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Phytochemical Study of *Urtica dioica* Extract and Evaluation of Sun Protection Factor (SPF)

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Abstract

Urtica dioica L., a medicinal plant from the Urticaceae family, is widely distributed in Europe, Africa, America, and parts of Asia due to its ability to adapt to various environments and climatic conditions. It is commonly used in traditional medicine for its numerous benefits. Its active compounds have the potential to contribute to the development of various medications, particularly for conditions such as skin cancer, by providing sun protection through sunscreens made from *U. dioica* extracts. The aim of our study is the phytochemical characterization and evaluation of the photoprotective activity of this plant. The identification of its components was carried out using phytochemical tests based on colorimetric reactions. The extraction of the compounds was performed through maceration with pure methanol, and the photoprotective activity was determined *in vitro* using spectrophotometry. The extraction yield was 8.75%. Phytochemical tests confirmed the presence of flavonoids, gallic tannins, sterols, terpenes, saponins, and alkaloids. The results showed a total polyphenol content 5.37 ± 0.17mg GAE/g DW in the methanolic extract, while the flavonoid content was 0.24 ± 0.12mg QE/g DW. The sun protection factor (SPF) was 22.56. *U. dioica* appears to be particularly promising for use in cosmetic products, providing excellent sun protection at a concentration of 2 mg/ml.

Keywords: *Urtica dioica*, phenolic extract, phytochemical screening, total polyphenols and flavonoids, photoprotective activity.

I. Introduction

According to the World Health Organization (WHO), 80% of developing countries continue to benefit from the use of traditional medicines derived from medicinal plants (Vaou *et al*., 2021). In Algeria, phytotherapy has long been a common practice in traditional medicine for treating various ailments, due to the richness of many plants in therapeutic compounds (Khalid *et al.,* 2019; Daira *et al.,* 2016). These active compounds are likely to play a key role in the development of numerous drugs aimed at treating various diseases, including cardiovascular, pulmonary diseases, certain types of cancer, and inflammatory disorders (Karima *et al*., 2022). The World Health Organization (WHO) estimates that 80% of developing countries continue to benefit from the use of traditional medicines derived from medicinal plants (Vaou *et al.,* 2021). In Algeria, phytotherapy has long been a traditional practice, widely used to treat various ailments due to the therapeutic properties of many plants (Khalid *et al*., 2019; Miara *et al*., 2013; Daira *et al.,* 2016; Warda *et al*., 2023). However, the regulations surrounding their use often lack precision and do not consistently consider contemporary therapeutic needs. In recent years, a great deal of research has aimed at improving traditional medicine by validating the effectiveness of the plants utilized and developing scientific guidelines for their application.

Among these medicinal plants, stinging nettle *Urtica dioica* L., also known as common nettle, is particularly notable. Although often recognized for its irritating touch, it also possesses significant medicinal properties. This wild plant, widely distributed in the Mediterranean basin, is often regarded as a weed (Bertrand, 2010; Daoudi *et al*., 2015; Aguirre Duran *et al*., 2022; Gülçin *et al*., 2004). Nettle reaches a height of 30 to 150 cm (Ţîţei, 2023) and is characterized by its opposite, oval, or heart-shaped leaves, dark green on top and lighter underneath (Testai*et al.,* 2002). It is a dioecious plant, with male and female flowers borne on different plants (Chavoutier *et al.,* 2000). The stem is robust, fibrous, and often simple, erect, hollow, and has a square section with deep vertical grooves (Singh and Sengar, 2021). The leaves and stems are covered with stinging hairs that release an irritating liquid upon contact with the skin (Said *et al.,* 2015).

Used for more than 2000 years, nettle has been a natural remedy throughout the ages (Said *et al.,* 2015). Medically, all parts of the plant are useful: seeds, leaves, and roots (Jan and Singh, 2017). Its main chemical components include flavonoids, tannins, fatty acids, sterols, terpenes, as well as vitamins and minerals (Fattahi *et al.,* 2014). Thanks to its high protein and vitamin content, including vitamin C, provitamin A, B2, B5, folic acid (B9), and vitamin K, nettle has gained a solid reputation

(Guil-Guerrero *et al.*, 2003; Rutto *et al.*, 2013). Additionally, it is rich in minerals such as iron, zinc, cobalt, potassium, and molybdenum (Said *et al*., 2015; Pradhan *et al.*, 2015; Rutto *et al.*, 2013).

