INTERNATIONAL JOURNAL OF CURRENT RESEARCH IN CHEMISTRY AND PHARMACEUTICAL SCIENCES
(p-ISSN: 2348-5213: e-ISSN: 2348-5221)
www.ijcrcps.com
DOI: 10.22192/ijcrcps Coden: IJCROO(USA) Volume 6, Issue 1 - 2019

Research Article

DOI: http://dx.doi.org/10.22192/ijcrcps.2019.06.01.005

Anti-inflammatory properties of *Melaleuca quinquenervia* (Cav.) ST Blake Myrtaceae (Niaouli) leaves' essential oil

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Abstract

Melaleuca quinquenervia is a plant well-known for its medicinal properties. Its leaves are mainly used for the treatment of respiratory diseases.
The present study aims was to appreciate the anti-inflammatory properties of the essential oil from the leaves of *Melaleuca quinquenervia* (Cav.) ST Blake Myrtaceae (Niaouli).
Phytochemical analysis of the essential oil, by CG/MS, revealed the major constituents such as: 1,8-cineole (30.14%), viridiflorol (29.92%), terpinene-4-ol (10.12%) α-terpineol (6.89%), limonene (4.36%). The study of the anti-inflammatory activity of this essential oil on wistar rats showed a decrease in the rate of the oedema evolution and displayed significant dose and time dependent of this oedema inhibition. The essential oil showed also strong analgesic and antipyretic properties. The dose of 1800 mg/kg showed a better activity than that induced by 50 mg/kg of acetylsalicylate of lysine. Altogether, this work demonstrates the anti-inflammatory property of *Melaleuca quinquinervia* leaves' essential oil suggesting its potential role as adjuvant therapeutic alternatives in dealing with inflammatory-related and respiratory diseases.

Keywords: Essential oil, *Melaleuca quinquenervia,* anti-inflammation, Wistar rats.

Introduction

Melaleuca quinquenervia is one of those plants that belongs to the Myrtaceae family. Its leaves are mainly used for the treatment of respiratory diseases [1]. It grows in New Caledonia, Australia, Madagascar and many tropical countries. It can reach 15 to 20 m in height [2]. In Benin, it is particularly found in southern Benin next to the village Attogon, in a forest of Niaouli called "Eco-Tourist Park" (Atlantic department) and at “Sèmè-Podji” located in the south of Benin (Ouémé department). Niaouli essential oil’s is commonly used in aromatherapy to cure certain ailments because it has multiple properties as antiviral, antiseptic and many other. Thus, essential oil of Niaouli obtained from freshly harvested leaves has many uses in Herbal Medicine. It is easy to use because for its various applications, whether for internal use, massage, friction or atmospheric diffusion. *Melaleuca quinquenervia* is well known for its importance as a medicinal plant and for its essential oil exploited industrially. The decoction of leaves is used in Africa as a febrifuge, against cooling, cutaneous affections, lung diseases, neuralgia, dermatosis, laryngitis, influenza, rhinitis, sinusitis and pharyngitis [3,4]. It would therefore be interesting to characterize the active constituents of this plant with analgesic, disinfecting, antiseptic, deodorizing, vasodilating, purifying and anti-inflammatory effects [2].

In the present study, we established firstly the chemical composition of *Melaleuca quinquenervia* leaves’ essential oil, and then evaluate their anti-oedema, analgesic and antipyretic activities on Wistar rats with the ultimate goal to fully harnessing the medicinal properties of this plant. Generally the early phase of acute inflammation involves cellular influx associated with the release of mediators such as histamine and serotonin followed by the production of bradykinin and prostaglandins [5], which ultimately lead to inflammation [6]. The inflammation can be revealed by many symptoms as oedema (swelling or tumor), painand warmth or fever (temperature) [7]. This essential oil can be used atthe pharmaceutical products place becoming more expensive for the indigenous population. Our data indicate that the *Melaleuca quinquenervia* essential oil contains chemical substances with great anti-inflammatory effects. There for chemical composition and the anti-oedema, analgesic and antipyretic activities of *Melaleuca quinquenervia* leaves’ essential oil on the rats were investigated.

Experimental Section

1. Material

1.1. Plant material

The plant materials used for this investigation are fresh leaves from *Melaleuca quinquernervia*, collected at Sèmè-Podji located in the south of Benin (Ouémé department). The leaves were air-dried in the laboratory sheltered from the sun and then ground before steam distillation. It was identified and authenticated by the National Herbarium of Abomey Calavi University where voucher specimen was deposited.

1.2. Animal material

The animal material is composed of young rats both sexes of Wistar strain of average weight 163 ± 14.16 g. They were acclimated to the conditions of the Human Biology Unit’s Laboratory, Faculty of Health Sciences, University of Abomey-Calavi, Benin, Institut des Sciences Biomédicales Appliquées (ISBA).They were housed in groups of 06 in standard cages steel tray floor, at 25 – 30 °C temperature, 70 to 80% for relative humidity and 12 h/12 h for light/dark duration. They were fed diet consisted of 53% crushed maize, 19% fish meal, 20% wheat bran, 5% groundnut oil, 1.5% vitamin complex (Olivitasol), and 1.5% NaCl. The chemical analysis of the diet showed that they contained 16.1% crude protein, 12.9% crude fiber and 2.6% crude fat [8]. Their have food and water *ad libitum*.

The daily time of animals treatment (extract administrations) was before 10 am;

2. Methods

2.1. Essential oil extraction and chemical analysis

Leaves collected in wet season in Southern Benin, West Africa were dried in laboratory at room temperature (25 - 30 °C). The oil extraction was obtained from dried leaves by hydrodistillation using Clevenger apparatus system [9] during 03 hours. Extracted oils were dried by anhydrous magnesium sulfate adjunction and stored at 4 °C before use.

