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Comparing the effect of ascorbic acid and conventional vape mod liquid to nasal mucociliary clearance, IL-6, stress oxidative, and lung function

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ABSTRACT

Background: The effects of vaping, or electronic cigarettes (e-cigarettes), on respiratory health are still debatable, even though it is thought to be a safer alternative to traditional cigarettes. Vape use may affect mucociliary function and increase oxidative stress and inflammation. Ascorbic acid has antioxidant and anti-inflammatory properties that can mitigate tissue damage from chemical exposure. This study aims to compare the impact of vape mod use, ascorbic acid supplementation with a vape mod, and non-smokers (control group) on nasal mucociliary clearance (NMC), interleukin-6 (IL-6), oxidative stress, and lung function to provide a clearer picture of the health risks associated with vape use.

Methods: 45 participants were recruited and randomized into 3 groups: conventional vape mod group, ascorbic acid vape mod group, and control group. The measurement of NMC using the saccharin test, obtained lung function (FVC, FEV1, and PEF) via spirometry, and measured IL-6, reactive oxygen species, and SOD3 levels by sandwich ELISA.

Results: The findings showed that a vape mod with ascorbic acid produced a better response than a conventional vape mod, based on NMC, IL-6, oxidative stress markers, and lung function.

Conclusion: Ascorbic acid use may have protective benefits against mucosal damage and inflammation resulting from chemical exposure, while conventional vape use may worsen respiratory health conditions and cause inflammation and oxidative stress.

Keywords: ascorbic acid, e-cigarette, NMC, IL-6, oxidative stress

INTRODUCTION

Smoking behavior remains a global issue that poses a threat to global public health every year. In Indonesia, according to the global adult tobacco survey, the overall prevalence of tobacco smoking has not significantly changed from 2011 to 2021. The current prevalence of tobacco smoking in 2011 and 2021 was 34.8% and 33.5%, respectively, or approximately 68.9 million adults (aged 15 or older) [1]. In 2019, the Institute for Health Metrics and Evaluation reported that cigarettes killed more than 8 million people, with over 7 million of these deaths attributed to direct cigarette use (active smokers) and around 1.3 million due to non-smokers exposed to second-hand smoke (passive smokers) [2]. Furthermore, tobacco smoking is a major global contributor to non-communicable diseases and a primary risk factor for cardiovascular and lung diseases [3].

Advances in technology have also contributed to mitigating the negative impact of tobacco smoking by creating alternative devices considered safer than conventional tobacco cigarettes, namely electronic cigarettes (e-cigarettes) [4, 5]. This has led to an increase in e-cigarette users in society, making it part of their lifestyle. The global adult tobacco survey reported a significant increase in the prevalence of e-cigarette users in Indonesia, rising from 0.3% in 2011 to 3.0% in 2021, or approximately 6.2 million adults [1]. A survey conducted by RISKESDAS in Central Java stated that e-cigarette users in the city of Semarang had the highest prevalence among all districts/cities in Central Java, at 8.46% [6]. The widespread use of e-cigarettes in society has reached a level where it is regarded as a lifestyle choice [7].

E-cigarettes or vape mods are battery-powered devices that produce inhalable aerosols by heating liquids containing nicotine, flavorings, and other chemicals. However, there are now many nicotine-free vape liquid options available [8]. Vape mod liquids typically contain propylene glycol (PG) and vegetable glycerine (VG) [9].

E-cigarette aerosol exposure significantly alters the upper-airway microenvironment, particularly affecting the nasal

mucosa. Inhalation of vape liquid aerosols—composed primarily of PG, VG, and chemical additives—disrupts the nasal epithelial barrier by altering tight junction integrity and decreasing airway surface liquid volume [10, 11].

Additionally, components such as nicotine impair ciliary beating frequency, prolonging nasal mucociliary clearance (NMC) time and compromising the sinonasal tract's primary defense against inhaled pathogens [12, 13]. These local physiological disruptions contribute to localized oxidative stress and trigger pro-inflammatory responses within the nasal mucosa [14, 15]. Understanding how e-cigarette aerosols impair nasal epithelial homeostasis is critical for establishing the pathological mechanisms of vaping-induced upper respiratory damage, providing a compelling rationale to investigate potential therapeutic interventions such as inhaled ascorbic acid.

