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Phytochemicals and Biological Activities of *Flueggea virosa* (Phyllanthaceae) Used in the Traditional Treatment of Benign Prostatic Hyperplasia in Mali

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Abstract: Worldwide, benign prostatic hyperplasia (BPH) is common in men over the age of 50. Hence there is a phytotherapy for BPH. In Mali, many medicinal plants are used in the traditional treatment of BPH. The current work aimed to characterize secondary metabolites and anti-radical constituents, to determine the acute toxicity and to evaluate the analgesic and anti-inflammatory activities of aqueous extracts from the leaves and stems of *Flueggea virosa*. Colour and precipitation reactions in tubes were performed to characterize the chemical constituents of the extracts. Anti-radical substances were determined through the free radical reduction method of 1,1 diphenyl, 2-picryl hydrazyl radical. The acute toxicity was performed *in vivo* using female mice. *In vivo* analgesic activity was determined through inhibition of induced pain in mice using 0.6% acetic acid. *In vivo* anti-inflammatory activity was determined by inhibiting inflammation caused with carrageenan in mice. The main chemical constituents of aqueous extracts were flavonoids, tannins and saponins. Polar extracts contained anti-radical substances. These extracts exhibited analgesic and anti-inflammatory activities. The decoction extracts administered orally in mice at the dose of 2000 mg/kg did not provoke toxic effects and mortality. The stem extract at 100 mg / kg exhibited the best analgesic activity with 64.82% inhibition and anti-inflammatory activity with 59.07% inhibition. These first results justify the traditional use of the plant in the medical management of BPH and will help to make data for the development of a new improved traditional medicine (ITM) based on the stems of *Flueggea virosa*.

Keywords: *Flueggea virosa*, Analgesic and Anti-inflammatory, Anti-radical Substances, Benign Prostatic Hyperplasia, Mali

1. Introduction

Benign prostatic hyperplasia (BPH) is a common disease in older men, with lower urinary tract symptoms caused by hyperplasia of the prostatic epithelium and stromal cells [1, 2]. Essential androgens for prostate growth during early development, puberty, and aging have been documented to play a role in enlarged prostate associated with other factors such as aging, diet, increased inflammatory mediators, hormones and oxidative stress [2]. Benign prostatic hyperplasia (BPH) is a histologic concept, sometimes with symptoms in the lower urinary tract: frequent, imperious and incomplete urination, weakness of the jet, dysuria and nocturia [3]. Currently, the main therapeutic drugs for BPH are 5-alpha reductase inhibitors and beta blockers [4, 5], such as finasteride and terazosin. However, these drugs have side effects such as fatigue, hypotension, ejaculation disorders, dysfunction and an increased risk of

prostate fibrosis [5, 6]. Furthermore, surgical treatment is another powerful remedy for BPH [7].

Nowadays, this option poses a lot of complications and the possibility of recurrence. Thus, the number of patients undergoing surgery for BPH is gradually decreasing [8]. Therefore, finding a curative drug that can effectively treat BPH with few side effects is critical. Herbal agents have gained considerable attention for the treatment of BPH and prostate cancer because they are thought to be safer, cost effective and have fewer side effects than conventional alternatives, especially in developing countries [9, 10]. New theories support that many potential herbs may inhibit the action of an essential hormone-regulating enzyme that converts testosterone to dihydrotestosterone, a process considered important in the development of an enlarged prostate and prostate cancer [11].

