obese males. Given the ever-increasing rates of obesity and cardiovascular disease in America (Capewell et al., 2010), it is important to have the most applicable knowledge and to utilize the best tools to combat this epidemic. It is unanimously agreed upon in the healthcare community that exercise can help improve body composition (Warburton et al., 2006). Exercises can also mitigate and reverse/reduce high levels of atherosclerosis, high levels of cholesterol and triglycerides, and balance the lipid profile (Warburton et al., 2006). However, it is unclear which intensity of exercise yields the most effective results. In this study, both lower and higher intensity exercises resulted in similar changes in LDL, HDL, TC, and TG, which were not statistically significant. One of the possible explanations for the lack of significant differences between the lower and higher intensity exercises in this study. This would support the claim of many other studies, which have reported that changes in blood lipids and lipoproteins are based on total calories burned, not the intensity of exercise (Crouse et al, 1995; Kraus et al., 2002; Tall, 2002). Thus, it would be better to focus on increasing and accumulating caloric expenditure

Journal of Health, Sports, & Kinesiology

daily, which will also lead to a decrease in body weight and improve body composition. It appears that weekly caloric expenditure from exercise that meets or exceeds the range for a healthy lifestyle is more important than the intensity of exercise. An adequate volume of physical activity is more sustainable for most individuals and should be encouraged (Kannan et al., 2014).

Although many precautions were taken to ensure that the study was successful, some limitations still remained. This study was limited to the sample size that was available. In addition, there was no control session. Future studies should include a more diverse sample size, involving more variations in age, sex, and ethnicities with control setting. Also, it is recommended that future research determine whether different intensities of chronic exercise requiring the same or higher volume of energy expenditure can positively alter the blood lipid profiles in obese males.

CONCLUSION

This study suggests that regardless of exercise intensity, an acute bout of aerobic exercise requiring 300 kcal energy expenditure may not be enough to significantly alter blood lipids and lipoproteins in physically healthy obese males. Therefore, we suggest that exercise volume, instead of exercise intensity, should be considered as a key factor for positively changing the lipids and lipid profiles in obese males.

REFERENCES

- Capewell, S., Ford, E. S., Croft, J. B., Critchley, J. A., Greenlund, K. J., & Labarthe, D. R. (2010). Cardiovascular risk factor trends and potential for reducing coronary heart disease mortality in the United States of America. *Bulletin of the World Health Organization*, 88(2), 120–130. https://doi.org/10.2471/BLT.08.057885
- Crouse, S. F., O'Brien, B. C., Rohack, J. J., Lowe, R. C., Green, J. S., Tolson, H., & Reed, J. L. (1995). Changes in serum lipids and apolipoproteins after exercise in men with high cholesterol: Influence of intensity. *Journal of Applied Physiology*, *79*(1), 279–286. doi:10.1152/jappl.1995.79.1.279
- Fiuza-Luces, C., Santos-Lozano, A., Joyner, M., Carrera-Bastos, P., Picazo, O., Zugaza, J. L., Izquierdo, M., Ruilope, L. M., & Lucia, A. (2018). Exercise benefits in cardiovascular disease: beyond attenuation of traditional risk factors. *Nature reviews. Cardiology*, 15(12), 731–743. https://doi.org/10.1038/s41569-018-0065-1
- Goldberg, A. C., Hopkins, P.N., Toch, P.P., Goldberg, A. C., Hopkins, P. N., Toth, P. P., Ballantyne, C. M., Rader, D. J., Robinson, J. G., Daniels, S. R., Gidding, S. S., de Ferranti, S. D., Ito, M. K., McGowan, M. P., Moriarty, P. M., Cromwell, W. C., Ross, J. L., Ziajka, P. E., & National Lipid Association Expert Panel on Familial Hypercholesterolemia (2011). Familial hypercholesterolemia: Screening, diagnosis and management of pediatric and adult patients: Clinical guidance from the National Lipid Association

Expert Panel on familial hypercholesterolemia. *Journal of Clinical Lipidology*, 5(3), Suppl., S1–S8. 10.1016/j.jacl.2011.04.003. Hansson, G. K. (2005). Inflammation, atherosclerosis, and coronary artery disease. *The New England Journal of Medicine*, 352(16),

1685-1695. doi:10.1056/NEJMra043430

Libby, P. (2002). Inflammation in atherosclerosis. Nature, 420(6917), 868-874. doi:10.1038/nature01323

