





# RESEARCH ARTICLE

# Spectral influence on secondary metabolites in *Jasminum* sambac CO. 1 under red and far-red light

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#### **Abstract**

Light quality plays a pivotal role in plant development and the biosynthesis of secondary metabolite. *Jasminum sambac* is a medicinally valuable plant known for its diverse phytochemicals with pharmacological significance. This study investigated the impact of red (600-700 nm) and far-red (700-750 nm) light treatments on the phytochemical profile of *J. sambac* CO. 1 using gas chromatography-mass spectrometry (GC-MS). Plants subjected to 80 % red and 20 % far-red light exhibited significant metabolic shifts compared to untreated controls, with enhanced accumulation of bioactive compounds such as 12-oleanen-3-yl acetate, cis-vaccenic acid and 9,19-cyclolanost-24-en-3-ol, each associated with anti-inflammatory, antimicrobial, antioxidant and anticancer properties. The findings highlight the role of light in modulating secondary metabolites, offering insights into optimized cultivation strategies for pharmaceutical and aromatic applications. This study underscores the potential of spectral light manipulation to enhance medicinal compound biosynthesis in *J. sambac* CO. 1.

Keywords: end-of-day light; GC-MS; Jasminum sambac CO. 1; metabolites; phytochemicals; red and far-red light

# Introduction

Jasminum sambac (L.) Aiton, a member of the family Oleaceae, is a widely valued ornamental and medicinal plant, renowned for its fragrant flowers and therapeutic potential (1). Traditionally, J. sambac has been utilized in the treatment of various ailments, including fever, abdominal pain, diarrhoea, asthma, skin diseases and insomnia (2). These effects are attributed to its rich reservoir of phytochemicals such as flavonoids, alkaloids, terpenoids, saponins, glycosides, phenolic acids and essential oils, including benzyl acetate, linalool and indole. Modern pharmacological research has further substantiated its bioactivities, revealing antimicrobial, antioxidant, anti-inflammatory, anticancer and anti-aging properties. Notably, compounds such as linally benzoate and benzene methanol have shown promising anti-diabetic effects through modulation of key enzymes like glucokinase (2). Other studies on related Jasminum spp. have demonstrated cytotoxic activity against various cancer cell lines (3).

The biosynthesis and accumulation of these bioactive metabolites are significantly influenced by environmental factors, with light quality being one of the most critical. Red (600-700 nm) and far-red (700-750 nm) wavelengths are sensed by phytochromes, which regulate plant morphogenesis and secondary metabolic pathways (4). Studies have shown that different light spectra can modulate the expression of genes involved in phenylpropanoid, flavonoid and terpenoid

biosynthesis, thus altering the concentration and composition of phytochemicals. For instance, far-red light has been shown to enhance photosynthetic efficiency and mediate metabolic regulation through key enzymes, influencing both plant development and the accumulation of secondary metabolites (4).

Despite the well-documented phytochemical richness of *J. sambac*, there is a paucity of research on how targeted light treatments affect its metabolic profile, particularly under controlled red and far-red illumination. Understanding the lightmediated modulation of its phytochemical constituents may reveal new strategies for enhancing the plant's therapeutic quality.

In this study, we aimed to investigate the effect of red and far-red light treatments on the phytochemical profile of *J. sambac* CO. 1. Mass spectrometry coupled with gas chromatography (GC-MS) was employed as the primary analytical technique to identify and quantify the bioactive constituents present under different light regimes. The primary objective of the study was to identify and analyze the metabolic and volatile compounds present in both control (untreated) and treated (80 % red: 20 % far-red) samples of *J. sambac* CO. 1. By characterizing the metabolite shifts induced by specific light wavelengths. This research seeks to provide insights into the photo regulation of medicinal compounds in *J. sambac* CO. 1, contributing to optimized cultivation strategies for pharmaceutical and aromatic applications.

# **Materials and Methods**

#### **Plant material**

The research was conducted in the Department of Floriculture and Landscape Architecture at Tamil Nadu Agricultural University (TNAU), Coimbatore, Tamil Nadu, during the period November 2024 to February 2025. It is located at 11°07'3.36" N latitude, 76°59'39.91" E longitude and an altitude of 411 m above mean sea level. *J. sambac* CO. 1 is a high-yielding variety of Arabian jasmine developed by Tamil Nadu Agricultural University, was selected as the experimental material for this study.

