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Article

Melia azedarach Flowers and Their Volatile Components Improved Human Physiological and Psychological Functions

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Abstract: In the present study, we examined the modulatory effects of *Melia azedarach* Linn flowers on human physiological and psychological behaviors. Inhalation of fresh flowers for 20 min decreased salivary amylase activity. Electroencephalogram analysis exhibit that inhalation of fresh flowers reduced alpha brainwave, while gamma, delta, and theta-brainwaves were increased. Moreover, systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were decreased after inhalation of flowers. Furthermore, inhalation of flowers reduced sympathetic nervous system (SNS) activity and increased parasympathetic nervous system (PSNS) activity. In addition, we extracted volatiles from the flowers by the solid-phase micro-extraction (SPME) method and the chemical composition was determined by mass spectrometry. Fifteen compounds were identified, among them benzaldehyde (68.50 %) and phenylacetaldehyde (22.26 %) were the major compounds. Similarly, inhalation of 0.25 % benzaldehyde or phenylacetaldehyde reduced SBP, DBP, HR, and SNS activity, whereas PSNS was increased. Furthermore, the profile of mood states (POMS) scores support that inhalation of fresh flowers significantly reduced depression, confusion, and tension. Anger, fatigue, and vigor were also decreased. These results suggest that *M. azedarach* flowers or their major compounds can be novel modulators of SNS dysfunction as well as aromatherapy.

Keywords: *Melia azedarach*, benzaldehyde, phenylacetaldehyde, autonomic nervous system, psychological behaviors.

Introduction

Essential oils and volatile components from plants have been used for emotional, cognitive, and physical healing since the beginning of recorded human history. Essential oils have been used extensively in aromatherapy for treating various psychophysiological disorders by major civilizations, including Chinese, Indian, Egyptian, Sumerian, and Mayan [1]. Recent studies have reported that olfactory stimulation by inhalation of essential oils and volatile components exerts various psycho-physiological disorders [2,3]. Stith

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et al reported that inhalation of cannabis flowers by human subjects resulted in positive anxiolytic effects [4]. Essential oil from *Canaga odorata* exposure to male mice significantly reduced anxiety and the major constituents responsible for this activity was reported as benzyl benzonate [5].

Melia azedarach Linn*,* popularly known as the "Chinaberry tree" is an ornamental tree of the mahogany family, *Meliaceae*. It is a deciduous and evergreen tree native to Asia and widely distributed in North and South America, Southern Europe, Northern Australia, and Africa [6]. It blooms in the spring, and its lilac flowers have a sweet fragrance. *M. azedarach* has the characteristics of rapid growth, broad root system, which helps soil and water conservation. *M. azedarach* is suitable for urban planting as street tree and landscaping, with its characteristics of heat resistance, early resistance, wind resistance, salt resistance, salt tolerance, and pollution resistance [7,8]. Also, *M. azedarach* was reported to have a phytoremediation property that can accumulate and stabilize cadmium and chromium in metal-contaminated regions [9].

M. azedarach was reported to have both pharmacological and toxicological properties. The leaves, fruits, bark, seeds, and roots of *M. azedarach* are used in traditional medicine in India, China, and Japan [10]. It has been shown to various pharmacological activities, including antifungal, antimalarial, antibacterial, hepato-protective, anti-oxidant, anti-fertility, anthelmintic, antipyretic, and cytotoxic [11-14], while the ingestion of foliage or fruit by cattle [15], pigs [16] and dogs [17] has caused intoxication with fatal outcomes. A case report study indicated that herbal formulation with *M. azedarach* caused gastro-intestinal, cardiovascular, respiratory, and neurological effects and death in severe cases [18].

Previous studies have demonstrated that volatiles of *M. azedarach* possessed strong antimicrobial activity [19,20]. Zakir-ur-Rahman, *et al*.[21] reported that oral administration of alcoholic and aqueous extract of flowers of *M. azedarach* was found to be non-toxic up to a dose of 1500 mg/kg along with mild gross physical and behavioral changes, including vasodilation, vasoconstriction, depression of respiration, and sedative mood. Whereas, intravenous administration resulted in mortality over a dose of 395 mg/kg in small experimental animals. This study indicates that toxicity depends not only on the dose but also on the route of administration. However, other pharmacological and toxicological effects of volatiles of *M. azedarach* were poorly investigated. Therefore, in this study, we aimed to investigate the effects of *M. azedarach* on physiological and psychological changes and look forward to being used as an aromatic healing tree.

Materials and methods

Flowers collection

The flowers used in this study were collected (500 g) from the campus of National Chung Hsing University (GPS, 24°07'15.2"N 120°40'29.8"E) in March 2019 and was identified by Prof Yen-Hsueh Tseng (Department of Forestry, National Chung Hsing University, Taichung, Taiwan). The voucher specimen was deposited in the herbarium of the same university (YHT0339 [TCF]). All the experiments were done with fresh flowers, which were collected on the same day.