Throughout history, *U. dioica* has found many applications, ranging from nutrition to textile production due to its strong fibers (Singh *et al*., 2019; Das *et al.*, 2015). It is also used as a natural fertilizer in the form of slurry (Garmendia *et al.*, 2018; Maričić *et al.*, 2022) and is an important source of chlorophyll for the food and pharmaceutical industries (Jan *et al.*, 2017; Manzoor *et al*., 2021).

Pharmacologically, *U. dioica* stands out for its antioxidant, analgesic, anti-inflammatory, and antiproliferative properties (Zhang *et al*., 2023; Cicero *et al.*, 2019). It has shown beneficial effects against benign prostatic hyperplasia (Saponaro *et al*., 2020), and its extracts inhibit platelet aggregation and inflammatory prostaglandins (El Haouari *et al*., 2006; Roschek *et al.*, 2009). Nettle also has antiviral (Kumaki *et al.*, 2011) and antimicrobial properties (Singh *et al*., 2013; Dar *et al*., 2013), as well as effects on gastrointestinal and liver disorders (Qayyum *et al.*, 2016).

Regarding sun protection, the growing demand for plant-based cosmetic products, including sunscreens, has led to further exploration of the photoprotective properties of nettle extracts. These natural products provide effective protection against ultraviolet (UV) rays, which are responsible for various skin damages (Napagoda *et al.*, 2016).

This study focuses on the phytochemical evaluation of *U. dioica* leaf extracts and the assessment of their sun protection factor (SPF) using methanolic extracts.

II. Materials and Methods

The *U. dioica* plant was collected in February 2022 from the Hassi Mameche region in the Wilaya of Mostaganem, characterized by a latitude of 35° 51' 40" North, longitude 0° 03' 13" East, and an altitude of 217 meters.

The aerial part (leaves) was carefully rinsed with distilled water to remove any particles or chemical residues. The freshly washed *U. dioica* leaves were gently dried with absorbent paper and then air-dried in the absence of light.

The dried leaves of the studied plant *U. dioica* were ground using an electric mill. The resulting powder was finely sieved to obtain an extremely fine consistency, ensuring better contact with the extraction solvent. The powdered *U. dioica* leaf sample, obtained after grinding and sieving, was stored in an airtight glass jar, kept in the dark for subsequent analyses.

II.1. Phytochemical Characterization

Phytochemical screening was conducted on the dried leaves of *U. dioica*. The analysis focused on detecting five bioactive compounds from secondary metabolism. The following compounds were examined:

- Alkaloids: Alkaloids were detected using the method described by Dohou *et al*. (2003), based on the reaction with Mayer's reagent;
- Flavonoids: The presence of flavonoids was identified through a colorimetric reaction in a basic medium, indicated by a light yellow color in the upper part of the test tube (Okmu, 2005);
- Gallic tannins: The method of Alain *et al*. (2011) and Hadduchi *et al*. (2016) was used, where the appearance of a dark blue-black color indicates the presence of gallic tannins;
- Sterols and terpenes: The formation of a brown or violet ring around the sample signals the presence of sterols and triterpenes (Daoudi*et al*., 2015);
- Saponins: The presence of saponins was detected through the formation of foam (Karumi *et al*., 2004).

II.2. Extraction of Polyphenols

The extraction was carried out according to the method described by Sujith *et al.* (2011). 10 g sample of ground plant material (leaf) was mixed with 100 ml of 96° methanol. The mixture was maintained in a water bath at 60°C for 20 minutes before being filtered. This process was repeated three times with the same plant material to ensure complete extraction of the active principles. The three filtrates were combined, and the solvent was removed using a rotary evaporator at 40°C.

II.3. Colorimetric Assay of Phenolic Compounds

II.3.1. Total Phenolic Content (TPC)

The colorimetric assay was performed according to the method of Li *et al*. (2013) using the Folin-Ciocalteu reagent. The protocol described by Singleton (1999) is as follows: In test tubes, 30 µl of methanolic extract of leaves and roots is added to 2.5 ml of Folin-Ciocalteu reagent diluted ten times. After 3 minutes of incubation, 2 ml of sodium carbonate solution (75 g/l) are added. The mixture is incubated in the dark at room temperature (28°C) for 30 minutes, and the absorbance is measured by spectrophotometry at 725 nm. According to Bentoumi (2019), the intensity of the blue coloration is related to the level of phenolic compounds present in the medium. The results are expressed as mg of gallic acid equivalents per gram of plant material (mg GAE/g PM), based on a gallic acid calibration curve.

II.3.2. Total Flavonoid Content (TFC)

The flavonoid content was determined according to the method described by Dowd, as adapted by Arvouet-Grand *et al.* (1994). 1 ml of extract is added to 1 ml of 2% aluminum chloride solution. The mixture is stirred and incubated in the dark for 10 minutes. Absorbance is measured at 415 nm. The flavonoid content is expressed as mg of quercetin equivalents per gram of plant material (mg QE/g PM).