Studies on conventional vape mod liquids containing PG and VG have reported that in vitro exposure of human bronchial cells to e-cigarette solutions containing PG and/or VG reduces cell metabolism, bronchial cell viability, ciliary activity, and increases mitochondrial oxidative stress [16, 17]. The composition of vape liquid containing VG and PG, when aerosolized by vaping, can dehydrate the surface fluid of the respiratory tract, leading to airway obstruction and inflammation [10].

Several studies on e-cigarette users have reported no changes in lung function parameters after vaping for 5 minutes, 2 hours, and more than 3 months [18-20]. However, research on e-cigarette users who have never smoked tobacco shows significantly lower forced expiratory volume in one second (FEV1), peak expiratory flow (PEF), and the FEV1/forced vital capacity (FEV1/FVC) ratio compared to controls (non-vapers and non-smokers) [21-24].

In contrast to conventional e-liquids that consist solely of PG and VG [9, 16], the ascorbic acid formulation evaluated in this study contains PG, VG, and 1000 mg of vitamin C [15, 25]. This study investigates the inhalation administration of aerosolized ascorbic acid to evaluate its direct local and systemic effects on the respiratory system [15, 26].

Both conventional vape mod liquid and ascorbic acid vape mod liquid function similarly and are compatible with vape mods. Inhaling ascorbic acid vape mod liquid may affect users' lung function, but no prior research has examined this. This study is the first population-based experimental study to investigate the short-term effects of using 1,000 mg of ascorbic acid-based liquid in vape mods. Therefore, researchers aim to explore differences in NMC, interleukin-6 (IL-6), reactive oxygen species (ROS), superoxide dismutase-3 (SOD-3) levels, and lung function among non-smokers, conventional vape mod liquid users, and ascorbic acid vape mod liquid users.

MATERIALS AND METHODS

Study Design

This prospective randomized controlled trial aimed to compare NMC, IL-6, ROS, SOD-3 levels, and lung function (FVC, FEV1, and PEF) between users of ascorbic acid vape mod liquid and conventional vape mod liquid, as well as a control group. This research took place at the Faculty of Medicine, Diponegoro University, Semarang, in 2023. Forty-five eligible participants who met the inclusion criteria, such as being 20-30 years old, being willing to be involved in this study by signing the informed consent and being in a healthy condition based on the doctor's examination, were permitted to participate in this research. Participants who were smokers; had a history of autoimmune disease, lung disease, heart disease, liver disease, and cancer; were pregnant; had allergic rhinitis and asthma; had hereditary and congenital diseases; were excluded.

Vaping history and washout protocol

To prevent baseline bias associated with prior tobacco or e-cigarette exposure, strict inclusion and exclusion criteria regarding smoking history were implemented [11, 21, 24]. Participants assigned to the control group (non-smokers/non-vapers) were required to have zero history of conventional cigarette or e-cigarette use [21, 24]. For participants allocated to the vaping intervention groups (conventional vape mod and ascorbic acid vape mod), eligible individuals were regular e-cigarette users without a history of conventional tobacco smoking (never-smokers) [23, 24].

To standardize baseline physiological parameters, we enforced a mandatory 48-hour washout period before baseline measurements [10, 21]. During this pausing period, participants were instructed to refrain completely from using any e-cigarettes, tobacco products, or nicotine replacement therapies [10, 21]. Adherence to the washout protocol before baseline biological sampling and baseline function tests [10, 14].

Sample size calculation

The required sample size was determined using the formula for comparing means across three independent groups in a one-way analysis of variance (ANOVA) design:

$$n = \frac{\left(Z_{1-\alpha/2} + Z_{1-\beta}\right)^2 \cdot 2 \cdot \sigma^2}{\delta^2}, \quad (1)$$

where $Z_{1-\alpha/2} = 1.96$ (corresponding to a 5% level of significance, $\alpha = 0.05$), $Z_{1-\beta} = 0.84$ (corresponding to 80% statistical power, $\beta = 0.20$), σ represents the estimated population standard deviation derived from prior literature on e-cigarette exposure and respiratory biomarkers [27, 28], δ denotes the expected minimum clinically meaningful difference between group means.