The analysis of the oil was carried out by gas chromatography coupled to a mass spectrum. The identification of volatile constituents was conducted by gas-chromatography in a Trace GC Thermo Quest gas chromatograph, CE Instruments. It is equipped with a flame ionization detector, a split/splitless injector and a DB-5 apolar column (30 mm 0.25 mm x 0.25 µm). The temperature of the furnace is programmed from 50 to 300°C at a rate of 5 °C/min. The flow rate of the hydrogen carrier gas is 35 mL/min that of the combustible gas is 350 mL/min. The amount of oil injected is from 1 µL to 5% in pentane. Injector's temperature was 240°C, column was at 60°C and 3°C.min^{-1} to 240°C during 7 min. Carrier gas (N_2) was at the flow of 1.0 mL.min^{-1}. The GC–MS analysis was carried out using a Hewlett Packard 5970 GC fitted with a DB-1 column (25 m 9 0.23 mm i.d.) with ionization energy of 70 Ev and Helium used as carrier gas at a flow rate of 0.9 ml/min.

The components are identified on the basis of their Kovatsretention indices which calculation method use the mixture of C8–C26 alkan chain molecules, and mass spectral fragmentation,

2.2. Anti-inflammatory properties

The experimental protocols have been approved by Benin Institute of Applied Biomedical Science Ethical Committee.

2.2.1. Induction of oedema and determination of its volume

The study of the anti-inflammatory activity is carried out by means of the indomethacin-based extract method according to the model of induction of oedema by injection of 0.1 mL of 1% (v/v) of formaldehyde solution in the right foot paw of the Wistar rats [7,11-14]. Measurements of foot volume are performed at 0, 30, 60, 120, 180 and 240 min after oedemainduction. The volume of the foot was determined by the immersion method which caused an increase in the water level [7,11-15]. Thirty minutes before the injection of the formaldehyde solution, the Wistar rats to be treated are received orally 1200 mg/kg and 1800 mg/kg of *Melaleuca quinquenervia* essential leaves' oil and 100 mg/kg of indomethacin used as a reference drug.

2.2.2. Analgesic/analgesic activity

Antalgic/analgesic activity is sought in rats by tail flick and Koster tests.

2.2.2.1. Method of immersion of the tail (tail flick test)

One hour after oral administration of the essential oil at 1200 mg/kg and 1800 mg/kg, the tail of each animal is placed in hot water maintained at 50 °C. The time which taked the animal to remove its tail is measured and will be considered as reaction time [11-14]. The same experiment is performed with control (untreated) and reference rats. Lysine acetylsalicylate (Aspegic) at 50 mg/kg wistar rat weight is used as a reference product.

2.2.2.2. Acetic acid method (Koster test)

Forty five minutes after oral administration of *Melaleuca quinquenervia* essential oil at 1200 mg/kg and 1800 mg/kg, 0.5% (v/v) acetic acid is injected intraperitoneally at 2 mL/kg to the animals. The number of abdominal cramps is evaluated 10 min after the injection of acetic acid for 10 min. Aspegic is used as a reference product at 50 mg/kg[14,16].

2.2.3. Antipyretic activity (yeast test)

Hyperthermia is induced by intraperitoneal abdomen injection of 2 mL/kg of an aqueous solution of brewer's yeast at 20% (g/v) to rats. The control rectal temperatures are measured 24 hours after the injection of the brewer's yeast[7,14]. The reference group received 50 mg/kg of lysine acetylsalicylate (Apegic), in a constant volume of 2 mL/kg. The two treated groups received respectively 1200 mg/kg and 1800 mg/kg of *Melaleuca quinquenervia* leaves essential oil. Rectal temperatures are taken again every hour for 5 h after the administration of the substances.

In the all experimental section the treated rats received only 2 mL/kg of virgin corn's oil.

3- Statistical Analysis

The results are expressed as Mean values ± Standard Error of Mean (SEM). The statistical treatments are achieved with the software STATISTICA 5.5 version, and the software Microsoft Excel 2013 of Windows 2013. The middle value comparisons have been done by means of the parametric tests: T test for independent samples. The results are considered statistically at probability level of $P < 0.05$

Results

1. Results

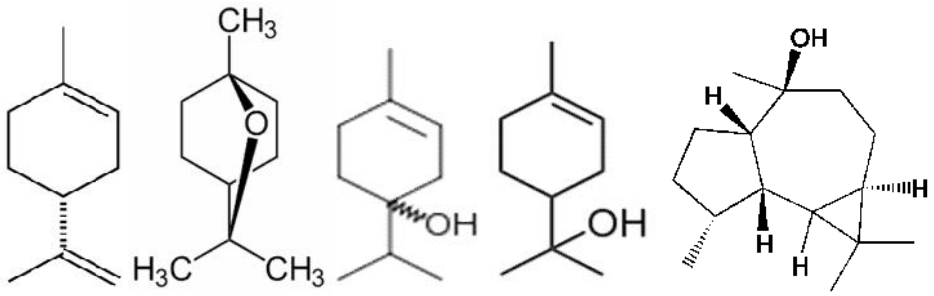
1.1. Essential oil chemical constituents

Melaleuca quinquenervia leaves' essential oil yield 1.5 %. The essential oil's specifications are: density : 0,889 ; refraction rating: 1,479 and rotatory power: +7°.

Chemical compositions of *Melaleuca quinquenervia* leaves' essential oils is given in table 1 in the order of the constituents' retention times. The result showed the major constituents such as: 1,8-cineole (30.14%), viridiflorol (29.92%), terpinene-4-ol (10.12%) α-terpineol (6.89%), limonene (4.36%) are in the essential oil of *Melaleuca quinquinervia* leaves. Their formulas are above.

Table 1: Chemical composition of the essential oils from *Melaleuca quinquinervia* leaves