#### **Experimental conditions**

The study consisted of two experimental conditions:

#### Control (untreated)

Plants were grown under short-day conditions (10 hr photoperiod) in an open field without any supplemental lighting.

#### Treatment (80 % red: 20 % far-red light)

Plants were also maintained under short-day conditions but received an end-of-day (EOD) light treatment for 5 hr inside a polyhouse. The EOD light consisted of a spectral composition of 80 % red light (600-700 nm) and 20 % far-red light (700-750 nm) using programmable LED panels under polyhouse condition. The light treatment continued daily during 6 pm to 11 pm for a period of 4 weeks.

## Leaf sample collection and metabolite extraction

At the end of the treatment period, approximately 50 g of fully developed mature leaves were collected from each group. These samples were immediately flash-frozen using liquid nitrogen and then finely ground. The powdered material was extracted with ethyl acetate at a 1:1 (w/v). This solution was subjected to shaking at 100 rpm on an orbital shaker for 96 hr at a constant temperature of 28 °C (5).

Post-extraction, the mixture was passed through Whatman no. 3 filter paper to separate the filtrate and concentrated through a rotary flash evaporator at 55 °C and 80 rpm. The resulting dried residue was dissolved in 1 mL of HPLC-grade methanol and filtered using a 0.22  $\mu m$  PVDF membrane filter (Himedia) for GC-MS analysis.

# Mass spectrometry coupled with gas chromatography (GC-MS) analysis

The GC-MS analysis was carried out using an Agilent 7890A gas chromatography connected to a 5975C mass spectrometer. A 1  $\mu$ L portion of the extract was injected in split mode at a ratio of 100:1, with helium as the carrier gas flowing at a constant rate of 1 mL/min. The injector was kept at a temperature of 280 °C. The oven temperature program began at 60 °C (held for 1.36 min), increased at a rate of 10 °C per min and reached a final temperature of 325 °C, which was held for 23 min (5).

Mass spectra data were collected over a scan range of m/z 50 to 350 using electron impact ionization at 70 eV. Identification of phytochemical constituents was performed by matching the obtained spectra with those in the National Institute of Standards and Technology (NIST) library, using a match score threshold of > 80% for compound confirmation.

# **Data analysis**

To identify the differences in the emission of volatile compounds between control and treatment (80 % red: 20 % far-red) samples, all peak area analysis were performed with Metaboanalyst software (http://www.metaboanalyst.ca/feces/home.xhtml) and hierarchical clustering heat map, principal component analysis and a correlation matrix was generated using Pearson's correlation coefficient. A Venn diagram highlighting the key metabolites and illustrates their overlaps between the control and treatment groups created using JVENN software (6).

## **Results**

GC-MS analysis of the leaf extracts from control (untreated) and treated (80 % red: 20 % far-red light) samples revealed the presence of diverse secondary metabolites and phytochemical constituents. The GC-MS chromatograms of the treated and control samples of J. sambac CO. 1, highlighting the retention times and abundance of the detected phytochemical compounds (Fig. 1 & 2). The identification of these metabolites was confirmed by analyzing the peak areas and metabolite characteristics.

Metabolites detected in control (untreated) group of *J. sambac* CO. 1, namely benzofuran, 2,3-dihydro- (8.80 %), benzaldehyde (6.76 %), oleic acid (6.26 %), butanoic acid, 4- (1,1-dimethylethoxy)-3-hydroxy-, methyl ester, (R)- (5.92 %), 2-cyclohexyldimethylsilyloxymethyl-tetra hydrofuran (5.32 %), 1,3-propanediol (4.56 %), 9,12-octadecadienoic acid (Z,Z)-, 2-hydroxy-1 (hydroxymethyl)ethyl ester (4.26 %), benzoic acid, 4- ethoxy-, ethyl ester (4.05 %), hexadecanoic acid, 2-hydroxy-1- (hydroxymethyl)ethyl ester (3.48 %), n-hexadecanoic acid (3.47 %), phytol (2.15 %), benzoic acid, 2-formyl-, methyl ester (1.63 %), 2,5-octadecadiynoic acid, methyl ester (1.19 %), 2-Allyl-2-methyl-1,3-cyclopenta nedione (0.50 %), as shown in Table 1.