Based on primary outcome parameters (IL-6 and ROS levels) from previous pilot data [15, 28], we calculated a minimum sample size of 12 participants per group. To account for potential dropouts or non-compliance during the 2-week intervention period, we recruited 15 participants per group (total N = 45).

Anthropometric and vital signs measurements

Trained medical staff measured anthropometric parameters and vital signs before the intervention to assess baseline homogeneity across groups [21, 22]. Body weight (kg) and height (cm) were measured using a calibrated digital standing scale and stadiometer (Seca, Germany) while participants wore light clothing and no shoes [23, 24]. Body mass index was calculated as body weight divided by height squared (kg/m^2).

Vital signs were measured after participants rested seated for at least 10 minutes in a temperature-controlled room [10, 21]. Blood pressure—systolic blood pressure (SBP) and diastolic blood pressure (DBP)—was measured using a

standard, calibrated digital sphygmomanometer (Omron Medical, Japan) with an appropriately sized cuff placed on the upper left arm at heart level [3, 21]. Radial pulse rate (bpm) and respiration rate (breaths per minute) were assessed manually over a full 60-second period [10, 24]. If the initial blood pressure reading exceeded optimal non-hypertensive thresholds (SBP ≥ 120 mmHg or DBP ≥ 80 mmHg), a second reading was taken 5 minutes later, and the lower value was recorded. The body temperature (°C) was recorded using a non-contact digital infrared forehead thermometer [21, 23].

E-Cigarette Devices and E-Liquid

The E-cigarette device used in this study was purchased from a vape shop (Semarang, Indonesia). The vape mod device was divided into 2 groups, with different liquid contents: ascorbic acid vape mod liquid or conventional vape mod liquid. Participants were randomly assigned 1:1 to each group and used the vape mod with the assigned liquid for two weeks. The control group was the participants who did not smoke (non-smokers and non-vapers).

Nasal Mucociliary Clearance

To measure NMC, the saccharin test is regarded as the accepted technique. Approximately 1 cm behind the anterior end of the inferior turbinate, a 0.5 mm saccharin particle was inserted. To prevent the particle from falling backward into any posterior nasal stream, the test is performed while the patient is seated with their head tilted back by roughly 10 degrees. The particle's nature is not disclosed to the patient. The clearance time is forward rather than backward, so it's crucial not to position it too far ahead. Advise the subject to drink every minute and to try to refrain from coughing and sneezing. The room should have no air currents and be completely dust-free. Record the time and stop it after tasting sweetness during the saccharin test.

Biomarkers Measurement

The IL-6, ROS, and SOD-3 levels were quantified in serum samples using quantitative sandwich enzyme-linked immunosorbent assay (ELISA) kits manufactured by R&D Systems (Minneapolis, MN, USA) [14, 28]. The kit specifications using Human IL-6 Quantikine ELISA Kit (Catalog # D6050; detection range: 3.12-300 pg/mL; sensitivity: 0.70 pg/mL), Human ROS ELISA Kit (Catalog # MET-5038; detection range: 15.6-1,000 pg/mL), and Human SOD3/EC-SOD Quantikine ELISA Kit (Catalog # DSOD30; detection range: 0.16-10 ng/mL; sensitivity: 0.04 ng/mL) [28, 29].

Venous blood samples (5 mL) were collected from each participant after an overnight fast [10, 21]. Samples were allowed to clot for 30 minutes at room temperature and centrifuged at 1,000 × g for 15 minutes at 4 °C to isolate serum [14, 28]. Serum aliquots were stored at -80 °C until assaying [28, 30]. Standards, controls, and serum samples were added in duplicate to microplate wells pre-coated with monoclonal antibodies specific for IL-6, ROS, or SOD3 [28, 29]. After incubation and washing, add enzyme-linked polyclonal detection antibodies [29, 30]. After washing, add the substrate solution and stop color development with 2 N sulfuric acid [28, 29].

The Absorbance was read at 450 nm with wavelength correction at 570 nm using a microplate reader (Bio-Rad Laboratories, Hercules, CA, USA) [28, 29]. Intra-assay and inter-assay coefficients of variation were maintained below 6.5% and 8.0%, respectively, to ensure analytical precision [14, 28].