N°	Temps de Rétention (min)	Indice de Kovats	Constituants	Pourcentage (%)
1	9.854	928	α-thujene	0.17
2	10.130	935	α-pinene	0.81
3	11.138	964	Benzaldehyde*	0.18
4	11.688	979	β–pinene	0.55
5	12.083	990	Myrcene	0.91
6	13.034	1019	α-terpinene	0.49
7	13.302	1027	**Limonene**	**4.36**
8	13.471	1032	**1,8-cineole***	**30.14**
9	13.601	1036	(Z)-β-ocimene	0.23
10	14.014	1048	(E)- β-ocimene	0.11
11	14.415	1060	Gamma terpinolene	0.77
12	15.292	1087	Terpinolene	0.51
13	15.751	1101	Linalol*	0.27
14	17.293	1152	Isopulegol*	0.19
15	17.995	1173	Borneol*	0.17
16	18.266	1184	**Terpinen-4-ol***	**10.12**
17	18.717	1199	**α-terpineol***	**6.89**
18	19.538	1228	Citronelol*	0.21
19	22.850	1349	Acétate d'alpha terpenyle*	0.93
20	24.476	1419	α-gurjuneme	0.70
21	24.819	14,25	β-caryophyllene	0.84
22	25.300	1445	Aromadendrene VI	0.73
23	25.698	1461	α-humulene	0.30
24	25.804	1465	Allo aromadendrene	0.48
25	56.098	1477	Gamma murolene	0.48
26	26.546	1495	Viridiflorene	1.28
27	26.682	1501	α-murolene	0.30
28	27.068	1517	Gamma cardinene	0.59
29	27.164	1522	Delta cardinene	0.82
30	28.129	1563	(E)-nerolidol*	0.64
31	28.446	1576	Ledol*	1.48
32	28.718	1588	Oxyde carophyllene*	0.43
33	29.029	1601	**Viridiflorol***	**29.92**
34	29.241	1611	Epi globulol*	0.88
35	30.032	1647	Epi alpha cardinol*	0.15
36	30.351	1661	α-carinol*	0.16
			Total identified	**98.19**
			Non- identified	**1.81**
			*** OxygenedCompnents**	**82.76**
			Non OxygenedCompnents	**15.43**



Limonene **1,8-cineole** **Terpinen-4-ol** **α-terpineol** **Viridiflorol**

1.2. Anti-inflammatory activity

The results obtained for the anti-inflammatory activity are as followed.

1.2.1. Anti oedema activity

1.2.1.1.Volume of oedema induced

The essential oil of *Melaleuca quinquenervia* leaves is given orally 30 min before the injection of formaldehyde solution. The results from the evolution of the oedema are as follows:

The analysis of Figure 1 shows that after induction of oedema with 0.1 ml of formaldehyde solution, the edema's rate change of the control group increased with time. Indeed, in the control rats treated with virgin corn's oil, the evolution rate of the oedema went from 0.00 ± 0.00% at the time $T_o$to 51.99 ± 0.18%, 67.22 ± 0.18%, 69.89 ± 0.21%, 70.84 ± 0.25% and 66.21 ± 0.24% respectively for the times 30, 60, 120, 180 and 240 min after formaldehyde solution injection.

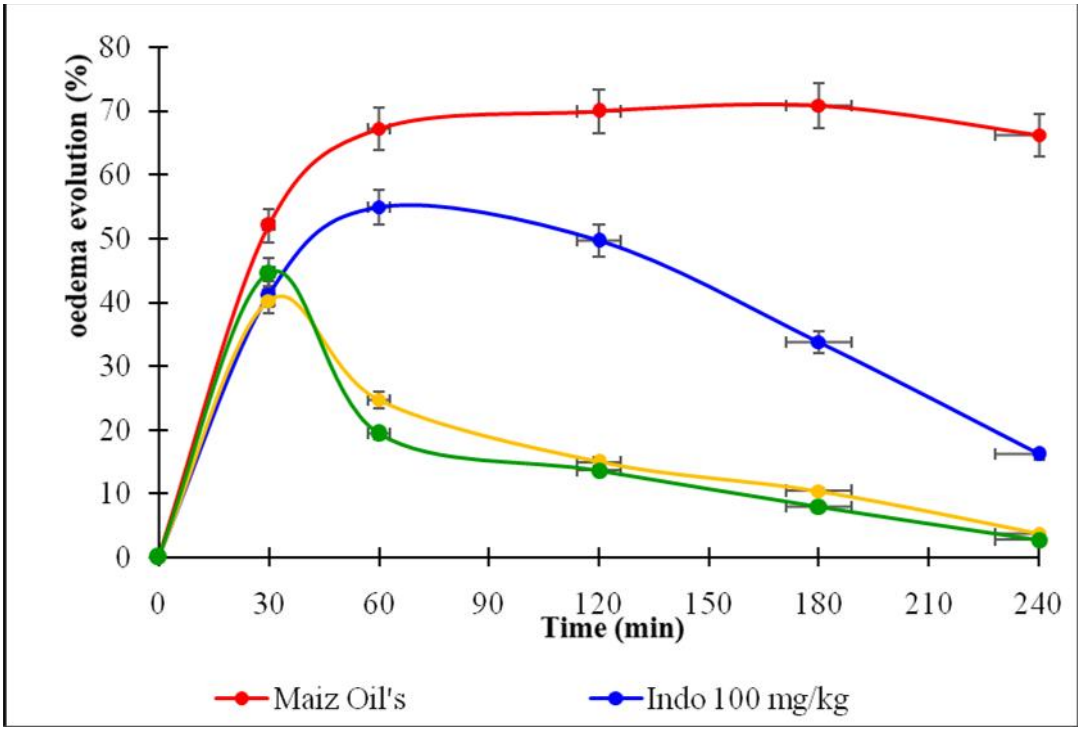


Figure 1: Curves of rats' right legs eodema's evolution, induced after the treatments during the anti-oedema activity's test of the essential oil. N = 6 per group, values are mean ± standard mean errors, $p < 0.05$ compared to the control group (ANOVA followed by the Student's test),
Indo = indomethacin, EO = Essential Oil.

The high percentage increase in the control group is evaluated at 70.84 ± 0.25% relative to the initial volume of the foot, three hours (180 min) after injection of the formaldehyde solution. So, in the rats treated with indomethacin and the essential oil of *Melaleuca quinquenervia*, there were a decrease in the rate of evolution of the oedema compared to the control group (respectively p = 0.02 for indomethacin, p = 0.006 for 1200 mg/kg and p = 0.002 for 1800 mg/kg). The decrease is most remarkable in rats treated with *Melaleuca quinquenervia* leaves' essential oil for sixty minutes (60 min) after induction of oedema.

1.2.1.2. Inibition of oedema's induced volume

From the observation of **figure 2** it appears that the doses of 1200 mg/kg and 1800 mg/kg of the essential oil of *Melaleuca quinquenervia* caused a significant inhibition of the oedema (respectively p = 0.004 and p = 0.001). The inhibition rates which increased after 30 minutes reached 93.89 ± 0.14% and 99.44 ± 0.12%, four hours after induction of oedema.