II.4. Dermal Photoprotection Activity

In nature, UV light induces the accumulation of flavonoids and other phenolic compounds in the epidermal tissues of plants. Research has focused on the use of UV-absorbing flavonoids and phenols as antioxidants in sunscreens to ensure protection against UV rays. This opens a new field for the use of natural antioxidants in the prevention of UV-induced diseases. Consequently, significant efforts have been devoted to developing *in vitro* techniques to assess the photoprotection of sunscreen compounds.

The polyphenols extracted from *Urtica dioica* leaves were dissolved in ethanol at a concentration of 2 mg/mL to evaluate their *in vitro* sun protection factor (SPF). The absorption spectra of the samples were recorded across the 290 to 320 nm wavelength range, with ethanol used as the blank. Absorption measurements were taken at 5 nm intervals, with five readings recorded for each wavelength. The SPF value was then calculated based on the data obtained, using the equation from Mansur *et al.* (1986).

$$\text{SPF spectrophotometric} = CF \times \sum_{290}^{320} EE(\lambda) \times I(\lambda) \times Abs(\lambda)$$

EE: Erythemal Effect;

I: Radiation Intensity;

Abs: Extract Absorbance;

CF: Correction Factor (=10).

Table 01: Normalized function used in the calculation of SPF

Wavelength (λ nm)	EE x I(normalized)
290	0.0150
295	0.0817
300	0.2874
305	0.3278
310	0.1864
315	0.0837

320	0.0180

III. Results and Discussion

III.1. Results of Phytochemical Screening

Phytochemical tests were conducted on the dried and ground leaves of *U. dioica* using specific reagents. The phytochemical screening revealed the presence of secondary metabolites in the plant tissues. The results of these tests are presented in Table 02.

Table 02: Phytochemical Screening Results of *Urtica dioica*

Compounds	Abundance
Alkaloids	+
Flavonoids	+
Gallic tannins	+
Sterols and terpenes	+
Saponins	+

These phytochemical tests reveal that *U. dioica* is rich in secondary metabolites, including alkaloids, gallic tannins, flavonoids, saponins, as well as sterols and terpenes. These findings are consistent with those reported by Karima *et al.* (2022). In contrast, phytochemical results for other species of the same genus, such as *U. urens*, *U. pilulifera*, and *U. membranacea*, show the presence of the same secondary metabolites but without alkaloids (Daoudi *et al.*, 2015; Farag *et al.*, 2013).

III.2. Yield of extractions of polyphenol

The yield of phenolic extracts from the dried leaves of *U. dioica* was 8.75%, which is similar to the result found by Karima *et al*. (2022) with a yield of 8% and close to the value reported by Bellabes *et al.* (2020), who recorded a yield of 10.94%. Furthermore, Zekovic *et al.* (2017) obtained a yield of 3.66% using 96% ethanol for polyphenol extraction from *U. dioica* leaves, and a yield of 1.50% when using ethyl acetate alone. According to Toubal *et al.* (2019), the extraction yield obtained from the whole *U. dioica* L. plant harvested in Dellys (Algeria) was 1.62±1.25% for the aqueous extract and 4.8±0.18% for the alkaloids. A study by Jakubczyk *et al*. (2015) on *U. dioica* harvested in Poland reported a methanolic extract yield of 17.45% from the aerial parts. However, Krajewska and Mietlinska (2022) found an aqueous extract yield exceeding 50%.These yields are lower than those observed in the current study, potentially due to differences in biotic conditions and the harvesting period. As noted by Silva et al. (2007), it's crucial to recognize that comparing results with previous studies can be challenging because of different influencing factors (solvents, extraction methods, plant material origin, etc.), which can affect the reliability of cross-study comparisons.

III.3. Total Phenolic Content (TPC)

The polyphenol content in the prepared extracts was determined by spectrophotometry using the linear regression equation of the standard curve, plotted with gallic acid (Fig. 01). The results are expressed in mg GAE/g DW. The equation of the curve shows a linear relationship with a strong coefficient of determination (R^2 = 0.9054), indicating a high correlation between absorbance and gallic acid concentration.

