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Research Article

Differential Contribution of Jasmine Floral Volatiles to the Aroma of Scented Green Tea

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Tea volatiles' generation and retention over manufacturing processes are crucial for tea quality. In this study, floral volatile adsorption and retention in green tea scented with *Jasminum sambac* flowers were examined over the scenting process. Out of 34 enhanced volatiles in the scented tea, β-ionone, β-linalool, indole, and methyl anthranilate were the most potent odorants with 5.1–45.2-fold higher odor activity values than the corresponding controls in the nonscented tea. Scenting efficiencies for the floral volatiles retained in the scented tea (the percentage of volatile abundance over its corresponding amount in jasmine flowers) ranged from 0.22% for α-farnesene to 75.5% for β-myrcene. Moreover, due to additional rounds of heat treatment for scented green tea manufacturing, some volatiles such as carotenoid-derived geraniol and β-ionone and lipid-derived (Z)-jasmone were heat-enhanced and others such as nonanal were heat-desorbed in the scented green tea. Our study revealed that dynamic volatile absorption and desorption collectively determined tea volatile retention and tea aroma. Our findings may have a great potential for practical improvement of tea aroma.

1. Introduction

Tea is a beverage globally consumed due to its pleasant flavor and health benefits against chronic pathologies such as cancer and cardiovascular diseases [1]. The aroma is an important criterion in the evaluation of tea quality. Extensive studies have been conducted to elucidate tea aroma formation [2, 3]. Intact fresh tea leaves hardly have any scent and distinct aromas of differently made teas are formed from their metabolic precursors present in tea leaves over their manufacturing processes [3]. For example, C13-norisoprenoid volatiles such as β-ionone and theaspirone are generated from carotenoids due to enzymatic and nonenzymatic degradation [4]. Fresh and greenish odorants such as (E)-2-hexanal and (Z)-3-hexanol are derived from lipid oxidation [5]. However, these volatiles generated from tea leaves over the manufacturing process are readily released into air and get lost. Meanwhile, substantial amounts of these volatiles are captured and retained in the tea leaf matrix. Therefore, tea aroma is determined not only by volatiles generation, but also by their retention in the processed tea leaves. It is obvious that odorants generated over the manufacturing processes are partially retained in the tea leaf matrix due to the dynamic volatile adsorption and desorption. Nevertheless, this dynamic process is crucial to tea flavor but is rarely investigated.

The jasmine flower scented green tea practically exemplifies floral scent enhancement of green tea owing to the consequence of tea adsorption and desorption of the volatiles released from the *Jasminum sambac* flowers. Generally, the manufacturing process for jasmine flower scented green tea (jasmine tea in short) includes multiple rounds of scenting and drying steps. For scenting, green tea processed in the conventional way is mixed with fully opened fresh jasmine flowers and piled up for several hours. Then, the flowers are removed and the scented tea leaves are heat-dried (at 90°C

to 100°C for 1 h) [6, 7]. Depending on the desired aroma intensity, this scenting (and heating) process can be repeated several times. In this way, the characteristic jasmine scented tea aroma forms [8]. The aroma constituents in the jasmine tea have already been profiled [8–10] and linalool and methyl anthranilate (in addition to a few other compounds) are identified as the potent odorants [8]. However, none of the studies has focused on the dynamic adsorption and desorption of jasmine floral volatiles and their differential contributions to the aroma quality of the scented green tea. Understanding the mechanisms underlying the adsorption/desorption of the floral volatiles will surely be helpful to better elucidate tea aroma formation and retention.

In this study, volatile profiles of jasmine scented and nonscented green teas and fresh jasmine flowers were compared for identifying the key floral odorants absorbed by the scented green tea and the factors affecting their adsorption/desorption over the manufacturing process. Our study revealed differential contribution of jasmine floral volatiles to the characteristic aroma of the scented green tea. Our findings not only shed light on the mechanism of scented tea aroma formation but also open a new horizon towards tea flavor improvement.

2. Materials and Methods

2.1. Chemicals. Authentic standards of linalool, (*E*)-linalool oxide A (furanoid), (*Z*)-linalool oxide B (furanoid), (*E*)-linalool oxide C (pyranoid), geraniol, citral, β-myrcene, D-limonene, β-ocimene, nerol, nerolidol, β-ionone, geranyl acetone, naphthalene, (*Z*)-3-hexen-1-ol, eugenol, nonanal, benzyl alcohol, benzene acetaldehyde, methyl salicylate, (*Z*)-3-hexenol acetate, 3-octen-1-ol, indole, and ethyl decanoate were purchased from Sigma-Aldrich (Shanghai, China). (*Z*)-Jasmone was purchased from Aladdin Industrial Inc. (Shanghai, China).

2.2. Plant Materials and Scenting Process. Shoot tips with two folded leaves were plucked from 10-year-old plants of *Camellia sinensis* var. *sinensis* cv. "Jin-Xuan" that were grown at Wanxiu district, Wuzhou city, Guangxi, China (23°47′58″N, 111°31′48″E). Green tea was prepared using a standard pan-fire process typically applied in local tea industries. This included indoor spreading of harvested tea crops at about 0.5–1.0 kg m^{-2} for 2-3 h at room temperature immediately after plucking, heat inactivation of enzymes in a pan at 220°C for 5 min, and rolling and drying (120°C for 1 h). For the scenting process, fully opened flowers of *Jasminum sambac* were excised and mixed with the preprocessed green tea at a ratio of 4 : 5 (w/w). The mixture of tea and flowers was piled up for 12 h at a temperature ranging from 38°C to 48°C. After scenting, the flowers were removed and the scented leaves were dried at 120°C for 1 h. Two additional rounds of the scenting process were performed as in the first round. All the scented and nonscented green teas with or without heat treatments were then maintained at room temperature for future volatile profiling.