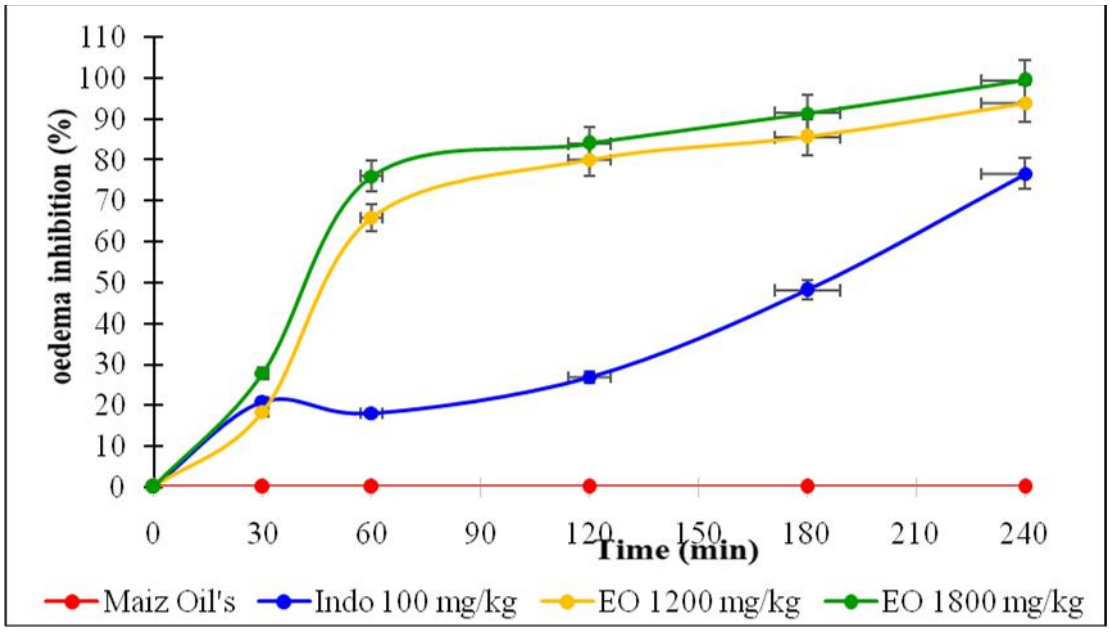


Figure 2 :Oedema's rates inhibition curves of rats' right paws after the treatments during the test of the anti-oedematous activity of the essential oil. N = 6 per group, values are mean ± standard mean errors, p < 0.05 compared to the control group (ANOVA followed by the Student's test). Indo = indomethacin, EO = Essential Oil.

The growth rate of inhibition of the 1200 mg/kg dose is lower than that of 1800 mg/kg. The degree of inhibition is then dose and time dependent. Before the first thirty minutes the two doses of the essential oil have inhibition rates comparable to that of indomethacin. But beyond thirty minutes, the different doses of the essential oil of *Melaleuca quinquenervia* are more effective than the reference product, ie 93.89 ± 0.14%,99.44 ± 0.12% and 76.67 ± 0.16% respectively for 1200 mg/kg, 1800 mg/kg and indomethacin.

1.2.2. Analgesic/analgesic activity

1.2.2.1. Tail flick method

Figure 3 observation revealed that in the control rats group, the duration time of the tail in water at 50 °C is 5.17 ± 1.16 second. When animals are protected, the length of stay is longer. *Melaleuca quinquenervia* leaves' essential oil at 1800 mg/kg gives a longer stay compared to 1200 mg/kg and Aspegic at 50 mg/kg. Those are respective durations of 39.83 ± 2.50, 19.33 ± 1.00 and 10.8 ± 1.00 sec. The stay time of the tail of rats in water at 50 °C is therefore dose dependent.

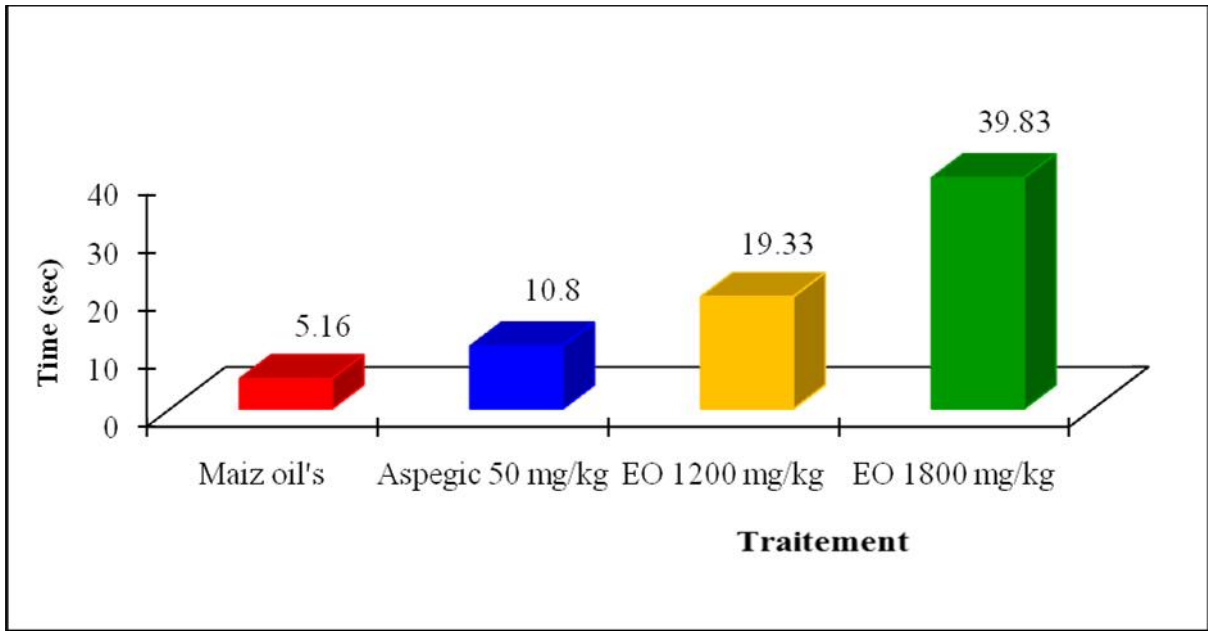


Figure 3 : Histograms of the staying times of the rats' tails in water at 50 °C after the treatments during the analgesic / analgesic activity test. N = 6 per group, values are mean ± standard mean errors, $p < 0.05$ compared to the control group (ANOVA followed by the Student's test).