Lung Function (FVC, FEV_1, and PEF)

Lung Function (FVC, FEV_1, and PEF) was obtained using a spirometry test (Mir Spirolab III Oxy), beginning with instructions for subjects to stand in their most comfortable position. Subsequently, the researcher closed the subject's nostrils with a clip-like device positioned just above the subject's nose. The subject then took a deep breath and held it for a few seconds before exhaling forcefully into the spirometer mouthpiece as forcefully and rapidly as possible.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA) [23, 24]. The normality test was performed using the Shapiro-Wilk test. For non-normally distributed data, we applied the Kruskal-Wallis test; when results were significant, we conducted post hoc pairwise comparisons using the Mann-Whitney U test [10, 23]. For normally distributed continuous data, one-way ANOVA, followed by the Games-Howell post hoc test to account for potential unequal variances [23, 24]. A two-tailed $\boldsymbol{p}$-value of <0.05 was considered statistically significant.

Ethics statement

Ethical clearance was obtained from the Commission on Medical/Health Research Bioethics, Faculty of Medicine, Sultan Agung Islamic University, Semarang, with registry number: 254/VII/2023/Komisi Bioetik. Participants were informed about the study's aims, objectives, benefits, research protocol, and potential side effects. Participants had the right to refuse or withdraw from this study. Participants willing to participate completed and signed the written informed consent form.

RESULTS

A total of 45 eligible participants were recruited and randomized into three groups. **Figure 1** shows the consolidated standards of reporting trials (CONSORT) flow diagram, and **Table 1** presents the baseline characteristics of the 45 participants.

The mean of NMC, IL-6, ROS, SOD3 levels, and spirometry test results are presented in **Table 2**. NMC transport analysis showed no significant differences between groups. However, the control group showed the longest average time in the NMC transport test (14.11 ± 8.07), compared with the ascorbic acid vape mod group (11.77 ± 6.50) and the conventional vape mod group (10.19 ± 4.39).

This study observed differences in IL-6, ROS, and SOD3 levels. The data showed significant differences across treatment groups. IL-6 and ROS levels in the ascorbic acid group were the lowest, at 0.72 ± 6.94 pg./ml ($p = 0.024$) and 61.48 ± 23.64 pg./ml ($p < 0.001$), respectively. The liquid conventional group showed very high ROS levels (1020.1 ± 105.4 pg./ml). This level was much higher than the other groups (61.48 ± 23.64 pg./ml and 76.11 ± 25.32 pg./ml). Measurement of SOD3 levels in each group also showed significant differences ($p = 0.001$), where the liquid conventional group had the highest SOD3 levels of 1.80 ± 0.82 ng/ml, ascorbic acid (1.64 ± 0.60 ng/ml), and the lowest was the control group (0.95 ± 0.33 ng/ml) (**Table 2**).

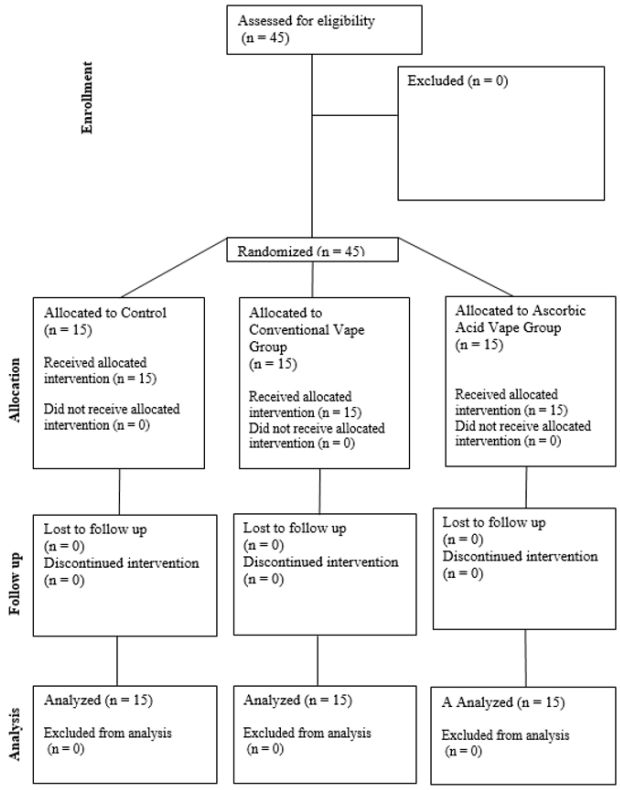

Figure 1. CONSORT flow diagram (the authors' own elaboration)

A box plot diagram presents a comparison of IL-6, ROS, and SOD3 levels (**Figure 2**).

