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Evaluation of Analgesic Activity for Ethanol Extract of Leaves of Pistacia Atlantica Grown in Libya

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ABSTRACT

Pistacia atlantica is a potential herb belonging to family Anacardiaceae. It is a well identified medicinal plant and used in many medicines all over the world. Different types of chemical compounds are isolated from the plant body and mainly the roots, these chemicals form many bioactive substances. Fresh mature green leaves from female Pistacia atlantica were collected from Kikla -Libya during October 2022. The common name of the plant is Atlantic Pistacia and known in Libya as batum. The leaves were washed with distilled water, shade-dried for 15 days and then ground to fine power by a mechanical grinder then macerated with ethanol 96% for 7 days with daily stirring. The resultant extract of Pistacia atlantica was tested for its analgesic activity using a hot-plate method, concentrations of the ethanolic extract of Pistacia atlantica (25,50 and 100 mg) were used in three animal groups (n=3 rats in each group), and the reaction time was recorded in three time intervals (30, 60, 120 minutes) then compared to control and paracetamol (100mg/kg) treated groups, Findings from this study demonstrated that the three different doses of ethanol extract prolonged the reaction time in the hot plate method. Thus, the ability of the extract to inhibit these behaviors on hot plate method indicates that it has a good analgesic activity in comparison with control and paracetamol. In the present study, the analgesic activity could be due to presence of specific phenolic compounds known as antimicrobial and anti-inflammatory molecules. In fact, in previous studies several biomolecules were identified in Pistacia atlantica leaves such as Flavonoids, tannins, saponins . All those compounds are known for their great and potent anti-microbial and anti-inflammatory activities. In conclusion, the ethanol extract for the leaves of the Pistacia atlantica displayed analgesic activity and supported the traditional use of this plant in pain relief. Further study is warranted to identify the active compounds present in this extract and to elucidate the mechanisms involved in its analgesic properties.

1. INTRODUCTION

Medicinal plants are a rich source for making phytochemical with great efficiency and selectivity. Since the middle of the nineteenth century, many natural products were obtained in a pure form from plants; most of these products are available to be used as active agents in modern medication. Despite the significant advances in synthetic drugs, side effects remain that necessitate the search for effective, inexpensive, and more accessible drugs. Medicinal plants may provide such valuable therapeutic alternatives. Use of traditional medicinal plants with analgesic effects has recently gained popularity worldwide because of their natural origin and fewer side effects (Uddin, G. et al. 2011). There has been considerable public and scientific interest in the use of natural products to combat human diseases such as cardiovascular disease, cancer, and inflammatory disease (which may in any case, actually include other chronic disease, like CVD, cancer and diabetes). In spite of major scientific and technological progress in combinatorial chemistry, drugs derived from natural products still make an enormous contribution to drug discovery today (Punj, V. et al. 2004). Most of the synthetic analgesics and anti-inflammatory drugs that are currently in use cause potential toxic effects, for example the risk of gastrointestinal bleeding is significantly associated with use of (NSAIDs) and respiratory depression and possibly dependence related to opioid. Drugs currently used for management of pain or inflammation exhibit toxic side effects upon chronic use (Alsabri, S.G. et al. 2012). Pain is a major problem affecting human. Most of analgesics consumed by patients associated with numerous side effects including stomach upset, constipation, drowsiness, rash and to some extent severe adverse drug reactions (Butler, D. S. et al. 2013). Therefore, there is a desire need for searching of alternatives to control pain with affordable efficacy and safety. Pistacia atlantica is one of the famous and well known medicinal plant grown in Libya, despite the claims of plant as potent, safe and of a great importance as mentioned by the Libyan folkloric traditional medicine experts, there are no enough studies from Libya that concern with the analgesic activity of Pistacia atlantica (Ermeli, N. et al. 2012). A painful sensory or emotional experience connected to existing or potential tissue damage, or expressed in terms of such damage, is what is meant by the term "pain." It is often started by unpleasant stimuli and communicated to the central nervous system (CNS) via specific neural networks where it is regarded as such. It serves as a safeguard against potential harm to the body (Świeboda, P. et al. 2013). Similar to how the body responds to infections and tissue damage, inflammation is a protective mechanism used by both the innate and adaptive immune systems (Benhammou, N. et al. 2008). The treatment of chronic pain should be multidirectional. There are pharmacological methods of treatment, physical, rehabilitation, neuromodulation, psychological methods and in some cases, invasive techniques. It is extremely important to ensure mindful and comprehensive care for the patient, and to clarify and obtain acceptance of the chosen method of treatment from the patient (Abbaszadeh, S. et al. 2019). The use of herbal medicine in the world has increased dramatically in recent years. These products are not regulated by the Food and Drug Administration with the same scrutiny as conventional drugs (Al-Said, M.S. et al. 1990) . Patients who use herbal supplements often do so in conjunction with conventional drugs. Pistacia as a genus of flowering plants, family Anacardiaceae, have around twenty species, five of them are more popular such as: P. vera, P. atlantica, P. terebinthus, P. khinjuk, and P. lentiscus. Which are native at all of Africa, and southern Europe, warm and semi desert area across Asia and United States (Amri, O. et al. 2017). This current study focused on the evaluation of its analgesic activity, and to investigate in vivo analgesic activity of ethanolic leaf extract of Pistacia atlantica using hot-plate method in rats.

