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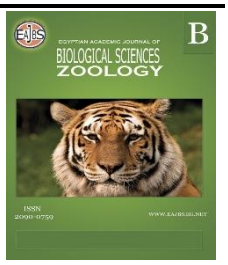

Contribution to the Study of The Antipyretic Effects of Aqueous Extracts of Two Plants « *Urtica dioica* and *Nerium oleander* ».

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ABSTRACT

The current treatment of febrile conditions involves non-steroidal anti-inflammatory drugs (NSAIDs), which are widely prescribed because of their efficacy in the management of pain, fever, and inflammation. However, their long-term therapeutic use is often associated with adverse effects such as gastrointestinal ulcers. Therefore, current research is based on the substitution of chemical treatments with natural treatments that are equally effective but have fewer side effects. One of the most widespread remedies is the use of substances of plant origin. Urtica dioica and Nerium oleander are two medicinal plants widely used for the treatment of various diseases in traditional medicine. The aim of this study was to evaluate the antipyretic effect of the aqueous extract of these plants in vivo. The administration of these extracts significantly reduced brewer's yeast-induced hyperthermia. The results of this study contribute to validating the medicinal virtues of these plants, especially in the treatment of febrile states. The phytochemical constituents are probably responsible for their pharmacological properties and could replace some drugs as they cause undesirable side effects.

INTRODUCTION

In the last two decades, research in herbal medicine has become one of the most important scientific concerns (Ezéchiel, L. J., *et al.*, 2022). As a result, WHO has set a strategy for traditional medicine that aims to maximize the potential of this form of medicine as a source of health care and to protect the raw material, especially in the case of plants (Chanda, R, 2002). It also recommends that developing countries initiate programs for the identification, preparation, cultivation, and conservation of medicinal plants and evaluate the quality and effectiveness of these remedies using modern techniques.

Algeria has a long history of traditional medicine. It is a country with a very varied geography and a very diverse flora (Lamia, S, 2022). Folk medicine continues to play an important role in the treatment of most diseases, particularly in rural areas (55% of the entire population) where people have limited access to modern medical care as opposed to the preparations used in traditional remedies, which are relatively cheap and easily accessible since they can be prepared from locally harvested plants (Aqil and Owais, 2006). In this socio-economic context, the study of plants can lead to adequate and low-cost therapeutic responses, combining proven scientific efficacy with cultural acceptability (Diallo, 2005). The scientific valorization of traditional medicine should lead to the development of plant-based medicines. The parameters in this field must be safety, efficacy, and quality. Our work focuses on the evaluation of the antipyretic effect of the aqueous extract of plants (Urtica dioica and Nerium oleander) on Wistar rats. The experiments were carried out in the biology laboratory of the University of Saida (Ain el-Hdjer) from October to May 2021.

MATERIALS AND METHODS

1-1-Biological material

Plant material

The plant material was purchased in dried form from the grocery shop located in Ain el Hajer in the Wilaya of Saida (**Table 1**), because of its major importance in Algerian culture as a culinary and even medical spice, and the plants (1 and 2) were used in a fresh and kept in a hermetically sealed glass jar to preserve their initial quality.This work was carried out at the laboratory of the University of Saida.

Table 1: description of the plants

Plants	Quantity of plant	The date of purchase	The origin of the plant	Condition
Plant 1 	300g	November	present in almost all regions of the world: from Europe and North Africa to Asia, as well as North and South America and South Africa.	Dry
Plant 2 	500g	November	Mediterranean countries, North Africa	Fresh

Animal Material:

The Rats: The experiments were carried out in the biology laboratory of the University of Saida, using white rats of the Wistar variety of the female sex, adults, aged 2 months, with a body weight of between 85 and 90g were used in the in vivo study. These animals were obtained from the Pasteur Institute of Algiers.

Evaluation of Antipyretic Effects:

The animals were kept at an ambient temperature of 22°C +/-4°C in conventional cages with a feeder and had free access to standard food, which corresponded to standard commercial food (al Alf).