Table 2 also illustrates the average increase FVC, FEV1, and PEF. Overall, the results indicate that there is a non-significant difference ($p > 0.05$) in the spirometry examination of FVC, FEV_1, and PEF in each group.

Post hoc tests on IL-6 and ROS using the Mann-Whitney test between the control group and the ascorbic acid vape mod and conventional vape mod groups found significant differences ($p < 0.05$). The Games-Howell test between the non-smoker group and the ascorbic acid vape mod and conventional vape mod groups for SOD3 showed significant differences ($p < 0.05$). Comparison between the ascorbic acid vape mod group and the conventional vape mod group in all three variables did not show significant differences (**Table 3**).

DISCUSSION

The popularity of e-cigarette vaping has been rising recently, and hence health concerns about vaping have attracted public attention. Previous research has indicated that immediate exposure to e-cigarettes may lead to inflammation, oxidative stress, and changes in the extracellular matrix [11, 31]. The health risks are attributed to the presence of chemicals and toxins in e-cigarettes, such as nicotine, which can harm the respiratory system. Furthermore, the long-term impact of vaping on overall well-being is not completely clear. Recent studies have suggested a possible connection between vaping and an elevated likelihood of lung dysfunction [27, 32].

The baseline mean SBP and resting pulse rates observed in our young adult cohort (averaging 130-132 mmHg and 86-91 bpm, respectively) reflect acute sympathetic activity and initial measurement anxiety (white-coat effect) common in clinical trial settings. Furthermore, transient vasoconstrictive effects from prior lifestyle or dietary habits (e.g., caffeine consumption or acute nicotine/vape liquid exposure prior to testing) may have contributed to slightly elevated baseline hemodynamic profiles [3, 21]. Standardized resting protocols and duplicate measurements ensured data reliability across all experimental groups.

Smokers had a lower NMC value than non-smokers, suggesting that smoking, including e-cigarette vaping, could hinder normal mucus clearance from the respiratory tract and elevate the likelihood of respiratory infections [12, 33]. In our

Table 1. The comparative baseline characteristics of subjects (N = 45)

Description		Control (non-smoker, non vaper) (n = 19)	Ascorbic acid's liquid (n = 14)	Conventional liquid (n = 12)	p
		M ± SD	M ± SD	M ± SD	
Age		21.21 ± 1.84	22.21 ± 1.48	22.42 ± 1.88	0.071‡
Anthropometry	Body weight	63.00 ± 9.69	78.76 ± 23.89	67.62 ± 9.81	0.075‡
	Height	169.47 ± 6.67	168.93 ± 4.78	171.63 ± 5.54	0.361‡
Vital signs	Blood pressure	130.20±24.45	131.89 ± 10.13	131.94 ± 12.03	0.585‡
	Pulse	88.13 ± 10.71	86.63 ± 18.70	91 ± 11.78	0.807‡
	Temperature	36.11 ± 1.22	36.20 ± 0.53	36.06 ± 1.19	0.314‡
	Respiration rate	19.27 ± 1.40	19.47 ± 3.20	19.69 ± 3.21	0.475‡

Note. ‡Kruskal-Wallis test

Table 2. Comparison of subject profiles of ascorbic acid liquid and conventional users (N = 45)

