WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.421
Volume 8, Issue 1, 297-306 Research Article ISSN 2278 – 4357

ANALGESIC ACTIVITY OF *ASPHODELUS MICROCARPUS* LEAVES EXTRACT

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Article Received on
12 Nov. 2018,

Revised on 03 Dec. 2018,
Accepted on 23 Dec. 2018,

DOI: 10.20959/wjpps20191-12945

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ABSTRACT

Our study aims to investigate the existence of the analgesic activity on methanolic extract from leaves of *Asphodelus microcarpus(A.m.)*. It's parts in the context valuation the traditional pharmacopoeia. The peripheral and central analgesic activities had evaluated by the Koster and Tail Flick tests respectively. The methanolic extract of leaves from *A.m.*, obtained by cold maceration (yield=17.62%), the extract was subject of a study of the peripheral analgesic effect. At the dose of 50 mg/kg, this extract showed a significant inhibitory effect on the number of abdominal cramps which exceeded of aspirin, used as a reference at the dose of 200 mg/kg. About the test Tail flick, methanolic extract didn't have a significant inhibitory effect compared to morphine at the dose of 5mg/kg, on the pain caused by the heat of the light beam. Consequently, the methanolic extract of leaves from *A.m.* has a peripheral analgesic actvity, and its uses in traditional medicine against rheumatic pain could be justified by this activity.

KEYWORDS: *Asphodelus microcarpus*, analgesic activity, Koster, Tail Flick, aspirin, morphine.

INTRODUCTION

Medicinal plants are the main man's refuge for the treatment of diseases. They still remain a source of medical care in developing countries in the absence of a modern medical system.[1]

The majority of people use medicinal plants to treat themselves, not only because of a lack of access to medicines prescribed by modern medicine, but also because these plants are often available at affordable prices, and affective against certain diseases.

Today, the know-how of traditional practitioners is less and less transmitted and tends to disappear. This is why ethnobotany and ethnopharmacology are working to identify, throughout the world, plants that are reputed to be active for which it is us to modern research to specifie the properties and validate their uses. In Africa , nearly 75% of the population use the plants around them to care for themselves.[3]

In Morocco, heterogeneous and varied climatic and ecological conditions have favored the proliferation of more than 42,000 plant species, including 800 endemic species and subspecies.[4]

Empirical knowledge of traditional herbal medicine in Morocco has been transmitted verbally through generations, and has been enriched by a strategic geographical location between North Africa and the Sahara.

Currently, researchers are increasingly relying on traditional medicine, and this traditional know-how, was able to extract the interesting molecules from plants. That can be used in therapy and also solve serious health problems.

As part of the enhancement of traditional medicine, there was a growing interest in recent decades, forthe study of medicinal plants and their traditional uses in different parts of the world. The use of these plants for the treatment of various diseases generates considerable economic benefits.

Asphodel is an important plant in traditional pharmacopoeia[5], it is used for its anti-rheumatic[6], anticancerous properties, and also against ear infections, vitiligo and white skin spots of all kinds[7], against mumps[8], hemorrhoids, fungi and abscesses[9], hemorrhoids and fungi[7], gastric ulcers and recommended as a diuretic,[10] and diabetes.[11]

The general objective of our study, which is part of the enhancement of traditional pharmacopoeia, is to highlight the peripheral and/or central analgesic activity of *Asphodelus microcarpus.*

MATERIALS AND METHODS

*Collection and drying of the plant

The plant was harvested in March 2015 in the area of Ain Aouda, near Rabat. It was identified by the botanists of the Scientific Institute of Rabat and a sample of *A.m.* is deposited under the number RAB78996, in the National Herbarium, whose Index Herbariorum is RAB[12] which corresponds to the name of the city of Rabat, seat of this herbarium.

*Extraction mode

After drying at room temperature and out of the sun, the *A.m.* leaves were crushed before being extracted by cold maceration with methanol, repeated until they were exhausted, followed by filtration. The filtrate is concentrated using a rotavapor (60°C) and the extract obtained is stored in opaque vials, in a cool and dry place.

1. Calculation of the yield

We determined the yields of the plant's dry matter samples by calculating the following ratio:

$$Yeld\ (\%) = \frac{W1 - W2}{W3} \times 100$$

W1 : Weight of the storage tank after evaporation ;

W2 : Weight of the empty storage tank;

W3 : Weight of the starting plant material.