2-1-Rat Rearing:

Rats are reared in cages lined with bedding that can be changed three times a week.

Feeding: The rats are fed pelleted food supplied by Sarl, a local producer in Bel Abess. This food is composed of barley, corn, bran, remoulage, and soya. They have free access to tap water and have been given an adaptation period of 7 days before use.

2-2-Group Allocation:

The rats were mated one week after arrival (three females and one male per cage). For this study, we used adult female rats of the Wistar strain with a body weight of between 75 and 104 grams from the central animal house of the university. The Rats were acclimated to our animal house for a period of two weeks prior to the trial.

On the first day of the trial, the rats were transferred to individual cages. They had free access to their food and drink. 4 batches, each consisting of 5 rats.

3. Preparation of the Aqueous Extract:

Decoction: In a ground flask, topped with a refrigerator. Mix 50 grams of plant material with 400 ml of distilled water.

- Heat to a steady boiling temperature for 2 hours in a stirring hot plate.

Allow the mixture to cool. Filter the mixture and recover the filtrate.

Store the filtrate in a bottle at 4°C.

3.3 Study of the Antipyretic Activity:

The objective of the work was to study the antipyretic effect of the aqueous decocts of the two plants studied (1 and 2) in order to popularize their use in traditional medicine.

Plant Material: The plant material was harvested in October 2017 in the Saida region and dried at room temperature.

Material: Brewer's yeast (*Saccharomyces cerevisiae*), Feeding probe, Stirrer, Magnetic bar, Watch glass, Spatula, erlenmayer, Paracetamol, Distilled water, Test tube, Thermometer and plant extract.

Preparation of the Decoctions:

50g of the plant material was boiled for 2 hours in 400 ml of distilled water.

Method: The antipyretic activity of the extracts was evaluated using fever-inducing brewer's yeast in rats (De Pasquale *et al.*, 1995). After rectal temperature taking, fever was induced in rats by subcutaneous injection in the dorsal lateral region of a 20% aqueous suspension of brewer's yeast at a dose of 20 ml/kg bw.

The animals fasted for seventeen (17) hours, the rectal temperature was taken again in each rat, and the different batches were given either distilled water or the plant decocts and the reference substance (paracetamol, 100 mg/kg) per os. One hour after the administration of the extracts, the temperature was taken every hour for four hours.

Four groups of animals, each containing five male rats, were given the following treatments orally:

Group I: Distilled water, which serves as the control,

Group II: received (U.D.) 100 and 200 mg/kkg bw, respectively,

Group III: received (N.O.) (100 and 200 mg/kkg bw) respectively,
Group IV: received paracetamol (150 mg/kkg bw) as a reference product.
These treatments were given with a volume of 10 ml per kg body weight 17 hours after fever induction. Rectal temperature was taken at 1, 2, 3, 4, and 6 hours after the treatments were given.

