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Anti-inflammatory Activity of *Taraxacum officinale* on Carrageenan-induced Paw Edema in Wistar Rats

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ABSTRACT

Background: *Taraxacum officinale* (dandelion) has been traditionally used to treat liver disorders and inflammation. This study investigates the anti-inflammatory effects of its ethanolic extract (EET) in a carrageenan-induced inflammation model in Wistar rats.

Methods: Twenty male rats were divided into four groups (n=5). Group 1 served as the negative control, while Groups 3 and 4 received a 3% carrageenan intra-dermal injection. Groups 2 and 3 were treated with EET (200 mg/kg body weight) twice daily for seven days. Blood samples were analyzed for antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase) and inflammatory biomarkers (PGE2, TNF-α).

Result: Carrageenan injection increased malondialdehyde, PGE2, TNF-α, blood glucose and fibrinogen while decreasing albumin, total proteins and antioxidant enzymes, leading to paw lesions. EET treatment significantly restored malondialdehyde (48.14%) and reduced PGE2 (20.95%) and TNF-α (23.75%). It increased albumin (48.48%) and total proteins (44.26%) while reducing blood glucose (47.91%) and fibrinogen (37.93%). Antioxidant enzymes improved (superoxide dismutase 67.58%, catalase 35.04% and glutathione peroxidase 34.40%), with notable lesion repair. These findings confirm the anti-inflammatory properties of *T. officinale*, suggesting its potential as a natural therapeutic agent for treatment of inflammation.

Key words: Carrageenan, Inflammation, Inflammatory biomarkers, *Taraxacum officinale*.

INTRODUCTION

Nature can contain miracle plants with significant nutritional and therapeutic potential, such as dandelion (Ürüºan, 2023) and *Bunium bulbocastanum* which are frequently found in Algeria (Bouhalla *et al*., 2023; Bouhalla *et al*., 2024). Interest in medicinal plants has grown due to their benefits in managing oxidative stress disorders and overall health (Petkova *et al*., 2015). Natural compound-based treatments often have fewer side effects than pharmacological alternatives.

Taraxacum officinale (dandelion), a perennial herbaceous plant from the Asteraceae family, is widely distributed in the Northern Hemisphere and traditionally valued for its medicinal properties (Jinchun and Jie, 2011).

Dandelion has demonstrated antidiabetic, choleretic, antirheumatic and diuretic effects. Studies suggest its potential in reducing inflammation and tumor risk,it exhibits diverse pharmacological activities, including diuretic, laxative, cholagogue, antirheumatic, anti-inflammatory, anticarcinogenic and hypoglycemic effects (Schütz *et al*., 2006).

This study investigates the in vivo anti-inflammatory activity of *T. officinale* in a carrageenan-induced paw edema model in Wistar rats.

MATERIALS AND METHODS

Collection and authentication of the plant

The aerial parts of *Taraxacum officinale* were collected from Tazgait, Mostaganem (Algeria) in March 2020. The plant was washed to remove debris and soil particles before extraction.

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Extraction

Plant extraction followed the modified protocol of You *et al*. (2010). The dried plant material was crushed and 200 g

was macerated in 1000 mL of 70% ethanol at room temperature for 48 hours in the dark. The extract was filtered (Whatman No. 4), concentrated using a rotary evaporator at 45°C to remove ethanol and stored in a dark glass bottle at 4°C.

Animals and housing

After two weeks of acclimatization, Wistar rats were assigned to four groups. G1 and G2 received 1 mL of physiological normal saline water (0.9%) orally, while G3 and G4 received 1 mL of *T. officinale* ethanolic extract (200 mg/kg). On the seventh day, one hour after the last dose, G2 and G4 received 100 µL of 3% carrageenan intradermally to induce paw inflammation (Onoja *et al*., 2017).

Four hours post-inflammation, rats were silenced with sedative and anesthetized with light chloroform and sacrificed. Blood was collected from the retro-orbital sinus into dry, heparin, EDTA and citrate *via*ls. The entire right-hind paw was rinsed with physiological normal saline water (0.9%), preserved in 10% formalin at room temperature and processed for histological examination.