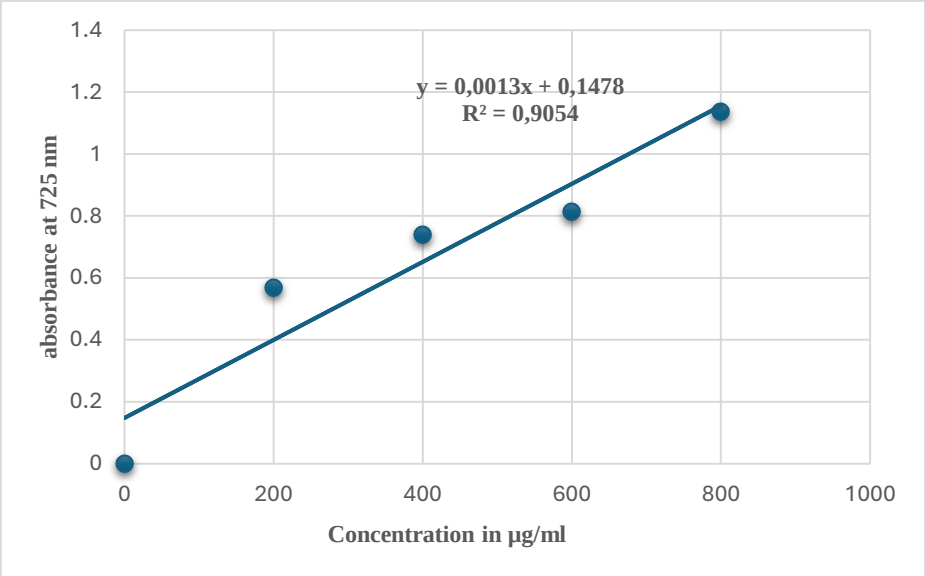

Figure 01: Calibration Curve of Gallic Acid

Methanol is capable of breaking down plant cells and releasing phenolic compounds. Additionally, as a more polar solvent than ethanol, it effectively dissolves polar phenolic compounds such as phenolic acids, glycol, and fatty acids. According to the findings of Tura and Robards (2002), methanol also inhibits the activity of polyphenol oxidases, which helps reduce the degradation of phenols.

Our results (5.37± 0,17GAE/g DW) are significantly lower compared to those of Taraseviči*ė*n*ė* *et al*. (2023), who obtained 21.60 mg GAE/g DW from *U. dioica* leaves using pure methanol with the same extraction method. Similarly, Bellebas *et al.* (2020) reported comparable results, with a yield of 4.57 ± 0.14 mg GAE/g DW. Furthermore, Karima *et al*. (2022) found 26.02 mg GAE/g DW using methanol extraction. The total phenolic content (mg GAE/g DM) in methanolic extracts, as reported by Asgarpanah and Mohajerani (2012), was 32 ± 0.148.

Indeed, the polyphenol content varies both qualitatively and quantitatively from one plant to another. This variation can be attributed to several factors such as: climatic and environmental conditions, genetic heritage, harvest period, and developmental stage of the plant (Chrubasik *et al.*, 1997). Additionally, the extraction method and quantification technique can significantly influence the estimation of total polyphenol content (Aguirre Duran *et al.*, 2022).

III.4. Total flavonoid content (TFC)

The results of total flavonoid content are expressed in quercetin equivalents, calculated using a calibration curve with the equation y = 0.0129 [Que] - 0.0085 and a determination coefficient (R^2) of 0.999 for the methanolic extracts of *U. dioica* leaves (Fig. 02).

