

Tanacetum Parthenium (L.) Sch Bip From Peru: Antioxidant Profile and The Antinociceptive Effect in An Experimental Model

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ABSTRACT

Background: *Tanacetum parthenium* (L.) Sch Bip known as “santa maria” (*Asteraceae* family) is used in Peru for inflammatory diseases and also in colic, stomachache, headaches, diarrhea, among other. **Objective:** The aim was to determine the antioxidant profile, and analgesic effect of ethanolic extract of flowers and leaves of *T. parthenium*. **Material and Methods:** Leaves and flowers of *T. parthenium* were soaked in 96% ethanol and the obtained extract was analyzed using chemical reactions for identifying each secondary metabolite, 2,2-Diphenyl-1-picrylhydrazyl (DPPH) was used to determine the antioxidant capacity, and the antinociceptive effect was determined by using tail flick method. **Results:** Qualitative phytochemical study indicates the presence phenolic compounds, alkaloids, flavonoids, saponins and steroids in both extracts. In DPPH assay IC₅₀ showed in leaves and flowers extract 452.10 ± 10.2 µg/mL and 270.70 ± 20.6 µg/mL respectively. The antinociceptive effect was better in leaves at doses 300 mg/Kg than flower extract. **Conclusions:** The ethanolic extract of flowers of *T. parthenium* showed a high antioxidant activity and antinociceptive effect in mice.

Key words: *Tanacetum parthenium*, Antioxidant, Polyphenols, Analgesic, Medicinal plants.

INTRODUCTION

The use of medicinal plants plays a vital role in managing of many diseases overall in those with an inflammatory component, because inflammation is the cause of many diseases, including cancer.¹ The herbal and natural products have been known throughout history and folk medicine and are safe depending on the doses or concentration used in dosage forms or traditional preparations.² Furthermore, it can be used as a parallel alternative to modern synthetic drugs.³ Additionally, maceration, infusions, and decoctions are the most utilized forms of preparation. Thereby, the use of medicinal plants and natural products has acquired interest in worldwide considering an alternative therapy to treat a variety of diseases in developing countries.⁴

Pain can be acute or chronic and is an unpleasant sensation, an emotional experience associated with actual or potential tissue damage.⁵ Pain is considered a prognostic or therapeutic indicator but also is a symptom in joint and musculoskeletal disorders trigger to loos function.⁶ Nonsteroidal anti-inflammatory drugs (NSAIDs) and narcotics are currently the most prominent class of drugs for pain management but they are at marked risk because of their serious side effects such as kidney and liver damage as well as gastrointestinal complications while constipation and dependence are associated with narcotic drugs.⁷

Tanacetum parthenium (L.) Sch Bip (*Asteraceae* family) is an herb that grows in Peru and is called “santa maria”, it possesses a fragrance and bitter taste. Traditionally is used for digestive problems such as diarrhea, abdominal pain, and other like

migraine and mountain disease.⁸ The extract of this plant has revealed the presence of sesquiterpene lactone like parthenolides and various phenolic compounds. The main metabolite isolated in *T. parthenium* named parthenolide presented analgesic effect after sciatic nerve injury.⁹ Thereby, the aim in this study was to determine the antioxidant capacity and antinociceptive effect of the ethanolic extract of leaves and flowers of *Tanacetum parthenium* (L.) Sch Bip.

MATERIALS AND METHOD

Collection and selection of botanical material

T. parthenium was collected in district of Cordova, province of Huaytara, department of Huancavelica in December 2022, between 3000 - 3500 masl. The collection was carried out in the early hours of the morning, and a sample of the entire plant (stem, flower and inflorescence) was taken for its subsequent botanical identification through a taxonomic classification in the Natural History Museum of the Universidad Nacional Mayor de San Marcos with certificate number (272-USM-2015). The plant was stored in kraft paper bags. The plant material obtained was approximately 3 kg.

Obtention of the ethanolic extract of *T. parthenium*

The ethanolic extract was obtained from the leaves and flowers separately, by the maceration method, which consisted of extracting the metabolites of the species under study until exhaustion, using 96% ethanol as solvent, then, it was proceeded to evaporate until complete dryness of the preparation with the help of a rotary evaporator at 40°C.