Determination of biochemical parameters

Glucose

Glucose levels were determined using the enzymatic (Hexokinase/G-6 PDH, Biomérieux, France) and colorimetric (Biolabo Kit, France) methods.

Albumin

Albumin was measured using bromocresol green, which shifts from yellow-green to blue-green in proportion to albumin concentration (Webster, 1977).

Total proteins

Proteins were quantified using a biuret reaction in an alkaline medium, producing a blue-violet complex proportional to protein concentration (Burtis and Ashwood, 1999).

Fibrinogen

Fibrinogen levels were determined using the chronometric method based on thrombin time (Clauss, 1957; Destaing *et al*., 1960), employing titrated calcium thrombin (Fibriprest Automate).

Antioxidant status

- Malondialdehyde (MDA) was measured following Yagi (1976).
- Catalase activity was assessed per Lück (1965).
- Superoxide dismutase activity followed Elstner and Heupel (1976).
- Glutathione peroxidase activity was determined using Paglia and Valentine (1967).

Inflammatory biomarkers

- Prostaglandin E2 (PGE2)

PGE2 levels were measured using an ELISA Kit *via* a competitive inhibition immunoenzymatic assay. The intensity of the yellow reaction product, detected at 412 nm, was inversely proportional to the PGE2 concentration.

- Tumor necrosis factor-α (TNF-α)

TNF-α levels were quantified in liver homogenates using a sandwich ELISA. A monoclonal anti-TNF-α antibody captured the cytokine, which was then detected using a biotin-conjugated antibody and Streptavidin-HRP. The final colorimetric reaction, proportional to TNF-α concentration, was measured at 450 nm.

Statistical analyses

Statistical analyses were performed using Statbox 6.04. Results were expressed as means±standard de*via*tion (n=5). A significance level of $p<0.05$ was applied.

RESULTS AND DISCUSSION

Biochemical parameters

Fig 1 represents the blood sugar level in Wistar rats treated or not by carrageenan. Compared with the rats of the negative control group, carrageenan increased the blood sugar level in the rats of the second group with a rate of 68.51%. A significant decrease ($P<0.05$) of this parameter is noted in the rats of the G4 group (47.91%), which received 200mg/kg of the ethanolic extract of *Taraxacum officinale* (EET) compared to the ratio to the second group.

High glucose levels in rats of group G2 (injected only with carrageenan), that inflammation can unbalance diabetes and *Taraxacum officinale* exerts a protective and preventive effect against carrageenan-induced hyperglycemia.

Ribezzo *et al*. (2016) show that oxidative stress plays a key role in the perpetuation of inflammation and by the release of cytokines and is observed in various diseases such as cardiovascular diseases, neurodegenerative diseases as well as diabetes that hyperglycemia is one of these signs, which is explained by the results of the positive control group.

Davaatseren *et al*. (2013) show that *Taraxacum officinale* has an antidiabetic role. Total proteins The serum concentrations of total proteins are reported in Fig 2.

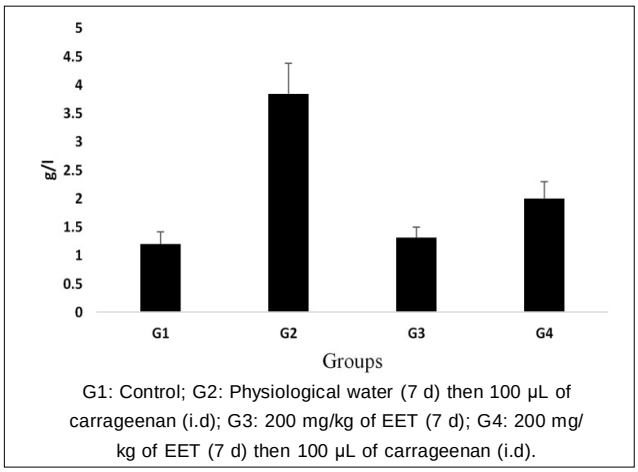
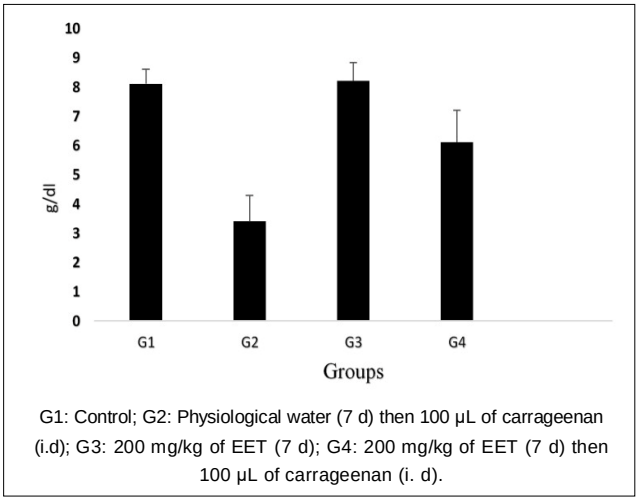


