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Phytochemical Investigation and Anti-Inflammatory Activity of Zilla Macroptera L

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ABSTRACT

In this work we have investigated the analgesic and anti-inflammatory activities of the organic and aqueous extracts of Zilla macroptera in male mice of strain NMRI Albinos. Evaluation of the analgesic activity showed that the aqueous extract at 150 mg/kg of the plant induced a decrease in the number of abdominal cramps caused by 1% acetic acid. The aqueous extract of the plant had an analgesic effect almost equal to that of Diclofenac; in fact, the latter caused a pain inhibition of 49-1.1% while Zilla macroptera caused a pain inhibition of 49-2.1%, at the concentration of 150 mg/kg. Evaluation of the percentage of inhibition showed that the aqueous extract of Zilla macroptera had a better anti-inflammatory activity compared to Diclofenac sodium during the treatment duration (69% - 56% at 60 min; 71% — 50% at 120 min, and 75% - 66% at 180 min). The results of this research indicate that Zilla macroptera inhibits inflammation and could explain its effective use in traditional medicine. The phytochemical investigation of the bioactive extract led to isolate two natural products: furanone derivative and oxymesterone, the structures were elucidate by using spectroscopic methods.

Keywords: Zilla Macroptera, Cruceferae, Analgesic Activity, Aqueous Extract Essential Oils, Plants, Fungi, Animals, Algae

Introduction

Natural products occupy an important place in the discovery of new drugs. It is estimated that nearly 50% of the therapeutic agents currently used come from natural sources (plants, fungi, animals, algae, etc.) [1-3]. It is also estimated that less than 10% of plant species have been studied for their biological activities. Inflammation and pain are two physiological processes that are intimately linked and implicated in a large number of acute or chronic diseases [4-5]. However, the drugs on the market (non-steroidal anti-inflammatory drugs, steroidal anti-inflammatory drugs, opioids, local anesthetics, etc.) are unsatisfactory, restrictive and cause many undesirable effects (gastric ulcers, immunosuppressive actions, convulsions, cardiovascular accidents [6-8]. Hence the need to research new molecules that could act directly on the mediators of inflammation and pain, thus having fewer side effects. Herbal medicine has been used for centuries to treat various ailments. In Algeria, plants have been used for a long time and their use is inspired by the experiences of the populations as well as by classical Arab medicine. However, this use does not follow precise rules and does not take into account the new necessities of current therapy, many studies have focused on the study of plants used in traditional medicine [9-12]. Zilla macroptera is used in traditional pharmacopoeia against imbalances of the gastrointestinal tract, cephalic pains, and bronchitis, and as an anti-inflammatory agent. Among the most used plants in the Southwest Algerian region Zilla macroptera known by the local name "Boukhlala". This plant is used to treat gastric problems, skin diseases, kidney problems [11-13] In this work we are interested in the evaluation of the anti-inflammatory activity of some pure products isolated from the aerial part of this plant

Materiel and Methods

Plant Material

The whole plants of zilla macroptera (crucefera) were collected from north region of Bechar (March 2014, Algeria). The botanical identification and voucher specimen were deposited in in the Medicinal Plant Encyclopedia Herbarium of bioactive molecules and Chiral Separation Laboratory (BMCS Lab) under accession number MPE11-7- E3. [14].

Extraction and Fractionation

Dried and ground aerial part of Zilla macroptera (500 g) were extracted with MeOH (70 %). The extract was concentrated, diluted with water and partitioned with hexane, methylene chloride, ethyl acetate and n-butanol (100 mL in 3 steps) [15].

Reagents

All chemicals were purchased from Sigma-Aldrich (St Louis, MO, USA).

Animals

Permission was obtained from the Committee of use of animal experiments (Approval # 943-19). The study was carried out on mice NMRI Albinos, 100% males, from the breeding laboratory of the Pasteur Institute of Algeria. Their weight was between 22 and 38 g. Mice were randomly housed in plastic cages with controlled temperature (250C) and under a 12 h light–dark cycle. Animals benefited from an adaptation period before use. They were fed and maintained under standard procedures, with access to water and standard food (Bovin fattening). The mice were with an empty stomach for 17 hours before each experiment [16].