Metabolites detected in the treatment group of *J. sambac* CO. 1 included γ-sitosterol (2.99 %), octadecanoic acid (1.56 %), cholest-5-en-3-ol, 24-propylidene-, (3 $\beta$ )- (0.39 %), tetradecanoic acid (0.36 %), catechol (0.35 %), 4H-Pyran-4-one, 2,3-dihydro-3, 5-dihydroxy-6-methyl- (0.34 %), stigmasterol (0.31 %), thymine (0.28 %), ethanone, 1-(2-hydroxy-5-methylphenyl)- (0.25 %), L-arginine, N2-[(phenylmethoxy) carbonyl]- (0.19 %), benzoic acid, ethyl ester (0.16 %), trichloroacetic acid, dodec-9-ynyl ester (0.16 %), tricyclo[2.2.1.0 (2,6)]heptane-3-methanol, 2,3-dimethyl- (0.15 %), diphenyl sulfone (0.15 %), squalene (0.15 %), hexadecanoic acid, methyl ester (0.14 %), as presented in Table 2.

Metabolites uniquely present only in treatment of *J. sambac* CO. 1 include (3 $\alpha$ )-12-oleanen-3-yl acetate (30.85%), *cis*-vaccenic acid (4.57%), 9,19-cyclolanost-24-en-3-ol, (3 $\beta$ )- (4.39%), 1,2,3,5-cyclohexanetetrol, (1 $\alpha$ , 2 $\beta$ , 3 $\alpha$ , 5 $\beta$ )- (1.03%), 6S-2,3,8,8-tetramethyltricyclo [5.2.2.0(1,6)] undec-2ene (0.96%),  $\alpha$ -D-glucopyranoside, O- $\alpha$ -D-gluco pyranosyl-(1 $\rightarrow$ 3)- $\beta$ -D-fructofuranosyl (0.66%), 9,12-octa decadiynoic acid, methyl ester (0.52%), 2,5-dimethyl-4-hydroxy-3(2H)-furanone (0.42%), 3-butene-1,2-diol (0.29%), vitamin E (0.22%), campesterol (0.18%), as given in Table 3.

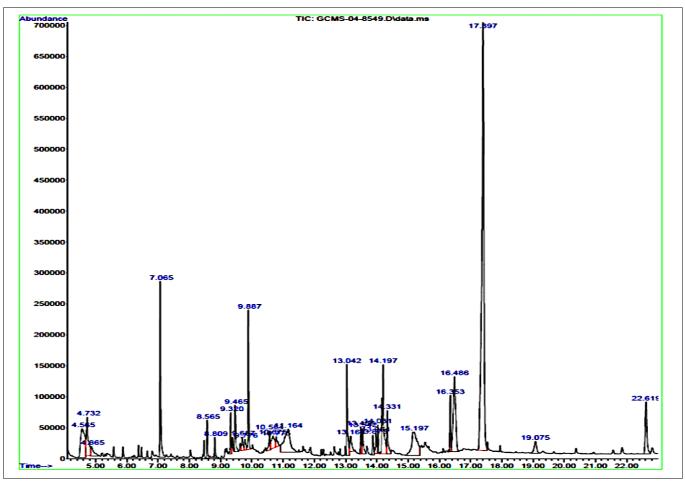


Fig. 1. Metabolite profiling of VOCs in leaf extracts of treatment (80 % red: 20 % far-red) of *J. sambac* CO. 1.