Fig 1: Glycemia (g/l) in rats treated or not with the ethanolic extract of *Taraxacum officinale* (EET) and/or carrageenan. The values represent the mean (m) of 5 determinations ±SEM (n=5).

Through the results obtained, the injection of carrageenan in G2 resulted in a significant decrease (P<0.05) in the total protein level which is of the order of 4.7 g/dl compared to the control group (G1) (8.1 g/dl).

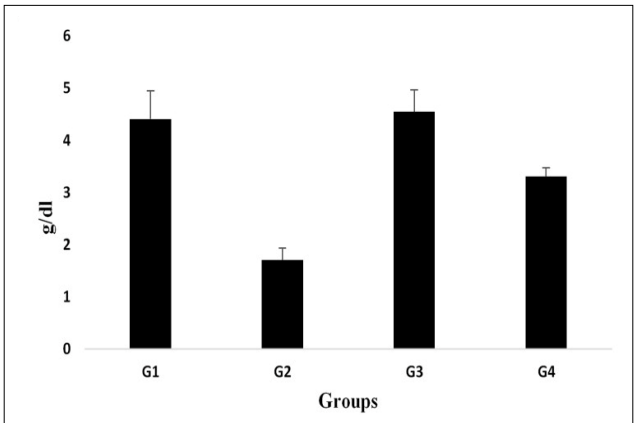
On the other hand, there is a significant increase (P<0.05) observed in rats pretreated with EET (G4), whose levels of total proteins (44.26%) are higher almost 2 times than those recorded in rats of the positive control group G2.

Fig 3 represents the serum albumin concentrations. Our results show that the administration of the EET extract does not significantly affect the albumin levels in group G3 (4.54 g/dl), these are almost similar for the negative control group G1 (4.4 g/dl).



G1: Control; G2: Physiological water (7 d) then 100 µL of carrageenan (i.d); G3: 200 mg/kg of EET (7 d); G4: 200 mg/kg of EET (7 d) then 100 µL of carrageenan (i. d).

Fig 2: Total proteins (g/dl) in rats treated or not with the ethanolic extract of *Taraxacum officinale* (EET) and/or carra geenan. Values represent the mean (m) of 5 determinations±SEM (n = 5).

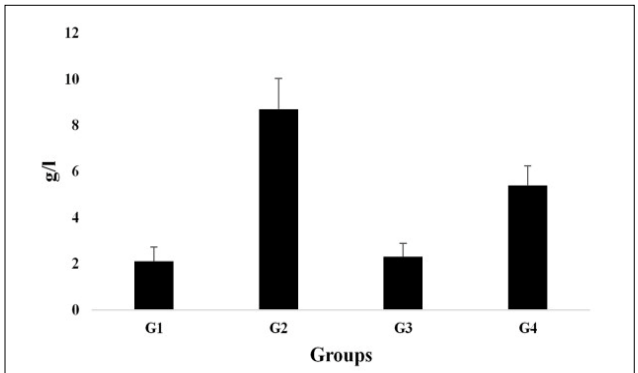


G1: Control; G2: Physiological water (7 d) then 100 µL of carrageenan (i. d); G3: 200 mg/kg of EET (7 d); G4: 200 mg/kg of EET (7 d) then 100 ìL of carrageenan (i. d).