Volatile extraction and chemical analysis

To obtain and analyze of floral of *M. azedarach*, the solid-phase micro-extraction (SPME) technique was performed to collect the volatile compounds. A SPME holder and carboxen-polydimethylsiloxane (75 µm) were purchased from Supelco Co. (Bellefonte, PA). Before being used, SPME fibers were conditioned by heating in a hot injection port of a GC at 250°C for 15 min to remove contaminants. The fresh flowers (80 g) were placed in a 125 mL Erlenmeyer flask, sealed with paraffin film, placed in a water bath at 40°C, and the volatile compounds were adsorbed by SPME for 30 min. The volatile compounds were analyzed by ITQ 900 mass spectrometer coupled with the DB-5MS column. The temperature program was as follows: 40°C for 2 min, then increased by 4°C/min to 100°C and then increased 10°C/min to 250°C holds for 5 min. The other parameters were injection temperature, 260°C; ion source temperature, 280°C; EI, 70 eV; carrier gas, He 1 mL/min and mass scan range 40-600 *m/z*. The volatile compounds were identified by Wiley/NBS Registry of Mass spectral databases (V. 8.0), National Institute of Standards and Technology (NIST) Ver. 2.0 GC/MS libraries and the Kovats indices were calculated for all volatile constituents using a homologous series of n-alkanes C_9-C_{24}. The components were identified by co-injection with standards (wherever possible). Quantification was done by an external standard method using calibration curves generated by running GC analysis of representative compounds, which are listed in Table. 1.

Participants and experimental procedure

One hundred undergraduate and post-graduate students volunteered to take part in this study. Before participation, each volunteer completed a health questionnaire and physiological measurements. All participants were self-reported that they were in good health and none were excluded from the study. The study was performed under the ethical standards of the 1991 Declaration of Helsinki. Briefly, "each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study". All subjects gave their informed consent before their inclusion in the study and were free to withdraw at any time. The detailed experimental procedures were described previously [24]. To understand the effect of the behavioral changes after inhalation of fresh flowers of *M. azedarach* or its major compounds, each volunteer's blood pressure, heart rate (HR), sympathetic nervous system activity (SNS), parasympathetic nervous system activity (PSNS), and heart rate variability (HRV) were recorded before the inhalation. After that, a bunch of fresh flowers was given to inhale during ordinary breathing for 5 min. On the other hand, its major compounds 0.25 % of benzaldehyde or phenylacetaldehyde (100 mL) applied to a piece of absorbent cotton (0.8 x 0.8 cm), and the cotton piece was fitted under the subject's nose and the odor of the compounds were inhaled during ordinary breathing for 5 min. Then, each subject's blood pressure, HR, HRV, SNS, and PSNS were measured using an ANSWatch wrist monitor (Taiwan Scientific Corporation, Taipei, Taiwan; Taiwan Department of Health, medical device product registration number 001525), as described previously [22,23].

Effects of volatile compounds on human physiology and sensory evaluation

To avoid age and gender influences, we randomly selected 13 male and 12 female college students within the age group of 20-30 years. All subjects were healthy and not undergoing any medical treatment during the experimental period. The subjects were instructed to have sufficient sleep the previous night and not to drink, eat, or be involved in sports for at least 2 hours before each test. Verbal and written informed consent was obtained from all volunteers after informing them of the study design, intervention, data collection, and the rights of the participants. Interventions and data collection were performed by the researcher and trained research assistants. The non-invasive human study was approved by the University Ethics Committee and performed in accordance with the ethical standards of the responsible committee on human experimentation outlined in the 1991 Helsinki declaration.

Salivary amylase activity test

The salivary amylase activity could reflect the psychological stress of the human [41]. To evaluate the modulatory effect of *M. azedarach* flowers on human psychological stress, salivary amylase activity was measured before and after inhalation of flowers. The saliva under the tongue of the subject was collected with a test strip for 30 seconds, and then the salivary amylase activity analyzer (Nipro Co., Japan) was used for analysis and data collection.

Electroencephalogram (EEG) analysis

EEGs are indicators of human cognitive physiology, which measure the electrical activity produced by neurons of the cerebral cortex by detecting signals at the scalp. The signal is amplified and presented graphically with electrical potential on the vertical axis and time on the horizontal axis. EEG waves are classified according to their frequency such as alpha (α, 8Hz

- 12Hz), beta (β, 12Hz-30Hz), theta (θ, 4Hz-7Hz), and delta (δ, 0.1Hz-3Hz). The detection of brainwave signals were performed by Neurosky mind wave mobile Ii brainwave starter kit (Neurosky, Inc., San Jose, CA, USA), placed on FP1 position according to international 10-20 system, to record the change of subject's EEG before and after smell the flowers. The subjects were monitored and measured in three stages. The first stage was monitored for 5 minutes before smelling, the second stage was monitored for 20 minutes during smelling, and the third stage was monitored for 5 minutes after the smelling. Then the recorded brainwaves were analyzed by brain wave monitoring and feedback management software (MindWave Mobile, Sheng Hong Precision Technology Co., Taipei, Taiwan).