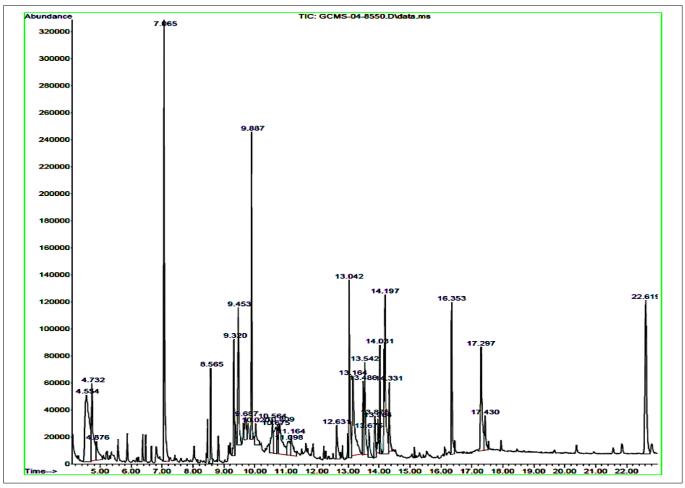


Fig. 2. Metabolite profiling of VOCs in leaf extracts of control (untreated) of *J. sambac* CO. 1.

**Table 1.** Phytochemical compounds detected in the leaf extracts of control (untreated) of *J. sambac* CO. 1.

S. No.	Compound name	Formula	Area %	RT time	Properties	References
1	Benzofuran, 2,3-dihydro-	C <sub>8</sub> H <sub>8</sub> O	8.80	7.06	Anticancer, antiviral activities	7
2	Benzaldehyde	$C_7H_6O$	6.76	4.55	Antihistamines, sedatives and anti- tuberculosis drugs	8
3	Oleic acid	$C_{18}H_{34}O_2$	6.26	14.19	Anti-inflammatory activity	9
4	Butanoic acid, 4-(1,1-dimethylethoxy)-3- hydroxy-, methyl ester, (R)-	$C_9H_{18}O_4$	5.92	9.68	Treating allergic diseases and asthma	10
5	2-Cyclohexyldimethylsilyloxymethyl- tetrahydrofuran	C <sub>13</sub> H <sub>26</sub> O <sub>2</sub> Si	5.32	9.45	Precursor in the production of polymers	11
6	1,3-Propanediol	C <sub>3</sub> H <sub>8</sub> O <sub>2</sub>	4.56	4.73	Building block in the production of polymers	12
7	9,12-Octadecadienoic acid (Z,Z)-, 2-hydroxy -1 (hydroxymethyl)ethyl ester	C <sub>21</sub> H <sub>38</sub> O <sub>4</sub>	4.26	17.29	Anti-inflammatory activity	13
8	Benzoic acid, 4-ethoxy-, ethyl ester	C <sub>11</sub> H <sub>14</sub> O <sub>3</sub>	4.05	9.88	Anti-inflammatory, antimicrobial activities	14
9	Hexadecanoic acid, 2-hydroxy-1- (hydroxymethyl)ethyl ester	C <sub>19</sub> H <sub>38</sub> O <sub>4</sub>	3.48	16.35	Anti-inflammatory activity	15
10	n-Hexadecanoic acid	$C_{16}H_{32}O_2$	3.47	13.04	Anti-inflammatory, antimicrobial activities	16
11	Phytol	C <sub>20</sub> H <sub>40</sub> O	2.15	14.03	Antioxidant, anti-inflammatory, antimicrobial, anticancer, anxiolytic activities	17
12	Benzoic acid, 2-formyl-, methyl ester	$C_9H_8O_3$	1.63	8.56	Anti-inflammatory activity	18
13	2,5-Octadecadiynoic acid, methyl ester	$C_{19}H_{30}O_2$	1.19	12.63	Antibacterial, antifungal activities	19
14	2-Allyl-2-methyl-1,3-cyclopentanedione	C <sub>9</sub> H <sub>12</sub> O <sub>2</sub>	0.50	9.19	Anti-inflammatory, antimicrobial, anticancer activities	20

**Table 2.** Phytochemical compounds detected in the leaf extracts of treatment (80 % red: 20 % far-red light) of *J. sambac* CO. 1.