Fig 3: Albuminemia (g/dl) in rats treated or not with the ethanolic extract of *Taraxacum officinale* (EET) and/or carrageenan. The values represent the mean (m) of 5 determinations ±SEM (n = 5).

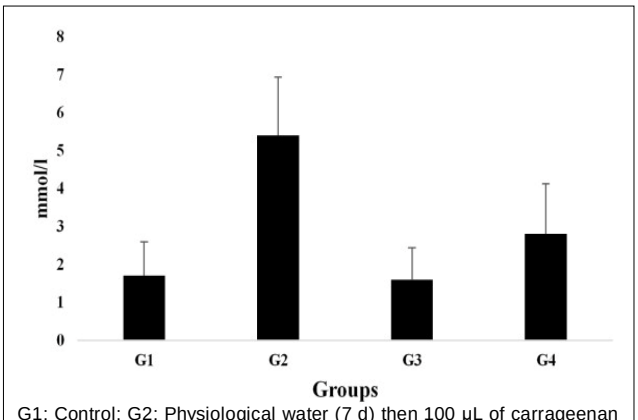
However, the intradermal injection of carrageenan significantly modified (P<0.05) the proportions of albumin in G2 animals, decreasing their levels with a rate of 61.36% compared with G1. And a significant increase (P<0.05) in the albumin level in rats pretreated with 200 mg/kg of ethanolic extract of *Taraxacum officinale* then injected with 100 µl of carrageenan of the order of 61.36% compared with G1.

Total proteins mainly include albumin, globulins (alpha 1, alpha 2, beta, gamma) are synthesized by the liver (Belier and Michaux, 2007). During tissue inflammation, there is normally vasodilation and capillary recruitment and at least transient increases in capillary permeability. This leads to



G1: Control; G2: Physiological water (7 d) then 100 µL of carrageenan (i. d); G3: 200 mg/kg of EET (7 d); G4: 200 mg/kg of EET (7 d) then 100 µL of carrageenan (i. d).

Fig 4: Fibrinogen (g/l) in rats treated or not with the ethanolic extract of *Taraxacum officinale* (EET) and/or carrageenan. Values represent the mean (m) of 5 determinations ±SEM (n = 5).



G1: Control; G2: Physiological water (7 d) then 100 µL of carrageenan (i. d); G3: 200 mg/kg of EET (7 d); G4: 200 mg/kg of EET (7 d) then 100 µL of carrageenan (i. d).

Fig 5: Malondialdehyde levels (mmol/l) in rats treated or not with the ethanolic extract of *Taraxacum officinale* (EET) and/or carrageenan. Values represent the mean (m) of 5 determinations ±SEM (n = 5).

extravasation of plasma proteins (Carlsson and Rippe, 1999) which was observed in the group subjected to inflammation (hypoalbuminemia and hypoproteinemia).

The plasma fibrinogen concentrations of rats exposed to inflammation are shown in Fig 4. According to our results, it is noted that the fibrinogen concentration increased significantly (P<0.05) by 75.86% in animals that received only a carrageenan injection at the paw (G2) compared to the control group (G1). In comparison with rats in group G2, the EET decreased the fibrinogen concentration in rats of group 4 with a level of 37.93%.

Fibrinogen is a soluble protein synthesized by the liver.It is a marker of inflammation (Louisot, 1983) so the increase in fibrinogen in the positive control group (G2) compared to the control group (G1) is a sign of the onset of inflammation.

Antioxidant status

The malondialdehyde level of the different groups is presented in Fig 5.