Autonomic system (ANS) activity analysis

To understand the effects of the ANS activity after smelling the flowers, each volunteer's blood pressure, heart rate (HR), sympathetic nervous system activity (SNS), parasympathetic nervous system activity (PSNS), and heart rate variability (HRV) is the physiological phenomenon of variation in the time interval between heartbeats and it is measured by the variation in the beat-to-beat interval were recorded by using an ANSWatch wrist monitor. ANSWatch test takes about 7 min and outputs 8 parameters, including systolic blood pressure, diastolic blood pressure, HR, SNS activity (low-frequency, LF), PSNS (high- frequency, HF), sympatho-parasympathetic balance index LF/HF, HRV, and several irregular heartbeats. The data obtained from the ANSWatch wrist monitor were analyzed by ANSWatch Manager Pro software.

Profile of mood states (POMS) analysis

In this study, the POMS, a globally standardized, self-administered, 65-item questionnaire (including 7 dummy items), was used to assess moods before and after inhalation of fresh flowers or their major compounds. Each item was rated on a 5-point Likert scale of 0 to 4, ranging from "not at all" to "extremely". These raw scores were added to generate 6 subscales of emotional state: tension-anxiety, depression-dejection, anger-hostility, vigor, fatigue, and confusion, as described previously [24].

Statistical analysis

Data are expressed as mean ± SD. All data were analyzed using the statistical software Graphpad Prism version 6.0 for Windows (GraphPad Software, La Jolla, CA). Statistical analysis was performed with Student's *t*-test. *P* values of less than 0.05*were considered statistically significant for pre-inhalation *vs* post-inhalation groups.

Results and discussion

Volatile analysis of M. azedarach flowers

The chemical composition of *M. azedarach* flowers was shown in Table 1. Based on SPME analysis, we found that benzaldehyde (68.50 %) and phenylacetaldehyde (22.26 %) were represented the major constituents of the flower essential oil. The remaining components were naphthalene (2.53 %) and chrysanthenone (0.96 %), Benzene (0.59 %), caryophyllene (0.58 %), α-copaene (0.41 %), *cis*-chrysanthemyl alcohol (0.30 %), cyclohexene (0.30 %), cyclohexene (0.24 %), benzyl alcohol (0.19 %), 4-anisaldehyde (0.17 %), 1-hexnaol (0.15 %), α-cubebene (0.15 %), and germacrene B (0.15 %). Our results were in accordance with a previous report that benzaldehyde and phenylacetaldehyde were the major compounds emitted by *M. azedarach* flower [25].

Effects of inhalation of *M. azedarach* flowers on salivary amylase secretion

Recently, salivary amylase has emerged as a valid and reliable marker for determining the autonomic nervous system activity in stress research and is, therefore, an important biomarker to consider in behavioral medicine [26]. The salivary amylase is regulated by the sympathetic-adrenal medullary system, therefore psychological stress would cause changes in salivary amylase [27]. Lim had studied the correlation between salivary α-amylase, anxiety, and game records in the archery competition. The results revealed that the increase of cognitive anxiety is directly proportional to the salivary α-amylase concentration, which decreased the overall performance during the archery competition [28]. This study suggested that during archery competition, anxiety hinders

Table 1. Chemical composition of essential oils of *M. azedarach* flowers

No.	Constituent	RT (min)	KI^{exp}	KI^{ref}	Percentage (%)
1	1-Hexnaol	5.10	831	865	0.15
2	Benzaldehyde	10.42	964	964	68.50
3	Benzyl alcohol	14.10	1039	1031	0.19
4	Phenylacetaldehyde	14.49	1047	1051	22.26
5	Chrysanthenone	17.94	1114	1121	0.96
6	*cis*-Chrysanthemyl alcohol	20.11	1160	1163	0.30
7	Benzene	20.39	1166	645	0.59
8	4-Anisaldehyde	24.75	1258	1239	0.17
9	Cyclohexene	28.09	1330	677	0.30
10	α-Cubebene	28.75	1346	1349	0.15
11	α-Copaene	29.98	1373	1372	0.41
12	Cyperene	31.30	1402	1399	0.24
13	Caryophyllene	31.82	1416	1415	0.58
14	Naphthalene	34.98	1491	1181	2.53
15	Germacrene B	37.74	1553	1558	0.15
	Total				97.48

KI^{exp}: Kovat index determined by the experiment
KI^{ref}: Kovat index from the literature[40]
RT: Retention time
Compounds 1, and 3 were alcohols; compounds 2, 4, and 8 were aldehydes; compounds 7, 9, and 14 were hydrocarbons; compounds 10, 11, 12, 13, and 15 were sesquiterpenoids; compound 5 and 6 were monoterpene

performance, and this effect may be related to the increase in salivary α-amylase levels. In this study, a decrease in salivary amylase content (18.60 to 15.85 kIU/L) was found after inhalation of *M. azedarach* flowers (Fig. 1). However, there was no significant difference between the pre-inhalation and post-inhalation of *M. azedarach* flowers for 20 min (Student's *t*-test), suggesting that the flowers of *M. azedarach* could partially reduce the psychological stress. Table 2 shows the socio-demographic characteristic details of the study participants. We also found that either gender of physical appearance of the participants were not influence the results.