The use of complementary and alternative medicine in the management and treatment of BPH has shown hope and is gaining popularity [12]. Some drugs like saw palmetto, *Cucurbita pepo* (pumpkin) have been shown to suppress the level of prostate specific antigen (PSA) in the blood [11]. In addition, studies of randomized trials and meta-analyses through recent literature suggest clinical efficacy and good tolerance of certain preparations, in particular extracts of *Serenoa repens* and also of *Pygeum africanum*, produced with high concentrations of β- sitosterol, and pumpkin seeds [13]. A recent literature review undertaken in Nigeria identified African medicinal plants or not with anti-BPH activity in animals [12]. These plant species belonging to different families were *Celosia argentea* F. Cristata (L) (Amaranthaceae), *Citrullus lanatus* (Thumb) (Cucurbitaceae), *Croton membranaceus* (Euphorbiaceae), *Cucurbita pepo* L. (Cucurbitaceae), *Raphia hookeri* G. Mann & H. A. Wendl. (Arecaceae / Palmaceae), *Secamone afzelii* (Asclepiadaceae), *Solanum macrocarpon* L. (Solanaceae), *Telfairia occidentalis* (Hook. F) (Cucurbitaceae), *Trischosanthes cucumerina.var. anguina* (Cucurbitaceae) and *Zapoteca portoricensis* (Jacq.) H. M (Fabaceae). These plants contain bioactive constituents and antioxidant agents such as flavonoids, terpenoids, saponins and steroids which contribute to their anti-inflammatory properties and thus to their anti-BPH activities [12]. Overall, the use of herbal remedies for benign prostatic hyperplasia is aimed at reducing symptoms associated with this disease. In Mali many medicinal species are used in the traditional treatment of BPH. The chemistry and biological activities of some of these plants including *Acanthospermum hispidum, Curculiigo pilossa, Piliostigma thonningii* and *Spilanthes uliginosa* have been documented [14, 15].

Flueggea virosa (Roxb. ex Willd.) Royle belonging to the Phyllanthaceae family is a shrub two to three meters long, with many branches starting from the base, thus forming an ellipse. It is used in traditional medicine in Mali and elsewhere to manage several diseases including diarrhoea, rheumatism, malaria, liver disease, inflammation and pain. The extracts of this plant also find their use in certain disorders of urinary and genital tracts [16]. The literature shows that this plant is chemically rich in alkaloids, triterpenoids, tannins, flavonoids, resins, steroids, cardiac glycosides, and anthraquinones [17]. The presence of these constituents confers to this plant a variety of pharmacological activities such as analgesic, anti-inflammatory, aphrodisiac, sedative, anti-arrhythmic, antidiabetic, antimalarial, anti-HIV, anti-hepatitis C, anti-diarrheal, cytotoxic, anti -microbial, antifungal, antioxidant, and laxative properties [17].

With the view for developing a phytomedicine for the management of BPH in Mali, the current work aimed to evaluate the analgesic, anti-inflammatory and antioxidant activities of aqueous extracts from the leaves and stems of *Flueggea virosa* used in the traditional treatment of BPH in Mali.

2. Materials and Methods

2.1. Plant Material

The stems and leaves of *Flueggea virosa* were collected in December 2012 by Mr. Oumar Diakité in Fouladougou-bangassi in the Kita circle of Mali.

The samples arrived in Bamako the same day and were identified at the Department of Traditional Medicine (DMT) of the National Institute for Public Health Research (INRSP) then dried for a week under shade at room temperature in the drying room of the DMT. After drying the two samples were pulverized using a Forplex type F1 mill available at DMT. The powders obtained were used for extractions, and phytochemical and biological investigations.

2.2. Animals

For this work authors used white mice male and female weighing between 18 and 35 g, of no consanguineous strain from CF1 (Carworth Farms strain 1) line of OF1 (Oncins France strain 1) race supplied by the animal facility of the National Support Center for Disease Control (CNAM) in Bamako. The animals were kept under standard environmental conditions. They had a 12 hour light /dark cycle. Animals were fed using mouse food made at DMT with free access to tap water.

2.3. Ethical Statement

The experimental procedures and techniques used in the study were in accordance with accepted principles for laboratory animal use and care. All protocols and techniques used in this study were approved by the National Institute for Public Health Research Ethic Committee.

2.4. Extractions

Different types of extracts have been made for antioxidant activity and biological tests.

2.4.1. Aqueous Extracts

10% Extemporaneous Decoction

Authors mixed 10 g of the drug and 100 ml of distilled water together in a flask then put the flask on a warmer and boil for 15 minutes. After cooling, the extract was filtered through a 40x40 compress. The volume of the filtrate was

measured and then used directly for the tests.

10% Decoction

Authors mixed 100 g of the drug in 1000 ml of distilled water and boiled for 15 minutes. After cooling, the extract was filtered through a compress and squeezed. Authors obtained a final volume of 690 ml for the leaves and 700 ml for the stems. These final volumes were concentrated in a rotary evaporator and then frozen before being lyophilized in a freeze dryer. The yield was calculated for each extraction.