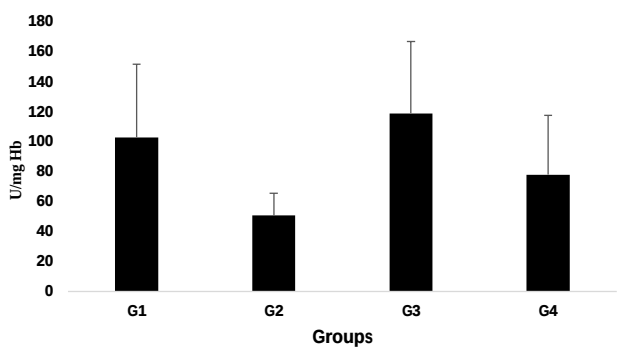
A very high level of malondialdehyde (68.51%) is noted in rats of group G2 injected with carrageenan compared to rats of the control group G1. Compared with the MDA level of rats of group G2, rats of group G4 pretreated with EET then carrageenan showed a reduced level of 48.14%. Our observations are in line with those obtained by (Park *et al*., 2011) who suggest that the two 'extracts: aqueous and methanolic of*T. officinale* root have a protective action by reducing lipid peroxidation (MDA) which observed in rats of the group pretreated with the ethanolic extract of *Taraxacum officinale* then undergone inflammation with carrageenan.

Oxidative status: Catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) levels

A highly significant (P<0.05) reduction in the enzymatic activity of catalase, superoxide dismutase and glutathione peroxidase to respective levels of50.77;78.29 and 50.29% is due to intradermal injection of carrageenan which induced inflammation in G2 rats compared to the control group (G1) (Fig 6,7 and 8). Furthermore, daily administration of EET at a dose of 200mg/kg attenuated carrageenan-induced inflammation in (G4) animals at estimated increases in the enzymatic activity of CAT, SOD and GSH Pxof the order of 57.40 ; 79.56 and 56.98% respectively, compared to G2.

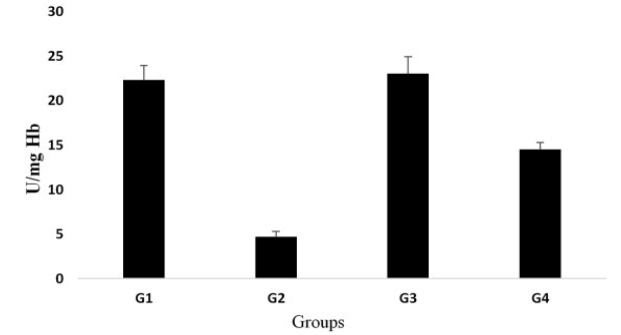
Superoxide radical produced during mitochondrial electron transport chain or as a product of nitric oxide synthase, NADPH and xanthine oxidase. Nitric oxide is formed by NO synthase from L-arginine and molecular oxygen. O_2 is dismutated by superoxide dismutase SOD to H_2O_2 which is then converted to OH or detoxified by catalase to water. In addition, NO and O_2 react spontaneously and rapidly to form peroxynitrite (ONOO) (Kandikattu *et al*., 2015; Hausladen and Stamlert, 2017).

Antioxidants recovered from medicinal plants and enzymes of different derivatives from various biological sources such as catalase, peroxidases and superoxide dismutase play



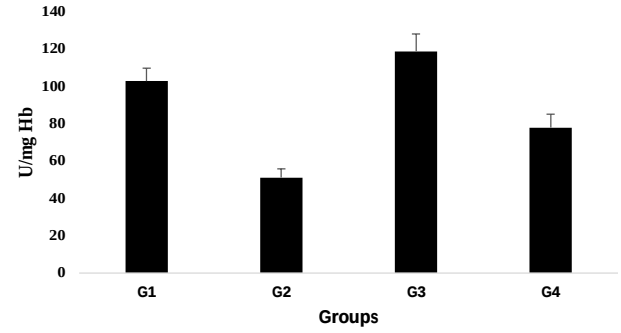
G1: Control; G2: Physiological water (7 d) then 100 µL of carrageenan (i. d); G3: 200 mg/kg of EET (7 d); G4: 200 mg/kg of EET (7 d) then 100 µL of carrageenan (i. d).

Fig 6: Catalase levels (Umg/Hb) in rats treated or not with the ethanolic extract of *Taraxacum officinale* (EET) and/or carrageenan. Values represent the mean (m) of 5 determinations ±SEM (n = 5).