Description		Control (non-smoker, non vaper) (n=19)	Ascorbic acid's liquid (n = 14)	Conventional liquid (n = 12)	p
		M ± SD	M ± SD	M ± SD	
NMC		10.19 ± 4.39	11.77 ± 6.50	14.11 ± 8.07	0.396‡
IL-6		2.50 ± 0.89	0.72 ± 6.94	1.03 ± 2.54	0.024‡*
ROS		76.11 ± 25.32	61.48 ± 23.64	1020.1 ± 105.4	< 0.001‡*
SOD-3		0.95 ± 0.33	1.64 ± 0.60	1.80 ± 0.82	< 0.001§*
Spirometry	FVC	3.77 ± 0.53	4.03 ± 0.60	3.56 ± 0.53	0.249‡
	FEV_1	3.47 ± 0.48	3.64 ± 0,51	3.29 ± 0.48	0.086‡
	PEF	8.52 ± 2.07	8.65 ± 0.85	8.62 ± 2.07	0.962‡

Note. *Significant ($p < 0.05$); ‡Kruskal Wallis; & §One-way ANOVA

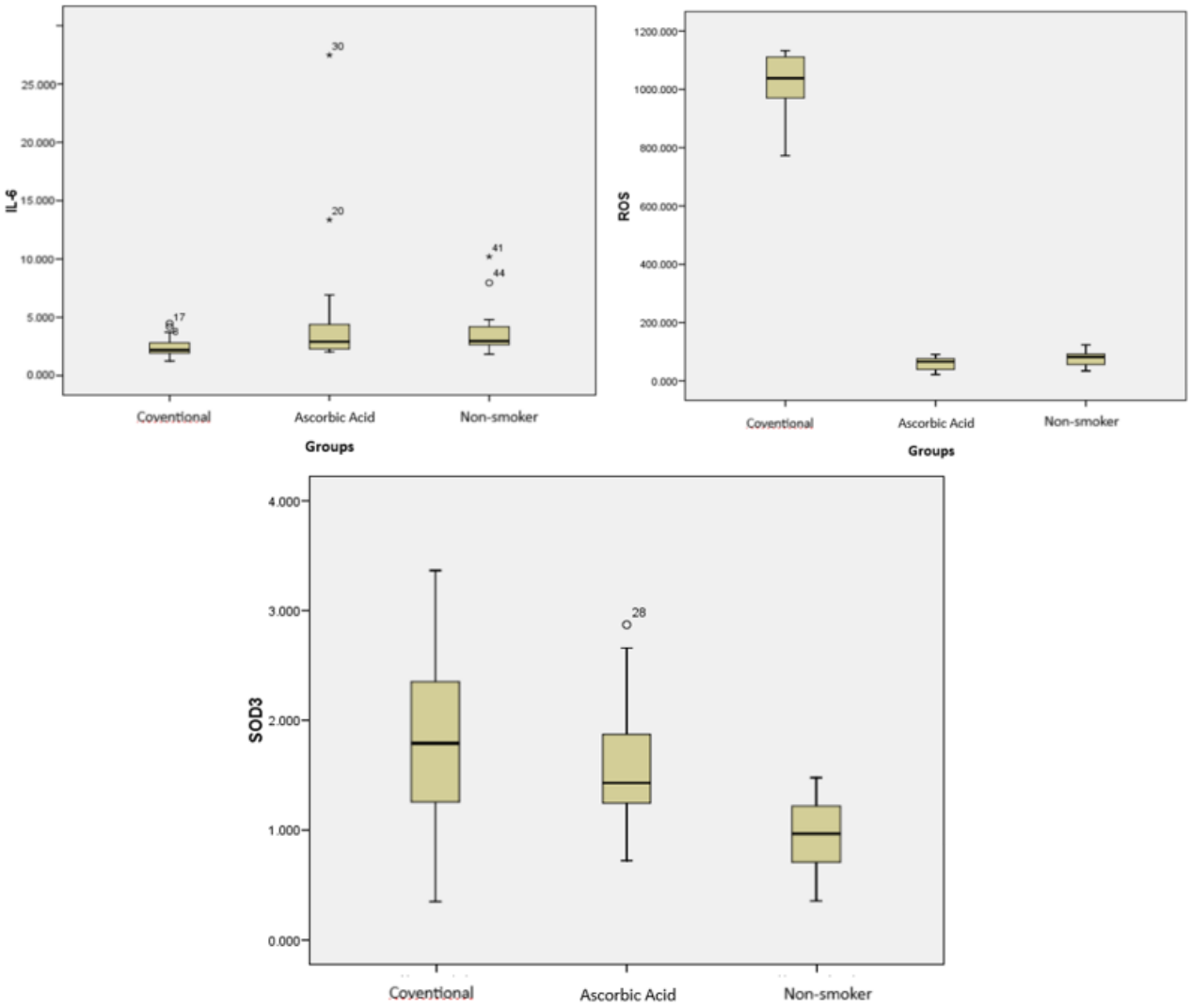

Figure 2. The differences between IL-6, ROS, and SOD3 levels in non-smoker, ascorbic acid vape, and conventional vape groups (the authors' own elaboration)