Effects of inhalation of *M. azedarach* flowers on electroencephalogram (EEG)

The brainwave frequency of the human is between 1-40 Hz. Gamma-wave is greater than 38 Hz, which means that is in a highly alert state; the beta-wave belongs to 12-38 Hz, that indicated in concentration or tension status. The brainwave of 8-12 Hz belongs to alpha-wave, which appears when the human body is relaxed [29]; Theta-wave and delta-wave are 4-8 Hz and 0.5-4 Hz, respectively, which are more likely to appear when sleeping [30]. Several studies have been reported the effects of fragrance on EEG activity, the major findings of those studies are a decrease of alpha-brainwaves during and after exposure to fragrances [1,31]. According to our results, it was found that inhalation of *M. azedarach* flowers for 20 min, decreased the levels of low-α (8-9 Hz) and high-α frequencies (10-13 Hz), whereas low-β (13-17 Hz) and high-β (18-30 Hz) levels were unaffected (Figure 2a-d). This data is consistent with Masago, *et al.*[32] reported that inhalation of plant volatiles, such as lavender, eugenol, and chamomile decreased α-1 (low-α) brainwave activity, whereas other brainwaves were unaffected. On the other hand, low-γ, high-γ, δ- and θ-frequencies were increased (Fig. 2e-h). Since, the δ- and θ- brain waves were recorded during low brain activities [33], these data indicating

Table 2. Socio-demographic characteristics of the study group (n = 100)

Variable	Treatment group
Gender	
Male (%)	55[a]
Female (%)	45[a]
Marital status	
Single (%)	100[a]
Married (%)	0[a]
Average age (years)	24.4 ± 6.79[b]
Average weight (kg)	67.03 ± 15.6[b]
Average height (cm)	168.76 ± 9.32[b]
Average BMI (kg/m^2)	19.79 ± 4.04[b]
Underweight (%)	40[a]
Normal (%)	55[a]
Overweight (%)	5[a]

[a]Data is presented as frequency (percent) (N = 100)
[b]Mean ± standard deviation

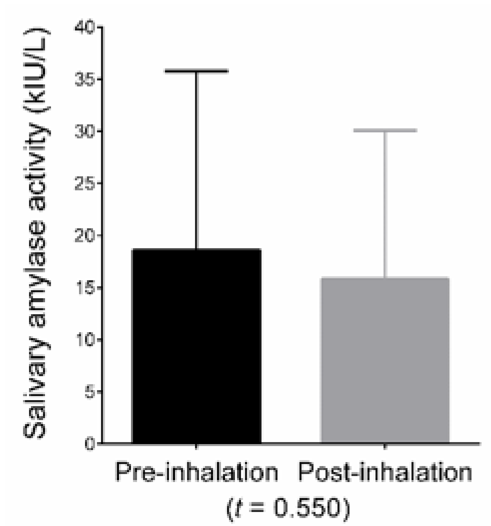

Figure 1. Changes of salivary amylase activity after inhalation of *M. azedarach* flowers. Values represented the differences between the pre-inhalation and post-inhalation activity (kIU/L). Values were expressed as the mean ± SD (n=20). Student's *t*-test was applied to evaluate the salivary amylase activity difference between pre- and post-inhalation of *M. azedarach* flowers. There were no significant differences in pre- and post-inhalation

that the fragrance of *M. azedarach* flowers may increase physiological and mental relaxation.

Effects of *M. azedarach* flowers on ANS activity

The human body's physiological activities include extremely complex checks, balance, and coordination processes that lead to homeostasis. The main function of ANS is to maintain a constant environment of the human body so that the functions and activities between various tissues and organs can maintain the most coordinated state [34]. In the human body, the ANS is mainly distributed in smooth muscle, myocardium, and various glands, while controlling breathing, circulation, digestion, metabolism, and other non-autonomous reflex

