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Anti-inflammatory and analgesic activities of extracts from *Balanites aegyptiaca* L. Delile (Balanitaceae) root bark: Plant used against liver diseases in Bukina Faso

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***Balanites aegyptiaca* (L.) Del has been used in various traditional medicines against inflammation and pain. The aim of this study was to evaluate the enzymatic, anti-oedmeatous and analgesic activities of ethanolic and aqueous extracts of *Balanites aegyptiaca* (L.) Del root bark in mice. The extracts were tested *in vitro* for their ability to inhibit the enzymes cyclooxygenase (COX)-1 and COX-2, 15-lipoxygenase (LOX) and phospholipase ($sPLA_2$). The anti-inflammatory and analgesic activity of ethanolic and aqueous extracts was determined by oral administration to healthy animals at doses of 100, 200, 400 and 600 mg/kg and their involvement in K_{ATP} pathways was verified. The percentage inhibition of the activity of the enzyme phospholipase A_2 was close to 50%, those of COXs (COX 1 and COX 2) comparable to those of the control. It has an ability to inhibit 15-LOX even if the IC 50 is lower than that of the reference compound (Zileuton). Pretreatment with the extract at doses of 100 to 600 mg/kg significantly reduced carrageenan-induced edema from 54.91 to 71.80%. The action of the extract significantly decreased the number of contortions with a percentage inhibition greater than 50% for doses of 400 and 600 mg/kg. The action of the extract is not involved in potassium channels (K_{ATP}) in nociception. Pharmacological observed activities provide the scientific basis for the medicinal use of the plant in the treatment of acute inflammation.**

Key words: *Balanites argyptiaca*, phospholipase A_2, cyclooxygenases, lipoxygenase, anti-edema activity, analgesic.

INTRODUCTION

Hepatitis is defined by inflammation of the hepatic parenchyma, associated with a more or less extensive necrosis of hepatocytes (Tata Kadiatou et al., 2018). This inflammation is the response to multiple aggressions of liver (virus, drug, toxins or autoimmune, etc), epithelial cells, endothelial cells and infiltrating inflammatory cells (Juhn et al., 2008). Infiltrating inflammatory cells produce the mediators of inflammation which are proteins, peptides, glycoproteins, cytokines, metabolites of arachidonic acid (prostaglandins and leukotrienes), nitric oxide and oxygen free radicals with the potential to fight infection, but also to damage the host (Juhn et al., 2008). Free fatty acids, such as arachidonic acid, substrate for cyclooxygenase (COX 1 and 2) and lipoxygenase (LOX), are products of the hydrolysis of phospholipids by phospholipase A_2 enzymes. These are involved in many cellular mechanisms, including membrane lipid digestion and uptake, angiogenesis, cell proliferation and migration, and innate immunity and in inflammatory diseases (Murakami et al., 2011). Pain and inflammation occur as nonspecific indicator of numerous disease conditions (Abiye et al., 2019). According to Belemlilga et al. (2019), pain is well defined as an unpleasant sensory and emotional experience that is associated with possible or actual tissue damage. Inflammations are accompanied most often by pain that can be acute or chronic. Steroidal and nonsteroidal anti-inflammatory drugs are generally used to treat the inflammatory process and block the action of certain pro-inflammatory enzymes. Currently, non-steroidal anti-inflammatory drugs (NSAIDs) are widely prescribed because of their efficacy in the management of pain, inflammation, and rheumatic disorders (Sdayria et al., 2018). Some molecules have the ability to inhibit phospholipase A2 (PLA2), cyclooxygenase (COX) and lipoxygenase (LOX) leading to a reduction in the production of prostaglandins (PGs) and leukotrienes (LTs) and inflammatory antagonism (Yahfoufi et al., 2018). However, their long-term therapeutic use is often associated with adverse effects such as gastrointestinal upset due to altered protective gastric mucosa (Wallace and Vong, 2008), renal damage and respiratory depression as well as possible dependence particularly with opioid analogues (Abiye et al., 2019). Some of drugs use ATP-sensitive potassium channel pathway leading to long-term cancer (Sharmin et al., 2016). More and more, people are falling back on traditional medicine especially on medicinal plants for their phytochemicals an active area of research for their anti-inflammatory properties. *Balanites aegyptiaca* L. Delile (Balanitaceae) is native of Arabia, India, ki, Latin America and North Africa and it colonized the Sahel and savannah of West and East Africa according to Boffa (1999). Different parts of the plant (fruits, seeds, barks and roots) are used in traditional medicine for the treatment of pathologies such as laxatives, stomachaches, sterility, mental diseases, epilepsy, yellow fever, syphilis and as a vermifuge, rheumatism, toothaches, jaundice, liver and spleen problems (Maydell, 1983; Tata Kadiatou et al., 2018). Several pharmacological activities have been developed with different parts of *Balantites aegyptiaca* around the world and more precisely in Burkina Faso where they have developed a galenic formulation of syrup against intestinal parasites (Salfo et al., 2018). The aim of this study is to evaluate the ability of ethanolic and aqueous root bark extract to inhibit the production of pro-inflammatory enzymes (phospholipase A2, COX 1 and 2 and LOX), to evaluate activity of anti-edematous, analgesic activity and observe whether they use the ATP-sensitive potassium channel pathway.

