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Phytochemical Profiles, *in vitro* Antioxidants, and Anti-inflammatory Activities of Flowers and Leaves of *Lantana camara* L. Grown in South of Tunisia

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Abstract

The current study assesses the photochemical profiles, the *in vitro* antioxidant (2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2′-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS), reducing power ferric and silver nanoparticule) and anti-inflammatory activity of *Lantana camara* L. leaves and flowers collected from the South of Tunisia. Bioactive extracts of two organs were prepared through an ultrasound-assisted extraction in ethanol. Herein, multivariate statistical analysis was performed to define the relationship between biological activities and the bioactive molecules content and composition. Phytochemical profiling showed higher phenolic and flavonoids contents in leaves extracts than in those obtained from flowers, while the condensed tannins was absent in both organs. LC-MS analysis identified 16 and 15 phenolic compounds from flowers and leaves extracts, respectively. The flowers extract was especially rich in Kaempferol, luteolin-7-O-glucoside, quinic acid and apigenin-7-O-glucoside. Kaempferol, luteolin-7-O-glucoside, quinic acid and syringic acid were identified as the prevalent compounds in leaves extract. The latter exhibited the highest DPPH and ABTS radical scavenging potentials. Whereas flowers extracts revealed the highest reducing potential of ferric and silver ions. However, the leaves and flowers extracts are unable to protect bovine serum albumin (BSA) from thermal denaturation. Furthermore, significant correlations ($p < 0.05$) were recorded between phytochemical profile and biological activities, as well as between different antioxidant studied assays. The obtained results present practical data for the potential application of *L. camara* as a sustainable source of multi-functional molecules in food and medicinal industries.

Keywords

Lantana camara L., phytochemical profile, biological activities, antioxidant potential, anti-inflammatory

1 Introduction

With global warming and the economic crisis threatening agricultural production in the Mediterranean basin, new challenges and opportunities for renewing herbs and plants have emerged [1]. In this regard, medicinal and aromatic plants have huge potential as multifunctional crops for a variety of environments, particularly human health, and the circular economy. Around 28,000 aromatic plant species have been used as bioactive compounds in a multitude of fields including pharmaceutical, agricultural, food, perfumery, and cosmetics [2]. Currently, there is an increasing interest to move towards a healthier lifestyle. In this sense, many investigations have been carried out related to health benefits of flowers species such as *Mentha pulegium* L., *Platycodon grandiflorum* (Jacq.), *Eleutherococcus nodiflorus* (Dunn), *Quararibea funebris*, *Rhododendron dauricum* L., *Lantana camara* L. and rose flowers [3–6]. This may be due to the presence of bioactive molecules such as essential oils, polyphenolics, alkanoids, flavonoids, terpenoids and antioxidant enzymes [6, 7].

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Lantana camara L. species have been gaining several attentions for flowers productions, which are a seasonal by-product [8]. In fact, *L. camara* is native to subtropical and tropical regions of the America and the Caribbean islands [9]. It can grow up to 10 m high even in extreme harsh climatic conditions and its presence has recorded in Brazil, Florida, Jamaica, Mexico, and Trinidad [10]. Later, *L. camara* has been naturalized in more than 60 countries by the intervention of nurserymen. While this species has often categorized as poisonous plant, included in top ten as invasive weeds, and considered too toxic to livestock and on the earth [11]. It can tend to expand more under the effects of wildfire, grazing, trimming, and cutting [12]. Besides, this ornamental weed has been introduced as a garden flower in various regions of North African including Tunisia. It can tolerate different agro-climatic conditions [13]. The effects considered as the invasion of *L. camara* species are the changes in soil condition and composition of native plants [14].

Thus, *L. camara* is well known as a useful hedge and its ability to improve the fertility of rocky, to enrich the soil, retain humus in deforested areas, examine soil erosion [8, 15], source of insecticidal activity [16] and sustenance of butterfly [14]. The pharmacology and photochemistry of *L. camara* contribute well to economic uses in medicines, foods, animal feeds, and cosmetics [17, 18]. The different organs (leaves, roots, flowers, and seed) of *L. camara* were used orally in traditional medicine to treat various human disorders [19]. Plant extracts have shown significant anti-cancer, anti-bilious fever, anti-itch, anti-cut, anti-tumor, anti-tetanus, anti-malaria, and anti-hypertension potential [20]. The infusions of leaves are mainly used to cure scratching, rheumatism, stomachache, wound healing, toothache, bronquitis, fever, eruptions, eczema biliary and antiseptic [21, 22].

The concoction of leaves is used for ulcers, cuts, swelling, and wounds [20]. In India, the leaves are used to treat asthma, colds, bronchitis, eye infections, cough, stomach pains, ulcers, and kidney disorders [23]. The flowers have been used to treat inflammation, epilepsy, poisoning, and rheumatism [24, 25]. The decoction flowers were recommended for the treatment of fever and influenza [26]. The infusion of *L. camara* flowers was given as pectoral for children [23]. The mixture of dried flowers and coconut oil was used to get relief from headache [27]. The fruits and the roots are frequently used to cure rheumatism and rash [28].