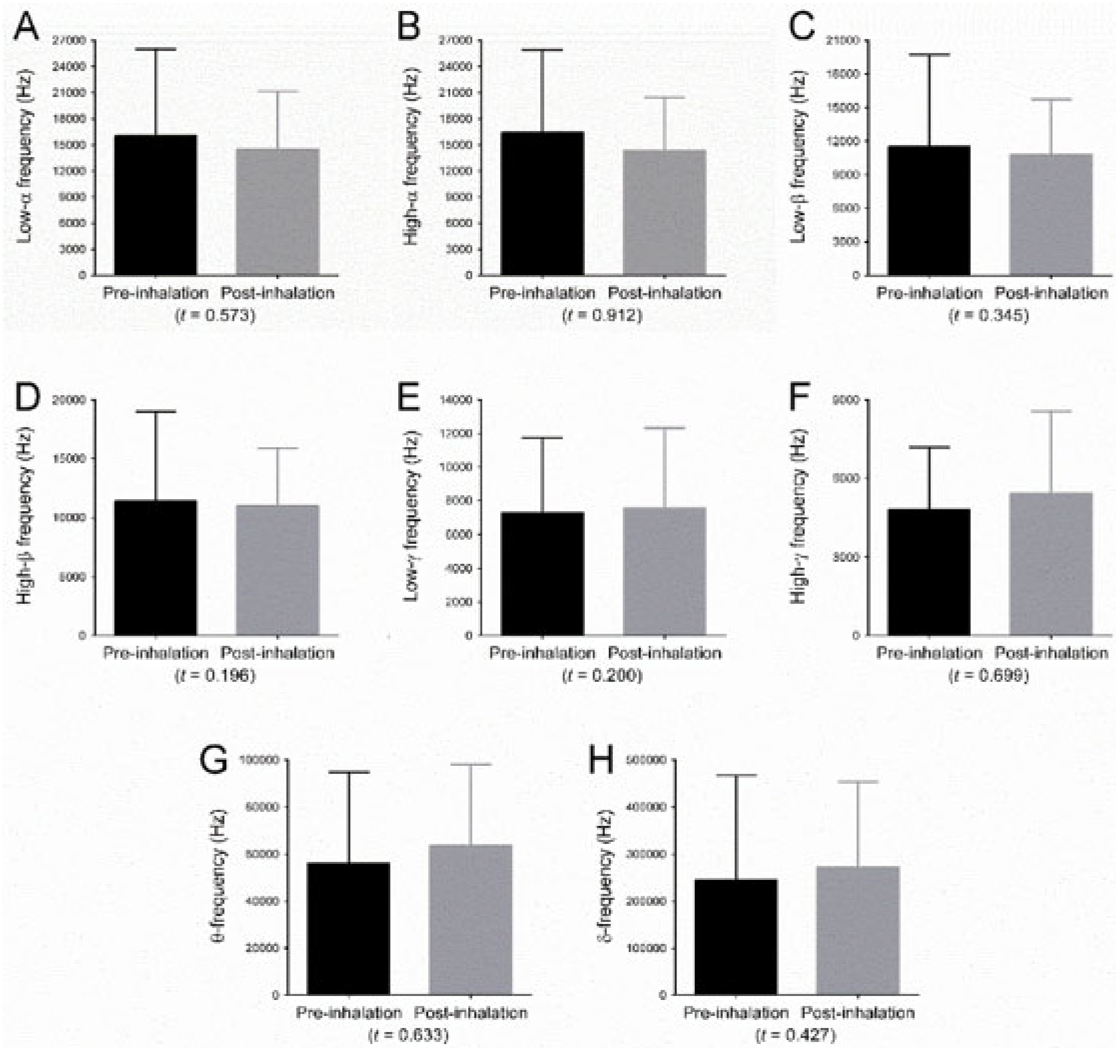

Figure 2. Effects of *M. azedarach* flowers on brainwave changes in human. Histogram represented the changes in (A) low-a, (B) high-a, (C) low-b, (D) high-b, (E) low-g, (F) high-g, (G) d and (H) q-brainwaves (Hz) between before and after inhalation of flowers. Values were expressed as the mean ± SD (n=20). Student's *t*-test was applied to evaluate the difference between pre- and post-inhalation of *M. azedarach* flowers. There were no significant differences in pre- and post-inhalation

processes necessary for life [22]. According to the results obtained in this study, the systolic blood pressure of participants was decreased (Fig. 3a), while the diastolic blood pressure was unaffected (Fig. 3b). In addition, the heartbeat frequency of subjects was slow down (Fig. 3c). Furthermore, the total ANS activity was increased, as indicated by the sympathetic nervous activity was decreased (Fig. 3d) and parasympathetic nervous activity was increased (Fig. 3e), whereas the total sympathetic/parasympathetic balance index (SNS/PSNS) was decreased after inhalation of the flowers for 20 minutes (Fig. 3f). This result was consistent with Igarashi, *et al*.[35] demonstrated that inhalation of fresh rose flowers significantly increased parasympathetic nervous activity as a sign of comfortable and natural feeling. Also, it was previously reported that alcoholic and aqueous extracts of fresh flowers and berries of M. *azedarach* exhibited mild central nervous system (CNS) sedative effects in experimental animals [21]. Therefore, it is noteworthy that the total ANS activity was improved, which means that individuals could look fresh after inhalation of flowers. Overall, the scent of *M. azedarach* flowers tends to relax.