MATERIALS AND METHODS

Chemicals

Carrageenan and acetylsalicylic acid were obtained from Sanofi Winthrop Industry (France). Acetaminophen, acetic acid, sodium tetraborate, boric acid come from Sigma (Saint Louis, USA). 1,2-diheptanoilthio-glycerophosphocholine (1,2dHGPC), secretory phospholipase A_2 ($sPLA_2$) from bee venom and 5,5′- dithiobis-2-nitrobenzoic acid (DTNB) were obtained from Cayman Chemical Co. (MI, USA). For the colorimetric inhibition of COX-1 and human COX-2, Screening Kit (Item No. 560131) manufactured by Cayman Chemical, USA, was used. Other products and reagents [methanol, dimethyl sulfoxide (DMSO), Solumedrol, 5-lipoxygenase (EC: 1.13.11.12) type 1-B (extracted from soybean 167 U / mL), (Prolabo), were also used.

Animals

NMRI male mice 1-2 months old weighing 25-30 g from the Institute of Research in Health Science (IRSS) pet shop was used for the acute toxicity studies. They were provided by the IRSS pet shop where they were fed wheat cake (29% protein) and running water. They were raised under air conditioning (23-25°C) and 60% humidity. All experiments were conducted in the morning in accordance with the Laboratory Animal Care Guidelines and the Ethical Guidelines for Painful Experimentation on Conscious Animals (Zimmermann, 1983).

Plants materials and extraction

The part of *B. aegyptiaca* L. Delille (Balanitaceae) were harvested

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in the locality of Ouagadougou in 2015. The plant was botanical identified by Professor Amado Ouédraogo (Laboratoire de Biologie et Ecologie Vegetale / University Joseph KI-ZERBO, Ouagadougou, Burkina Faso) and a specimen was deposited at the herbarium of the university against a code number T4263. Plant material was dried at room temperature, ground (mill with East Gladiator type blades) and stored in an airtight bag until use.

Fifty (50) mg of powder was mixed with 500 ml of distilled water and boiled under reflux for 30 min. After cooling, the mixture is centrifuged and the supernatant is frozen for lyophilization. Two hundred and fifty (250 g) of the powder were extracted by exhaustion with a mixture of ethanol: water (9: 1). Rotary vacuum evaporator was used to remove the solvent and extract was freeze dried. The lyophilizate obtained (26.5 g for ethanolic extract and 11.95 g for aqueous extract) was stored in a vacuum desiccator for later use.

In vitro anti-inflammatory activity

Phospholipase A_2 inhibition test

$sPLA_2$ activity was determined using method of Cayman Chemical Co. (MI, USA) (D'Almeida et al., 2013). For the assay, the wells (enzyme test) received 10 µl of methanol (HPLC) plus 10 µl $sPLA_2$ and the inhibition wells received 10 µl of reconstituted $sPLA_2$ then 10 µl of extract (8mg / ml) or of the reference compound. The blank consisted of 10 µl of methanol (HPLC) with 10 µl of buffer. The reaction was initiated with the addition of 200 µl of Diheptanoythiol-PC substrate and each mixture is made of triplicate then the entire device is allowed to incubate for 15 min at 25°C. After 15 min, 10 µl of DTNB was added to each well to stop the reaction. Mixing of the plate was carried out for 1 min and the reaction mixture was analyzed spectrophotometrically (spectrophotometer BioRad model 680, Japan) at the wavelength of 405 nm. All tests were done in triplicate and the percent inhibition of $sPLA_2$ was calculated by the following formula:

% Inhibition = [(AEA - AIA) / AEA] X 100

-AEA: Activity enzyme test absorbance;
Enzyme Activity Test: Abs Enzyme test - Blank abs
-AIA: activity inhibition test absorbance
Activity Inhibition Test: Abs Inhibition test - Blank Abs

Enzymatic cyclooxygenase (COX1 and COX2) inhibitory activity

The COX activity assay kit (Catalogue No. 560131, Cayman Chemical, Ann Arbor, MI, USA) measures the peroxidase activity of cyclooxygenase. The peroxidase activity is assayed colorimetrically by monitoring the appearance of oxidized N,N,N',N'-tetramethyl-p-phenylenediamine (TMPD) at 590 nm (Kulmacz and Lands, 1983). For the assay, in the reaction medium, the test enzyme batch consisted of 150 µl of assay buffer, 10 µl of heme and 10 µl of the COX 1 or COX 2 enzymes and 10 µl of the dimerization solvent (DMSO). The inhibition test batch consisted of 150 µl of assay buffer, 10 µl of heme, 10 µl of COX 1 or COX 2 enzymes and 10 µl of ethanolic and aqueous extracts of root bark (2.2 mg / ml) or positive control such as aspirin and indometacin. The blank consisted of 160 µl of assay buffer, 10 µl of Heme and 10 µl of dimerization solvent (DMSO). The mixture was shaked for a few seconds and incubated for 5 minutes at 25°C. Twenty microliter of colorimetric substrate was added to each well used and the reaction was initiated by adding 20 µl of arachidonic acid solution to all wells used. The plate was carefully dried for a few seconds to mix and incubate for 2 min at 25°C. Absorbance was read at 590 nm using a plate reader (Epoch, BioTeck instruments, USA). All tests were done in triplicate. the percent inhibition of COX 1 or COX 2 was calculated by the following formula:

% Inhibition = [(AEA - AIA) / AEA] × 100

-AEA: Activity enzyme test absorbance
Enzyme Activity Test: Abs Enzyme Test - Blank abs
-AIA: activity inhibition test absorbance
Activity Inhibition Test: Abs Inhibition Test - Blank Abs

Lipoxygenase (LOX) inhibitory activity

The inhibition of lipoxygenase was assayed according to the spectrophotometric method described by E Malterud and Rydland (2000) with slight modifications. Briefly, 100 µl of enzyme solution (200 U/ml) prepared in boric acid buffer (0.2 M; pH 9.0) was mixed with 25 µl of aqueous and ethanolic extracts of *B. aegyptiaca* (8 mg/ml in DMSO) and then incubated at room temperature for 3 min. Reaction was then initiated by the addition of 125 µl of the substrate (250 µM of linoleic acid) and the velocity was recorded for 3 min at 234 nm with a microplate reader (Epoch, BioTeck instruments, USA). All tests were done in triplicate and DMSO was used as a control while Zileuton, positive control, were used as reference compounds. Percentage of lipoxygenase inhibition was calculated according to the equation:

% Inhibition of lipoxygenase= $[(V_0$ Control− V_0 Sample)/ V_0 Control] ×100

V_0 Control: Enzymatic activity without inhibitor, V_0 Sample: Enzymatic activity in presence of extract or reference compounds.

In vivo anti-inflammatory activity

Anti-edematous activity

The experimental study of the anti-inflammatory activity was carried out according to the method described by Winter et al. (1962) slightly modified by Noufou et al. (2012) according to which the inflammation is induced by injection of carrageenin at the level of the plantar arch of the paw right of the rat. The edema caused by this carrageenin will be translated into volume and measured by the Plethysmometer (Ugo Basile) which makes it possible to follow the evolution of the inflammatory process. Six batches of seven mice used (weight between 20-30 g) were fasted 17 h before the test. The mice were grouped into:

Control group: The mice of this batch receive the vehicle solution (physiological saline) orally, 01 hour before the injection of 50 µl of carrageenin (1% in NaCl 0.9%) into the plantar arch of the right leg of the mouse.
Reference group: The mice in this batch were treated with acetylsalicylic acid (ASA) at a dose of 100 mg / kg bw, 1 h before the injection of carrageenan.
Tests group (04 groups): The extracts to be tested are administered to mice orally at doses of 100, 200, 400 to 600 mg / kg; 01h before the injection of carrageenan.