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Preliminary phytochemical screening and antioxidant activity

Identification and coloring reactions were carried out for each type of secondary metabolite present in the ethanolic extract of leaves and flowers, with the specific reagents; The results indicated the presence or absence of the metabolites: 5 mg of each extract was redissolved in its respective solvent, to then add 5 drops of reagents respectively in the sample to be tested. The antioxidant activity was carried out against the 2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical according to Herrera et al. ⁵

Determination of the analgesic effect of the ethanolic extract of leaves and flowers of *T. parthenium*

Experimental animals: Albino mice of Balb/C 53 strain of both sexes were obtained from the National Institute of Health's Bioterio. The animals were kept under ambient conditions, having free access to a standardized diet and fresh water *ad libitum*. Then, mice were kept in boxes with a controlled temperature of 25 ± 2 °C, with 12 h of light and 12 h of shade. Mice were divided into 6 groups of 6 mice each, fasting 18 h before the experiment. Tramadol (Tramal ®) 1mg/Kg was used as a positive control.

Procedure: The lower portion of the tail, approximately 5 cm, was submerged in a beaker of water maintained at 55 ± 0.5 °C. The time in seconds for the tail to withdraw from the water was taken as the reaction time. The cut-off points for not injuring the animal was 10 s. The reaction time was measured 1 h before and 1 h after the administration of the extracts. The control drug was administered subcutaneously 30 minutes before the test.⁵

After the test, the animals were euthanized with sodium thiopental at a dose of 100mg/Kg subcutaneously.

Experimental group n Treatment

Group I: Control (distilled water (10 mL/Kg)

Group II: Tramadol 1 mg/Kg s.c.

Group III: Ethanolic extract of *T. parthenium* flowers 100 mg/Kg v.o.

Group IV: Ethanolic extract of *T. parthenium* flowers 300 mg/Kg v.o.

Group V: Ethanolic extract of *T. parthenium* leaves 100 mg/Kg v.o.

Group VI: Ethanolic extract of *T. parthenium* leaves 300 mg/Kg v.o.

Statistical analysis

Data were processed using the statistical package SPSS (statistical package for social sciences), version 24.0. A $p < 0.05$ was considered significant, with a confidence interval of 95%. The mean and standard error of the individual values obtained were determined.

RESULTS

Yield percentage of the ethanolic extract of leaves and flowers

An equation was used to determine the yield percentage of the ethanolic extract (% EE) of leaves and flowers respectively, obtained with the following expression:

$$\% EE = \frac{\text{Final weight of the ethanol extract}}{\text{Initial weight of the used plant}} \times 100$$

$$\% EE \text{ of leaves} = 16.10$$

$$\% EE \text{ of flowers} = 10.40$$

Table 1: Phytochemical screening of the ethanolic extract of leaves and flowers.

Chemical group	Reaction	Evidence	Leaves	Flowers
Phenolic compounds	FeCl3	Dark green	+	+
Tannins	Gelatin	Precipitate	-	-
Flavonoids	Shinoda	Red	+	+
	Dragendorff	brick red precipitate	+	+
Alkaloids	Wagner	brown precipitate	-	+
	Mayer	white precipitate	+	+
Triterpenes and Steroids	Lieberman Burchard	Dark green	+	+
Saponins	Foam	persistent foam	+	+
Amino acids	Ninhydrin	violet	+	+
Quinones	Bontrager	Red	-	-

Negative (-), Positive (+).

Table 2: Determination of the antioxidant activity against DPPH of the ethanolic extracts of *T. parthenium* leaves and flowers.

Extract	IC ₅₀ µg/mL ± SD
Ethanolic extract of <i>T. parthenium</i> leaves	452.10 ± 10.2
Ethanolic extract of <i>T. parthenium</i> flowers	270.70 ± 20.6
Trlox (antioxidant standard)	0.54 ± 0.12