2.3. Volatile Profiling. Tea infusion volatile collection, identification, and quantification were conducted according to Han et al. [11] using a 20 mL glass vessel and a headspace-solid phase microextraction (HS-SPME) fiber, coupled with gas chromatography (Agilent 7697A) and mass spectrometry (Agilent 7890A) (GC/MS). In brief, tea infusions were prepared using 1 g of tea (accurate to four decimals) added to 100 mL boiling double distilled water. After incubation for 5 min, 5 mL of each infusion was transferred to the sampling vessel and headspace volatiles were collected using a 65 μM PDMS/DVB fiber (Supelco, Bellefonte, PA, USA) for 1 h and then deadsorbed in the GC injection port for 5 min at 250°C and resolved by a DB-5 capillary column (30 m × 0.25 mm × 0.25 μm, Agilent) for GC/MS analysis. The oven temperature was programmed according to Han et al. [11]. The assays were carried out in triplicate for each sample. Ethyl decanoate (0.01%, 5 μL) was added to the samples as the internal standard. Volatile compounds were identified by comparing the retention indices (times) with those of either commercial standard substances or the NIST database, according to Wei et al. [12]. Quantification of these compounds in tea infusions was carried out based on the internal standard or the calibration curves prepared with authentic commercial standards [13]. Freshly excised jasmine flowers (1 g, accurate to four decimals) were also placed in the sampling vessel and their headspace volatiles were collected at 38°C and analyzed using the methods described above. The relative concentrations of the volatiles were expressed as μg·kg^{-1} based on SPME sampling and comparison with internal standard (ethyl decanoate).

2.4. Statistical Analysis. The data for all the assays were represented as mean ± SD from three biological replicates (tissue or infusion types). One-way analysis of variance (Duncan's multiple range test) was performed using the DPS software package (http://www.chinadps.net/index.html) for statistical analysis. For detecting variations among samples and to identify a subset of volatiles most important for defining the major variations between the two tea infusions and jasmine flowers, supervised orthogonal partial least-squares discriminant analysis (OPLS-DA) was conducted using volatile compound IDs, tissue/infusion types, and volatile concentrations collected, as input data [14]. Compound ID numbers were plotted onto a 2-dimensional graph with positive values representing compounds that make a positive contribution and negative values representing a negative contribution to tea scent according to Trygg et al. [14] (Figure 1). Data points were identified as being variables of importance (VIP) in the projection based on the OPLS-DA analysis [15].

3. Results and Discussion

3.1. Distinct Volatile Profiles of Scented and Nonscented Green Tea Infusions and Jasmine Flowers. In this study, volatile emission profiles of fresh jasmine flowers (JF) and the infusions of scented (ST) and nonscented (NT) green teas were compared using OPLS-DA approach. Volatile profiles showed good reproducibility and high separability among
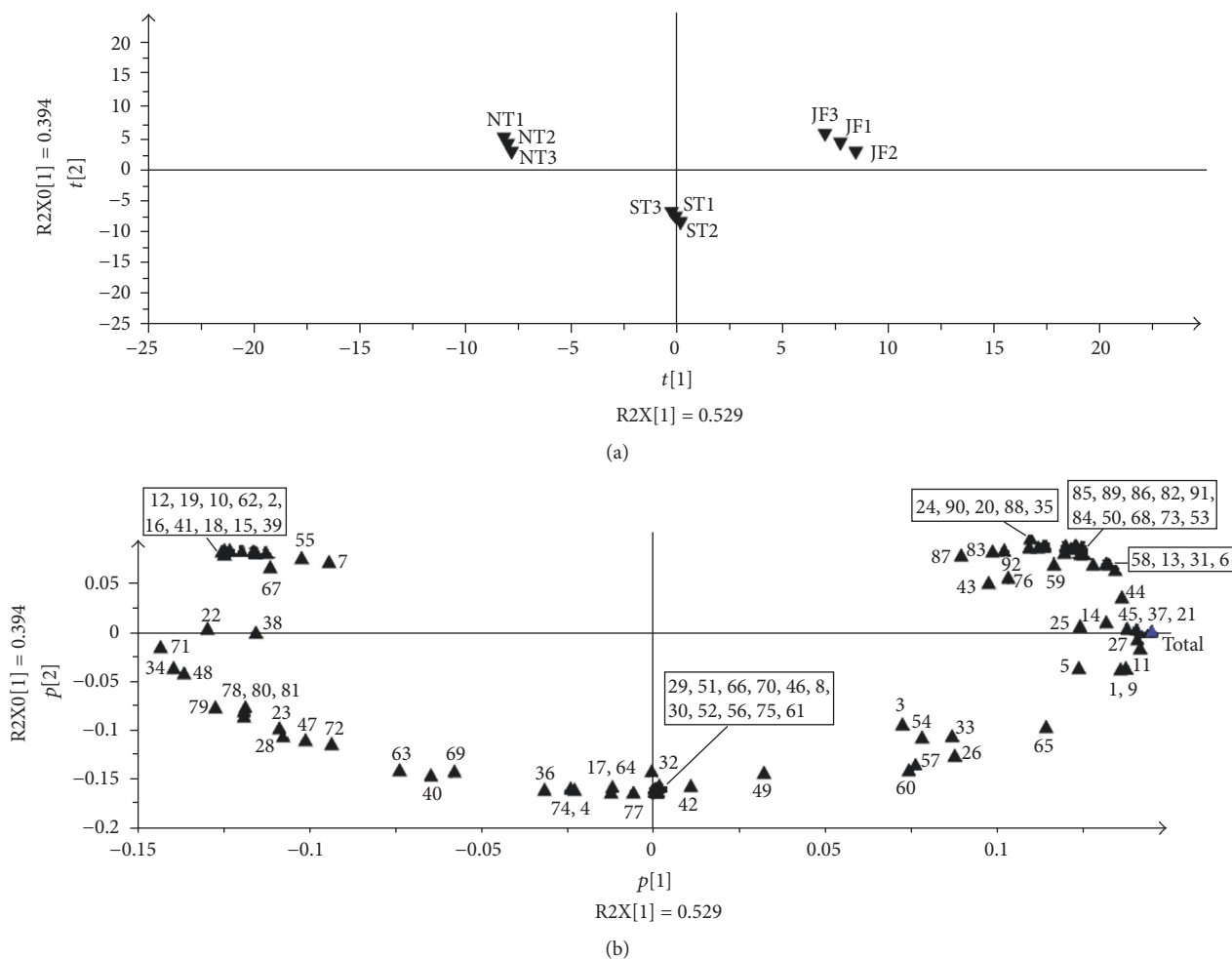
(a)