The volume of the treated paw was measured before 01 h, and at 01, 03 and 05 h after the carrageenan injection. The anti-inflammatory activity was evaluated as a percentage of edema reduction in treated mice compared to blank controls according to the following formula:

Table 1. Phospholipase A_2, cyclooxygenase (COX 1 and COX 2) and 15-lipoxygenase inhibition activity.

Enzyme	Phospholipase A2	COX 1	COX 2	LOX
%	Inhibition percentage (at 100 µg/ml)			IC_{50} µg/ml
Ethanolic extract	45.82±1.3	42.35±1	33.1±2	83.75±20.09
Aqueous extract	42.84±1.5	54.12 ±2	10.22±3	110.66±6.21
Indomethacin	nd	nd	58.71±0.41	nd
Zileuton	nd	nd	nd	2.92±0.24

Inhibition % = ((A - B)/A) × 100

A represents the average difference of the volume of increase of the paw of the mice of the blank control group at the times T 01, T 03 and T 05h and B represents the average difference of the volume of increase of the paw of the mice of the treated batches at the times T 01, T 03 and T 05h. These averages are plotted on a curve to follow the evolution of the edema for each group. The determination of the percentage of inhibition of edema (IOP) makes it possible to evaluate the anti-inflammatory potential of the extract studied and to compare it with that of the reference product.

Analgesic activity: Writhing test

The analgesic effect of the extracts was evaluated according to the number of abdominal contortions induced by the intraperitoneal injection of acetic acid (0.6%) according to the method described by Noufou et al. (2012). Lots of seven were randomly constituted. The white control group received distilled water, the reference group, acetaminophen (paracetamol) a dose of 200 mg / kg and the other lots received the aqueous and ethanolic extracts of the root rinds at doses ranging from 100, 200, 400 to 600 mg / kg. One hour after extracts or reference administration, the animals intraperitoneally received acetic acid 0.6% at the dose of 10 ml / kg. Five minutes after the injection of acetic acid, the number of contortions was counted in each mouse for 15 min. The analgesic effect was evaluated according to the following formula:

Inhibition % = ((Nb-Nt)/Nb) × 100

Nb is the average of the number of contortions of the mice of the blank control group and Nt is the average of the number of contorted mice of the batch treated.

Non-morphine analgesic activity: Involvement of ATP-Sensitive K^+ Channel Pathway

The non-morphine analgesic activity involving the K^+ channels was evaluated by the method described by Perimal et al. (2010), with slight modifications. Four groups of 7 mice were divided as follows: the control group receives only the vehicle (saline), the second group receives glibenclamide (an ATP sensitive K^+ channel inhibitor) and the last two groups receive respectively the ethanolic and aqueous extracts at a dose of 400 mg / kg of body weight. All mice except the first were pretreated with glibenclamide (10 mg / kg) 15 min before administration of saline or both extracts. Mice were injected with acetic acid, 1 hour after treatment. Five minutes after the acetic acid injection the number of contortions was recorded for 15 min. The analgesic effect was evaluated according to the following formula:

Inhibition % = ((Nb-Nt)/Nb) x100

Nb is the average of the number of contortions of the mice of the blank control group and Nt is the average of the number of contorted mice of the batch treated.

Statistical analysis

Experiments were carried out in triplicate and results expressed as mean ± SEM. The analysis of the results was done on the basis of statistical processing of Graph Prism software version 6 and One way Analysis of Variance followed by Dunnett's test was used as a statistical treatment. The differences were considered significant when $p \leq 0.05$ compared to the control.

RESULTS

In vitro anti-inflammatory activity

The percent inhibition of the activity of the phospholipase A2 enzyme was close to 50% for both extracts as indicated in the Table 1. The inhibition percentages of cyclooxygenases 1 and 2 gave results on both sides comparable to the control for COX 2. The percentage inhibition of COX 1 by the two extracts was close to 50% whereas for COX 2 this percentage is very low with the aqueous extract than that ethanolic (Table 1). The results of the IC 50 of the LOX are shown in Table I. Of the two extracts, the ethanol extract has a lower IC 50 than the aqueous one even though both have a lower enzymatic activity than that of the reference compound the Zileuton.