10% Infusion

Authors mixed 100 g of the drug in 1000 ml of boiling distilled water. After cooling we filtered on a compress and squeezed. Authors obtained a final volume of 830 ml for the leaves and 820 ml for the stems. These volumes were concentrated and then frozen before being lyophilized. The yields were then calculated.

2.4.2. Hydroethanolic (70% EtOH and 30% EtOH) Extractions

Authors mixed 5 g of drug and 50 ml of solvent in a flask containing a magnetic rod then put this flask on the stirrer for 1 hour. Authors then filtered, evaporated to dryness in a rotary evaporator, weighed the extracts, then their yields were calculated.

2.5. Phytochemical Screening

Certain major groups of secondary metabolites have been investigated in drugs according to conventional methods of characterization. Tannins and polyphenols were identified by the $FeCl_3$ test; flavonoids by reaction to cyanidin; saponins by the foam test; the triterpenes and steroids by the Liebermann-Burchard test and finally the alkaloids by the tests of Mayer and Dragendorf [18, 19].

For the characterization of the anti-free radical constituents, the plates were revealed with the methanolic solution of 1,1 Diphenyl-2-Picryl-Hydrazyl (DPPH), in the proportion 2 mg/10 ml. When present the anti-radical constituents appear as yellow spots on a purple background.

2.6. Biological Activities

2.6.1. Determination of Acute Toxicity

The acute oral toxicity test was performed according to the guidelines of the Organization for Economic Co-operation and Development (OECD) [20]. The mice were fasted for 18 hours with free access to water. With a weight varying between 19 and 25 g, they were divided at random into five groups of three female mice and treated orally with a single dose of dry aqueous extract from the leaves or stems of *F. virosa* (2000 mg/kg), 20% extemporaneous extract of each plant organ (20 ml/kg) or distilled water (20 ml / kg) used as negative control. After administration, the animals were observed for the first 2 hours before feeding them and then observed for another two hours to record cases of immediate deaths or cases of behavioural change relating to the skin, hair, eyes, mucous membranes, respiration etc and once a day on 14 days to record late deaths.

2.6.2. Analgesic Activity

Analgesic activity was tested using 30 male mice (weighing 22-34 g). The animals were randomized into six groups of five mice. Groups I and II were treated orally with distilled water (20 ml/kg) used as negative control group and Paracetamol (100 mg/kg) used as reference drug respectively. Groups III and IV received orally 20 ml/kg of 10% extemporaneous decoction from the leaves and stems of the plant respectively. While groups V and VI were respectively treated orally with 250 mg/kg of dry 10% decoction extract from leaves and with 100 mg/kg of dry 10% decoction extract from stems. One hour after these treatments, the animals received by intra-peritoneal (IP) injection 0.6% acetic acid solution at a dose of 10 µl/g of body weight. Immediately after their injection, the mice were placed in plastic cages, observed to count the twists performed by each mouse during the 25 minutes following the intra-peritoneal injection of acetic acid as described by Siegmund et al. [21] with a few modifications. The time to onset of the first twist and the number of twists were noted for each mouse.

The mean value for each group was calculated and compared to the negative control group. The percentages of inhibition were calculated using the following formula:

$$\%\ Inhibition = \frac{(Wc - Wt) \times 100}{Wc} \quad (1)$$

Wc represents the mean of the number of contortions of the mice in the negative control group;

Wt is the mean of the number of contortions of the mice in the groups treated with extracts and Paracetamol.

2.6.3. Anti-inflammatory Activity

The acute inflammation was induced by the injection of carrageenan under the plantar fascia of the right hind paw of mice as described by Winter et al [22] with slight modifications. Male mice were randomized into six groups of five animals. Groups I and II were treated orally with distilled water (20 ml/kg) used as negative control group and indomethacin (10 mg/kg) used as reference drug respectively. Groups III and IV received orally 20 ml/kg of 10% extemporaneous decoction from the leaves and stems of the plant respectively. While groups V and VI were respectively treated orally with 250 mg/kg of dry 10% leaf decoction and 100 mg/kg of dry 10% stem decoction. One hour after the treatments 0.025 ml of a 1% carrageenan suspension in physiological saline was injected in the right hind paw of each animal to induce the œdema. The paw thickness was measured using a digital calliper. The measurements were determined at 0 h or initial thickness (E0) before injection of the carrageenan) and after the injection of the carrageenan, the thickness of the paw was then measured every hour until the fifth hour (ET). The difference between ET (1, 2, 3, 4 and 5 h) and E0 was considered as the œdema value. The average paw thickness for each group was calculated and compared to the negative control group according to the following formula.