(b)

FIGURE 1: OPLS-DA score plot (a) and corresponding loading plot (b) derived from the integrated volatile emission data sets of jasmine flowers (JF) and the infusions of scented (ST) and nonscented (NT) green teas. Data were derived from three independent biological replicates. Names of numbered compounds in panel (b) are outlined in Supplementary Table 1. $t[1]$ and $p[1]$ represent principal component 1 (volatile compounds). $t[2]$ and $p[2]$ represent principal component 2 (sample group). Equations R2X[1] = 0.529 and R2X0[1] = 0.394 represent, respectively, the contributions of principal component 1 (R2X[1]) and component 2 (R2X0[1]) to the variation among the ST, NT, and JF. Compounds in the left two quadrants of panel (b) make a negative contribution to tea odor discrimination and compounds in the right two quadrants make a positive contribution. Criteria for selecting top volatiles of importance were in accordance with the SIMCA-P program where a VIP value more than 1 was considered as a positive contributor.

three biological replicates for fresh jasmine flowers and infusions of scented and nonscented green tea (Figure 1(a)). Data points for nonscented green tea were mainly positioned in the top left quadrant, separate from jasmine flower in the top-right quadrant, with scented tea in between and mainly positioned in the lower two quadrants. Replicates of both scented and nonscented green teas were closely localized, while those for jasmine flowers exhibited somewhat high variation, probably due to flowers not strictly picked at the same developmental stage. Generation of many jasmine floral scents (as well as expression of corresponding genes) varies, depending on the flower's developmental stages [16]. An OPLS-DA loading plot showed the correlation of the loading compounds towards different samples, and compounds positioned in the top-right quadrant contributed more to the differences among the three groups than those in other

positions (Figure 1(b)). β-Linalool (#21), indole (#45), benzyl alcohol (#11), and methyl salicylate (#37) were among the top 10 variables of importance (VIP) that mainly specified the volatile profile differences among the three samples (Supplementary Table 2, in Supplementary Material available online at https://doi.org/10.1155/2017/5849501).

In addition, for nonscented tea, nonanal ($14.8 \pm 6.1\,\mu g\,kg^{-1}$) and methyl anthranilate ($10.6 \pm 5.6\,\mu g\,kg^{-1}$) were the most abundant volatiles. For the scented tea, the most abundant volatiles were benzyl acetate ($329.2 \pm 15.8\,\mu g\,kg^{-1}$) and β-linalool ($231.1 \pm 30.5\,\mu g\,kg^{-1}$). For jasmine flower, α-farnesene was the highest at $495.4 \pm 38.8\,\mu g\,kg^{-1}$, followed by β-linalool ($440.5 \pm 2.1\,\mu g\,kg^{-1}$). These results indicated clearly that the increased amounts of β-linalool in the scented tea resulted from the adsorption from jasmine flowers. Although many compounds were common to more

than one emission profile, some were unique to each of them as well (Supplementary Table 3). These dominant volatiles were reported earlier from tea infusions and jasmine flowers [8, 11, 17]. A high level of eugenol was found in the jasmine tea infusion, as reported before [7, 8], but not in the green tea infusion in this study, although this compound was reported as a potent odorant of green tea [17], probably because the manufacturing procedures applied for green teas in this study and previous ones were different. This phenylpropanoid compound is produced by the action of eugenol synthases using coniferyl acetate as a substrate in plants [18], but it is undetectable in the headspace of jasmine flowers [19, 20]. These data together suggest that the enhanced eugenol in jasmine tea might be generated due to possible hydrothermal conversions over the multiple rounds of scenting process, not due to direct adsorption from jasmine flowers, although the details require further investigation. In addition, high levels of β-phenethyl acetate and benzyl tiglate were also found in jasmine tea, but not from green tea or jasmine flowers in this study. β-Phenethyl acetate is reportedly detected from a jasmine flower grown in Egypt [19], but not from those grown in China [20], suggesting a possible difference between cultivars. Benzyl tiglate is emitted from the *Quisqualis indica* flowers but not from jasmine flowers [21]. Further investigation is required to learn the mechanisms for the enhanced levels of the two compounds in jasmine tea.

3.2. Potent Odorants in the Infusions of Scented and Non-scented Green Teas and Jasmine Flowers. Instead of aroma extract dilution analysis [17], the odor activity value (OAV, volatile abundance over its perception threshold) was deployed in this study to evaluate the odor characteristics of tested samples, to avoid losses of highly volatile compounds during extraction, and to eliminate matrix interference with the volatility of an odorant [22]. OAVs were determined for all 27 volatiles detected from the headspaces of tea infusions and jasmine flowers with known threshold values from the literature. Those with OAV > 1 are presented in Figure 2.

For nonscented green tea, out of six compounds possessing odor activity values over 1, β-ionone (OAV, 142.3) and nonanal (14.7) were the most potent odorants (Figure 2), and both derived from metabolite degradation during the manufacturing process [3]. In jasmine flowers, β-linalool was the most potent odorant with OAV of 550.7, followed by indole (393.9). In the scented tea odor, activities of β-ionone and β-linalool were significantly enhanced to 731.3 and 288.9, respectively, which were 5.1- and 45.2-fold higher than the corresponding OAVs in the nonscented tea (Figure 2(a)). Odorants methyl salicylate (OAV, 1.7), geraniol (OAV, 1.7), and (Z)-jasmone (OAV, 3.6) exhibited 18.5-, 7.6-, and 4.7-fold higher odor activity in scented tea than their counterparts in the nonscented tea as well (Figure 2(b)). In addition, based on threshold values obtained, an additional 6 compounds (OAV < 1) had higher OAVs in scented tea than in nonscented tea, including monoterpenoids D-limonene, β-ocimene, and (E)-linalool oxide A (furanoid). These compounds might synergistically contribute to the characteristic jasmine scented tea flavor which was described by Ito and Kubota [9].