2. METHOD

Plant materials: Fresh mature green leaves from female pistacia atlantica were collected from Kikla -Libya during October 2022. The leaves were washed with distilled water, shade-dried for 15 days and then ground to fine power by a mechanical grinder.

Chemicals: 96% Ethanol, distilled water, paracetamol.

Instruments and other materials: Rotary evaporator, electrical grinder, polypropylene cages, sensitive balance, autoclave, graduated syringe, water bath.

Animals and experimental design: A total of 15 adult male Albino rats with body weights of 250-300 g were attained from the Laboratory Animal Unit of the National center of medical sciences Al zawia-libya. The rats were housed in polypropylene cages (3 rats /cage) in a ventilated room with a controlled light (12 hr): dark (12 hr) cycle and temperature (25 ± 2 0C). Food and water were provided. The animal management protocol and the experimental design were accepted by the Research Ethics Committee of the National center of medical sciences Al zawia-libya. After one week of acclimatization, rats were randomly divided into 5 different groups: 3 animals in each group. The rats in the 1st group were administered normal saline as a control, and in the 2nd group were administered paracetamol as a standard.

The animals in 3rd, 4th and 5th groups were administered pistacia atlantica ethanol extract using Intraperitoneal injection (IP) at doses of 25, 50mg, and 100 mg dried extract/kg body weight, respectively, in 0.5 mL of saline for time of 30 minute, 60 minute and 120 minute respectively.

Preparation of plant extract: Exactly 100 g of ground leaves was extracted with 96% ethanol by a cold maceration method. The extract was filtered through filter paper (No. 1) and then evaporated under reduced pressure at 50 0C using a rotary evaporator. The extract was stored in a 5 0C refrigerator for further.

Evaluation of analgesic activity of pistacia atlantica extract: Hot-plate method was used in the current study (Al-Said, M.S. et al. 1990, Jallali, I. et al. 2022). A total of 15 Adult male Albino rats with body weights of 200-300 g were attained from the Laboratory Animal Unit of the National center of medical sciences Al zawia-libya.
The rats were housed in polypropylene cages (3 rats/cage) in a ventilated room with a controlled light (12 hr): dark (12 hr) cycle and temperature (25 ± 2 0C). Food and water were provided. The animal management protocol and the experimental design were accepted by the Research Ethics Committee of the National center of medical sciences Al zawia-libya. After one week of acclimatization, rats were randomly divided into 5 different groups: 3 animals in each group. The rats in the 1st group were administered normal saline as a control, and in the 2nd group were administered paracetamol as a standard. The animals in the ,3rd, 4th and 5th groups were administered pistacia atlantica ethanol extract using Intraperitoneal injection (IP) at doses of 25, 50mg, and 100 mg dried extract/kg body weight, respectively, in 0.5 mL of saline for time of 30 minute, 60 minute and 120 minute respectively.

Statistical analysis
Data obtained are presented as means ± standard error of the mean (S.E.M) for the number of animals in each group (n=3), groups by SPSS SOFTWARE.

3. RESULT

Analgesic activity
The results in table 1 and (fiqure 1), demonstrated that the ethanol extracts exhibited a significant analgesic activity at the doses tested. The analgesic activities are comparable with the reference analgesic agent (Paracetmole) used in the present study with significant increase in the reaction time (in second) ($p < 0.05$) for the three plants extract under investigation in comparison with the control group.

Table 1:- Analgesic activity of ethanol extract of pistacia atlantica using hot plate method (Mean ± SD).

Treatment group	Dose Mg/kg	Mean reaction time (in second)		
		30 Min Mean±SD	60 Min Mean±SD	120 Min Mean±SD
Control	----------	8.67±0.47	8.83±0.31	8.43±0.25
Plant extract	25	11.16±0.98	7.40±1.02	9.96±1.12
Plant extract	50	9.90±0.67	9.56±0.85	8.40±0.32
Plant extract	100	15.80±0.23	8.06±1.09	8.01±0.87
Paracetamol	100	15.16±0.65	12.56±0.98	9.43±1.03