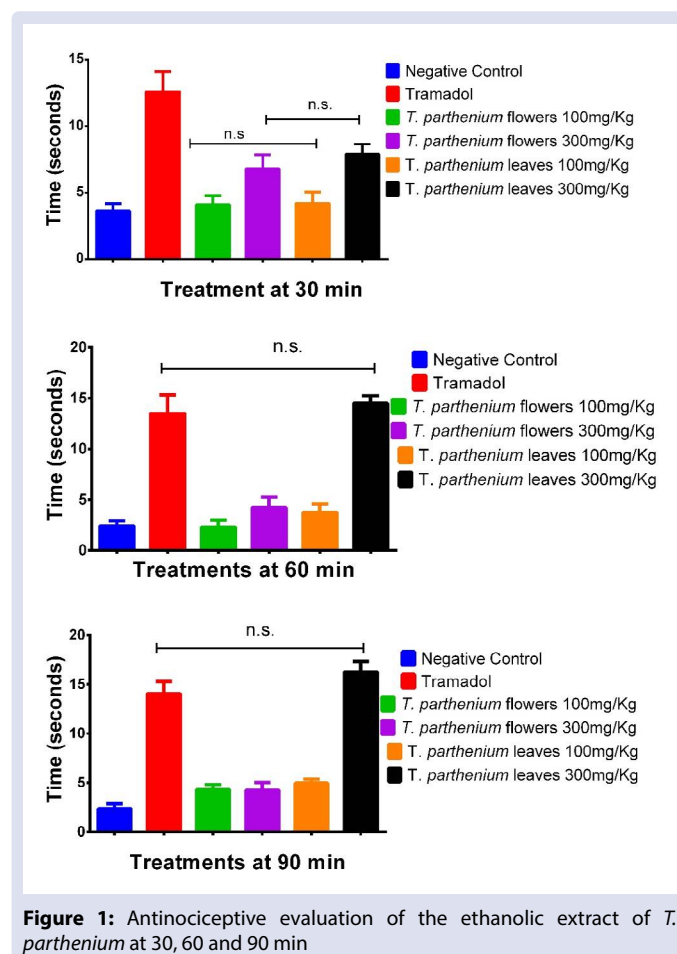


Figure 1: Antinociceptive evaluation of the ethanolic extract of *T. parthenium* at 30, 60 and 90 min

Phytochemical analysis

The results of the phytochemical Screening of the ethanolic extract of *T. parthenium* leaves and flowers are shown in table 1. As is shown the flowers

extract presented the same compounds than leaves extract, only there was not a reaction with Wagner reagent in leaves extract but it was positive in Dragendorff and Mayer, which indicates the presence of alkaloids.

Antioxidant activity

Regarding the antioxidant activity, the better effect was observed in flowers extract compared to leaves extract. However, both extracts were less than the control Trolox. (Table 2)

Evaluation of the antinociceptive effect in mice

The ethanol extract of *T. parthenium* presented better results at 100 and 300 mg/kg at 60 min post administration by oral route. In the evaluation, non-significant effect was observed between tramadol and the ethanol extract at 100 and 300 mg/kg ($P = 0.5666$) at 60 and 90 min of evaluation. (Figure 1)

DISCUSSION

T. parthenium, is a medicinal plant used among the rural population of the department of Huancavelica to generally ameliorate digestive problems. The study carried out gives us an idea of the possible active principles of the plant, responsible for the analgesic and anti-inflammatory effects, as well as antioxidants. In the phytochemical study, the ethanolic extract of flowers and leaves presented similar secondary metabolites. The secondary metabolites determined in the present study are related to the results reported by Enciso *et al.*⁸

In the *in vitro* antioxidant capacity assay against the DPPH radical, the ethanolic of flower extract had a high antioxidant capacity than the leaf extract, which shows that the *in vitro* antioxidant activity, however the extracts did not exceed the standard antioxidant Trolox. Since the most representative metabolite are triterpenes and steroids, according to Jain *et al.*,¹⁰ polyphenols are also recognized for their property as free radical scavengers due to their property of donating electrons, their antioxidant activity depends on the stability of different systems as well as on the number and the location of hydroxyl groups.¹¹

The tail withdrawal test (Tail-Flick Test or D'Armour & Smith test) is a test that assesses sensitivity to pain by evaluating the tail withdrawal latency in response to a thermal stimulus in rats. and mouse.¹² When the rodent feels discomfort, it tries to remove the tail (tail flick) from the heat source. Changes in the tail flick latency times or reaction time of the animal then reflect the pain sensitivity of the animal.¹³ In the present study, the ethanolic extract of the leaves (300 mg/Kg) presented a better effect compared to the flowers (100 and 300 mg/Kg) and similar to the standard used tramadol (1 mg/Kg). The mechanism is still unknown because it is an extract with mixtures of different compounds, but a study carried out by Parvin *et al.*, demonstrated that the ethanol extract of *T. parthenium* at 40 mg/Kg and 80 mg/Kg has an analgesic effect in rats by intraperitoneal administration.¹⁴ On the other hand, parthenolide is an active constituent (0.856%) in *T. parthenium* extract, and could be responsible of the analgesic effect in both extracts. Although in this study, it was not evaluated the presence of this sesquiterpene lactone, a study confirms its analgesic effect being superior to nimesulide (an analgesic drug) at 2 mg/Kg.¹⁰

CONCLUSION

As a result of the phytochemical analysis carried out on the ethanolic extract of leaves and flowers of *T. parthenium* have been identified the presence of phenolic compounds, triterpenes and/or steroids, alkaloids, and flavonoids. The ethanolic extract of leaves and flowers of *T. parthenium* presented antioxidant activity against the DPPH radical,

having an IC_{50} of $472.16 \pm 15.2 \mu\text{g/mL}$ for the leaf extract and an IC_{50} of $246.75 \pm 25.6 \mu\text{g/mL}$ for the ethanolic flower extract. The ethanolic extract of the leaves of *T. parthenium* presented better analgesic effect at a dose of 300 mg/Kg than flower extract.

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