1.2.2.2. Acetic acid method (Koster test)

From the observation of the histograms of Figure 4, it appears that the essential oil of *Melaleuca quinquenervia* dosed at 1800 mg/kg high significantly ($p = 0.00005$) reduces the number of abdominal cramps induced by acetic acid. This number is 23.33 ± 3.26, 26.00 ± 1,300, 33.67 ± 3.33 respectively for 1800 mg/kg and 1200 mg/kg of the essential oil and 50 mg/kg of Aspegic against 53.33 ± 6.00 for the controls.

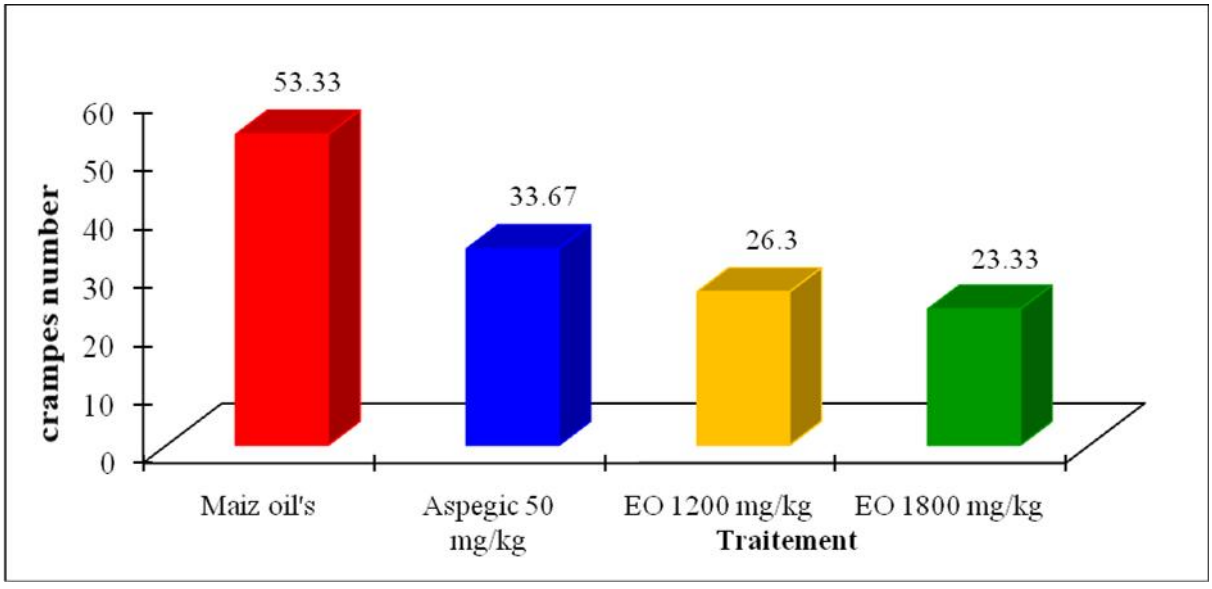


Figure 4 : Histograms of the abdominal's cramps number 10 min after the injection of acetic acid and after treatments during the analgesic/analgesic activity test. N = 6 per group, values are mean ± standard mean errors, $p < 0.05$ compared to the control group (ANOVA followed by the Student's test)

1.2.3. Effects of *Melaleuca quinquenervia* leaves' essential oil on hyperthermia

The initial temperature (before induction) is 35.49 ± 0.27 °C. After the injection of the brewer's yeast, it'swentto 37.51 ± 0.26 °C (hyperthermia)24 hours later (Figure 5).

Oral administration of the essential oil of *Melaleuca quinquenervia* twenty four hours after the injection of the brewer's yeast reduces the increase of the temperature compared to Aspegic. From the observation of Figure 5, it appears that, from the hyperthermia establishing to respectively one, two and five hours, *Melaleuca quinquinervia* leaves' essential oil decreased the rats' anal temperature. It was from 37.45 ± 0.23 °C (hyperthermia) to 35.58 ± 0.19 °C, 35.23 ± 0.32 °C and 33.50 ± 0.32 °C for 1800 mg/kg and from 37.62 ± 0.26 °C (hyperthermia) to 36.00 ± 0.63 °C, 35.53 ± 0.23 °C and 34.22 ± 0.28 °C for 1200 mg/kg. Whereas for Aspegic 50 mg/kg it was from 37.25 ± 0.25 °C (hyperthermia) to 36.52 ± 0.35 °C, 36.42 ± 0.3 °C and 34.98 ± 0, 22 °C. Therefore 1200 mg/kg ($p = 0.019$) and 1800 mg/kg ($p = 0.007$) doses of *Melaleuca quinquinervia* leaves' essential oil lowered significantly rats' rectal temperature against Aspegic 50 mg/kg ($p = 0.04$). *Melaleuca quinquinervia* leaves' essential oil at 1200 mg/kg and 1800 mg/kg are more effective than Aspegic 50 mg/kg.