S. No.	Compound name	Formula	Area %	RT time	Properties	References
1.	γ-sitosterol	C <sub>29</sub> H <sub>50</sub> O	2.99	22.61	Anti-inflammatory, antioxidant activities	21
2.	Octadecanoic acid	$C_{18}H_{36}O_2$	1.56	14.33	Anti-inflammatory, anti-microbial activities	22
3.	Cholest-5-en-3-ol, 24-propylidene -, (3 $\beta$ )-	C <sub>30</sub> H <sub>50</sub> O	0.39	22.81	Anti-inflammatory, anticancer activities	23
4.	Tetradecanoic acid	$C_{14}H_{28}O_2$	0.36	11.64	Antimicrobial, anti-inflammatory activities	24
5.	Catechol	$C_6H_6O_2$	0.35	6.80	Antioxidant, antimicrobial activities	25
6.	4H-Pyran-4-one, 2,3-dihydro-3,5- dihydroxy-6-methyl-	C <sub>6</sub> H <sub>8</sub> O <sub>4</sub>	0.34	6.36	Antioxidant, anti-inflammatory activities	26
7.	Stigmasterol	C <sub>29</sub> H <sub>48</sub> O	0.31	21.85	Anti-inflammatory, antioxidant, anticancer activities	27
8.	Thymine	$C_5H_6N_2O_2$	0.28	5.57	Antiviral, anticancer activities	28
9.	Ethanone, 1-(2-hydroxy-5- methylphenyl)-	$C_9H_{10}O_2$	0.25	8.03	Antioxidant, anti-inflammatory and antimicrobial activities	29
10.	L-Arginine, N2-[(phenylmethoxy) carbonyl]-	C <sub>14</sub> H <sub>20</sub> N <sub>4</sub> O <sub>4</sub>	0.19	5.22	Roles in cardiovascular health, immune support and wound healing	30
11.	Benzoic acid, ethyl ester	$C_9H_{10}O_2$	0.16	6.65	Anti-microbial and anti-fungal activities	31
12.	Trichloroacetic acid, dodec-9- ynyl ester	$C_{14}H_{21}Cl_3O_2$	0.16	16.11	Anti-cancer, anti-microbial activities	32
13.	Tricyclo[2.2.1.0(2,6)]heptane-3- methanol, 2,3-dimethyl-	$C_{10}H_{16}O$	0.15	12.28	Anti-inflammatory activity	33
14.	Diphenyl sulfone	$C_{12}H_{10}O_2S$	0.15	12.98	Antibacterial, anti-inflammatory activities	34
15.	Squalene	C <sub>30</sub> H <sub>5</sub> 0	0.15	17.95	Antioxidant activity	35
16.	Hexadecanoic acid, methyl ester	C <sub>17</sub> H <sub>34</sub> O <sub>2</sub>	0.14	12.81	Anti-inflammatory, antioxidant, antimicrobial activities	36

Table 3. Phytochemical compounds uniquely present only in the treatment (80 % red: 20 % far-red light) of J. sambac CO. 1.

S. No.	Compound name	Formula	Area %	RT	Properties	References
1.	(3α)-12-Oleanen-3-yl acetate	C <sub>32</sub> H <sub>52</sub> O <sub>2</sub>	30.85	17.39	Anticancer, antimicrobial and antioxidant activities	37
2.	cis-Vaccenic acid	$C_{18}H_{34}O_2$	4.57	14.19	Anti-inflammatory, anticancer activities	38
3.	9,19-Cyclolanost-24-en-3-ol, (3β)-	C <sub>30</sub> H <sub>50</sub> O	4.39	15.19	Anti-inflammatory, anticancer, antioxidant activities	38
4.	1,2,3,5-Cyclohexanetetrol, $(1\alpha,2\beta,3\alpha,5\beta)$ -	$C_6H_{12}O_4$	1.03	10.67	Antidiabetic, antiviral, antimicrobial activities	39
5.	6S-2,3,8,8-Tetramethyltricyclo[5.2.2.0(1,6)] undec-2 ene	$C_{15}H_{24}$	0.96	19.07	Anti-inflammatory, antimicrobial, antioxidant activities	40
6.	α-D-Glucopyranoside, O-α-D-glucopyranosyl- (1+3)-β-D-fructofuranosyl	$C_{18}H_{32}O_{16}$	0.66	9.19	Antioxidant, anti-inflammatory activities	41
7.	9,12-Octadecadiynoic acid, methyl ester	$C_{19}H_{30}O_2$	0.52	12.63	Antimicrobial, anti-inflammatory, anticancer activities	42
8.	2,5-Dimethyl-4-hydroxy-3(2H)-furanone	$C_6H_8O_3$	0.42	5.35	Antioxidant, antimicrobial, anti-inflammatory activities	43
9.	3-Butene-1,2-diol	C <sub>4</sub> H <sub>8</sub> O <sub>2</sub>	0.29	5.86	Antiviral, anticancer, antimicrobial activities	44
10.	Vitamin E	$C_{29}H_{50}O_2$	0.22	20.37	Antioxidant activity	45
11.	Campesterol	C <sub>28</sub> H <sub>48</sub> O	0.18	21.56	Anti-inflammatory, antioxidant, anti-cancer activities	46