Table 3. Post hoc test of IL-6, ROS, and SOD3

Group		Variable		
I	II	IL-6	ROS	SOD3
Non-smoker	Ascorbic acid	0.023*	< 0.001*	0.003*
	Conventional	0.022*	< 0.001*	0.011*
Ascorbic acid	Conventional	0.979	0.198	0.842

Note. *Significant ($p < 0.05$)

study, NMC among non-vapers, ascorbic acid vape mod users, and conventional vape mod users, as measured by the saccharin test, showed that the conventional vape user group needed the longest time. The consequence of impaired NMC and the potentially toxic effects of chemicals present in e-cigarettes raise concerns about the respiratory health risks associated with vaping [12, 13].

NMC in e-cigarette smokers was affected by oxidative stress caused by nicotine exposure through transient receptor potential channel A1 (TRPA-1) receptors. These receptors reduce airway surface liquid volume and decrease mucus density. Additional research has indicated that formaldehyde from E-cig-generated aerosols can cause DNA strand breaks and cell death, while PG thickens the respiratory epithelium by promoting goblet cell proliferation and increased mucin production within these cells [14].

Continuous vaping can trigger respiratory tract inflammation and affect the cytokines involved in the inflammatory process [28, 30]. Inflammation is a vital part of the immune response against pathogens and bodily harm. It involves controlled molecular actions that usually happen briefly. Prolonged inflammation can be harmful, potentially leading to chronic inflammation and possibly even tumor formation [34]. IL-6 is an essential cytokine involved in immune response and inflammation. In line with the results of our study, IL-6 levels in conventional vape mod users were detected to be the highest. This clearly shows that the use of conventional vape mods, which most people consider a healthier alternative to smoking, is wrong. This is reinforced by other studies that also mention that e-cigarette vape mod exposure can cause inflammatory reactions and harm the functioning of the respiratory system [27]. The negative effects of e-cigarette vape mods were often made worse by the flavoring added to e-cigarettes. Inhaling e-cigarette aerosol may trigger IL-6 signaling in the respiratory tract. E-cigarette aerosols stimulate the production of pattern-recognition receptors like toll-like receptor and the release of pro-inflammatory cytokines such as IL-1β and tumor necrosis factor-α, along with their respective receptors. In the oral cavity, vaping e-cigarettes disrupts the natural balance of the

oral microbiota by suppressing beneficial bacteria and promoting the growth and biofilm formation of cariogenic bacteria, especially with sweet flavors that contain sugar. Suppression of IL-4 further facilitates colonization by pathogenic bacteria. In human airway epithelial cells, e-cigarette aerosols also increase the production of inflammatory cytokines, such as IL-6 and IL-8, which macrophages secrete in response to e-vapes. Acrolein, a component of e-cigarette vapor, impairs neutrophil function and inhibits the Fc receptor [29, 34].

An alternative to conventional vape mods was tested in this study using ascorbic acid liquid. As a result, the group of vape users with liquid ascorbic acid showed the lowest IL-6 levels. In the human body, ascorbic acid is one of the fundamental low-molecular antioxidants [35]. It helps control ROS concentrations and supports the activity of other antioxidants. Even in the early stages of ROS formation, ascorbic acid helps control their levels. The primary producers of ROS are the mitochondrial respiratory chain and particular enzymes like xanthine oxidase and NADPH oxidases [36, 37].