2. Analgesic activity

2.1. Peripheral analgesia

The study of peripheral analgesic activity of the aspirin type is performed by the Koster test [14]; a batch of 6 mice was tested to identify the effect of methanolic extracts from *A.m.* leaves, for each dose of 25 and 50 mg/kg orally. To determine peripheral nociceptive sensitivity, acetyl salicylic acid (aspirin) is used as a reference to 200 mg/kg oral dose. After 30 min, the animals receive 0.1 ml acetic acid by intraperitoneal injection and are placed in individual cages to be observed for 20 minutes. The parameter taken into account is the total number of cramps or frank abdominal twists, making it possible to calculate, for each treated batch, the percentage of protection against cramps, measured according to the following formula[15]:

$$\frac{Number\ of\ control\ batch\ cramps - Number\ of\ processed\ batch\ cramps}{Number\ of\ control\ batch\ cramps} \times 100$$

The number of cramps is noted 5 minutes after the injection of acetic acid and for a period of 20 minutes.

The mices used in this test are male swiss mice housed in the animal experimental centre of the Faculty of Sciences of Rabat, aged from 2 to 2.5 months and weighing 20 to 30 g.

2.2. Central Analgesia

The morphinic analgesic activity is evaluated by the Tail Flick test, (Figure 1) which is the experimental device used to produce heat. It consists of a bulb emitting radiant heat of 55 to 60°C, a stopwatch that is triggered at the same time as the radiant heat source, and a photoelectric cell that automatically stops the stopwatch as soon as the animal removes its tail.

Figure 1: Caudal Analgesiometer.

Before any treatment, we had sorted the animals, only rats with a normal reaction time, manifested by a tail withdrawal, less than or equal to 6 seconds were selected for the experiment.

Methanolic leaves extract at 50 and 100 mg/kg orally (Figure 2) and morphine (reference substance) at 5 mg/kg subcutaneously (Figure 3) were administered 30 minutes before the test. Tail removal reflex time is measured at 15, 30, 45, 45, 60 and 120 min after administration of extracts in batches of 6 rats.[13]

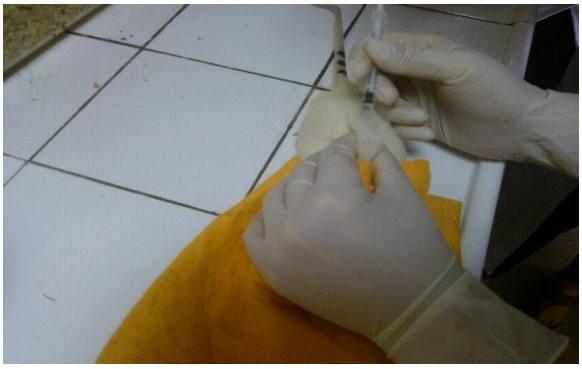

Figure 2: Injection of morphine.

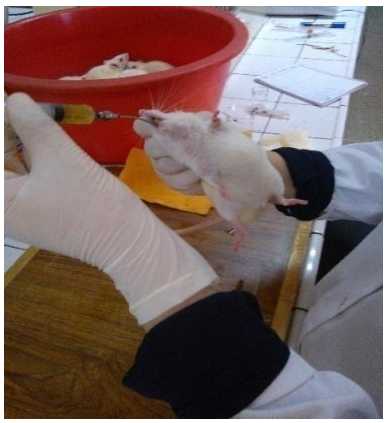

Figure 3: oral feeding of extracts.

The animals used for this test are male Wistar Rats, from the Faculty of Science in Rabat, weighing between 200 and 300 g, fasted 24 hours before the test.

The tail removal reflex is assessed before and after administration of extracts, this time is prolonged in case of analgesia, a time greater than 6 seconds reveals a central analgesic action.[13]

RESULTS

1. Extraction efficiency

The methanol extraction yield obtained by cold maceration with methanol of the leaves of *Asphodelus microcarpus* is 27.3% (w/w).

2. Analgesic activity

2.1. Peripheral analgesia

The number of cramps performed by the animal following intraperitoneal injection of 3% acetic acid and the percentage of inhibition of cramp, at different concentrations of methanolic extracts from the leaves of *A.m.* are presented in the table 1.

Table 1: Peripheral analgesic action of the methanolic extract of *Asphodelus microcarpus* leaves: aspirin type (Koster test).

Treatment	Dose	Number of cramps	% of Inhibition
Aspirin	200 mg/kg	24,5± 2,87	49,79 **%**
Leaves extract	50mg/kg	17,66± 2,42	63,81 **%**
Leaves extract	25mg/kg	43,25±3,4	11,37 **%**
Control	0	48,8±3,27	0 **%**

The results of this test show that the number of cramps induced by acetic acid was reduced by the methanolic extract from the leaves of the plant studied.

At a dose of 50 mg/kg, a significant inhibitory effect of methanolic extract was observed on the number of cramps with a percentage of 63.81%.

2.2. Flick Tail Test

The tail removal reflex is evaluated before and after administration of the extract, a reflex time greater than 6 seconds reveals a central analgesic action (Figure 4).