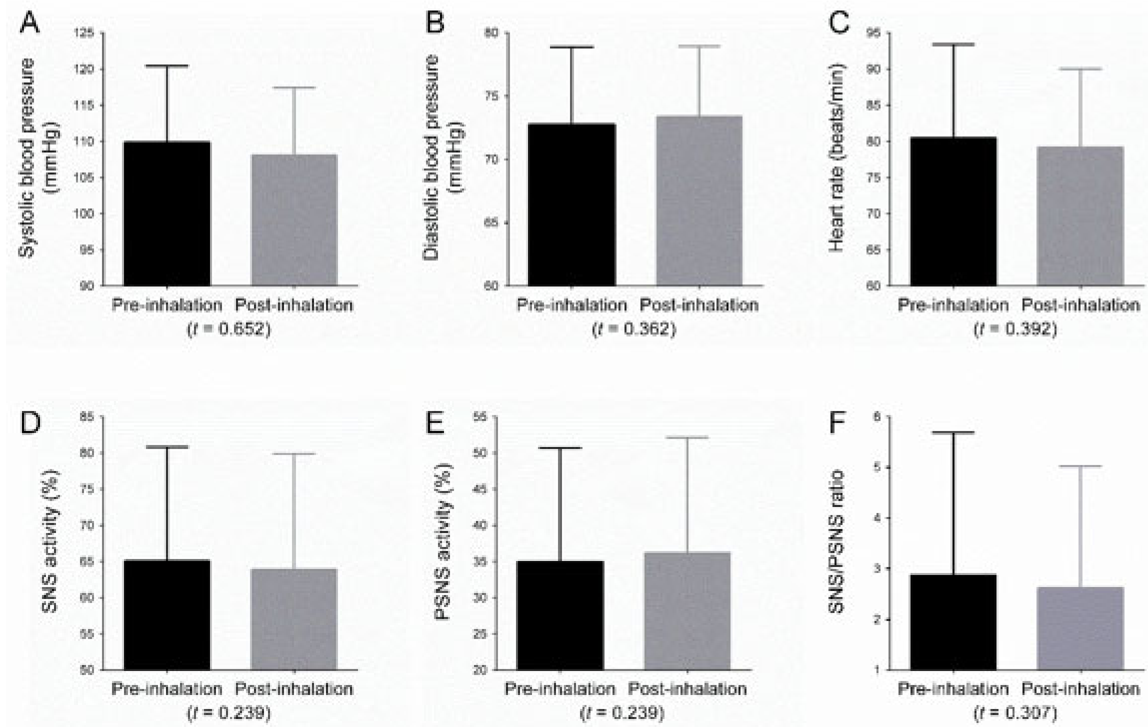

Figure 3. Effect of *M. azedarach* flowers on human autonomic nervous system activity. Histogram represented the changes between (A) SBP: systolic blood pressure; (B) DBP: diastolic blood pressure; (C) HR: heartbeat frequency; (D) SNS: sympathetic nerve activity; (E) PSNS: parasympathetic nerves activity and (F) ANS/PNAS ratio of before and after inhalation of flowers. Values were expressed as the mean ± SD (n=20). Student's *t*-test was applied to evaluate the difference between pre- and post-inhalation. There were no significant differences in pre- and post-inhalation

Effects of *M. azedarach* flowers on mood states (POMS)

Understanding the effects of inhalation of *M. azedarach* flowers on the subject's mood states, the Profile of Mood States (POMS) test was used to assess mood changes after inhalation of *M. azedarach* flowers for 20 min. As shown in Fig. 4a-c, inhalation of *M. azedarach* flowers significantly decreased the average scores of depression from 8.36 to 4.6 (P = 0.045), tension from 8.88 to 5.6 (P = 0.03) and confusion from 9.8 to 6.48 (P = 0.02). In addition, inhalation of *M. azedarach* flowers decreased the average score of anger, fatigue, and vigor from 5.58 to 3.56 (P = 0.235), 10.0 to 8.08 (P = 0.106), and 15.7 to 15.3 (P = 0.413), respectively, however, these reductions were not statistically significant (Fig. 4d-f). The POMS scores after inhalation of *M. azedarach* flowers are comparable with baseline scores. The *M. azedarach* flowers-mediated reduction in depression was in agreement with a previous study that alcoholic and aqueous fresh flower extracts mildly increased CNS sedation in lab animals [21]. Taken together, these data strongly support the result of ANS analysis. These results postulated that inhalation of *M. azedarach* flowers could partially reduce negative emotion and improved behavior functions.

Effects of major compounds of *M. azedarach* flowers on ANS activity

Matsubara and Kawai [36] studied physiological relaxative effects of volatiles of Japanese cedar and found that the participants exposed to cedar volatiles decreased salivary amylase activity and ANS activity and emotion were improved. Later, it was reported that D-limonene and α-pinene, are the functional components of Japanese cedar, which enhanced PSNS activity and decreased heart rate [37,38]. Fabes [39] examined olfaction and young children's odor preference and found that children's behavioral preferences were signi-