Interestingly, the potent odorants nonanal and decanal, both as potent odorants of green teas (nonscented) made from different tea cultivars [11], had higher odor activity values (OAV > 1) in the nonscented green tea than those in the scented tea. We speculated that these might be due to more pronounced heat desorption of these volatiles from scented tea, since several additional rounds of heat treatment were applied for scenting tea manufacturing process. It is known that linalool exhibits strong floral, fruity, and citrus-like scents [23]; indole has fecal, animal-like, floral odor [24]; jasmone has somewhat fruity, floral, and woody aroma notes [25]; and ionone has woody and floral aroma notes [3, 24] (Supplementary Table 4). Since the majority of these floral scent volatiles were more abundant in the infusion of scented tea than that of nonscented tea, the jasmine scented green tea infusion possessed a strong floral scent. Nonanal and decanal contribute waxy, fatty, and aldehydic aromas [26] and thus their reduction in scented green tea might also improve its aroma quality.

3.3. Scenting Enhanced Volatiles in Scented Green Tea. Over the scenting process, the nonscented dry green tea (NT) was mixed with the fresh jasmine flowers (JF) at the ratio of 5/4 (dry tea/fresh flowers, W/W). Floral volatiles whose abundances were higher than those of green tea in the mixed headspace shared by both flowers and tea would be dynamically adsorbed onto the tea leaf matrix until an equilibrium was reached. In order to determine contribution of different JF volatiles to the aroma of scented green tea (ST), headspace volatile profiling was conducted not only for the infusions of NT and ST, but also for JF with an emphasis on the compounds which were identified with authentic standards or exhibited a significantly changed abundance after the scenting process.

Compared to NT, ST possessed 34 enhanced and 3 reduced compounds (Figures 3 and 5). Among the enhanced compounds, seven were dominant volatiles in ST with the abundances 18.2-fold to 173-fold higher than their counterparts in NT (Figure 3(a)). β-Linalool, indole, and benzyl acetate in ST were enhanced 45.3-, 42.4-, and 33.6-fold, respectively. Similarly, another 10 volatiles, but less abundant in ST, were 8.2- to 48.7-fold higher than their corresponding volatiles detected in NT (Figure 3(b)). Moreover, an additional 10 volatiles were detected in ST only, but not in NT (Figure 3(c)). The majority of these compounds are common tea volatiles [2, 27] and all of them were found to be abundant in JF (Figure 3(d)) (except for geraniol and several other compounds) as reported previously [19]. However, a direct abundance comparison of the volatiles detected from tea infusions with those from fresh jasmine flowers was not adequate, due to inconsistent volatile sampling methods applied in this study and the unknown release efficiencies of individual volatiles from solid plant matrix to the headspaces of the volatile sources. The abundances of the JF volatiles presented in Figure 3(d) might be slightly different from the abundances of the floral volatiles the green tea was actually scented with, because the dry green tea used for scenting was 1.2-fold more than JF in this study. Moreover, 27 volatiles, all present in the headspace of JF in high quantities (Figure 3(d))
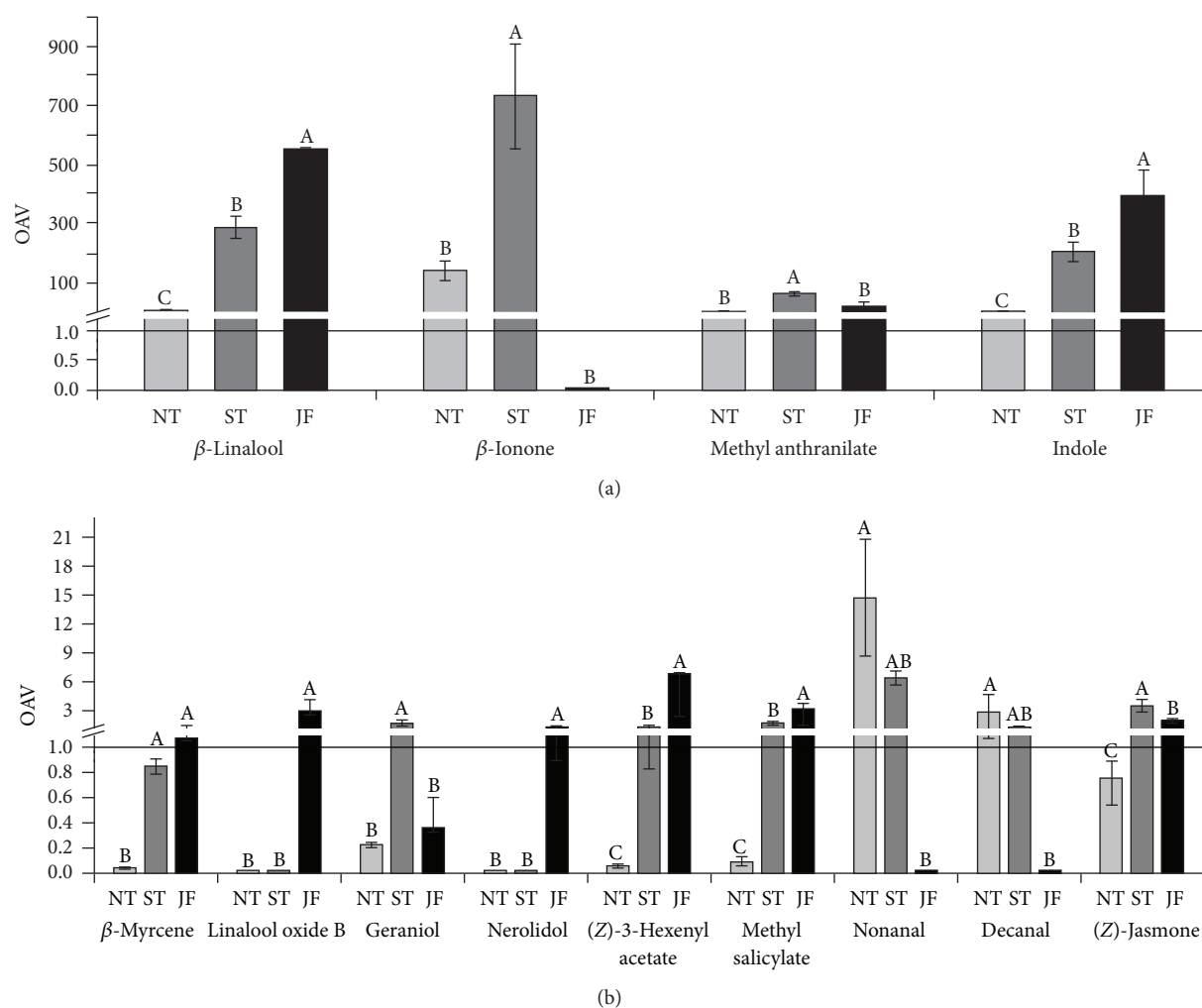
(a)