Inflammation is strongly linked to both high and low ROS levels [38]. Numerous antioxidant enzymes, proteins, and non-protein antioxidants also possess anti-inflammatory properties. Inflammation triggers the generation of ROS, reactive nitrogen species, and other reactive molecules, intensifying oxidative stress and damaging vital macromolecules [15, 39]. This statement is consistent with the results of a previous study that showed an increase in endogenous ROS in a group of rats given toxic exposure to e-cigarettes [40]. Compared with the conventional vape group, the ROS level in the ascorbic acid vape user group was lower. This result may reflect ascorbic acid's role as a respiratory tract lining fluid, helping modulate ROS production in the respiratory tract [36]. Ascorbate not only inhibits free-radical production or directly reduces their levels but also boosts the cellular antioxidant system by increasing low-molecular-weight antioxidants and activating antioxidant enzymes to prevent oxidative stress or lessen its damaging effects on cellular compartments [41].

A major molecular mechanism underlying both traditional and e-cigarette smoking is the disturbed oxidative balance. Superoxide radicals are converted to hydrogen peroxide by SOD. Prior research has indicated a decrease in SOD levels associated with traditional tobacco smoking [15, 42]. Inconsistent results have also been observed. In this study, the highest SOD3 levels were found in the conventional vape mod group. The non-smoker and ascorbic acid vape mod user groups had lower SOD3. In this case, higher SOD3 activity may help reduce elevated superoxide radicals and prevent oxidative stress caused by conventional vaping. Inconsistent results were also reported before, where the traditional smoker group had the highest SOD3 levels, while the conventional vape group had the lowest levels [31].

For the FVC parameter, although the results are not significant, the ascorbic acid vape mod group shows higher results than the others. This phenomenon may occur because ascorbic acid functions as an antioxidant, neutralizing oxidative stress [43]. Toxic components in vape aerosols, if not reduced, can cause damage to lung tissue, leading to airway obstruction and affecting lung function [11]. This aligns with cross-sectional study findings suggesting a correlation between higher ascorbic acid intake and higher FVC values. However, it is essential to note that the cited research measured ascorbic acid obtained from direct food and fruit consumption, not through inhalation methods as in this study [44, 45]. For the FEV1 and PEF parameters, the ascorbic acid vape mod group showed insignificantly higher values, suggesting the antioxidant potential of ascorbic acid in lung function. This result is also supported by previous cross-sectional studies that reported a correlation between higher serum antioxidant levels and elevated FEV1 values [46-50]. Another study conducted in healthy adults also reported an improvement in PEF with ascorbic acid supplementation [51].

This is the first study to replace conventional vape mod liquid with ascorbic acid mod liquid tested in vape users. Internal and external factors influenced the study results. Users' compliance and vaping habits may have influenced the results. Participants' respiratory illness history can also affect the study's results. Further research is needed on the histopathological effects of using ascorbic acid vape mod and conventional vape mod, with more participants included in the study and a longer study period for vape mod usage.

Several limitations should be acknowledged. First, the relatively small sample size may limit the statistical power to detect subtle differences in certain secondary clinical parameters, such as spirometric pulmonary volumes. Second, the 2-week intervention period evaluates only short-term physiological and biomarker responses; consequently, the long-term biological safety, chronic tissue remodeling, and potential adverse effects of inhaled ascorbic acid remain to be established. Third, participant compliance regarding vaping protocols and adherence to pre-testing dietary/lifestyle restrictions relied partly on self-reporting. Future research with larger sample sizes, extended intervention timelines, and histopathological evaluations is warranted to validate these preliminary findings.

CONCLUSION

In summary, ascorbic acid vape mod liquid has greater anti-inflammatory potency compared to conventional vape mod liquid. Ascorbic acid use may have protective benefits against mucosal damage and inflammation resulting from chemical exposure, while conventional vape mod use may worsen respiratory health conditions and cause inflammation and oxidative stress. In fact, research on its long-term impacts on human health is needed.

Author contributions: AP: conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing – original draft; **RA:** conceptualization, data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, writing – original draft; **JB:** conceptualization, writing – review & editing. All authors have agreed with the results and conclusions.

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Ethical statement: This study was approved by the Ethics Committee of the Faculty of Medicine, Sultan Agung Islamic University, Semarang (protocol code: 254/VII/2023/Komisi Bioetik). It was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all the subjects involved in the study.

AI statement: The authors stated that no generative AI or AI-based tools were used.

Declaration of interest: No conflict of interest is declared by the authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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