# **Metabolomics data analysis**

The heat map was generated to visualize the range and relative abundance of volatile organic compounds (VOCs) present in control and treatment leaf samples of *J. sambac* CO. 1. A high degree of correlation was found for the volatiles present in the control and treatment (Fig. 3). A principal component analysis

(PCA) score plot and loading plot were constructed, showing that PC1 explains 99.3 % and PC2 explains 0.6 % of the variance (Fig. 4-6). Additionally, correlation matrix representing the correlogram was generated for control and treatment whereas the results were categorized into the strong direct and strong inverse correlation (Fig. 7). Differentiation and overlapping of

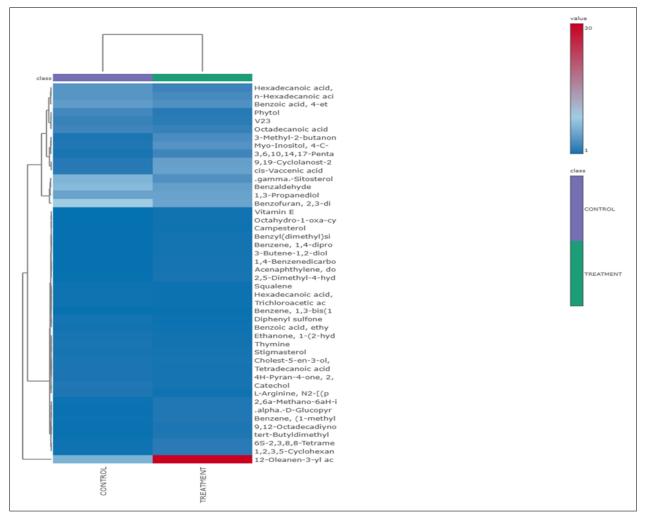
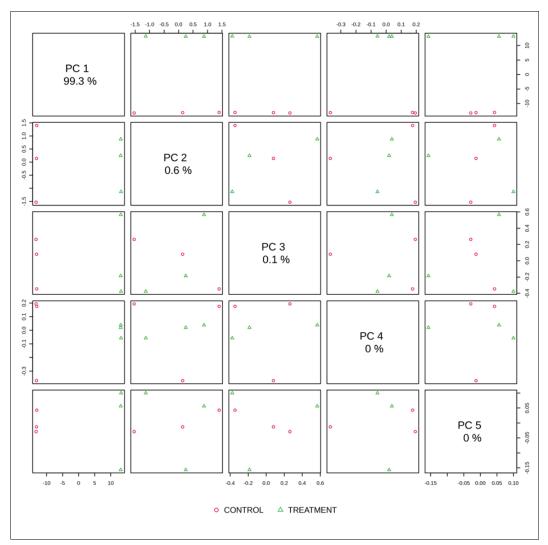
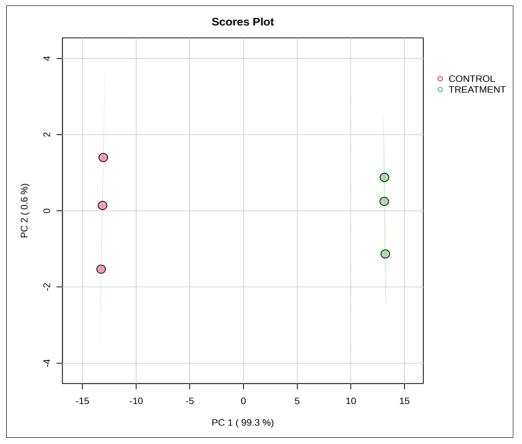


Fig. 3. Heat map analysis of metabolites peak area (%) in control (untreated) and treatment (80 % red: 20 % far-red light) of J. sambac CO. 1.