(b)

FIGURE 2: Odor activity values of volatiles (>1) found in the infusions of scented (ST) and nonscented (NT) green teas and jasmine flowers (JF) based on volatile abundances and their thresholds. Duncan's new multiple range test was performed and the columns labeled with the same letter within the same compound had no significant difference among the three sample types, $P < 0.05$. (a) Volatiles with high OAVs. (b) Volatiles with low OAVs.

with a few exceptions (geraniol, neo-allo-ocimene, and δ-terpinene), were found to be more abundant in ST than in NT (Figure 3), suggesting that the enhancement of these volatiles in ST could substantially result from tea adsorption of these floral volatiles over the scenting process. For geraniol and geranyl acetate, their abundances in the JF headspace were quite low, but both were found to be more abundant in ST infusion than in NT infusion (Figure 3(b)). It is known that tea aroma compounds geraniol and its derivatives can be generated from heat-induced degradation of carotenoids and possibly also from hydrolysis of its glycoside precursor [3]. Our data suggested that chemical conversion, in addition to adsorption, might also occur over the scenting process.

The percentage of the abundance of a volatile in scented tea subtracted from the amount of the counterpart in the non-scented tea over the abundance of the corresponding compound in jasmine flowers was proposed to estimate its scenting efficiency, although differential contributions of floral volatile adsorption and chemical conversion to its