L. camara, in fact, produces a wide range of secondary metabolites. Bioactive compounds derived from the various organs of *L. camara* have gained popularity as alternative treatments for many kinds of ailments. The medicinal value of *L. camara* plant lies in some chemical constituents (phytochemicals) that produce a definite physiological function as well as medicinal activity on the human body. The major bioactive compounds of the flower extracts are phenolic compounds and flavonoids [29]. Recent studies have reported that *L. camara* leaves extract exhibit a wide range of bioactivities, such as anthelminthic, antioxidant, anti-proliferative, insecticidal and anti-inflammatory [18, 24]. Mediterranean countries, including Tunisia, have several plants flowers used in folk medicine, such as *L. camara*. Despite the widespread use of these plants across many applications and the distinctive climate of Tunisia, no research has been conducted on the phytochemical information and antioxidant activity of *L. camara* growing in Tunisia. Arid climate in south Tunisia may have a positive impact on the phenolic composition and the biological activity of the *L. camara* plant.

In the present study, phytochemical properties, and biological capacities (antioxidant and anti-inflammatory), ferric and silver ions reducing power of *L. camara* collected in southern of Tunisia were investigated. The identification and quantification of the extractable phenolic were carried out via LC-MS and colorimetric method. The antioxidant activity was evaluated using four different methods and the anti-inflammatory propriety was estimated against the thermal denaturation of bovine serum albumin (BSA). Furthermore, the relationship between the phytochemical composition and biological potential was determined by multivariate analysis. The obtained results implied that *L. camara* plant could be a useful source of bioactive medicinally and food industry components.

2 Materials and methods

2.1 Chemical and reagent

All the chemical and reagents purchased were of analytical grade and used without additional purification. 2,2-Diphenyl-1-picrylhydrazyl (DPPH), ethanol (C_2H_5OH), Folin-Ciocalteu reagent, sodium carbonate (Na_2CO_3, ≥ 99.5%), gallic acid ($C_7H_6O_5$, ≥ 98%), aluminum nitrate ($Al(NO_3)_3$, ≥ 98%), methanol (CH_3OH), hydrochloric acid (HCl, ≥ 32%), catechin ($C_{15}H_{14}O_6$, ≥ 98%), bovine serum albumin (BSA) solution, Tris-HCl buffer (50 mM, pH 6.6), diclofenac sodium ($C_{14}H_{10}C_{l2}NO_2Na$, ≥ 98%),

silver nitrate (≥ 99%), sodium citrate ($Na_3C_6H_5O_7$, ≥ 97%), phosphate buffer (0.2 mol/L, pH 6.6), potassium ferricyanide ($K_3Fe(CN)_6$, ≥ 99%), trichloroacetic acid ($C_2HCl_3O_2$), ferric chloride solution ($FeCl_3$), 2,2′-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) diammonium salt ($C_{18}H_{24}N_6O_6S_4$, ≥ 98%), DPPH, folin–Ciocalteu phenol reagent, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (Trolox), potassium persulfate ($K_2S_2O_8$, ≥ 99%), formic acid (CH_2O_2, ≥ 98%), vanillin ($C_8H_8O_3$, ≥ 99%), aluminum chloride ($AlCl_3$, ≥ 99%) were purchased from Sigma-Aldrich. Distilled water was used for the preparation of all chemical solutions.

2.2 Instrumentation

Phytochemical composition of plant material extracts was done on a UV/Vis spectrophotometer (T60 UV–visible) versus a blank sample. The absorption was measured in the range of 423–765 nm. Total phenols, flavonoid, condensed tannins content, antioxidant and anti-inflammatory activity in the extract solutions were calculated using the gallic acid, rutin, catechin, Trolox and diclofenac as gram equivalents per 100 g of dry weight (DW), respectively.

The bioactive component was analyzed and identified qualitatively using a liquid chromatography mass spectrometry/mass spectrometry LC–MS-2020 quadrupole mass spectrometer (Shimadzu, Kyoto, Japan) equipped with an electrospray ionization source (ESI) and operated in negative ionization mode. Mass spectrometer was coupled online with an ultra-fast liquid chromatography system consisted of a LC-20AD XR binary pump system, SIL-20AC XR autosampler, CTO-20AC column oven and DGU-20A 3R degasser (Shimadzu, Kyoto, Japan). The analytical column was equipped with Aquasil C18 guard column (10 mm × 3 mm, 3 µm, Thermo Electron) and Aquasil C18 column (Thermo Electron, Dreieich, Germany) (150 mm × 3 mm, 3 µm). The mobile phase consisted of a mixture of A (0.1% formic acid in H_2O, v/v) and B (0.1% formic acid in methanol, v/v) with a linear gradient elution: 0–45 min, 10–100% B; 45–55 min, 100% B. Between each individual run, there was a regulated equilibration interval of 5 minutes. The injection volume was 5 L, the mobile phase flow rate was 0.4 mL/min, and the column's temperature was set at 40 °C. Spectra were monitored in mode Selected Ion Monitoring (SIM) and processed using Shimadzu Lab Solutions LC–MS software.