Hruby, A. & Hu, F.B. (2015). The epidemiology of obesity: A big picture. Pharmacoeconomics, 33(7), 673-689.

https://doi.org/10.1007/s40273-014-0243-x

- Kannan, U., Vasudevan, K., Balasubramaniam, K., Yerrabelli, D., Shanmugavel, K., & John, N. A. (2014). Effect of exercise intensity on lipid profile in sedentary obese adults. *Journal of Clinical and Diagnostic Research*, 8(7), BC08–BC10 doi:10.7860/JCDR/2014/8519.4611
- Keytel, L.R., Goedecke, J.H., Noakes, T.D., Hiiloskorpi, H., Laukkanen, R., van der Merwe, L., & Lambert, E. V. (2005). Prediction of energy expenditure from heart rate monitoring during submaximal exercise. *Journal of Sports Sciences*, 23(3), 289–297.
- Kraus, W. E., Houmard, J. A., Duscha, B. D., Knetzger, K. J., Wharton, M. B., McCartney, J. S., Bales, C. W., Henes, S., Samsa, G. P., Otvos, J. D., Kulkarni, K. R., & Slentz, C. A. (2002). Effects of the amount and intensity of exercise on plasma lipoproteins. *The New* England Journal of Medicine, 347(19), 1483–1492. https://doi.org/10.1056/NEJMoa020194
- Meyers, M. R. & Gokce, N. (2007). Endothelial dysfunction in obesity: etiological role in atherosclerosis. Current Opinion in Endocrinology, Diabetes and Obesity, 14(5), 365-369. doi: 10.1097/MED.0b013e3282be90a8.
- Nystoriak, M. A., & Bhatnagar A. (2018). Cardiovascular effects and benefits of exercise. *Frontiers in Cardiovascular Medicine*, 5, 135. https://doi.org/10.3389/fcvm.2018.00135
- Riebe, D., Franklin, B. A., Thompson, P. D., Garber, C. E., Whitfield, G. P., Magal, M., & Pescatello, L. S. (2015). Updating ACSM's Recommendations for Exercise Preparticipation Health Screening. *Medicine and Science in Sports and Exercise*, 47(11), 2473– 2479. https://doi.org/10.1249/MSS.00000000000664
- Tall A. R. (2002). Exercise to reduce cardiovascular risk--how much is enough?. *The New England Journal of Medicine*, 347(19), 1522–1524. https://doi.org/10.1056/NEJMe020117
- Wang, Y., & Xu, D. (2017). Effects of aerobic exercise on lipids and lipoproteins. Lipids in Health and Disease, 16(1), 132. doi:10.1186/s12944-017-0515-5
- Albarrati, A. M., Alghamdi, M. S. M., Nazer, R. I., Alkorashy, M. M., Alshowier, N., & Gale, N. (2018). Effectiveness of Low to Moderate Physical Exercise Training on the Level of Low-Density Lipoproteins: A Systematic Review. *BioMed Research International*, 5982980. https://doi.org/10.1155/2018/5982980

- Warburton, D. E. R., Nicol, C. W., & Bredin, S. S. D. (2006). Health benefits of physical activity: The evidence. CMAJ: Canadian Medical Association Journal, 174(6), 801–809. https://doi.org/10.1503/cmaj.051351
- Yoshida, H., Ishikawa, T., Suto, M., Kurosawa, H., Hirowatari, Y., Ito, K., Yanai, H., Tada, N., & Suzuki, M. (2010). Effects of supervised aerobic exercise training on serum adiponectin and parameters of lipid and glucose metabolism in subjects with moderate dyslipidemia. *Journal of Atherosclerosis and Thrombosis*, *17*(11), 1160–1166. https://doi.org/10.5551/jat.4358

Author Information

Jinkyung Park, Ph.D., Corresponding Author https://orcid.org/0000-0003-4888-8881 Assistant Professor, Department of Exercise Science School of Health and Human Performance Georgia College & State University, Milledgeville, GA, USA. jinkyung.park@gcsu.edu Yunsuk Koh, Ph.D. https://orcid.org/0000-0001-9280-5786 Associate Professor & Director of Exercise Physiology Department of Health, Human Performance, and Recreation College of Health and Human Sciences Baylor University, Waco, TX, USA. yunsuk_koh@baylor.edu

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationship that could be constructed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.



Copyright © 2020-2021. This work is licensed under a CC BY-NC-SA 4.0 International license. This is an open access article distributed under the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.