abundance change in jasmine tea are unknown. For those enhanced volatiles, the efficiencies varied, ranging from 0.22% for α-farnesene to 75.5% for β-myrcene (Figure 4). This finding suggested that scenting effectiveness was compound specific and might result from multiple causative factors. Chemical and physical properties, including volatility represented by vapor pressure (mmHg at 25°C), water solubility (mg/L at 25°C), and polarity represented by topological polar surface area, were examined for each volatile in Figure 4 through the public chemical structure databases (http://www.chemspider.com and https://pubchem.ncbi.nlm.nih.gov/) with an emphasis on their correlation with scenting effectiveness. It was noted that majority of the volatiles with high scenting effectiveness (>40%) had high water solubility, ranging from 421.5 mg/L for ethyl benzoate to 32322.0 mg/L for benzyl alcohol. (Z)-3-Hexenol and linalool both possessing high scenting efficiencies (Figure 4) have 16000.0 mg/L and 1590.0 mg/L water solubility, respectively. Exceptions were found for β-myrcene and D-limonene,
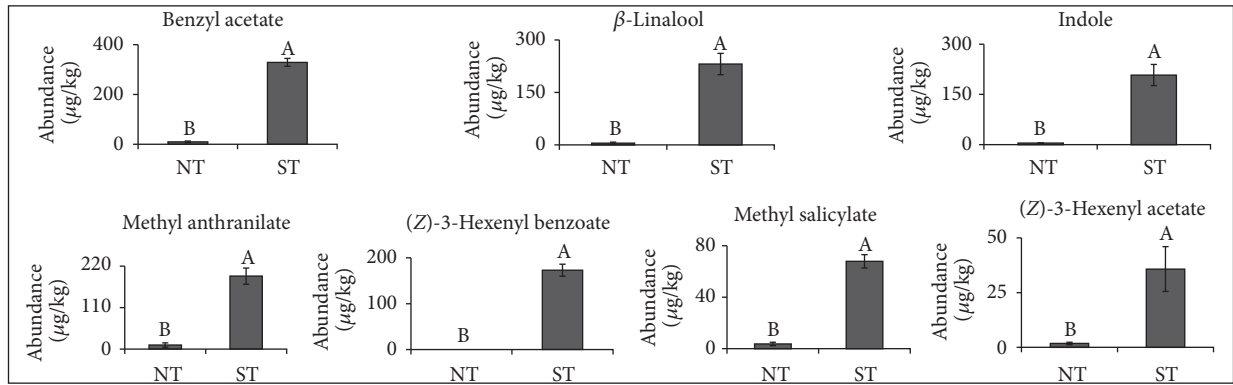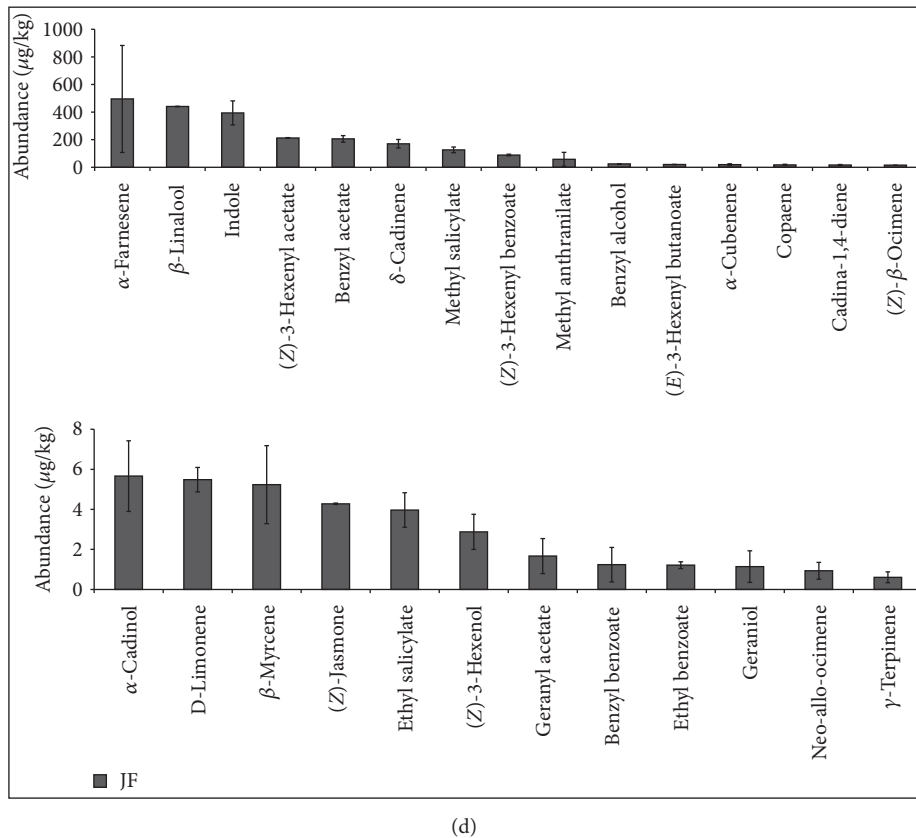
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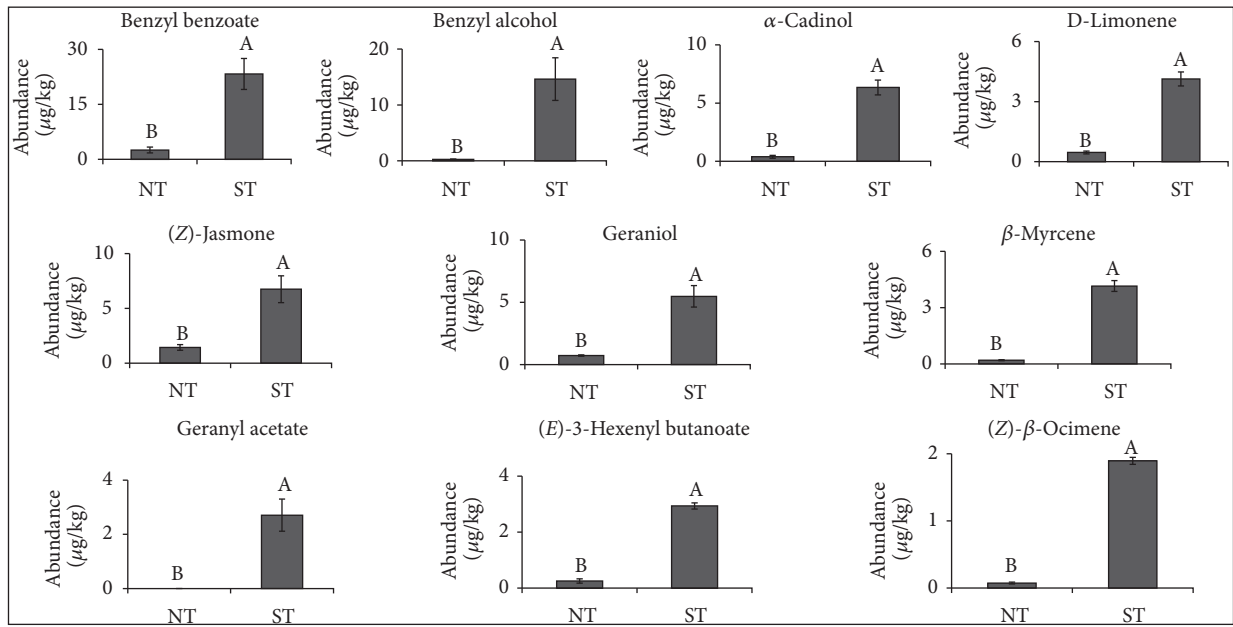
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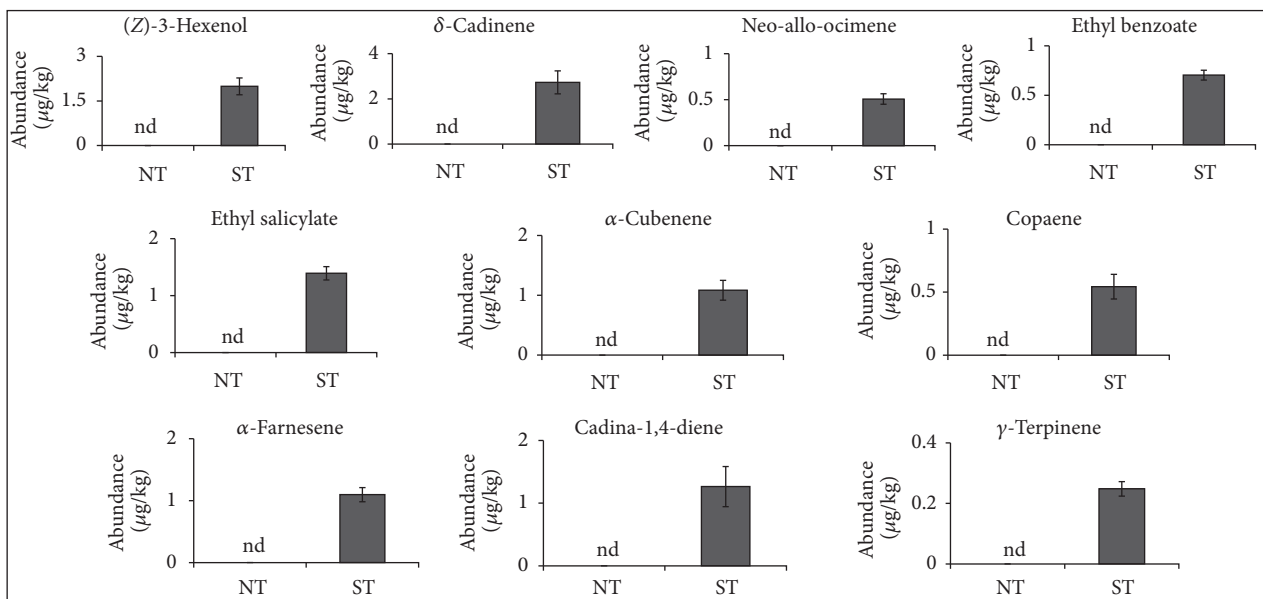
(c)

Figure 3: Continued.