G1: Control; G2: Physiological water (7 d) then 100 µL of carrageenan (i. d); G3: 200 mg/kg of EET (7 d); G4: 200 mg/kg of EET (7 d) then 100 µL of carrageenan (i. d).

Fig 7: Superoxide dismutase levels (Umg/Hb) in rats treated or not with the ethanolic extract of *Taraxacum officinale* (EET) and/or carrageenan. Values represent the mean (m) of 5 determinations ±SEM (n = 5).



(i. d); G3: 200 mg/kg of EET (7 d); G4: 200 mg/kg of EET (7 d) then 100 µL of carrageenan (i. d).

Fig 8: Glutathione peroxydase levels (Umg/Hb) in rats treated or not with the ethanolic extract of *Taraxacum officinale* (EET) and/or carrageenan. Values represent the mean (m) of 5 determinations ±SEM (n = 5).

an important role in minimizing the rate of oxidation of other compounds (D'Angelo, 2009).

Our results show the anti-inflammatory effect of the EET and they corroborate with that (Park *et al*., 2011) which suggest that the ethanolic and aqueous extract of *Taraxacum officinale* reduced antioxidant enzyme activities including: Superoxide dismutase, catalase, GSH-peroxidase and GSH-reductase.

Biomarkers of inflammation

- Prostaglandin E2 (PGE2) levels

Fig 9 shows the prostaglandin levels in rats treated or not with the ethanolic extract of *Taraxacum officinale* and/or carrageenan Rats in group G2 treated only with carrageenan recorded a very significant increase ($P<0.05$) in the serum level of PGE2 of 60.67%, compared to the control group G1. While group G4 (which received 200 mg/kg of EET) showed a significant decrease of 20.95% in the concentration of PGE2 compared to the positive control group G2.

- TNF-α Levels

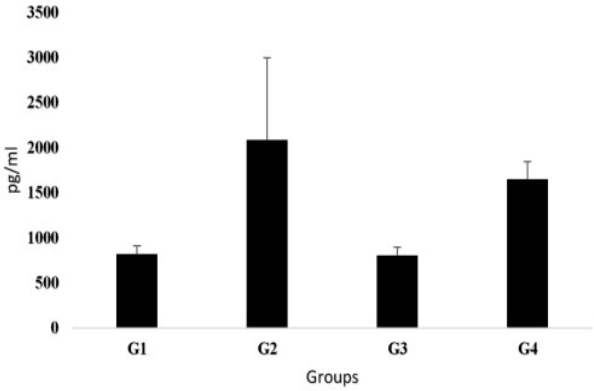
The level of tumor necrosis factor TNF-α ng/g in rats treated or not with the EET and/or carrageenan is shown in Figure 10. According to our results shown in the following figure, it is noted that there is a significant increase ($P<0.05$) (47.45%) in the serum level of TNF-α in rats of the second group G2 (which were injected with carrageenan only) compared to rats of the first group G1 (86.2 ng/g). Compared with the level of rats of group G2, rats of group G4 pretreated with EET extract and then carrageenan showed a reduced level of 23.75%.

Inflammation is a complex biological process that acts as a primary defense system to counteract harmful stimuli against foreign organisms such as bacteria and viruses. The inflammatory mechanism induces IKK and p-65 which activates cytokines and releases prostaglandins (PGE) (Loram *et al*., 2007; Turner *et al*., 2014).

Then inflammation is confirmed in the positive control group leading to a significant increase in prostaglandin levels because Bahmani *et al*. (2014) reported that flavonoids have effects on opioid receptors and alpha-adrenergic receptors which can inhibit enzymes involved in inflammation and pain. In addition, flavonoids in inflamed tissues inhibit cyclooxygenase, so they can prevent the formation of prostaglandins (PGE) Pilehvarian *et al*. (2010). This was recorded in rats in the group pretreated with 200 mg/kg of EETbecause our plant is rich in flavonoids. Our results corroborate those of Liu *et al*. (2010) who show that *Taraxacum officinale* also inhibits the production of inflammatory cytokines TNF 6 hours after lipopolysaccharide challenge in a dose-dependent manner in mice.