In vivo anti-inflammatory activity

Anti-edematous activity

The results of the anti-edematous activity of the two extracts are shown in Figures 1 and 2. The effect of carrageenan on the mice which received the vehicle led to an increase in the volume of the paw from the first hour and reached the maximum at the fifth hour Pretreatment with different types of extracts at doses of 100, 200, 400 and 600 mg / kg significantly reduced carrageenan-induced edema. The reduction of edema by the extracts was dose-dependent and their percent inhibition was nevertheless lower than that of the reference,

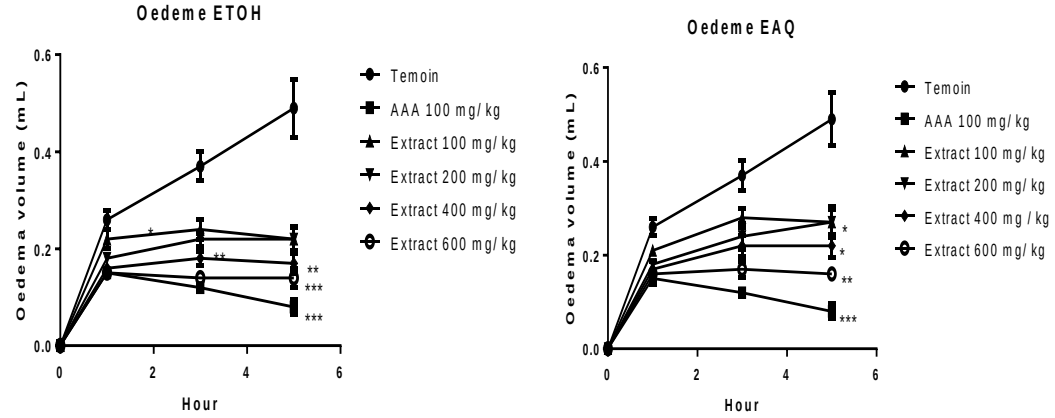

Figure 1. Effect of ethanolic (Oedema ETOH) and aqueous (Oedema EAQ) extracts at different doses on carrageenan-induced mouse paw edema. Values are mean ± S.E.M. n = 7. *, **, *** indicate a significant difference respectively at p <0.05, P <0.01 and p <0.001 compared to the control (ANOVA, post test Dunnett).

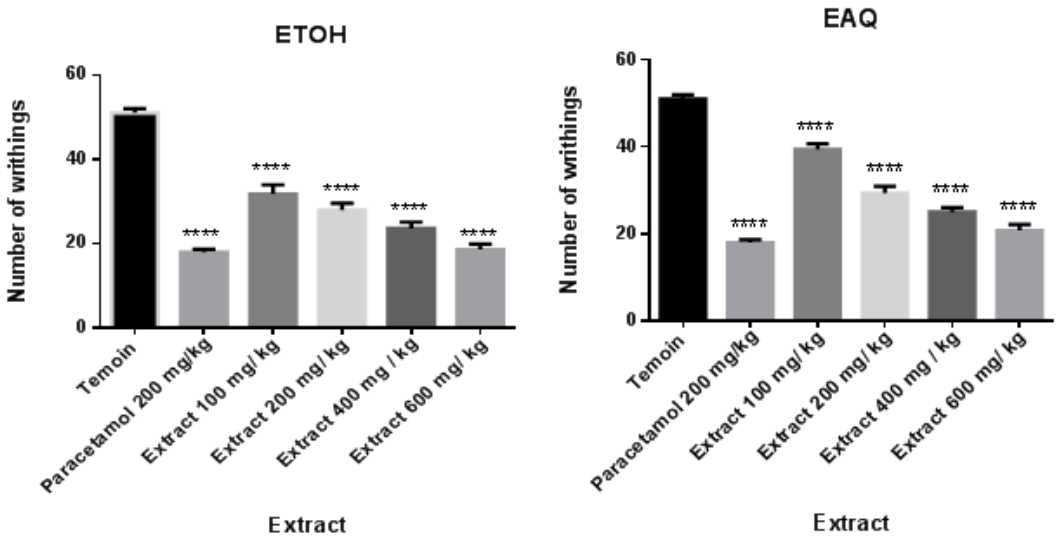

Figure 2. Effect of ethanolic (ETOH) and aqueous (EAQ) extracts on acetic acid induced writhing in mice. Values are mean ± S.E.M. n = 7. ***: P<0.001 indicate significance compared with control normal group (one way ANOVA analysis followed by Dunnett's test).

acetylsalicylic acid dosed at 100 mg/kg which was 83.56% at the fifth hour.