Anti-Inflammatory Activity

The anti-inflammatory activity study was evaluated by the method of inhibition of 1% formalin-induced mouse paw edema. The mice before each experiment were with an empty stomach for 17 hours, at which time inflammation is induced by injecting formalin into the plantar arch of the left mouse paw. Measurements of the volumes of the right hind paw of each mouse were performed prior to induction of edema and every 1 h, 2 h, 3 h, 4 h and 5 h after the formalin injection [17]. Half an hour before the formalin injection, the different lots of mice received the different treatments: A control group of 6 mice's treated IP with physiological water, according to body weight. A reference batch of 6 mice's treated by IP with Diclofenac Sodium (20 mL). A batch of 6 mice's treated with the extract IP with the plant extract Bubonium graveolens at a dose of 150 mg/kg, according to body weight. The anti-inflammatory activity of the products was tested and its evolution was estimated by the determination of the average percentages of inhibition of the edema, calculated according to the formula:% d'inhibition = V_0: represents the volume of the paw at t = 0 (before injection of formalin). V_t: represents the volume of the paw at any time t.

Apparatus

The LC system consisted of a liquid chromatography (Si-gel : 230-400 mesh (MerK) were used for column chromatography) operating at room temperature with a flow rate of 1 mL·min^{-1} and the UNICAM UV 300 spectrophotometer detector operating at wavelength of 210 nm. The IR spectra (υmax) were determined on an AVATAR 320 FT-IR spectrophotometer. The NMR spectra were obtained on a Bruker Avance DRX 300 FT spectrophotometer operating at 300 MHz for 1H NMR, and 125 MHz for ^{13}C NMR. For the ^{13}C NMR spectra, multiplicities were determined by a polarization transfer (DEPT) experiment.

Results and Discussion

Phytochemical Study

In our work, three compounds A, B, C were isolated the first two compounds A and B separated from fractionation of the ethyl acetate extract (extraction liq-liq) the compound C separated by fractionation of the extract of ethyl acetate (flavonoid extraction) gives the following frontal ratios: 0.77, 0.88, 0.92.analysed by the HPLC apparatus to confirm the separation, which it gives the chromatograms of the compounds A, B, C.

Compound A: oxymesterone, $C_{20}H_{30}O_3$, Yellow poder, 190 mg, Tr=10.967 min, k'=2.34 , C18 column, 82.096%, UV(MeOH) : 277 nm

IR (KBr): 3400(OH), 2919, 2850 (CH_2 , CH_3), 1717(C=O), 1665(C=O), 1461 (CH), 1977(OH), 1170(C-O), 1029(C-O), 720 (CH aromatic, CH2) cm^{-1}

^{1}H NMR (300MHZ, CDCl3) : 0,89(s, 3H, H-19) , 1,18(s, 6H, H-18, H-20), 1,09-1,44(m, 11H, H-1,H-7, H-11, H-12, H-14, H-15), 1,50(s, 2H, H-16) , 2,50(t, 2H, H-6), 3,27(t, 2H, H-2), 4,05(s, 1H, OH)

^{13}C NMR (75MHZ, CDCl3) : 38,95(C-1) , 28.94(C-2) , 170,29(C-3) , 121.92 (C-4) , 59.71(C-5) , 20.71(C-6 , C-15) , 38.65(C-7, C-10, C-16) , 40.19(C-8, C-9), 40.04(C-11) , 39.49(C-12), 39.76 (C-13, C-14) , 48.55 (C-17) , 14.03 (C-18, C-19, C-20). (Figure 1).