2.3 Plant materials and extracts preparation

The green leaves, the yellow-pink flowers of *L. camara* were collected freshly during spring 2021, from the Higher Institute of Applied Sciences and Technology of Gabes, Tunisia (latitude 10°05'26.80"E and longitude 33°52'49.29"N). To standardize the conditions, the freshly plants were harvested at the morning. The study site has a typical Mediterranean climate with mild rainy winters and hot dry summers in the north of Tunisia, semi-arid conditions in the center, and arid conditions in the south [30]. The mean annual temperature varies between 30 °C in July and 12 °C in December [30]. The schematic pathway for the source material and solvent extract of starting from *L. camara* is shown in Fig. 1. In brief, the leaves and petals of *L. camara* were separated and kept at room temperature for drying. Afterwards, the dried petals and leaves were manually ground to fine powder and stored at 4 °C. Each sample powder (5 g) was dispersed

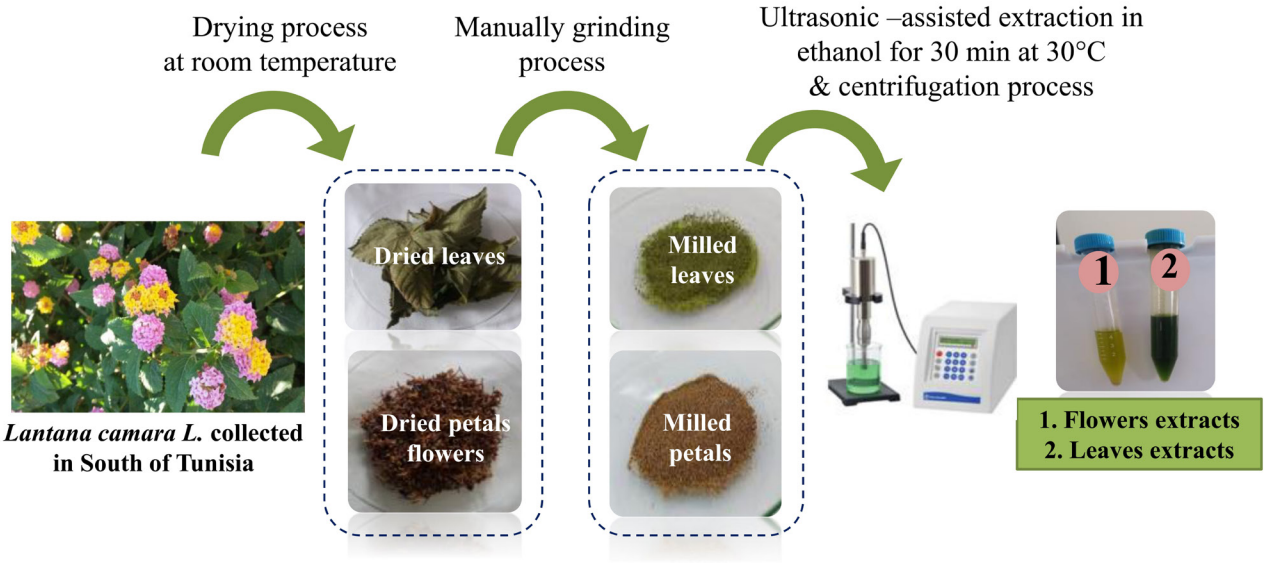

Fig. 1 Experimental setup for the plant material and extracts preparation from *Lantana camara* L. collected in South of Tunisia

in 100 mL ethanol. The mixing was kept in an ultrasonic bath model Clean-120hd (200 W, 40 kHz) for 30 min at 30 °C. After the ultrasonic process, the resulting suspension was filtrated using a filter paper. The filtrate was centrifuged at 4500 rpm for 10 min. The final extracts were stored under shade at 4 °C for further analysis.

2.4 Phenolic compounds determination

2.4.1 Total phenolic content

Total phenolic content was performed by following the Folin-Ciocalteu method according to Gasmi et al. [31]. Each 100 µL of extract was mixed with 500 µL of concentrate Folin-Ciocalteu reagent and 4 mL of sodium carbonate solution (1 M). The absorbance was measured at 765 nm by using a spectrophotometer after 90 min of incubation. The total phenolic was calculated by using the equation of linear regression obtained from the gallic acid standard curve and expressed as gram gallic acid equivalent (GAE) per g dried weight (DW) of sample.

2.4.2 Total flavonoids content

The total flavonoid content was evaluated according to the colorimetric assay described by Ben Othmen et al. [32]. A volume of 1 mL of each extract was mixed with 1 mL of aluminum nitrate solution (10%). The mixture was incubated for 30 min at room temperature and the absorbance was measured at 430 nm. Flavonoids content was determined using the calibration curve realized using rutin. The obtained results were expressed as gram of rutin equivalents (RE) per g of dry weight (g RE per g dried sample (DW)).

2.4.3 Condensed tannins content

The condensed tannins were determined as per the method described by Hayder et al. [33]. Briefly, each 250 µL of ethanol extract was placed in test tube and mixed with 1.5 mL of methanol vanillin solution at 4% concentration and 750 µL of concentrated hydrochloric acid (32%). The prepared samples were incubated at room temperature for 15 min. The absorbance was measured at 500 nm. Catechin was used as a standard. The condensed tannins content was expressed as gram catechin equivalents (CE) per 100 g of dry weight (g CE/100 g DW).

2.5 Characterization of phenolic compounds by LC-MS analysis

The phenolic compounds were performed by LC-MS spectrometry. Before the injection of samples into the HPLC column, leaves and petals flowers extracts were dissolved in methanol (10%), and then filtered twice using filter paper and membrane filter (0.45 mm). The mass spectrometer was operated in negative ion mode with a capillary voltage of −3.5 V, a nebulizing gas flow of 1.5 L/min, a dry gas flow rate of 12 L/min, a dissolving line (DL) temperature of 250 °C, a block source temperature of 400 °C, a voltage detector of 1.2 V and the full scan spectra from 50 to 2000 Da. The phenolic compounds found in various samples were identified by comparing retention times and spectra with those of standard compounds. The measurement results were expressed as mg/100 g of dry weight.