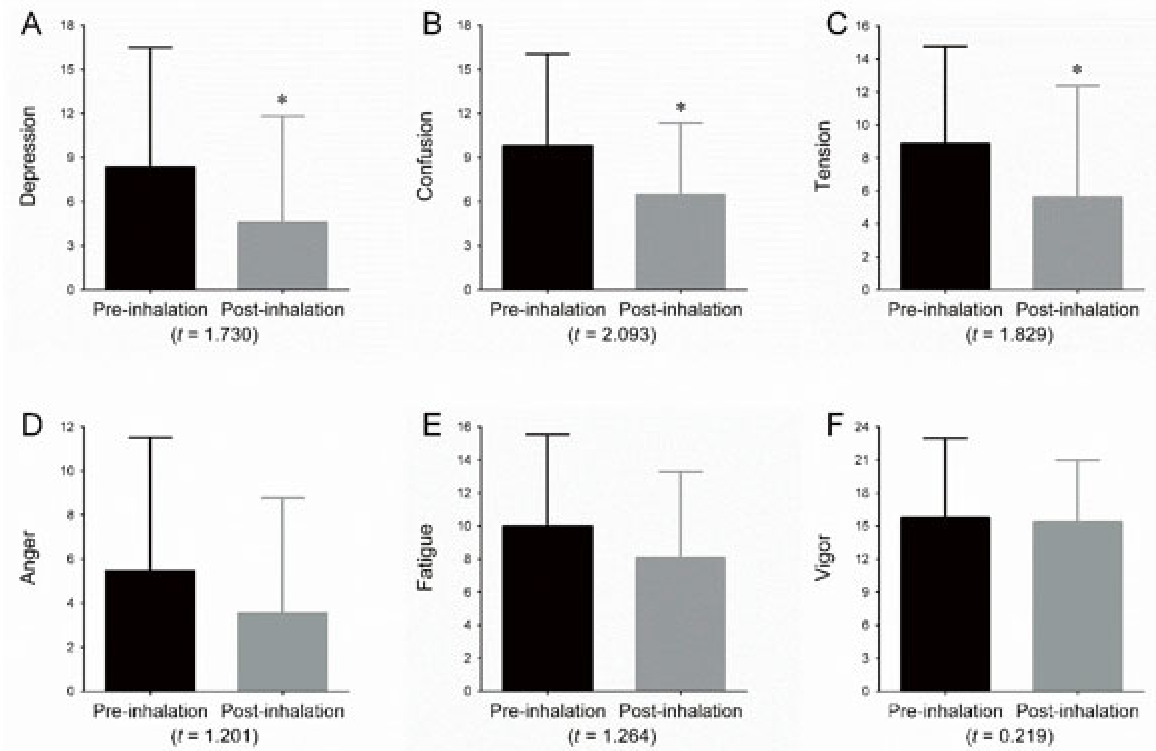

Figure 4. Effects of *M. azedarach* flowers on profile of mood states (POMS) in human. Values represent the POMS cores between pre- and post-inhalation of *M. azedarach* flowers. The POMS score was sub-scaled in to (A) depression, (B) confusion, (C) tension, (D) anger, (E) fatique and (F) vigor. Values were expressed as the mean ± SD (n=20). Student's *t*-test was applied to evaluate the difference between pre- and post-inhalation. There were no significant differences in pre- and post-inhalation. * P<0.05 was statistically significant compared with pre-inhalation

ficantly influenced by odor, indeed benzoldehyde is the most preferred odor of the children. However, detailed physiological and psychological changes in human subjects by penzaldehyde were poorly explored. Therefore, we sought to examine whether benzaldehyde and phenylacetaldehyde, which are major components of *M. azedarach* flowers have ANS regulatory effects. Volunteers were exposed to 0.25 % benzaldehyde with olive oil and 0.25 % phenylacetaldehyde with jojoba oil to determine which compound may have a potent effect on human physiology and psychology. Our result showed that inhalation of 0.25 % benzaldehyde decreased systolic blood pressure, heart rate, and SNS activity, while PSNS actively was increased (Fig. 5a-f). Similarly, inhalation of 0.25 % phenylacetaldehyde decreased SNS activity and increased PSNS activity (Fig. 6a-f). However, the decrease of SNS and increase of PSNS by either 0.25 % benzaldehyde or 0.25 % phenylacetaldehyde were not statistically significant.

Conclusions

This study suggests that volatiles of *M. azedarach* flowers tent to relax the human body and reduce negative emotion. Inhalation of *M. azedarach* flowers and its major compounds benzaldehyde and phenylacetaldehyde partially slow down blood pressure, decrease SNS activity, and increased PSNS activity. Therefore, we infer that the major components benzaldehyde and phenylacetaldehyde may responsible for the improved physiological or physiological functions of *M. azedarach* flowers. The volatile components of *M. azedarach* flowers can be a considerable candidate for aromatherapy.

Declaration of competing interests

The authors declare no conflict of interest.