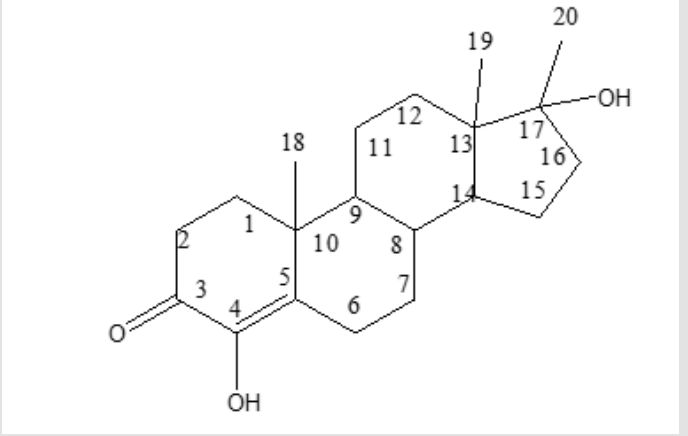

Figure 1:

Compound C : 8-hydroxy-15-(hydroxymethyl)-11, 12-dimethyl-octahydrooxireno [1,12] cyclo deca- furan-8-one

Yellow powder ,180 mg, Rf= , Tr=6.775 min, k'=9.423 , C18 column, 98.088%, UV(MeOH) : 284 n m, IR(KBr) : 3398(OH) , 2851, 2919, 2955 (CH2 , CH3) , 1633(C=O) , 1461(C=C) , 1377(OH) , 720(CH2) cm^{-1}

1H NMR (300MHZ, CDCl3) :4,29 (m, 1H, H-1), 4,07 (m, 1H, H-2), 2,50 (ddd, j^2, j^3, j^3, 1H, H-3a) , 2,50 (ddd, j^2, j^3, j^3, 1H, H-3b), 1,06 (m, 1H, H-4), 2,85 (ddd, j^2, j^3, j^3, 1H, H-5a), 2,85 (ddd, j^2, j^3, j^3, 1H, H-5b), 4,29

(dd, j^3, j^3, 1H, H-8), 3,25 (ddd, j^2, j^3, j^3, 1H, H-9a), 3,25 (ddd, j^2, j^3, j^3, 1H, H-9b), 1,94 (m, 1H, H-10), 1,06 (d, j3, 3H, H-11), 2,50 (d, j^3, 3H, H-12), 4,21 (s, 2H, H-15), 5,40(s,2H, OH)

^{13}C NMR (75MHZ, CDCl3) : 59.98(C-1) , 55.98(C-2) , 40.33(C-3) , 25.05(C-4) ,40.05 (C-5), 115.33 (C-6) , 166.9(C-7) , 67.33 (C-8) , 39.11 (C-9) , 28.23(C-10) , 20.66(C-11) , 13.88(C-12) , 170.29 (C-13) , 128.58 (C-13) , 55.98 (C-15). (Figure 2).

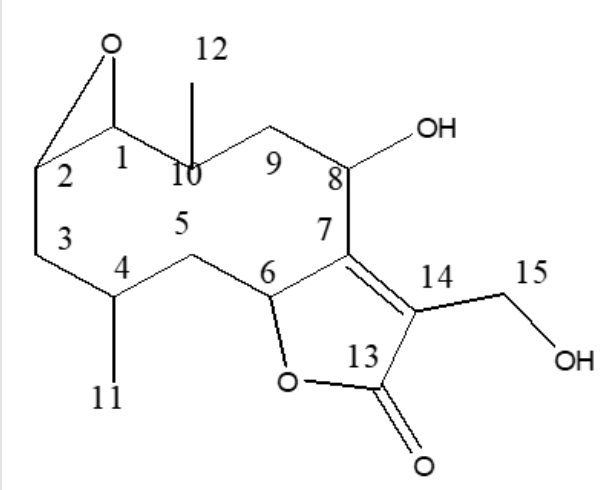

Figure 2:

Anti-Inflammatory Activity

Assessment of Edema

(Table 1).

Table 1: Variation in mean volumes of mice paws treated with Voltarene (diclofenac), water and organic and aqueous extracts of the aerial part of Zilla macroptera. (1: ether 2: diclofenac 3: water 4: Hexan 5:dichloromethan 6: ethyle acetate 7:butanol 8: essential oil).