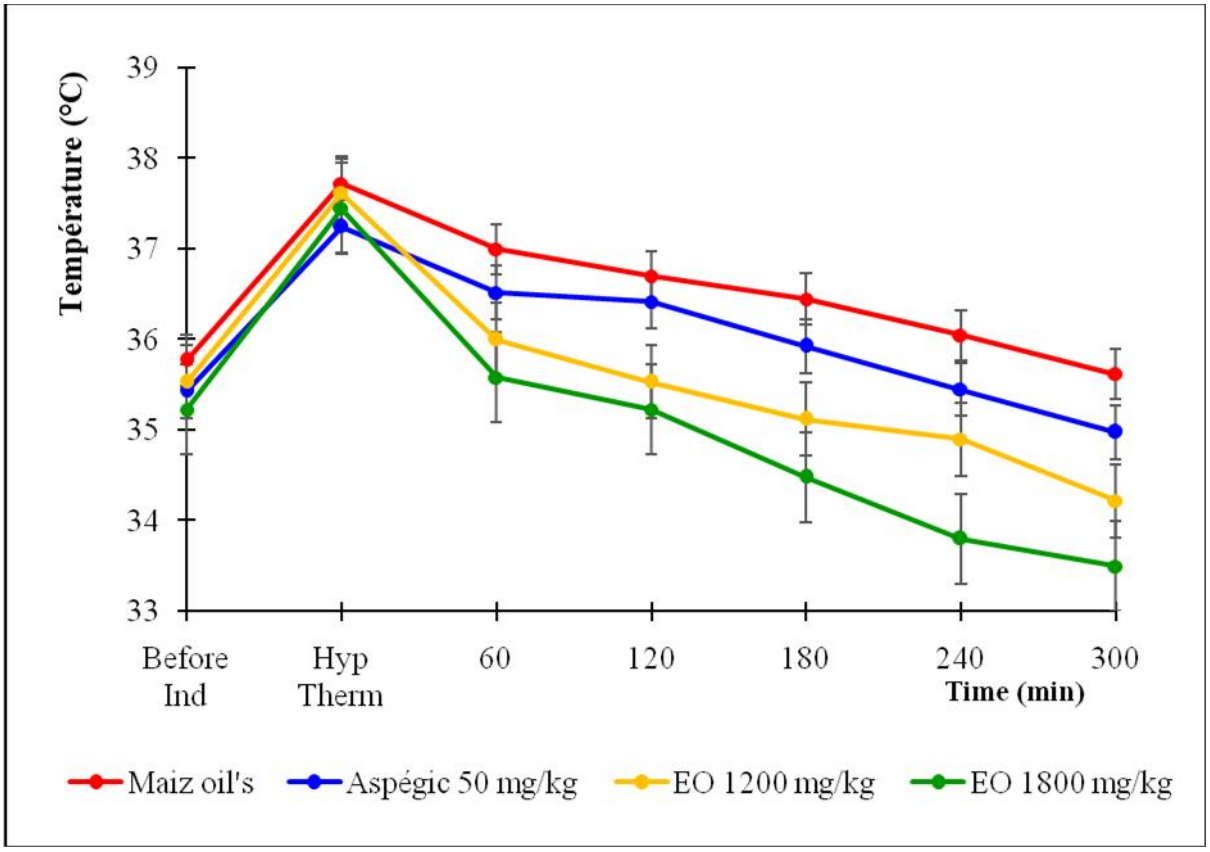


Figure 5: Curves of the evolution of rats' rectal temperatures after induction of hyperthermia followed by treatments. N = 6 per group, values are mean ± standard mean errors, $p < 0.05$ compared to the control group (ANOVA followed by the Student's test)

2. Discussion

The result of GC and GC-MS analysis of the essential oil indicated the presence of 05 major constituents representing 81.43% of the total identified components of the essential oil: 1,8-cineole (30.14%), viridiflorol (29.92%), terpinene-4-ol (10.12%),α-terpineol (6.89%), limonene (4.36%). Those chemical compounds have medicinal importance in the essential oil of *Melaleuca quinquinervia* leaves. This justifies the fact that, on an industrial scale and in the manufacture of medications, those leaves constitute a source of essential oil rich in 1,8-cineol and viridiflorol[4]. The percentages of major constituents of *Melaleuca quinquenervia* leaves' essential oil are differented of those of author[17] and the same with those in previous work and there for belong to type II Niaouli essential oil's chemotype[4]. It has been reported that α-pinene, linalool, β-caryophyllene, and β-caryophyllene oxide have anticholinesterase activity

[18,19]. It has been indicated that the presence of these compounds gives the essential oil its activities [20]. Indeed, these compounds have multiple biological properties. They are anti-infectious and antiseptic; anti-inflammatory and antihistamines [2]. Histamine is a neurotransmitter that promotes vasodilation, pain and increased vascular permeability in inflammatory reactions [21]. It contributes to the passage of liquid and plasma proteins to the extracellular medium, responsible for oedema [22]. Oxygen compounds and terpenoids in the essential oil have the ability to inhibit the action of histamine produced by mast cells. The high percentage (82.76%) of oxygenated compounds has been benefic for our Niaouli's essential oil in its inflammatory reactions.

The injection of formaldehyde solution in the right foot paw of the Wistar rats has caused local inflammation caused by tissue injury that results from the action of the prostaglandins and histamine produced. These mediators increase the permeability of the capillaries of the region. As a result, the exudate escapes from the bloodstream to the interstitial space. This exudate is the cause of localized oedema, which, in turn, compresses the nerve endings and thus determines a sensation of pain [22-24].

The protection of rats with the essential oil of *Melaleuca quinquenervia* decreases the oedema significantly by initially blocking the synthesis of histamine and 5-hydroxytryptamine which promote vasodilation, plasma transudation and oedema; secondly, it inhibits the synthesis of kinins that increase vascular permeability and finally inhibits the synthesis of prostaglandin associated with leukocyte migration in the inflamed area [25]. Our results are close to those of [26] who observed a significant decrease in the leucocyte and prostaglandin levels produced after administration of the essential oil of the different parts of *Tetraclinis articulata* in guinea pigs. These results corroborated those of [7] and [27] who observed an inhibition of pro-inflammatory substances (bradykinin, prostaglandins, thromboxane A2 leukotrienes etc.) after respective administration of aqueous extract of *Stercula setigera* and essential oil of *Eucalyptus camaldulensis* in wistar rats and ethyl acetate fractions of *Bidens pilosa* (asteraceae) leaves in white mice. The presence, in the essential oil of *Melaleuca quinquenervia* of active compounds such as: the majority 1,8-cineole,viridiflorol, terpinene-4-ol, α-terpineol, and minority α-pinene, β-pinene and limonene, known to have anti-inflammatory properties, could be responsible for its inhibitory effects. In this work, the 1800 mg/kg dose was more effective and significantly inhibited formaldehyde solution induced oedema compared to the negative control treated with virgin corn oil and the various positive controls treated with indomethacin (reference drug). This suggests that our essential oil at the dose of 1800 mg/kg has more effective anti-inflammatory properties compared to the reference molecules used but the effect decreases over time, which can be explained by the resorption of certain components of this oil or elimination by urine or stool [7,14,20] because, during the experiment, the rats urinated enough.