 $\textbf{Fig. 4.} \ \ \textbf{Overall view plot of principal component analysis (PCA)}.$ 



**Fig. 5.** Principal component analysis (PCA) - score plot.

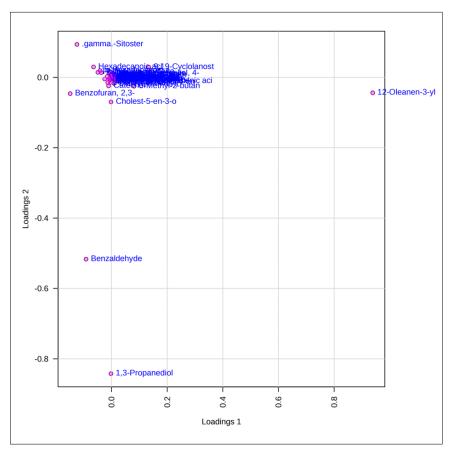
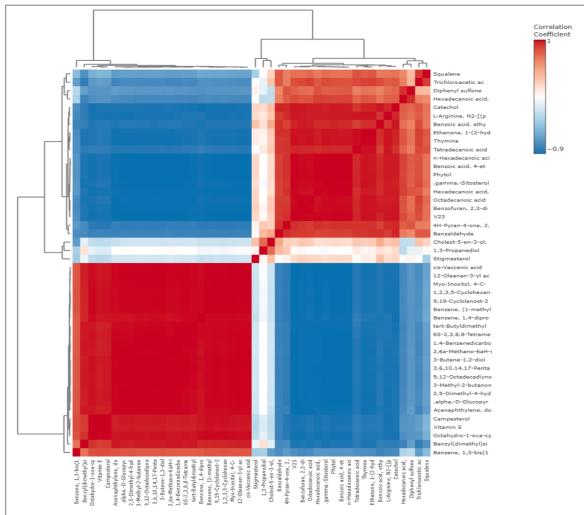
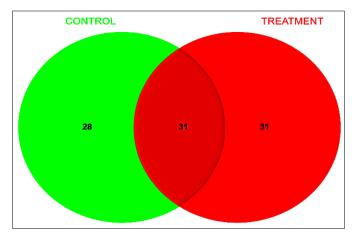


Fig. 6. Principal component analysis (PCA) - loading plot.



**Fig. 7.** Correlation matrix based on Pearson correlation coefficient among different volatile compounds between control (untreated) and treatment (80 % red: 20 % far-red light) of *J. sambac* CO. 1 with dendrogram.



**Fig. 8.** Comparative metabolomics: Distinct and shared metabolites between control (untreated) and treatment (80 % red: 20 % far-red light) of *J. sambac* CO. 1.

the metabolites and the interactions among them were represented by Venn diagram (Fig. 8).

#### **Discussion**

GC-MS analysis of leaf extracts from both untreated and treated with 80 % red: 20 % far-red conditions revealed the presence of various phytochemicals and the compounds identified were known to exhibit diverse pharmacological potentials. For instance, they possess antifungal properties capable of either fungicidal or inhibiting their growth (fungistatic), acting through mechanisms such as disruption of fungal cell walls or membranes, interference with metabolic processes or inhibition of cell division (47). Among the compounds identified, 2,5-octadecadiynoic acid, methyl ester and benzoic acid, ethyl ester possess anti-fungal properties (19, 31). Additionally, several compounds showed antiviral potential including benzofuran, 2,3-dihydro-, benzoic acid, 4-ethoxy-, ethyl ester, tetradecanoic acid, 1,2,3,5-cyclohexanetetrol, (1 $\alpha$ , 2 $\beta$ , 3 $\alpha$ , 5 $\beta$ )- and thymine (7, 14, 24, 28, 39).