Extract	Dose	T0	T1	T2	T3	T4	T5
1	0.025ml/kg	0.11±0.01	0.15±0.04	0.15±0.04	0.17±0.03	0.17±0.03	0.16±0.03
2	8mg/ml	0.11±0.01	0.16±0.01	0.15±0.03	0.13±0.03	0.13±0.02	0.13±0.02
3	100mg/ml	0.11±0.01	0.17±0.02	0.17±0.03	0.17±0.03	0.18±0.03	0.16±0.04
	200mg/ml	0.11±0.02	0.15±0.03	0.16±0.03	0.16±0.04	0.19±0.02	0.18±0.02
4	100mg/ml	0.11±0.01	0.12±0.02	0.12±0.02	0.12±0.02	0.13±0.02	0.12±0.02
	200mg/ml	0.11±0.01	0.12±0.02	0.12±0.02	0.12±0.02	0.12±0.02	0.12±0.02
5	100mg/ml	0.11±0.01	0.14±0.02	0.15±0.02	0.16±0.02	0.15±0.02	0.15±0.02
	200mg/ml	0.11±0.02	0.13±0.02	0.15±0.02	0.15±0.02	0.15±0.02	0.15±0.02
6	100mg/ml	0.11±0.01	0.17±0.02	0.15±0.02	0.14±0.02	0.13±0.02	0.13±0.02
	200mg/ml	0.11±0.02	0.15±0.02	0.14±0.02	0.13±0.02	0.13±0.02	0.12±0.02
7	100mg/ml	0.11±0.01	0.18±0.02	0.19±0.02	0.20±0.02	0.20±0.02	0.20±0.02
	200mg/ml	0.11±0.01	0.19±0.02	0.19±0.02	0.19±0.02	0.19±0.02	0.19±0.02
8	2ml pure	0.11±0.01	0.11±0.01	0.11±0.01	0.11±0.01	0.11±0.01	0.11±0.01

Evaluation of the Anti-Inflammatory Activity

The organic extract of ethyl acetate at a dose of 100 and 200 mg / kg already acts at the first hour, which shows an effect on the primary phase of the inflammation and remains in a positive rhythm up to the fifth hour. The dose 100 mg / kg gives a clear effect only at the third hour [18]. The dose 200 mg / kg gives an effect more than diclofenac. The difference in paw volume increase over time between the treated groups and the control group is still statistically significant. (Table 2) The organic ethyl acetate extract from the aerial part of zilla macroptera slightly prevents the formation of edema or gives a significant effect of anti-inflammatory activity.

Table 2: Inhibition of edema of mice treated with diclofenac and the aqueous extract and organic extracts of the aerial part zilla macroptera. (1:water 2: Hexan 3: dichloromethan 4:ethyle acetate 5: butanol 6: diclofenac 7: essential oil).

Extract	Dose mg/mL	1h	2h	3h	4h	5h
1	100	54.54%	54.54%	54.54%	63.63%	45.45%
	200	36.36%	45.45%	45.45%	72.72%	63.63%
2	100	9.09%	9.09%	9.09%	18.18%	9.09%
	200	9.09%	9.09%	9.09%	9.09%	9.09%
3	100	27.27%	36.36%	45.45%	36.36%	36.36%
	200	18.18%	36.36%	36.36%	36.36%	36.36%
4	100	54.54%	36.36%	27.27%	18.18%	18.18%
	200	36.36%	27.27%	18.18%	18.18%	9.09%
5	100	63.63%	72.72%	81.81%	81.81%	81.81%
	200	72.72%	72.72%	72.72%	72.72%	72.72%
6	8	45.45%	36.36%	18.18%	18.18%	18.18%
7	5ml	0%	0%	0%	0%	0%

Conclusion

According to the results obtained in this study, we can say that the ethyl acetate extract of zilla macroptera has a good anti-inflammatory activity [19]. We found for the anti-inflammatory activity by the method that the ethyl acetate extract of the studied plant has the capacity to reduce the mouse paste after provocation of the edema.

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