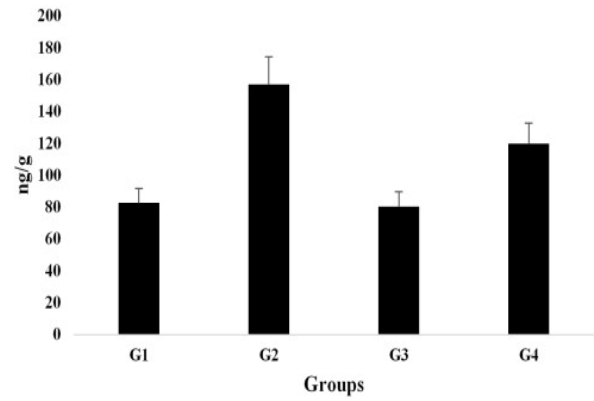
Histological study

Microscopic observation carried out on a topographical staining of histological sections of paws reveals the inflammatory action due to the injection of 100 µL of carrageenan intradermally (G2) at the level of the paw of rats Fig 11. This chronic inflammation is reflected at the level of tissue architecture by the presence of congestions, associated with edema between the muscle bundles at the level of the deep dermis (Fig 11 G2). Furthermore, an architectural aspect showing a normal striated muscle of the legs of the rats of the G3 group (which received only 200 mg/kg of *Taraxacum officinale*) as almost that of the control group (G1) (Fig 11 G3). However, the rats of G4 responded positively and effectively to the pre-treatment by the EET extract from which their structures seem to be restored compared to that found in the positive control group (Fig 11 G4).



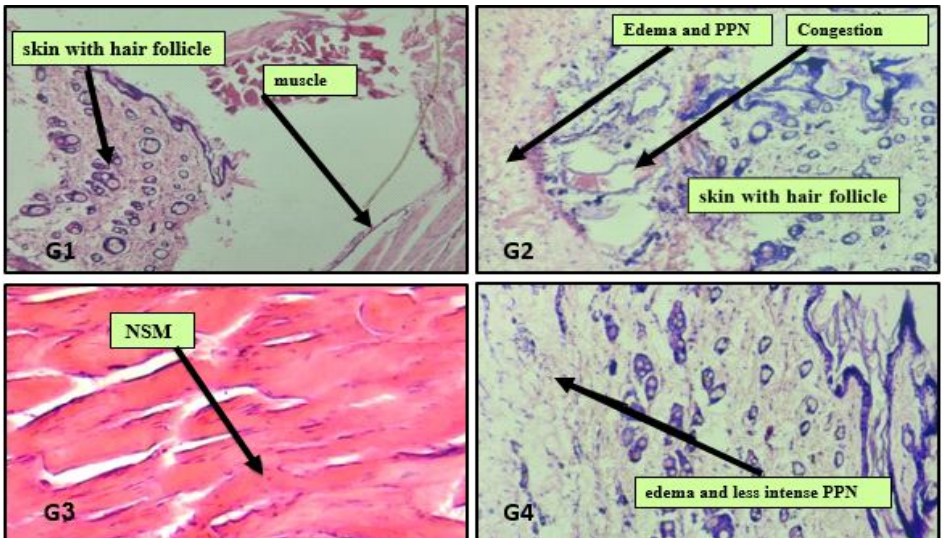
G1: Control; G2: Physiological water (7 d) then 100 µL of carrageenan (i. d); G3: 200 mg/kg of EET (7 d); G4: 200 mg/kg of EET (7 d) then 100 µL of carrageenan (i. d).

Fig 9: Prostaglandin levels pg/ml in rats treated or not with the ethanolic extract of *Taraxacum officinale* (EET) and/or carrageenan. Values represent the mean (m) of 5 determinations ±SEM (n = 5).



G1: Control; G2: Physiological water (7 d) then 100 µL of carrageenan (i. d); G3: 200 mg/kg of EET (7 d); G4: 200 mg/kg of EET (7 d) then 100 µL of carrageenan (i. d).