In order to highlight the action of our essential oil on the pain caused by the compression of nerve endings by oedema[22-24], we realized in a first time the tail flick's test and in a second time that of Koster's.

The reduction in the number of abdominal cramps of the first test could be explained by a probable blocking of the excitation of the nociceptive afferent nerve endings. In fact, the intraperitoneal administration of acetic acid in rats resulted in severe abdominal contractions. These contractions are due to the production and release of algogenic mediators via cyclooxygenases (COX) and the biosynthesis of prostaglandins [28], especially PGE2 produced by COX-1 [29]. These released mediators sensitize cholinergic and histamine peritoneal nociceptors. The administration of Aspegic (50 mg/kg) as a preventive treatment to rats inhibited significantly the algogenic action of acetic acid. This analgesic activity of Aspegic results from the suppression of the formation of mediators of pain in the peripheral tissues, because this analgesic inhibits the activity of COX-1 and COX-2 [30]. The results obtained show that *Melaleuca quinquenervia* essential oil has a significant analgesic effect by reducing the number of abdominal contractions at all doses. This suggests that the *Melaleuca quinquenervia* essential oil has compounds that act in the same way as Aspegic, and therefore inhibits COX-1 and COX-2, preventing the synthesis of prostaglandins. Since all analgesics have the property of inhibiting abdominal contractions induced by acetic acid, this test is useful for performing a first sorting of substances with analgesic action [31], but does not allow to give precisely the mode of action of the substance tested.

The central analgesic activity of the essential oil of *Melaleuca quinquenervia* was evaluated by testing its effect on pain induced by a thermal stimulus (water bath) in Wistar rats. For this test, only central analgesics increase the reaction time of the animal [7]. Results from this study indicate that Aspegic (50 mg/kg) significantly inhibited pain in the water bath test. Aspegic acts at the central level and its analgesic power is due to an agonist activity of the central receptors, associated with a neuronal reuptake inhibitory activity of serotonin and norepinephrine. This activity is enhanced by downstream inhibitory control at the spinal level [32]. The essential oil of *Melaleuca*

quinquenervia significantly inhibited the pain in a dose-dependent manner induced by water maintained at 50 °C. These results suggest that our essential oil would act via the same mechanisms as Aspegic, and would therefore be an inhibitor of the central processes of pain. In all these tests, the 1800 mg/kg dose was more effective and significantly inhibited the different pain models compared to the negative control treated with virgin corn oil and the different positive controls treated with the reference product. This suggests that our Niaouli's essential oil at the dose of 1800 mg/kg has more effective analgesic properties compared to the reference molecules used. On the basis of these results, it appears that the essential oil of *Melaleuca quinquenervia* possesses central and peripheral analgesic properties. Similar results were obtained by [32] with the ethyl acetate fraction of the leaves of *Bidenspilosa* and [14] with the essential oils of *Cimbopogon citratus* and of *Eucalyptus citrodora*.

As any synthesis of prostaglandin in the inflammatory reaction is conditional on a rise in temperature (fever) [33], we tested the antipyretic effect of the essential oil of *Melaleuca quinquenervia*. The results of this test showed that our essential oil is anantipyretic powerful. It has decreased significantly the temperature compared to Aspegic. Indeed, it reversibly blocks COX which prevents the production of prostaglandins responsible for fever (central antipyretic effect), and blocks the sensitization of peripheral nociceptors (peripheral analgesic effect) [33] such as salicylate and non-steroid anti-inflammatory drugs [34,35]. In our essential oil these anti-inflammatory effects are suggested to be carried out by the oxygenated compounds. In this test the dose of 1800 mg/kg was more effective and significantly lowered the temperature compared to the 1200 mg/kg dose and Aspegic. These results are close to those found by [7-14].The identification in the essential oil of *Melaleuca quinquenervia* bioactive compounds such as: *Melaleuca quinquenervia* of active compounds such as: the majority 1,8-cineole, viridiflorol, terpinene-4-ol, α-terpineol, and minority α-pinene, β-pinene and limonene, known to have anti-inflammatory properties, could be responsible for the effects analgesic and antipyretic observed. This would justify its empirical use as a pain reliever.

It should be noted that during Physical Education and Sports (PES) practice, the athlete is often confronted with pain-inducing trauma. This pain is accompanied by the inflammatory reaction[36]. PES was responsible for 25 % of cases of trauma for girls and 20 % for boys in the world. Instead of using high-cost pharmaceuticals to relieve the pain that accompanies the inflammatory response, taking *Melaleuca quinquenervia* essential oil may be advisable. This would relieve these practitioners because the cost is less expensive.

Conclusion

The essential oil *Melaleuca quinquenervia* contains mostly compounds such as: majority 1,8-cineole, viridiflorol, terpinene-4-ol, α-terpineol, and limonene and minority α and β-pinene. This justifies the fact that, the leaves constitute a source of essential oil rich in 1,8-cineol and viridiflorol and in the manufacture of medications. The oral administration of *Melaleuca quinquenervia* leaves' essential oil to wistar rats has been shown to have anti-edematous, analgesic and antipyretic effects. These effects are however time and dose dependent. The latter is therefore the most effective dose against oedema, analgesic/analgesic and antipyretic activities show that the essential oil of *Melaleuca quinquenervia* at a dose of 1800 mg/kg has a positive effect on pain and fever. This allows us to say that this essential oil alleviates the pain and hyperthermia that accompany inflammation. These results confirm and validate the traditional therapeutic indication of the leaves of *Melaleuca quinquenervia*.

References

[1]J Kerharo, JC Adam. La pharmacopée Sénégalaise traditionnelle: plantes médicinales et toxiques, Vigot et frères, Paris, **1974**, 1019p.

[2] J Albahary. Huiles essentielles, 2 familles biochimiques majeures: Monoterpénols et oxydes monoterpéniques, 2 HE de reference: *Melaleuca alternifolia (tea-tree), Melaleuca quinquenervia* (Niaouli), *Cinnamomumcamphora*, **2010**, 16p.

[3] A Akoègninou, WJ van der Burg, LJG van der Maesen, V Adjakidjè, JP Essou, B Sinsin, H Yédomonhan. Flore Analytique du Bénin. Backhuys Publisher: Cotonouet Wagenigen, **2006**, 1034p.