The compound 2,5-octadecadiynoic acid, methyl ester has anti-bacterial activity causing bacterial cell wall disruption and oxidative stress in pathogens to protect plants from microbial infestation, potentially aiding in the treatment of microbial skin infections (19). Furthermore, the compounds displayed strong antioxidant properties by neutralizing reactive oxygen species (ROS), stabilizing cellular components, mitigating oxidative stress and preserving cell membrane integrity-crucial for plant survival under stress conditions. Antioxidant compounds identified included phytol, *y*-sitosterol, catechol, 4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-and stigmasterol) (17, 21, 25-27).

Several compounds were found to have anticancer activity, functioning by causing cytotoxic effects, meaning they trigger the death of cancer cells or suppress their ability to grow and multiply. Nearly 60 % of anticancer medications currently in use are derived from plants, as these are rich sources of bioactive constituents such as flavonoids, phenols, alkaloids and terpenoids. The anti-cancer compounds such as benzofuran, 2,3-dihydro-, phytol, 2-allyl-2-methyl-1,3-cyclopentanedione, stigmasterol, (3 $\alpha$ )-12-oleanen-3-yl acetate, *cis*-vaccenic acid and 9,19-cyclolanost-24-en-3-ol, (3 $\beta$ )-

(7, 17, 20, 27, 37, 38). Compounds with antimicrobial properties were also detected, including n-hexadecanoic acid (16), phytol, 2-allyl-2-methyl-1,3-cyclopentanedione, octadecanoic acid, cholest-5-en-3-ol, 24-propylidene-, (3 $\beta$ )-, tetradecanoic acid and catechol (17, 20, 22, 23, 24).

Light treatment enhances biosynthetic pathways by activating photoreceptors like phytochromes, which regulate genes involved in secondary metabolite production. Red and far-red light modulate transcription factors such as elongated hypocotyl 5, promoting enzymes like phenylalanine ammonialyase and chalcone synthase that drive flavonoid terpenoid biosynthesis. This photoregulatory mechanism increases the accumulation of pharmacologically active compounds (4). In J. sambac CO. 1, such treatments improved the yield of metabolites like 12-oleanen-3-yl acetate and cisvaccenic acid. These findings align with prior reports on lightmediated metabolic regulation in medicinal plants. Notably, (3α)-12-oleanen-3-yl acetate was the most abundant compound found with the highest peak area percentage (30.85 %) under the treated possess strong antiophidic (anti-snake venom) activity, making it a promising candidate for further research in anti-serum development (48).

# Conclusion

This study has effectively demonstrated the effect of red and farred light treatments on the phytochemical composition of J. sambac CO. 1. The observed changes in metabolite profiles under red and far-red light treatment were statistically significant (p < 0.05) and biologically meaningful, as they corresponded to elevated levels of key pharmacologically active compounds such as 12-oleanen-3-yl acetate and cis-vaccenic acid with antiinflammatory, antioxidant and antimicrobial activities. Most particularly, the increased yield of 12-oleanen-3-yl acetate, a compound that has anti-snake venom activity, underlines the prospect of treating *J. sambac* CO. 1 with targeted light therapies to optimize its therapeutic activity. These findings have significant implications for both agricultural and pharmaceutical applications. In agriculture, controlled light treatments could be integrated into greenhouse cultivation systems to enhance bioactive compound production in J. sambac, increasing crop value and therapeutic efficacy. For the pharmaceutical industry, this light induced biosynthesis of bioactive molecules enables scalable production of plant-derived pharmaceuticals with consistent potency.

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# **Authors' contributions**

KDK conceptualized the research article and designed the methodology for the literature search. SK guided the research

work by formulating the concept and approving the final manuscript. MG critically reviewed and edited the manuscript for intellectual content. SKR and KV helped in editing, summarizing and revising the manuscript. All authors read and approved the final manuscript.

# **Compliance with ethical standards**

**Conflict of interest:** Authors do not have any conflict of interest to declare.

**Ethical issues:** None

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