(d)

FIGURE 3: Enhanced floral volatiles in scented tea probably due to tea adsorption. (a) Volatiles with high abundances present in the scented tea; (b) volatiles with less abundances present in the scented tea; (c) volatiles present in scented tea only. (d) Volatiles present in the headspace of fresh jasmine flowers. ST: scented green tea infusion; NT: nonscented tea infusion; JF: jasmine flower; ND: not detected. Duncan's new multiple range test was performed and the columns labeled with the same letter within the same compound had no significant difference among the tested samples, $P < 0.05$. NS: no significant difference detected.
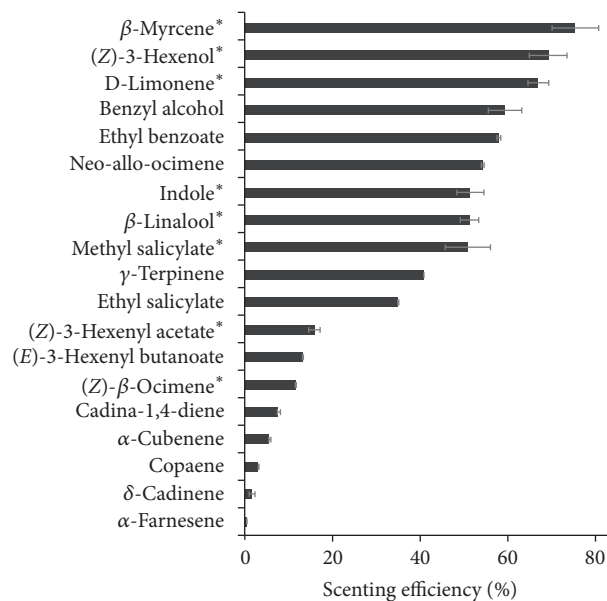

FIGURE 4: Differential scenting efficiencies of jasmine floral volatiles to the scented green tea. Scenting efficiency was calculated as the percentage of the volatile abundance detected in the scented tea subtracted from that of the same compound in nonscented tea over the abundance of the counterpart present in jasmine flower. Compounds labeled with "∗" were identified and quantified with authentic standards.
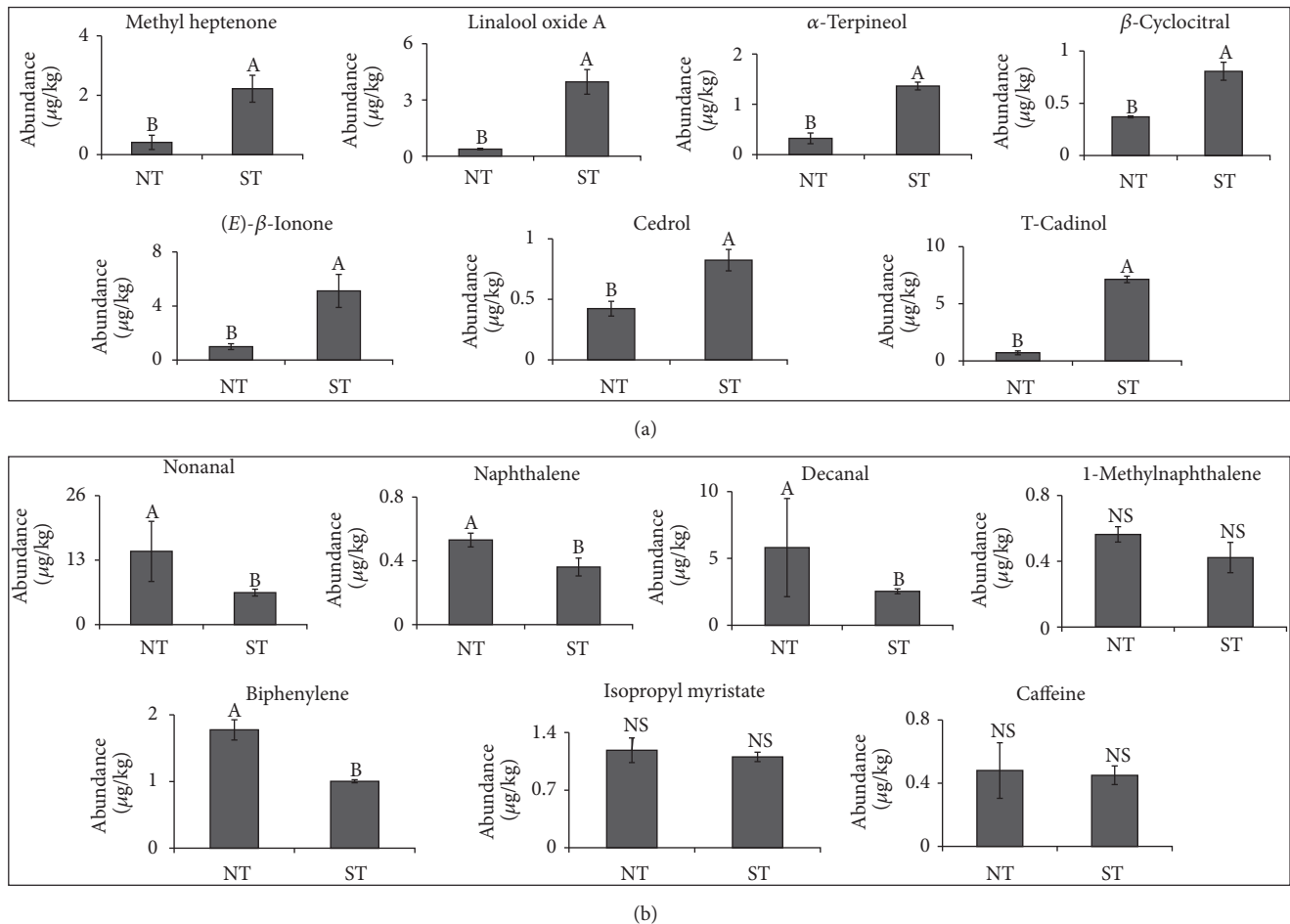
(a)