[4] JD Gbénou, M Moudachirou. *J. Essent. Oil. Res.*, **2007**, 19: 101-104.

[5] M Di Rosa, JP Giroud, DA Willoughby. *J. Pathol.*, **1971**, 104: 15-29

[6] S Arya, VL Kumar. *Mediat. Inflamm.*,**2005**, 4: 228-232

[7] JDGbénou, JF Ahounou, P Ladouni, WKDD Agbodjogbé, R Tossou, P Dansou, M Moudachirou. *Int. J. Biol. Chem. Sci.*, **2011**, 5(2), 634-641,

[8] AOAC, Official Methods of Analysis, 16th ed. Association of Official Analytical Chemists, Washington, DC, **2008**.

[9] PFandohan, BGnonlonfin, ALaleye, JDGbenou, RDarboux, MMoudachirou.*Food. Chem. Toxicol.,***2008**, 46: 2493-2497

[10]RP Adams. Identification of essential oils by Ion Trap Mass spectroscopy. Academic Press, London, **1989**

[11] AA Abena, P Kibori, D Bioka. *Pharmacopée et Médecine Traditionnelles Africaines*, VIII éd, **1995**, 67-72
[12]AAAbena, JM Ouanba, A Keita. *Pharmacopée et Médecine Traditionnelles Africaine*s, IX éd **1997**, 48-55
[13] AA Abena, JD Gbénou, E Yayi, M Moudachirou, RP Ongoka, JM Ouamba, T Silou. *Afr. J. Trad. Compl. Alt.Med.*, **2007**, 4(3), 267-272.
[14]JD Gbénou, JF Ahounou, HB Akakpo, A Laleye, E Yayi, F Gbaguidi, L Baba-Moussa, R Darboux, P Dansou, M Moudachirou, SO Kotchoni. *Molecular Biology Reports*, **2013**, 40(2), 1127-1134.
[15]KR Bhatt, RK Mehta, PN Shrivastana. *Indian J. Physiol. Pharmacol*., **1997**, 21: 399–400.
[16]RKoster, M Anderson, E de Beer. *J. Fed. Froc*.,**1959**, 18: 412
[17]AMKpochémè. Memor for graduation professional master in teaching physical education and sports, INJEPSUAC, Benin,**2007**, 75p. [18] SSavelev, E Okello, NSL Perry, PM Wilkins, EK Perry. *PharmacolBiochemBehav*. **2003,** 75: 661–668
[19]SSavelev, EJ Okello, EK Perry.*PhytotherRes*. 18:315–324.
[20] J Bruneton, Pharmacognosie : Phytochimie Plantes médicinales, Edition Technique et Documentation Lavoisier, 4ème éditions, Paris, **2009**, 1120p.
[21]D Gonçalves.Mémoire présenté pour l'obtention du grade de maître ès sciences en sciences expérimentalesdela santé, **2010,** 82p
[22]Co Phat. Collège Français des Pathologistes : la réaction inflammatoire. Les inflammations, **2012**,
[23] B Devulder, PY Hatron et E Hachulla*Physiologie de l'inflammation*. Edition Cedex Paris, **2002**, 15: 480.
[24] MC Rousselet, JM Vignaud, P Hofman, FP Chatelet. Inflammation et pathologie inflammatoire.Paris Maloine*,* **2005**, 320-331
[25] K Lindsey, AK Jager, DM Raidoo, van Staden. *J. Ethnopharmaco*, **1999**, 64(1), 9-14
[26] MBourkhiss, M Hnach, J Paolini, J Costa, A Farah, B Satrani. *Bulletin de la société royale des sciences de liège*, **2010**, 79: 141-154
[27] A FotsoFotso. Etude des propriétés analgésiques de la fraction a l'acétate d'éthyle des feuilles de*Bidenspilosa* (Asteraceae) chez la souris blanche (*Mus musculus*). Mémoire présenté en vue de l'obtention du Diplôme de Professeur de l'Enseignement Secondaire 2ème grade (DI.P.E.S. II), **2012**, 1-44
[28] E Elisabetsky, AA Tânia, RR Albuquerque, DS Nunes et A Cavalho. *J.Ethnopharmacol,* **1995**, 48: 77-83.
[29]S Ito, E Ouda-Ashitaa,TMianami. *Neurosci. Res,* **2001**, 41: 299-332.
[30] K Hirose, H Jyoama, Y Kojima, M Eigyi, H Hatakyama.*Neurosci. red*., **2015**, 280-286.
[31] D Le Bars, M Gozariu, SW Cadden. *Pharmacol Rev.,***2001**, 53: 597-652.
[32] S Paola, B Mauro, B Manfredi, AE Panerai. *Pain.***1997**, 325-330.
[33]Y Touitou. Pharmacologie générale 10e Ed.Masson*,* Paris, **2000**, 181-189.
[34]MR Santin, AO dos Santos, CV Nakamura, BPD Filho, ICP Ferreira, T Ueda-Nakamura. *Parasitol. Res*., **2009**, 5:1489-1496
[35] SJuglal, R Govinden, B Odhav. *J. Food. Prot.,***2002**, 65: 683-687
[36]D Piette, Y Coppieter, D Favresse, C Bazelman, L Kohn, P Desmet. *Bruxelles, Ecole de santé publique,***2003**,189: 2-5.

Access this Article in Online

Website: www.ijcrcps.com

Subject: Pharmaceutical Sciences

Quick Response Code

DOI: 10.22192/ijcrcps.2019.06.01.005

Article Info

Article History:

Received: 22nd January 2019
Received in Revised form: 23rd January 2019
Accepted: 26st January 2019
Published online: 31st January 2019

How to cite this article:
Emile ACHA, Judith F AHOUNOU AÏKPE, Jacques ADOVELANDE, M Fidèle ASSOGBA, Grégoire AGOSSOU, Alphonse SEZAN, H Pierre DANSOU, Joachim D GBENOU. (2019). Anti-inflammatory properties of *Melaleuca quinquenervia* (Cav.) ST Blake Myrtaceae (Niaouli) leaves' essential oil. Int. J. Curr. Res. Chem. Pharm. Sci. 6(1): 30-40.
DOI: http://dx.doi.org/10.22192/ijcrcps.2019.06.01.005