2.6 Antioxidant activity determination

2.6.1 DPPH free radical scavenging activity

The scavenging activity against DPPH free radical was determined based on the method recorded by Benchikh et al. [34]. An aliquot of 180 µL of the DPPH solution (0.2 mM in ethanol) was mixed with 20 µL of each extract in a 96-well microplate. The mixture was incubated for 30 min at room temperature in the dark before sample analysis by microplate reader at 517 nm wavelength. Trolox was used as reference antioxidants and the free radical scavenging activity was expressed as grams Trolox equivalents per 100 g dry weight (g Trolox E/100 g DW).

2.6.2 ABTS free radical scavenging activity

ABTS scavenging activity was assessed according to the method described by Elfalleh et al. [35]. The ABTS solution (7 mM in ethanol) was incubated with 2.45 mM of potassium persulfate ($K_2S_2O_8$) for 16 h in the dark and room temperature and then diluted until obtaining an absorbance of 0.7 at 734 nm. A 20 µL of tested solution was mixed with 180 µL of diluted $ABTS^+$ solution in a 96-well microplate. The absorbance reading of samples was measured at 734 nm, after 10 min incubation at 30 °C. Trolox was used as antioxidant standards. The antiradical effect was expressed as grams Trolox equivalents per 100 g dry weight (g Trolox E/100 g DW).

2.6.3 Reducing power (FRP)

The reducing power of *L. camara* extracts was evaluated following the method reported by Deng et al. [36]. Briefly, 1 mL of each extract was mixed with 2.5 mL of phosphate buffer (0.2 mol/L, pH 6.6) and 2.5 mL of potassium ferricyanide (1%). The mixture was incubated at 50 °C for 20 min. Then, a volume of 2.5 mL of trichloroacetic acid solution (10%) was added to the mixture. The resulting solution was mixed with 2.5 mL of distilled water and 0.5 mL ferric chloride solution ($FeCl_3$, 0.1%), and the absorbance reading of samples were recorded at

700 nm. The reducing power was determined according to a standard curve prepared from Trolox solution and was expressed as grams Trolox equivalents per 100 g dry weight (g Trolox E/100 g DW).

2.6.4 Silver nanoparticle assay (SNP)

Silver ion reduction was carried out according to the procedure reported by Bakhouche et al. [37]. An aliquot of 20 µL of examined extract or standard molecules was mixed with 50 µL of distilled water and 130 µL of SNP solution (1 mM $AgNO_3$, 1% citrate solution). After 30 min at room temperature, the absorbance was monitored at 423 nm using plaque reader. Trolox was used as standards and the reducing potential was expressed as grams Trolox equivalents per 100 g dry weight (g Trolox E/100 g DW).

2.7 Anti-inflammatory activity

The anti-inflammatory activity was evaluated *in vitro* by the thermal denaturation of Bovine Serum Albumin (BSA) [38]. A volume of 1 mL of extract was mixed with 1 mL of BSA (0.2%) prepared in Tris-HCl buffer (50 mM, pH 6.6). The resulting mixture was allowed to stand for 15 min at 37 °C and then heated in a bathwater at 72 °C for 5 min. The absorbance was read at 660 nm. Diclofenac sodium was used as a standard. The protective effect of samples against the denaturation of BSA was presented as inhibition percentages being calculated by Eq. (1):

$$I(\%) = \frac{ABS(c) - ABS(s)}{ABS(c)} \times 100 \quad (1)$$

where $I(\%)$ is the inhibition percentage, $ABS(s)$ is the absorbance of the test sample and $ABS(c)$ is the absorbance of control.

2.8 Statistical analyses

All analysis experiment was carried out in triplicates and the data were presented as means ± standard deviation. The analysis of the variance with one factor (ANOVA) was determined using XLSTAT 2014 software to determine significant differences between results. The relationship among all parameters in examined extracts was described as Pearson correlation coefficient (r).

3 Results and discussion

3.1 Total polyphenols, total flavonoids, and condensed tannins contents

Phenolic compounds of *L. camara* leaves and flowers were commonly extracted in ethanol by using ultrasound-assisted process. This later was used not only to prevent bioactive degradation from high temperature, but also to improve extraction performance. In this study, ethanol was used as solvent for plant material due its efficiency in degrading of plant cell wall, its low price and renewable source [39]. The obtained organic extracts were investigated for their total polyphenol content by the Folin–Ciocalteu assay, for their total flavonoids by $AlCl_3$ reagent and for their condensed tannins concentration using acidified vanillin. The studied extracts showed high phenolic contents with a significant difference between both organs (Fig. 2). This abundance, in particular the phenolic contents may be in part explained by their interesting role in ultraviolet (UV) screening effect [40]. The leaves extract showed a higher total polyphenol content (57.65 ± 0.39 g GAE/100 g DW) and total flavonoids content (7.11 ± 0.09 g RE/100 g DW). These results are similar to those obtained in the previous studies [41–43]. The total flavonoids and polyphenols content of locally *L. camara* leaves were shown to be higher than the Brazilian and Pakistani *L. camara* leaves, the values were (227.10 µg GAE/mg DW and 46.55 µg RE/mg DW) and (40.86 mg GAE/g DW and 53.11 mg RE/g DW), respectively [28, 42].