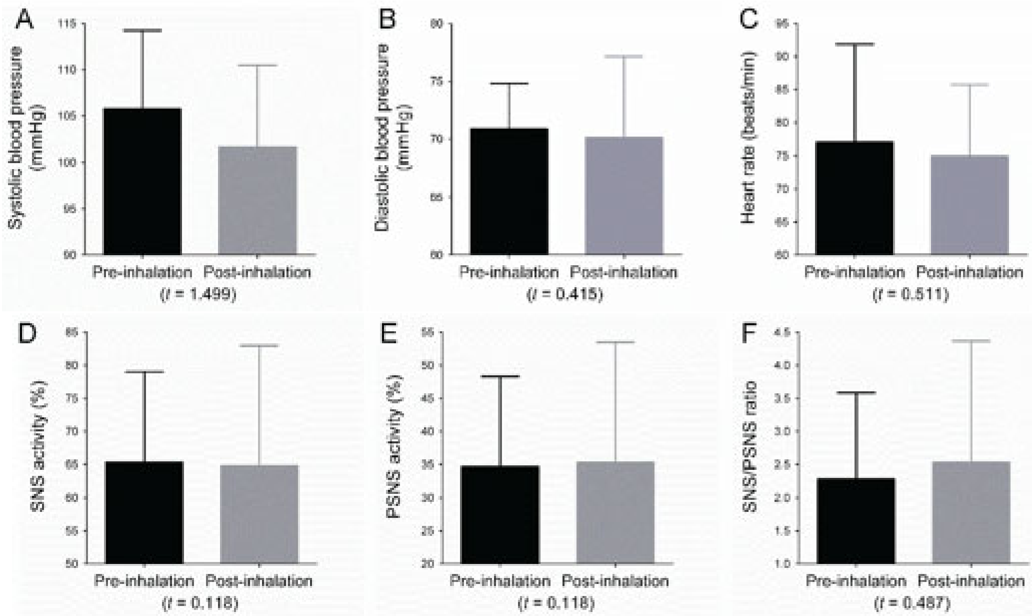

Figure 5. Effect of 0.25 % benzaldehyde on human autonomic nervous system activity. Histogram represented the changes between (A) SBP: systolic blood pressure; (B) DBP: diastolic blood pressure; (C) HR: heartbeat frequency; (D) SNS: sympathetic nerve activity; (E) PSNS: parasympathetic nerves activity and (F) ANS/PNAS ratio of before and after inhalation of 0.25% benzaldehyde. Values were expressed as the mean ± SD (n=20). Student's *t*-test was applied to evaluate the difference between pre- and post-inhalation. There were no significant differences in pre- and post-inhalation

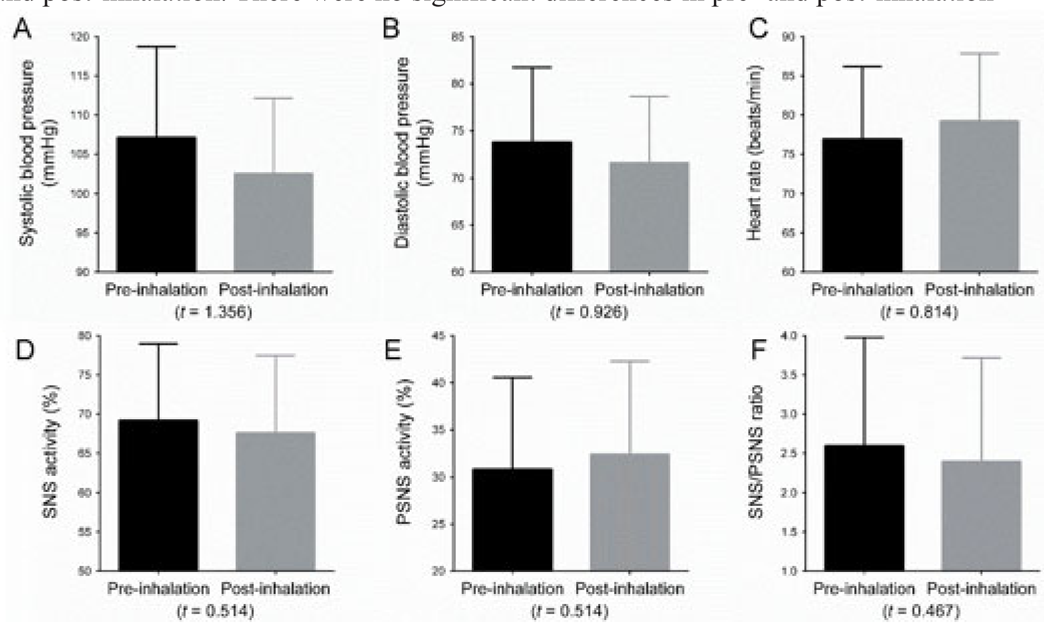

Figure 6. Effect of 0.25% phenylacetaldehyde on human autonomic nervous system activity. Histogram represented the changes between (A) SBP: systolic blood pressure; (B) DBP: diastolic blood pressure; (C) HR: heartbeat frequency; (D) SNS: sympathetic nerve activity; (E) PSNS: parasympathetic nerves activity and (F) ANS/PNAS ratio of before and after inhalation of 0.25% phenylacetaldehyde. Values were expressed as the mean ± SD (n=20). Student's *t*-test was applied to evaluate the difference between pre- and post-inhalation. There were no significant differences in pre- and post-inhalation

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