(b)

FIGURE 5: Volatiles with differential abundances between scented and nonscented teas but undetectable in the jasmine flower headspace. (a) Enhanced volatiles in the scented tea; (b) reduced volatiles in the scented tea. ST: scented green tea infusion; NT: nonscented tea infusion; ND: not detected. Duncan's new multiple range test was performed and the columns labeled with the same letter within the same compound had no significant difference among the three samples, $P < 0.05$. NS: no significant difference detected.

whose water solubility values are relatively low (6.9 mg/L and 4.6 mg/L, resp.), but their volatility values (2.3 mmHg and 1.3 mmHg, resp.) are higher than those of many other aliphatic volatiles presented in Figure 4. Moreover, α-farnesene and δ-cadinene possessing the lowest scenting efficiencies have the lowest values of water solubility (0.01 mg/L and 0.05 mg/L, resp.). It was assumed that volatiles possessing high water solubility could be partially dissolved into the aqueous phase in tea leaf matrix over the scenting process, in which tea leaves could adsorb moisture substantially released from the fresh jasmine flowers. Upon tea infusion preparation with hot water, those volatiles retained in the scented tea would be largely released due to their volatility. Further investigation is required to clarify the correlation between scenting effectiveness and water solubility and volatility of a volatile.

Moreover, surface compounds on the tea leaf matrix might discriminate volatiles with different polarity, which has been found for wool types used with natural and solid adsorbents [28]. In addition, many volatiles are known to be readily modified by the action of plant enzymes, such as

conversion of linalool and geraniol to many other derivatives in plants [29, 30]; hydrothermal conversions of these volatiles also occur. For instance, sesquiterpene α-farnesene is stress induced [31] and can be easily degraded due to photochemical allylic oxidation, hydroxylation, and epoxidation [32]. Consistently, α-farnesene was found to be abundant in the headspace of excised jasmine flowers, but much lower in the jasmine tea and undetectable in green tea in this study.

3.4. Heat-Affected Volatiles in Scented Green Tea.
Over the scenting and heating procedure, 14 volatiles were detected from the infusions of the two teas only, but with differential abundances ($P < 0.05$). These volatiles were undetectable in the jasmine flower headspace, suggesting that the observed differences between the two teas might unlikely result from the direct tea adsorption of these volatiles (Figure 5). Among these volatiles, 7 were found with higher levels in the scented tea compared to the nonscented tea, including linalool oxide A, β-ionone, and another four terpenoids (Figure 5(a)). The observed enhancement of these terpenoids in the scented tea might be the consequence of the heat-induced degradation or

chemical conversion. Mcgraw et al. [33] observed that terpene compounds degraded at high temperatures and turned into other terpene hydrocarbons and oxide terpenes. Tatum et al. [34] reported that α-terpineol component is formed by oxidative degradation of limonene. In this study, it was also observed that abundance of α-terpineol was significantly increased after the scenting process although it was not detected in the jasmine flowers (Figure 5), suggesting that it was likely derived from the hydrothermal conversion over the scenting process.

In addition, reduced levels of a few compounds were found in scented tea compared to nonscented tea (Figure 5(b)), including lipid-derived aldehydes nonanal and decanal [3]. These lipid-derived compounds are heat-induced and most likely also heat-released. Multiple additional rounds of heat treatments after scenting could result in the reduction of these volatiles in the scented tea infusion. Nonanal abundance in green tea is enhanced by steam processing but suppressed by pan-fire processing [11].

4. Conclusions

Our study revealed that jasmine flower scented green tea possessed an enhanced floral scent due to the adsorption of floral scent-related volatiles from the fresh jasmine flowers. This revealed that dry tea had the capacity to adsorb substantial amounts of volatiles from jasmine flowers. Differential contribution of jasmine floral volatiles to the aroma of scented green tea was observed. Moreover, chemical conversion also contributed to the differential abundances of some volatiles between scented and nonscented teas. Our study suggests that adsorption and retention of the volatiles generated endogenously from tea leaves were crucial for maintaining tea aroma and improving tea aroma quality practically.

Additional Points

Practical Applications. This work reveals the differential contributions of jasmine floral volatiles to the scented green tea and suggested that dry tea has a great capacity to adsorb substantial amounts of volatiles from jasmine flowers. Based on what was found in this study, heat treatment may be applied to premade teas with fine-tuned temperatures to desorb those off-flavor compounds. Moreover, pleasant aroma either from natural sources or from artificial mixtures can also be applied to enhance tea aroma with a specific desired odor.

Conflicts of Interest

The authors declare that they have no conflicts of interest regarding the publication of this paper.

Authors' Contributions

Shu Wei designed the experiments and interpreted the results. Jian-Xia Shen and Guo-Feng Liu helped to do OPLS-OD data analysis. Mohammad M. Rana drafted the manuscript. Tie-Jun Ling and Margaret Y. Gruber revised the manuscript. Jian-Xia Shen and Mohammad M. Rana are equal contributors.
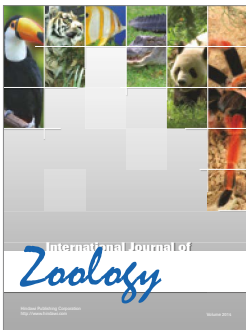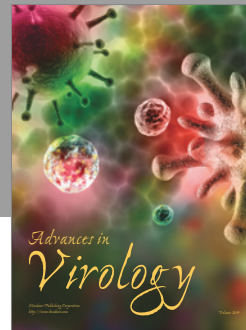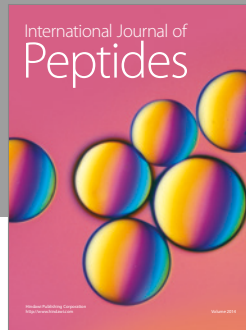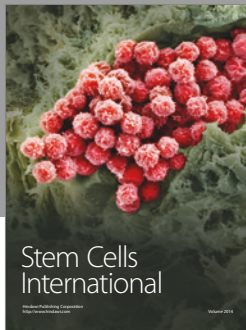
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