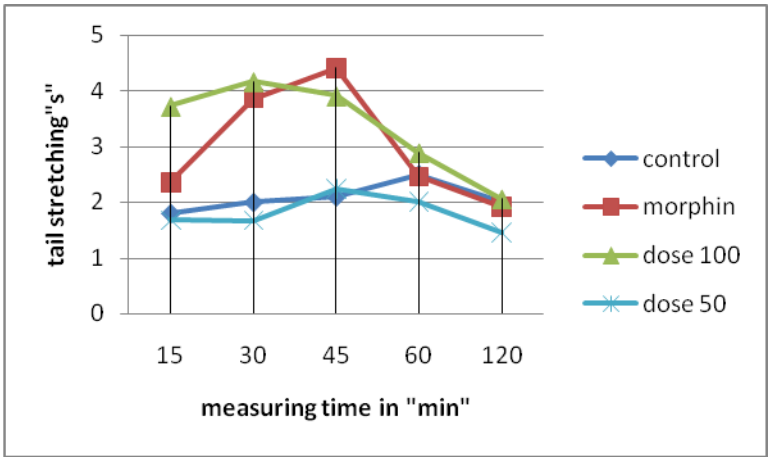

Figure 4: Central analgesic activity of methanolic extract from *Asphodelus microcarpus* leaves.

The Tail Flick test shows that tail removal time has gradually increased in rats treated with methanolic extract at a dose of 50mg/kg compared to the control batch and from 45 minutes onwards, it becomes at the same level as the reference (morphin) after 60 min, the effect of the extract disappears after 120 min and the rats return to their initial states. However, at 100 mg/kg, the results are similar to those of morphin.

DISCUSSION

Our study focused on the evaluation of analgesic effect of methanolic extract from the leaves of *Asphodelus microcarpus*. Koster and Tail Flick tests are used to determine the analgesic activity of the test substance.[16]

Acetic acid involves the peripheral mechanisms of the pain. It induces the release of many chemical mediators involved in pain such as histamine, prostaglandins, serotonin, bradykinin.[17] These mediators have been found in high proportions in rodent peritoneal exudates after injection of acetic acid.[18]

So the methanolic extract from *A.m.* leaves at a dose of 50 mg/kg with a significant analgesic effect may have an inhibitory effect on the release of mediators involved in peripheral pain. Our study on the leaves of the *A.m.* is the first to show a peripheral analgesic effect of this plant.

This analgesic effect is similar to that of many plants used in traditional medicine in painful syndromes whose extracts subjected to the Koster test showed an inhibition of abdominal cramps. For examples, we can quote Rumex abyssinicus Jacq (Polygonaceae)[20], a plant used in Ethiopian traditional medicine, and Drynaria quercifolia (L.) J. Smith (Polypodiaceae)[21], a plant used in Indian traditional medicine.

In 2017, Di Petrillo and al found that the leaves of *Asphodelus microcarpus* are rich in flavonoids[22] including Luteolin-6-C-glucoside; luteolin-6-C-acetilglucoside; luteolin-C-glucoside; luteolin, isoorientin. The analgesic effect observed for our extract may therefore be due to the presence of these flavonoids.

With regard to the central component of analgesic activity, the different doses of methanolic extract from the leaves of *Asphodelus microcarpus* administered by gavage do not inhibit the heat-induced pain of the light beam projected on the mouse tail. The Tail Flick test using thermal stimulus involves a spinal reflex, but could also involve neural structures. This method is used to identify central analgesics.[23] Thermal stimuli are selectively inhibited by central analgesics and not by peripheral analgesics.[24,25]

Methanolic extract from the leaves of *Asphodelus microcarpus* did not show central analgesic activity, unlike morphine, used as a reference substance.

Therefore, methanolic extract from the leaves of *Asphodelus microcarpus* would not have central analgesic activity at the doses used.

CONCLUSION

The use of *Asphodelus microcarpus* in traditional medicine for rheumatic pain could be justified by its significant peripheral analgesic effect from 50mg/kg and higher than that of acetylsalicylic acid (aspirin). While the central analgesic action of the morphine type is very low at the 100 mg/kg dose, against morphine, used as a reference substance.

Therefore, methanolic extract from the leaves of *Asphodelus microcarpus* would not have central analgesic activity at the doses used.

ACKNOWLEDGMENT

The author Hanae HOSNI wants to thank Pr Taleb Mohhamed Sghir and Dr Halim KHAMAR of scientific institute, Rabat for their help in identification of the species.

Also, we would like to thank Dr Kaoutar DIB for the English revision. And Dr El Houcine Bouidida for his valuable contribution and help.

Special thanks to all colleagues and professors at the Laboratory of Pharmacology and Toxicology, Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco especially Pr. Zellou Amina his kind advice during the experimental work.

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