Analgesic activity: writhing test

Figure 2 show the number of contortions due to the injection of acetic acid (0.6%). the number of fractions significantly decreased with the action of paracetamol at the dose of 200 mg / kg. the action of the extracts was dose-dependent and the percentage of the extracts was greater than 50% for the doses of 400 and 600 mg / kg compared with paracetamol.

Non-morphine analgesic activity: Involvement of ATP-Sensitive K^+ Channel Pathway

The writhing number of the mice receiving glibenclamide was comparable to that of the control mice that received the vehicle (Figure 3). Both extracts reduced the number of contortions by 50.98 and 53.73% respectively for the

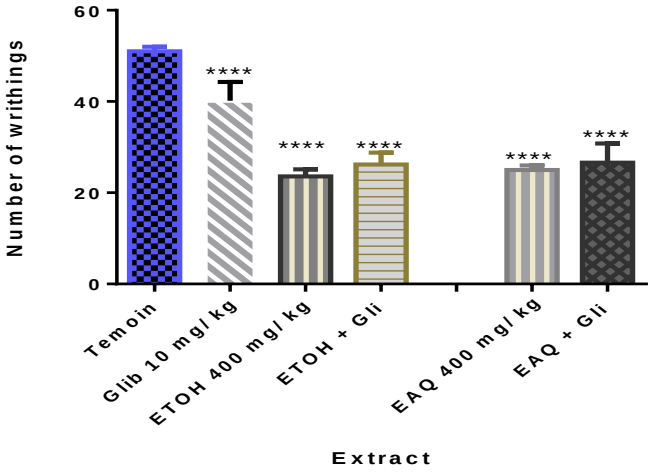

Figure 3. Effect of pretreatment of animals with glibenclamide (Glib) on the involvement of the K^+ channels of the ethanolic (ETOH) and aqueous (EAQ) extracts against the acetic acid-induced abdominal resistance test in mice.Values are mean ± S.E.M. ***: P<0.05 indicate significance compared with control normal group (one way ANOVA analysis followed by Dunnett's test).

aqueous extract and the ethanol extract in the absence of glibenclamide and in its presence its percentages decreased by less than 50% at 47.84 and 48.63% respectively. The action of glibenclamide increased the number of contortions.

DISCUSSION

Lipoxygenase enzymes (LOX) as well as cyclooxygenases, pro-inflammatory enzymes, are heavily involved in many diseases including atherosclerosis, cancer and diabetes (Vidal et al., 2007). Its enzymes cause the production of eicosanoids, which are the finished products of arachidonic acid metabolism. Phospholipase A2 is a key enzyme in the metabolism of membrane phospholipids and its cellular stimulation is the crucial step in the production of pro-inflammatory mediators, prostaglandins (COXs) and leukotrienes (15-LOX) (Khanum et al., 2005). In this study, the enzymatic activity of the ethanolic and aqueous extracts of Balanites aegyptiaca root bark was demonstrated through the inhibition of Phospholipase A_2 enzymes, COX 1 and 2 and lipoxygenase *in vitro*.

Activity of phospholipase A_2 was inhibited by the extracts thus blocking the production of arachidonic acid. Extracts would able to block phospholipases A2 which of its activation is due by stimuli such as bradykinin, tumor necrosis factor interleukin-1 or calcium ionophore A23187 (Feghali-Bostwick and Wright, 1997).

COX1 is constitutive and plays a physiological role in maintaining the integrity of tissues, while COX2 is inducible by inflammatory stimulation (Jouzeau et al., 1997). The extracts inhibited the activity of the COXs to different degrees. The extract acting on both COX 1 and COX 2, would have better anti-inflammatory and analgesic properties (COX 2) (Blobaum and Marnett, 2007; Burdan et al., 2004). These results are in agreement with those of Eldeen and Van Staden (2008) who in these studies found that the ethanolic extract of the roots of *Balanites aegyptiaca* inhibited the isoenzymes (COX-1 and 2).