As shown in Fig. 2, the locally *L. camara* flowers extracts exhibited lower total polyphenol and flavonoid content (28.53 ± 0.00 g GAE/100 g DW and 1.51 ± 0.01 g RE/100 g DW) compared to the leave's extracts (57.65 ± 0.39 g GAE/100 g DW and 7.11 ± 0.09 g RE/100 g DW). Whereas previous studies stated that flowers fraction contains higher amount of polyphenol compound than this content in leaves extract [43–45]. Therefore, in a recent research [19] were reported that the total polyphenol concentration isolated from *L. camara* flowers by using methanol (80%) as solvent extract was 21.45 g GAE/100 g DW),

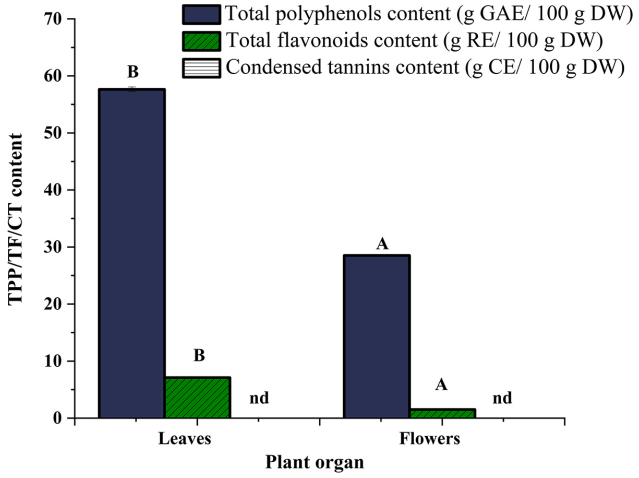

Fig. 2 Total polyphenols, total flavonoid contents and condensed tannins of flowers and leaves of *L. camara*. Different capital letters represent significant variation ($p < 0.05$) between leaves and flowers. The nd means "not detected".

which was lower to those obtained results, while it had higher total flavonoids content (13.76 g CE/100 g DW). These differences may be due to several internal and external factors, such as geographical origin, ripening date, extraction processes and solvents and the analytical techniques [33]. As seen in Fig. 2, the condensed tannins content in leaves and flowers extracts are totally absent, this can be explained that the extraction method and the nature solvent have great effects on this phenolic class.

According to the findings, both organs of *L. camara* contain significant amounts of total polyphenols, which have the ability to absorb and neutralize free radicals as well as quench reactive oxygen species [24]. They can additionally induce an inflammatory response [45]. Hence, it is important to investigate in detail the individual phenolic compounds and the biological potential of each extract.

3.2 Identification and quantification of phenolic components of *L. camara* extracts

The phytochemical analysis of leaves and flowers organic extract of *L. camara* were performed on LC-MS. The results of total phenolic acid and flavonoids content of Tunisian *L. camara* species have been evaluated and are summarized in Table 1. According to the results from LC-MS analysis, the edible species showed 16 and 15 compounds from flowers and leaves extracts, respectively, in which 13 compounds were found common in both extracts with variable concentration. Traces of gallic acid and ferulic acid were specific to flowers extract whereas syringic acid was detected only in leaves fraction with an interesting level 7.49 mg/100 g DW. The flowers fraction revealed the presence of seven phenolic acids (11.32 mg/100 g DW) with lower level, and nine flavonoids (1091.70 mg/100 g DW) with higher concentration, being quinic acid, luteolin-7-O-glucoside, apigenin-7-O-glucoside and kaempferol the major compounds identified. This richness in flavonoids was significantly related to its interesting role to define the color and the aroma of flowers to attract pollinators [46]. In the leaves sample, five phenolic compounds (23.74 mg/100 g DW) were detected with the predominance of quinic acid, syringic acid, and ten flavonoids (93.65 mg/100 g DW), being luteolin-7-O-glucoside and kaempferol the most prevalent molecules.

To situate Tunisian *L. camara* among those described in the existing literature, a comparison based on the identified phenolic compounds and respective concentrations

Table 1 Qualitative and quantitative data of the extractable phenolic acid in flowers and leaves of *L. camara*

Peak	Compound	RT (min)	m/z	Flowers (mg/100 g DW)	Leaves (mg/100 g DW)
	Phenolic acid				
1	Quinic Acid	1.58	191	**7.99**	**14.82**
2	1.3-Dicaffeoylquinic acid	1.61	515	0.31	0.93
3	Gallic acid	1.62	169	0.09	Nd*
4	Protocatechic Acid	4.61	153	0.88	0.38
5	Chlorogenic acid	9.00	353	1.94	Nd*
6	Syringic acid	Nd*	197	Nd*	**7.49**
7	Paracoumaric acid	16.28	163	0.04	0.12
8	Ferulic Acid	19.51	193	0.06	Nd*
	Total			11.32	23.74
	Flavonoids				
9	Rutin	21.75	609	0.55	1.08
10	Hyperoside	22.08	463	2.47	1.86
11	Luteolin-7-O-Glucoside	22.28	447	**33.82**	**73.82**
12	Quercitrin	24.38	447	2.67	1.82
13	Apigenin-7-O-Glucoside	24.59	431	**7.48**	3.46
14	Quercetin	29.03	301	3.92	0.99
15	Kaempferol	29.19	285	**1035.27**	**9.88**
16	Naringinin	31.41	271	2.05	0.18
17	Apigenin	31.95	269	3.47	0.10
18	Luteolin	Nd*	285	Nd*	0.45
	Total			1091.70	93.65