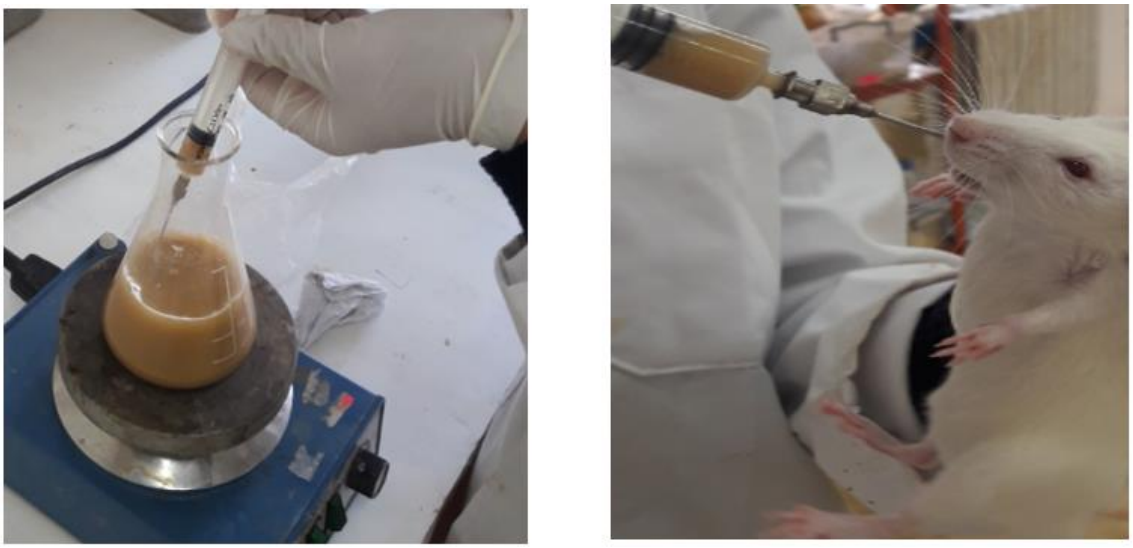

Fig. 1: Photo of preparation and administration of brewer's yeast by gavage.

Statistical Analysis:

The results of the tests carried out are expressed as a mean SD. An analysis of variance (ANOVA) is used to test the differences between the groups. Dunnett's multiple comparison is used to determine the significance of differences between the mean values of the treatment groups at the 0.05 level. The statistical studies were analyzed with the SPSS 20.00 software.

RESULTS

The injection of the brewer's yeast suspension causes a rise in rectal temperature after 17 hours. In fact, in the rats, the temperature rose from 34.2 to 36.7°C in the T+ batch, from 34.5 to 39.61°C in the UD batch, and from 36.2 to 37.2°C in the NO batch. The intraperitoneal administration of the aqueous extract significantly reduced the rise in temperature from 39.56/39.32°C to 34.48/34.68°C at the second hour of the measurement. Acetylsalicylic acid at a dose of 100 mg/kg bw lowered the rectal temperature of hyperthermic rats to 34.4 °C at the 2nd hour (Fig. 2).

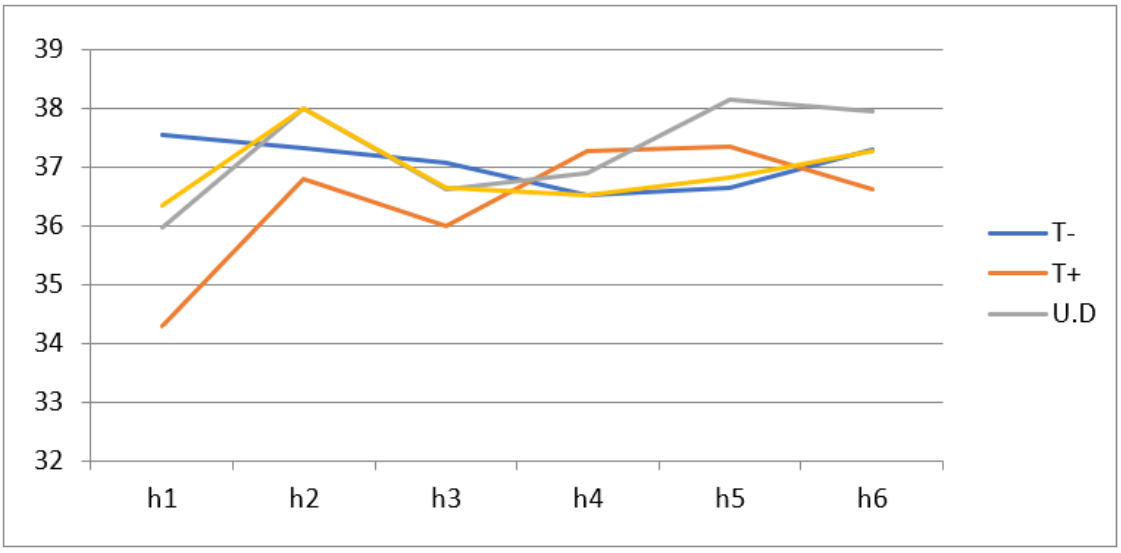

Fig. 2: Variation in temperature.