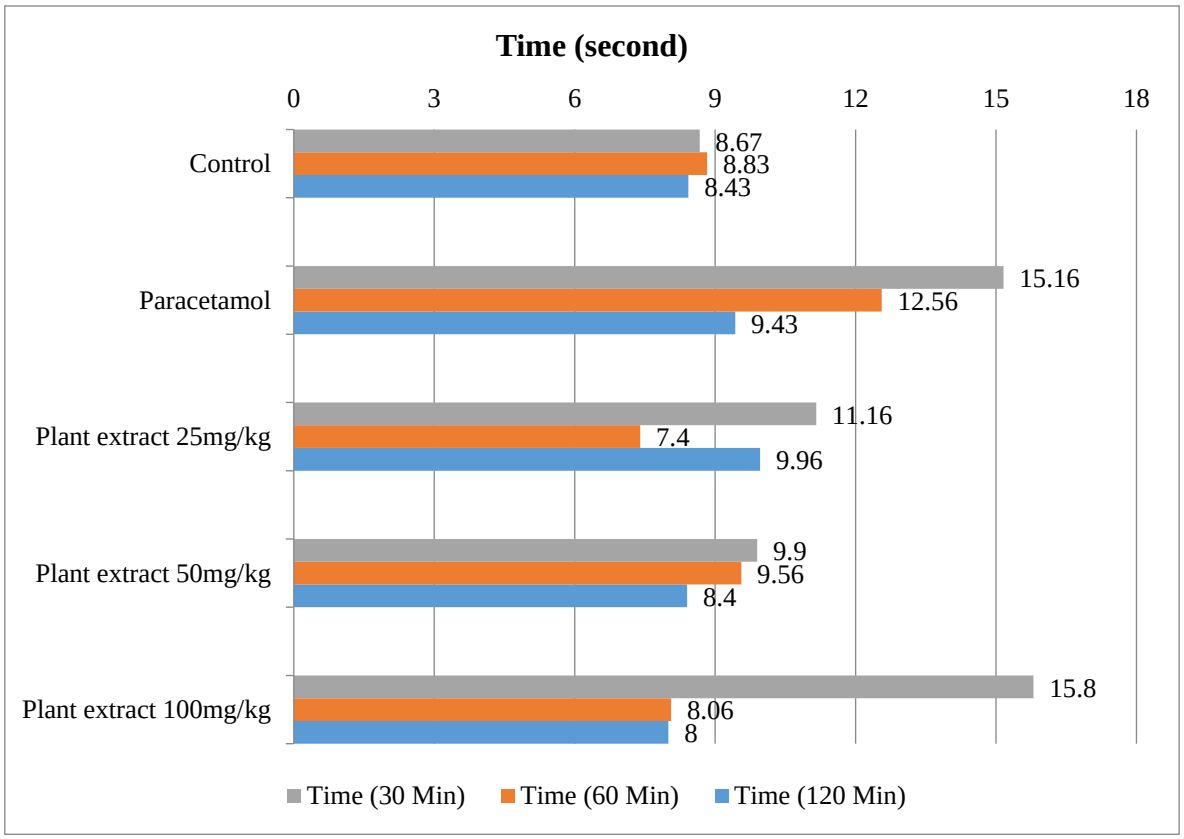

Figure 1:- The effects of the Pistacia atlantica ethanol extract administration on the reaction time in the Hot-plate method.

4. DISCUSSION

Analgesics are drugs that act on peripheral or central nervous system to selectively relieve pain without significantly altering consciousness (Alsabri, S.G. et al. 2012, Yimer, T. et al. 2020). Centrally acting analgesics act by raising the threshold for pain and also altering the physiological response to pain. On the other hand, peripherally acting analgesics act by inhibiting the generation of impulses at chemoreceptor site of pain (Hussein, S. et al. 2020). The animal models employed for screening of analgesic activity in this study are pain-state models using thermal stimuli which include tail-flick and hot plate methods. Both methods are useful in illustrating centrally mediated antinociceptive responses which focus generally on changes above the spinal cord level (Lebedev, M. A. et al. 2017). The ethanol extract from the leaves of pistacia atlantic caused increase the reaction time of the rats on hot plate method in this study. The difference in the mean reaction time of the extract and the control groups was statistically significant during all observation times. Analgesia in paracetamol treated rats was at 30, 60 and 120 minute. No significant analgesic effect was observed between three doses (25, 50 and 100 mg/kg) of the extract tested. Hot plate method produces two measureable behavioral components in response to thermal pain, with regard to their reaction times. Responses such as paw licking and jumping in rats are considered to be supraspinally integrated. Thus, the ability of the extract to inhibit these behaviors on hot plate method indicates that it has a good analgesic activity in comparison with control and paracetamol. Findings from this study demonstrated that the three different doses of ethanol extract prolonged the reaction time in the hot plate method. A number of alkaloids, flavanoids, steroids, and tannin isolated from medicinal plants have been reported to possess significant analgesic activity (Pekacar, S. et al. 2022). In the present study, the analgesic activity could be due to presence of specific phenolic compounds known as antimicrobial and anti-inflammatory molecules as mentioned in the previous studies (Shah, J. P. et al. 2015, Shareef, H. et al. 2019, Tanideh, N. et al. 2021).

5. CONCLUSION

In conclusion, the ethanol extract for the leaves of the pistacia atlantica displayed analgesic activity and supported the traditional use of this plant in pain relief.

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