* Nd: No definite

was made. According to Jain et al.'s [47] study, the phenolic constituents *L. camara* leaves extract were revealing the presence of 14 phenolic molecules, with the predominance of *p*-hydroxybenzoic, syringic, ferulic, *p*-coumaric and *m*-coumaric. Sousa et al. [48] have revealed the presence of five phenolic compounds (quercetin, rutin, gallic acid, caffeic acid and chlorogenic acid) in the ethanolic extracts of *L. camara* leaves and roots. The HPLC analyses by Sousa et al. [48], Ifora et al. [26] showed that the root extract had a higher concentration of phenolic content in relation with the leaf extracts. Swamy et al. [49] have identified 32 compounds belonging to different chemical classes of phenolic compounds in methanol extract of *L. camara* leaves, which known to display several biological activities. Ghisalberti [50] has cited six flavonoids' constituents in the leaves of different *Lantana* species, such as 3-methoxy- 3, 7 dimethoxy- and 3, 7, 4′-trimethoxyquercetin, pectolinarigenin 7-O-*β*-D-glucoside, hispidulin and a camara side glycoside. The HPLC fingerprint of fresh leaves aqueous extract showed the presence of six phenolic compounds salicylic acid, gentisic acid, *β*-resorcylic acid, coumarin, ferulic acid and 6-methyl coumarin [51]. The difference in *Lantana* species composition could be attributed to several factors; including the geographical origin [33], collection conditions [28], storage conditions [52], differences in isolation and identification procedures, type of extraction and nature of the solvent [50].

The obtained results point to the need for further research. Indeed, all the phytochemicals isolated from the extracts studied have been shown to have a wide range of biological activities, including antioxidant and anti-inflammatory properties. Therefore, the *in vitro* DPPH-ABTS free radical scavenging capacity, ferric and silver ions reducing potential, and anti-inflammatory were investigated.

3.3 Antioxidant capacity and contents

Several methods, including free radical scavenging, reducing capacity, and oxygen radical absorbing capacity, have been employed to investigate the antioxidant activity of plants. However, no standardized way is available to estimate an antioxidant. Moreover, four antioxidant assays were used for assessing the antioxidant effectiveness of studied extracts. Our data revealed that all employed methods have proven the effectiveness of the studied fractions compared with the reference antioxidant; (S)-6-methoxy-2,5,7,8 tetramethylchromane-2 carboxy-lic acid (Trolox), with significant difference between plant organs.

3.3.1 DPPH and ABTS radical scavenging abilities

The ability of the extracts to quench radicals was evaluated using the DPPH and ABTS radical scavenging methods, which were wieldy used due to their simplicity, stability, and reproducibility. Fig. 3 shows the DPPH and ABTS radical scavenging abilities of *L. camara* leaves and flowers extracts. Both extracts have an important radical scavenging capacity capability, and a significant difference was observed between organs due to their different composition. The lowest content of DPPH and ABTS scavenging capacity was observed in flowers extract (224.00 ± 0.47 g Trolox E/100 g DW and 378.39 ± 2.67 g Trolox E/100 g DW, respectively), while the leaves was found as the best donor of electrons to $DPPH^+$ and $ABTS^+$ (327.77 ± 3.63 g Trolox E/100 g DW and 525.11 ± 4.98 g Trolox E/100 g DW, respectively). These results are similar to those obtained in the previous studies [28, 41, 53]. Whereas, in a recent study, Mansoori et al. [43] were found that the DPPH and ABTS free radical of *L. camara* flowers exhibited higher content than the leaves one. The percentage inhibition of flowers and leaves fraction was 71.47 ± 0.80% and 17.81 ± 0.39% at concentration about 260 µg/mL, respectively.

Therefore, based on the above discussion, the DPPH radical and $ABTS^+$ radical cation scavenging activity of *L. camara* may primarily be related to their Hydrogen atom donation ability [54]. In addition, *Lantana* species is rich in natural antioxidants. These results suggest that the *L. camara* plant may possess strong antioxidant activity against the free radical mediated oxidation as bio-compounds in cosmetic, pharmaceutical and food industries.

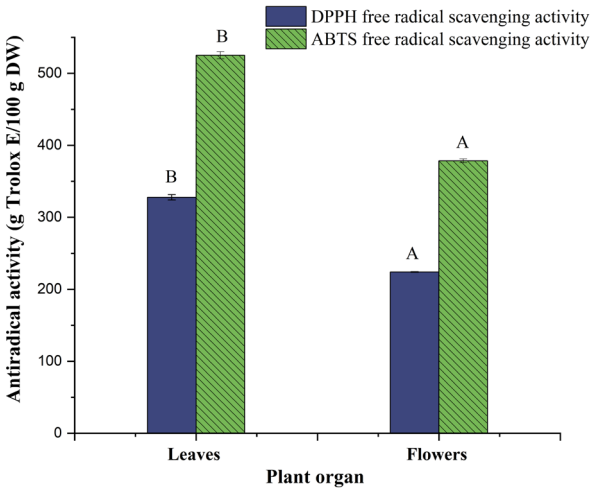

Fig. 3 Variation of DPPH and ABTS radical scavenging activities of leaves and flowers of *L. camara*. Different capital letters represent significant variation ($p < 0.05$) between both organs.