Fig 10: Tumor necrosis factor levels TNF-α ng/g in rats treated or not with the ethanolic extract of *Taraxacum officinale* (EET) and/or carrageenan. Values represent the mean (m) of 5 determinations ±SEM (n = 5).



(a) G1: Control; (b) G2: Physiological water (7 days) then 100 µL of carrageenan (3%) i.d; (c) G3: 200 mg/kg of EET (7 days) (d): G4: 200 mg/kg of *Taraxacum officinale* (7 days) then 100 µL of carrageenan (3%) id. PPN: polymorphonuclear neutrophils NSM: normal striated muscle.

Fig 11: Histological sections of the leg of the groups.

Liu *et al*. (2010) showed that *Taraxacum officinale* has been frequently used as a remedy for inflammatory diseases. The administration of (250 mg/kg) dandelion has a beneficial effect in decreasing catalase, glutathione peroxidase and superoxide dismutase, reducing lipid peroxidation (Ömür *et al*., 2017).

Our results are corroborated with those of Onoja *et al*. (2017) with the methanolic extract of *Justicia secunda* leaves. Hu and Kitts (2004) confirm that *Taraxacum officinale* contains luteolin which is possessed an anti-inflammatory effect. Jeon *et al.* (2008) demonstrated that *Taraxacum officinale* can be used in anti-inflammatory therapy with the advantage of having fewer side effects. Inflammation is a complex pathophysiological process mediated by various signaling molecules produced by leukocytes, macrophages and mast cells (Aoki *et al*., 2008). Symptoms result from increased blood flow to damaged or infected tissues, causing fever, redness, swelling and pain. Macrophages are major inflammatory cells and immune effector cells. A major function of macrophages is the phagocytosis of cellular and acellular debris during inflammation and healing (Scull *et al*., 2010).

Activated macrophages are present in inflamed tissues and play an important role in inflammatory disease *via* the release of inflammatory mediators. *Taraxacum officinale* has long been used as a medicinal plant to treat inflammatory diseases such as hepatitis, arthritis, rheumatism, breast abscess, lung abscess, intestinal abscess, scrofula, sore throat and swelling (Schutz *et al*., 2006; Park *et al*., 2011). In addition, various studies on *Taraxacum officinale* extracts and their components have demonstrated anti-inflammatory, antinociceptive, antioxidant and anticancer activities (Jeon *et al*., 2008; Choi *et al*., 2010; You *et al*., 2010), which is consistent with the results obtained during this work.

CONCLUSION

This study confirms that herbal medicine remains widely used for the treatment and prevention of inflammatory diseases. Intraperitoneal carrageenan injection led to increased blood glucose, fibrinogen, TNF-α and PGE2 levels, indicating acute inflammation. Histological analysis revealed inflammatory infiltrates, congestion and cellular necrosis, confirming tissue damage.

Administration of *Taraxacum officinale* extract (200 mg/kg/day) significantly mitigated these effects, restoring lipid profiles and reducing inflammatory biomarkers (PGE2 and TNF-α). Additionally, the extract enhanced antioxidant defenses by increasing superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-Px) activity, suggesting a protective antioxidant role. These findings highlight the potential of *T. officinale* as a natural anti-inflammatory agent.

Therefore, it would be interesting to note that this study will serve as a reference for the proper use of *Taraxacum officinale* and it would also be wise to conduct experiments with a view to producing a phyto-medicine based on this plant.

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Disclaimers

The views and conclusions expressed in this article are solely those of the authors and do not necessarily represent the views of their affiliated institutions. The authors are responsible for the accuracy and completeness of the information provided, but do not accept any liability for any direct or indirect losses resulting from the use of this content.

Informed consent

All animal procedures for experiments were approved by the Committee of Experimental Animal care and handling techniques were approved by the University of Animal Care Committee (Approval number by IAEC: 34/25, In May 2, 2025).

Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this article. No funding or sponsorship influenced the design of the study, data collection, analysis, decision to publish, or preparation of the manuscript.

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