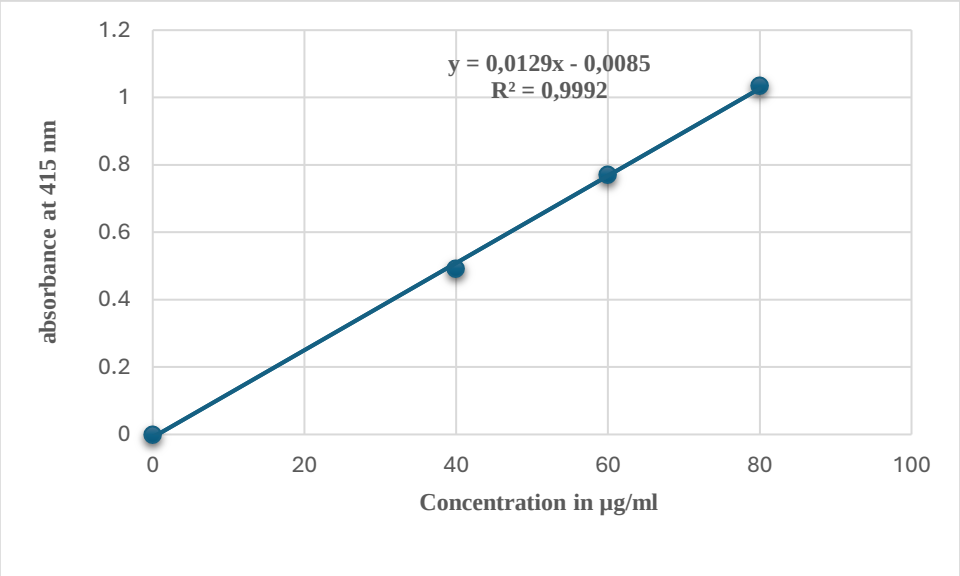

Figure 02: Quercetin Standard Curve

According to the results, the total flavonoid content in the extracts from nettle leaves was 0.24± 0,12 mg QE/g DM, which is close to the values obtained by Belabbas *et al.* (2020), who reported 1.73 ± 0.56 mg QE/g DM. Furthermore, Tarasevičienė *et al*. (2023) found significantly higher results using the same extraction solvent, reaching 20.11 mg QE/g DM.

III.4. Evaluation of Dermatoprotective (Photoprotective) Activity

Sunscreens, used as photoprotective agents against UV rays, have gained popularity due to their ability to absorb, reflect, or scatter sunlight. The Sun Protection Factor (SPF) is a key indicator of their effectiveness in preventing sunburn, with higher SPF values indicating greater protection (Mishra *et al.*, 2011).

However, prolonged exposure to UV rays, particularly UV-B (280-320 nm), increases the risk of skin conditions such as skin cancer and photoallergic reactions. In recent years, research has shifted towards using natural substances as promising alternatives for sun protection, due to their UV-absorbing capabilities and antioxidant properties (Ahmida *et al*., 2024).

Table 03: The average absorbances of each extract for the SPF test

λ (nm)	Abs	SPF
290	3,39 ± 0,20	0,5
295	3,09 ± 0,21	2,52
300	2,58 ± 0,06	7,41
305	2,02 ± 0,4	6,62
310	1,97 ± 0,16	3,67
315	1,94 ± 0,13	1,62
320	1,24 ± 0,18	0,22
Total		**22,56**

Skin cancers have become a major public health issue, with an increasing incidence over the past fifty years. The primary risk factor is exposure to ultraviolet (UV) rays (Fera *et al.,* 2023). UV rays, located in the ultraviolet spectrum between 290 and 320 nm wavelength, are primarily responsible for sunburn, skin aging, and the development of skin cancers (Zago *et al.,* 2024). Sunscreen factors (SPF) are generally classified into four categories: low protection (SPF between 2 and 15), moderate protection (SPF between 15 and 30), high protection (SPF between 30 and 50), and very high protection (SPF above 50) (Schalka and Reis, 2011).

The extracts from *U. dioica* leaves tested show moderate protection with an SPF of 22.56. In comparison, an aqueous extract containing 4% moringa leaves would provide an SPF of 2.01 (Baldisserotto *et al*., 2018). Rue (*Ruta graveolens*) is presented by Spanish, Portuguese, and Brazilian teams as a potential source of UV filters. The tested extract (200µg/mL) provides an SPF of 5.34 ± 0.13. The whole fruit extract of pink pepper at a dosage of 15 mg/mL provides an SPF of 20.15 (Oliveira *et al.,* 2020). For *Crataegus*, the effect is striking. At a dosage of 2 mg/mL, the extract obtained with a Soxhlet extractor is poor, with an SPF of 0.152, which is surprising since this value should not be below 1. However, the extract obtained using ultrasound is excellent, with an SPF of 24.47 (Ebrahimzadeh *et al.,* 2014).

Conclusion

In the context of valorizing natural plant-based substances and seeking biologically active compounds, *U. dioica* (stinging nettle) emerges as a notable Algerian species with numerous applications, particularly for its therapeutic properties.

This study focuses on a phytochemical screening of *U. dioica* collected from the northwestern region of Algeria, specifically from Mostaganem. We were able to evaluate the levels of phenolic compounds, including total polyphenols and flavonoids, as well as assess their *in vitro* photoprotective activity (SPF).

Phytochemical analysis of the aerial parts of the plant confirmed the presence of alkaloids, flavonoids, sterols, terpenes, gallotannins, and saponins. The extraction yield was 8.75%. The total polyphenol content was approximately 5.37 ± 0.17 mg GAE/g RS, and the flavonoid content was around 0.24 ± 0.12 mg EQ/g MS. The plant demonstrated a photoprotective activity with an SPF of 22.56, indicating its potential value in cosmetic products, particularly sunscreens.

Future studies should focus on evaluating the suitability of these compounds in cosmetic formulations to enhance their dermatological use. Additional *in vivo* studies are necessary to confirm the safety and efficacy of these bioactive compounds.

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