3.3.2 Ferric and silver ions reducing potentials

Reducing power capacity was determined by ferric reducing potentials (FRP) and silver nanoparticle (SNP) assay, which serve to evaluate their abilities to reduce ferric and silver ions, respectively. The test results of the FRP and SNP of *L. camara* extracts were shown in Fig. 4. The flowers fraction showed higher FRP and SNP (23.98 ± 0.16 g Trolox E/100 g DW and 68.15 ± 0.28 g Trolox E/100 g DW) than leaves extract (18.67 ± 0.37 g Trolox E/100 g DW and 27.36 ± 0.46 g Trolox E/100 g DW). These different values are in order with their phenolic content. Other study indicated that the methanolic fraction isolated from different varieties of *L. camara* leaves showed different FRP values, which were related to their phytochemical composition [51]. The study done by Mansoori et al. [43] described varied FRP values for different *L. camara* tissues and reported that both leaves and flowers fractions exhibited interesting electron-donating by reducing Fe^{3+} to Fe^{2+} and proved that leaves fraction was more power to act as an electron donor. Concerning SNP assay, there is no previous report of *L. camara* organs, which makes it difficult to compare the results from the present study, but both extracts were able to act as interesting reductants by electron transfer.

The results revealed that ferric and silver ions reducing capacity of obtained fractions was attributed to phenolic compounds and some types of flavonoids, as well as to other constituents which are not quantified in this report. Indeed, *L. camara* fractions contained a complex mixture of different phenolic constituents and other active compounds (alkaloids, sterols, saponins and terpenoids) [24, 42] with diverse structures, and displayed antagonistic or synergistic

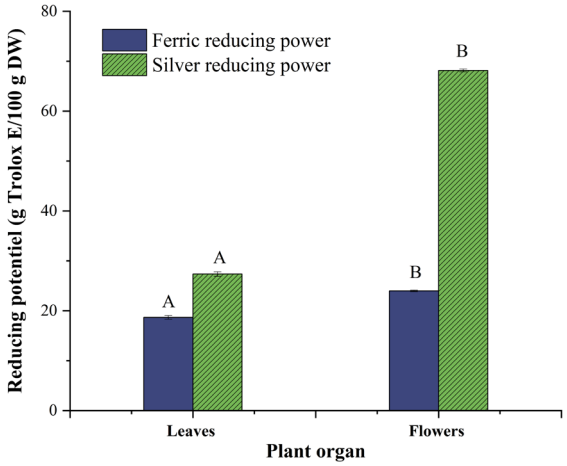

Fig. 4 Variation of ferric and silver ions reducing power of leaves and flowers of *L. camara*. Different capital letters represent significant variation ($p < 0.05$) between leaves and flowers.

effect, which cannot be neglected [54, 55]. These might justify the variation in antioxidant properties of leaves and flowers extracts. Globally, these results encourage the authors to further investigate and test the anti-inflammatory ability of the studied plant.

3.4 Anti-inflammatory effect

In folk medicine, many plant species are used in traditional medicinal preparations due to a complex mixture of compounds [56]. The *L. camara* belongs to the Verbenaceae family, which known as a renewable and abundant source of bioactive molecules, and which are reported to have anti-inflammatory potential [48]. In the literature, there are several studies on anti-inflammatory activity of *L. camara* on diverse cellular model. Mane et al. [18] cited that the aqueous extract of *L. camara* exhibited anti-inflammatory activity in albino rats. Moreover, Wu et al. [57] demonstrated that triterpenoids isolated from aerial parts of *L. camara* showed anti-inflammatory effects by inhibiting NO release in LPS-induced BV-2 cellular models. Additionally, Millycent et al. [58], who studied the anti-inflammatory potential of *L. camara* aqueous extract using animal models, stated that leaves exhibited highly significant edema diminishing effect.

The test results of the *in vitro* anti-inflammatory activity of *L. camara* extracts in BSA were shown in Fig. 5 and the percentages of inhibition were compared to diclofenac solution. The results showed that both extracts were unable to stabilize the BSA structure against thermal denaturation, despite they contain effective compounds known by their anti-inflammatory effects and can modify the thermal stability of protein [59]. Kalita et al. [60] stated that phenolic compounds can link with several protein polypeptide chain segments, keeping them stable even when subjected to thermal stress. Terpenoids and saponins, which were quantified with high levels in aerial parts of *L. camara* [42], were able to inhibit the thermal coagulation of albumin [61]. Ifora et al. [26] was found a strong relationship between the flavanol quercetin concentration and the anti-inflammatory potential of *L. camara* leaves.

On the other hand, previous study has indicated that *L. camara* essential oils displayed an interesting protective against the denaturation of BSA induced by heating at 72 °C, with IC_{50} values in the range of 15.45 ± 0.04 to 17.75 ± 0.07 µg/mL. The highest anti-inflammatory activity was observed in leaf essential oil and was probably associated with the high proportions of (E)-β-caryophyllene and α-humulene [45].

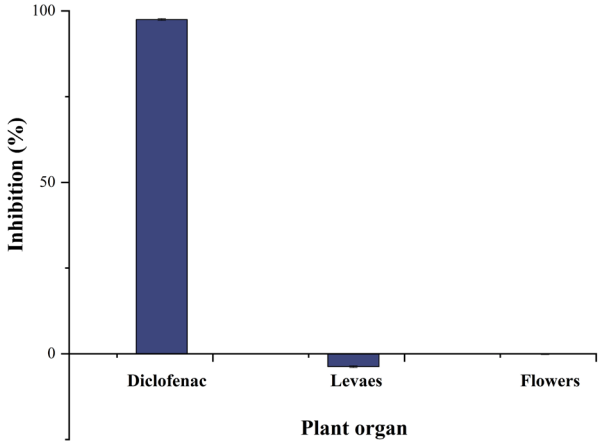

Fig. 5 *In vitro* anti-inflammatory effect of *L. camara* extracts and diclofenac