According to Chung et al. (2009), it would be judicious that an extract having the inhibitory therapeutic effects of COX-1 and COX-2 be studied in the process of LOX inhibition it could be the only preferred route of conversion of arachidonic acid. in leukotrienes (leukotriene B 4, LTB 4) which play the major role in the inflammatory response. Both ethanolic and aqueous extracts of *B. aegyptiaca* showed moderate activity (41-70% inhibition) in the inhibition of 15-LOX according to the classification explained by Chung et al. (2009). The two extracts having an action on the inhibition of COX 1 and 2 enzymes and 5-LOX could have a synergistic effect in blocking the production of prostaglandins and leukotrienes (Irrera and Bitto, 2017). Both extracts inhibit the enzymatic activities of phospholipase A2, COX 1 and 2 and 5-LOX at different percentages and at each stage of the inflammatory process so it would be a good anti-inflammatory to fight against inflammatory diseases (George et al., 2014).

The method of induction of edema by carrageenan was

used for inflammatory activity in vivo. According to Chatter and Tarhouni (2009) the method of induction of carrageenan would be simple, rapid in the induction of symptoms characteristic of inflammation (development of edema within one hour after injection, with an effect maximum after 5 hours) and reproducible. The induction of the inflammatory process by the carrageenan is manifested in 3 stages: The early stage (the first 90 min) during which histamine and serotonin are released; the second stage (90-150 min) which is driven by the release of kinin; and the third step (after 180 min), which is mediated by prostaglandin (Guo et al., 2011) (Rock et al., 2018).

B. aegyptiaca extracts significantly reduced ($p < 0.05$) carrageenan-induced edema in a dose-dependent manner by acting progressively on it with strong inhibition observed at the fifth hour. The action of the extracts would reduce the inflammation by inhibition of the enzyme cyclo-oxygenase responsible for the production of prostaglandins and thromboxane (Etamé Loé et al., 2018). Similar results have been found with different parts of the plant such as aerial parts (Gaur et al., 2008) and seeds (Ali et al., 2014) in reduction of edema.

The writhing test is occasionally classified as a visceral pain model, but both visceral and somatic structures are activated by intraperitoneal injection of acetic acid (Berge, 2011). The analgesic effect of *B. aegyptiaca* extracts was studied by inducing pain with acetic acid. This induced pain is thought to be due to the released chemical mediators (histamine, bradykinin, substance P and prostaglandins) that would stimulate peripheral nociceptive and induce an increase in vascular permeability (Noufou et al., 2012). This high vascular permeability leads to the formation of an exudate compressing the nerves at the origin of the sensation of pain (Etamé Loé et al., 2018). The action of the extracts reduced the number of contortions in a dose-dependent manner with a 50% inhibition with the 400 mg / kg dose with both ethanolic and aqueous extracts. The extracts would have an inhibitory effect on pro-inflammatory chemical mediators. The inhibitory effects of these extracts could be attributed to their inhibitory action on the enzymes involved in the synthesis of prostaglandins and leukotrienes.

This study also revealed the mechanisms including involvement of ATP-sensitive K^+ channels in the antinociceptive activities of *B. aegyptiaca* extracts. The single dose of 400mg / ml extracts that inhibited the number of contortions in the writhing test by 50% was used for non-morphine analgesic activity involvement of ATP-sensitive K^+ channel pathway. The action alone of glibenclamide (an ATP-sensitive potassium channel antagonist) did not significantly alter the number of contortions caused by the injection of acetic acid. The number of contortions significantly decreased the antinociceptive effects of *B. aegptiaca* with injections of extracts and glibenclamide (<0.05). According to Nushrat and al., glibenclamide specifically blocks only drugs sensitive to ATP- K^+ channels, but does not affect other types such as Ca^{2+} activated and voltage-gated K^+ channels (Sharmin Ani et al., 2016). Scientific studies have shown that K + channels play a major role in pain, and that their opening causes a hyperpolarization of the cell membrane, leading to a decrease in cell excitability (Lawson, 2000). The blocking of K + channels did not have too much effect on the action of the extracts, which could be explained by the fact that the extracts do not follow the K_{ATP} path. Extracts do not seem to take the path of K_{ATP} which would mean that their long-term use will have virtually no carcinogenic effect on the body.

Conclusion

In conclusion, ethanolic and aqueous extracts of *B. aegyptiaca* root bark showed good inhibitory activity of pro-inflammatory enzymes such as phospholipase A2, COX 1 and 2 and 5-LOX. The extracts showed dose-dependent anti-inflammatory and analgesic activities in the different models used in this study and they do not seem to follow the K_{ATP} pathway. The present study could confirm the traditional uses of *B. aegyptiaca* against inflammatory pathologies.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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