DISCUSSION

This study evaluated the antipyretic effect of the aqueous extracts of both plants on experimental animal models, whose hyperthermia was induced by yeast beer. The extract significantly reduced rectal temperature. This reduction is similar to that of the standard antipyretic drug, acetylsalicylic acid. Based on the data obtained from our study, it can be said that both extracts showed significant antipyretic, temperature-lowering activity. Thus, it can be deduced that these extracts inhibit the synthesis of prostaglandins. These results reflect that the extracts have some influence on prostaglandin biosynthesis, as the latter is considered a regulator of body temperature. Brewer's yeast was chosen for its similarity to an immunological binding protein called lipopolysaccharide (LBP), which causes the production of endogenous pyrogen leading to the synthesis and release of prostaglandins (Chan *et al.*, 2004; Taesotikul *et al.*, 2003). It is now generally accepted that prostaglandin E2 (PGE2) is the final mediator of fever in the brain, particularly in the pre-optic area of the anterior hypothalamus (Kripa *et al.*, 2011). In a state of rising body temperature, the temperature regulation system dilates blood vessels, causing increased sweating to lower the body temperature by a neural response mechanism (Li *et al.*, 2008; Aronoff *et al.*, 2001). Commonly prescribed antipyretics today include paracetamol, acetylsalicylic acid, and other non-steroidal anti-inflammatory drugs (NSAIDs). The major action of antipyretics lies in their potential to inhibit the enzyme cyclooxygenase (COX), which causes the interruption of inflammatory prostaglandin synthesis (Abe, S *et al.*, 2008). Previous studies have shown that the antipyretic effect of the Rosa genus on rats can be attributed to the presence of flavonoids (Hajare *et al.*, 2008). Furthermore, flavonoids and tannins are known to inhibit prostaglandin synthesis (Ramaswamy *et al.*, 1985). From our results and those of the above-mentioned authors, we can say that flavonoids, tannins, and other chemical compounds present in the methanolic extract are components responsible for the antipyretic effect. It would therefore be interesting to isolate the bioactive principles that are responsible for this activity.

The extracts of both plants reduced the hyperthermia caused by the brewer's yeast injection. The antipyretic effect of the extracts could be due to the reduction of cytokine release and prostaglandin biosynthesis (Bose *et al.*, 2007). Salicylic acid decreases fever of infectious, inflammatory, or neoplastic origin by counteracting the synthesis of

cytokine-induced prostaglandins PGE2 in the thermoregulatory center, which is the hypothalamus and increases heat loss by causing skin vasodilation (LeFevre, 2006). Compared to extracts of other plants, such as aqueous extracts of Pterocarpus erinaceus (Fabaceae) leaves at 400 mg/kg and Ximenia americana (Olacaceae) leaves at 400 mg/kg, which reduced hyperthermia by 0.70°C (Ouédraogo *et al.*, 2012) and 0.68°C, respectively (Soro *et al.,* 2009), the ethanolic extracts of Genista ferox and Clematis flammula are considered potent antipyretics.

Conclusion:

In this study, the aqueous extracts of Urtica dioica and Nerium oleander plants were obtained by decoction. In this work, we evaluated the antipyretic activity of the extracts of the 2 plants.

The evaluation of the biological activities on an animal model using Wistar-type rats by aqueous extracts of U.D. and N.O. against the diseases very widespread in the world like pain and fever.It can be concluded that the aqueous extracts of Urtica leaves were able to inhibit the sensation of pain and have analgesic activity in Wistar rats in a dose-dependent manner. Therefore, it can be deduced that the NO extracts showed antipyretic analgesic activity and also have an antipyretic effect that could help prevent fever complications.

The results obtained in this study are interesting, but further studies are needed to understand the molecular and cellular mechanisms of these effects. These studies should also be directed towards the determination of active compounds in NOUD extracts and the evaluation of their effects on the signaling involved in fever processes.

Finally, the Nerium oleander plant can be proposed as an alternative compound for fever prevention.

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