3.5 Correlation analysis

The ability of phenolic acids, flavonoids and their derivatives to scavenge free radicals and reduce ions has been commonly reported in literature. This antioxidant potential is related to its chemical structure, partition coefficients and rate of reaction with the molecules of interest [62]. Deng et al. [36] reported that some phenolic acids, such as ferulic acid displayed pro-oxidation activity. Santos et al. [63] found that quinic acid isolated from plants tissues was present as free radical scavengers. In addition, flavonoids and its derivatives compounds, including flavonols and flavones can act as singlet oxygen quenchers, reduction agents and superoxide radical scavengers [64]. Liu et al. [65] showed that luteolin and Kaempferol, major phenolic compounds, in both examined extracts is an effective antioxidant. However, some reports stated that there is no significant correlation between polyphenols contents and total antioxidant capacities [66].

Table 2 provides the results of correlation analysis. The obtained results were performed to investigate the linear relationships between phenolic content, and composition and the corresponding radical scavenging and reducing capacities of *L. camara* extracts. The experimental data showed that the ability of studied extracts to quench different radicals displayed significant positive correlation with polyphenols and flavonoids content, with correlation coefficient exceed 0.96. Previously several studies revealed a strong correlation between phenolic levels and antioxidant capacity of different plants tissues [35, 67], but some other studies have not reported this relation [60].

DPPH and ABTS scavenging capacities were positively correlated and quinic acid and luteolin-7-O-glucoside concentrations. The kaempferol and the DPPH and ABTS values were negatively correlated ($r = -0.99$ and $r = -0.99$, respectively). A significant and high negative correlation was also observed between ferric and silver ions reducing power and total phenolic ($r = -0.95$ and $r = -0.99$), total flavonoids ($r = -0.95$ and $r = -0.99$), quinic acid concentrations ($r = -0.96$, $r = -0.99$), and luteolin-7-O-glucoside levels ($r = -0.96$, $r = -0.99$). Moreover, inverse correlations were found between reducing ability and kaempferol content with correlation coefficient higher than 0.96.

These results suggest that the free radical scavenging abilities were related to high levels of phenolic, flavonoids, quinic acid and luteolin-7-O-glucoside. The kaempferol content was found as the main contributor for the reducing ions potential of *L. camara*, but it cannot be solely responsible for the activity, and the observed effect might be attributed to other constituents which are not quantified in this study.

A strong positive correlation was found between DPPH and ABTS scavenging ability on the one hand, and between ferric and silver ions reducing potential on the other hand

Table 2 Correlation coefficients (r) between phytochemicals contents and composition and antioxidant activities of the Tunisian *L. camara* leaves and flowers

Correlation between	Correlation coefficient
TP-DPPH	0.99
TP-ABTS	0.99
TP-FRP	−0.95
TP-SNP	−0.99
TF-DPPH	0.98
TF-ABTS	0.99
TF-FRP	−0.96
TF-SNP	−0.99
DPPH-ABTS	0.97
DPPH-FRP	−0.98
DPPH-SNP	−0.99
ABTS-FRP	−0.94
ABTS-SNP	−0.98
FRP-SNP	0.96
Quinic acid-DPPH	0.99
Quinic acid-ABTS	0.99
Quinic acid-FRP	−0.96
Quinic acid-SNP	−0.99
Luteolin-7-O-glucoside-DPPH	0.99
Luteolin-7-O-glucoside-ABTS	0.99
Luteolin-7-O-glucoside-FRP	−0.96
Luteolin-7-O-glucoside-SNP	−0.99
Kaempferol-DPPH	−0.99
Kaempferol-ABTS	−0.99
Kaempferol-FRP	0.97
Kaempferol-SNP	0.99

(r = 0.97 and r = 0.96, respectively). While the scavenging capacity and the reducing power were related negatively. However, previous study has suggested there is a linear correlation between the different mechanism of action of antioxidants compounds of some plant extracts [68, 69].

4 Conclusion

The phytochemical profile and the biological activity in different parts (leaves and flowers) of Tunisia *L. camara* species were investigated. To estimate the phenolic compounds, antioxidant potential, anti-inflammatory activity, reducing power ferric and silver nanoparticle of *L. camara* leaves and flowers fractions were prepared by using ultrasound-assisted process. The results showed that *L. camara* leaves revealed the highest amounts of polyphenol and flavonoids in quantitative terms (57.65 ± 0.39 g GAE/100 g DW and 7.11 ± 0.09 g RE/100 g DW, respectively) and were richer in phenolic acids (23.74 mg/100 g DW). Nonetheless, the flowers showed the highest flavonoids content (1091.70 mg/100 g DW). Both studied organs showed significant potential in all antioxidant tests compared to the reference antioxidant Trolox. The leaves fraction showed the highest DPPH and ABTS radical scavenging capacity. The flowers extract showed the highest ferric and silver reducing power (23.98 ± 0.16 g Trolox E/100 g DW and 68.15 ± 0.28 g Trolox E/100 g DW). Furthermore, the examined fractions did not protect the BSA from thermal degradation. The radical scavenging potential of the studied extracts were highly correlated with their total polyphenols, flavonoids, quinic acid and luteolin-7-O-glucoside contents, while the observed reducing power was only related to the level of kaempferol. These findings suggest that *L. camara* is a promising source of phenolic component with high antioxidant potential, which could explain some of its traditional uses.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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