$$\%\ Œdema = \frac{(ET - E0) \times 100}{E0} \quad (2)$$

E0=Initial thickness of the mouse paw; ET=Thickness of the paw after injection of carrageenan and treatment

The percentages of inhibition were then calculated using the following formula:

$$\%\ Inhibition = \frac{(P0-PT)x\ 100}{P0} \quad (3)$$

P0=% increase of the paw in the negative control; PT=% increase of the paw in the treated batch.

2.7. Statistical Analysis

The results were expressed as Mean ± SD. The data were analysed by Student's t test. A value of $P<0.05$ was considered significant.

3. Results

3.1. Yields of Aqueous and Hydroalcoholic Extracts

The yields of the various extractions with polar solvents on the leaves and the stems are reported in Table 1. The yields of the leaf extracts were higher than those from the stem. The best yield was 41.60% for the 30% ethanolic extract from the leaves.

3.2. Phytochemical Data

The information on the chemical groups sought in the two parts analysed is noted in Table 2. The anti-free radical substances present in the polar extracts from the two organs of the plant are illustrated by yellow spots in Figure 1.

Table 1. *Yields of different extractions with polar solvents on the leaves and stems of Flueggea virosa.*

Extracts	Yields (%)	
	Leaf	Stem
10% Decoction	25.35	8.56
10% Infusion	25.14	10.70
10% Extemporaneous Decoction	28.60	8.70
70% EtOH	22.60	14.40
30% EtOH	41.60	16.00

Table 2. *Secondary metabolites analysed by tube reactions.*

Chemical Groups	Results	
	Leaf	Stem
Flavonoids	++	+++
Alcaloids (Mayer-Dragendorff)	-	-
Tannins (reaction with $FeCl_3$)	++++	+++
Gallic tannins (reaction of Stiasny)	++	+++
Catechic tannins	-	+++
Steroids and triterpenes	++	+++
Anthocyanins	-	-
Leucoanthocyanins	+	+
Saponins	±	±

Key: ++++=Highly abundant; +++=Abundant; ++=Moderate; +=Low; ±=Trace; -=Absent.

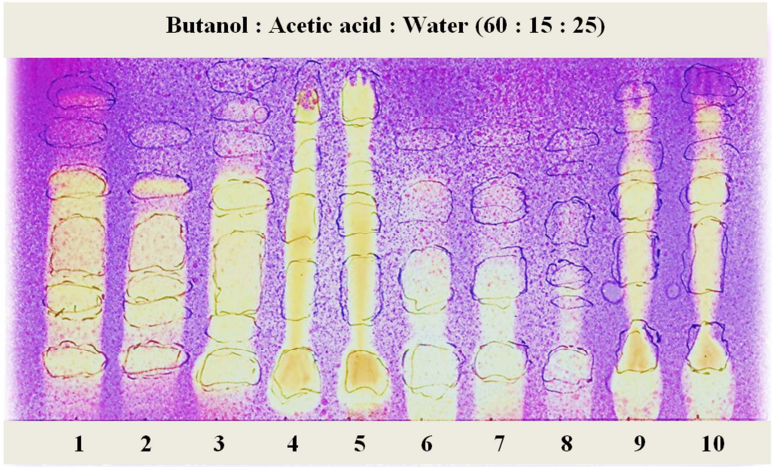

Figure 1. *Chromatogram showing the anti-free radical constituents stained in yellow on the plate revealed with DPPH after migration in Butanol: Acetic acid: Water (60:15:25).*

Key: 1=10% leaf decoction, 2=10% leaf infusion, 3=10% leaf Extemporaneous decoction, 4=70% leaf ethanol extract, 5=30% leaf ethanol extract, 6=10% stem decoction, 7=10% stem infusion, 8=10% stem Extemporaneous decoction, 9=70% stem ethanol extract and 10=30% stem ethanol extract.

3.3. Biological Activities

3.3.1. Acute Toxicity Data

From our experimental conditions, the 20% extemporaneous decoction (20 ml/kg) and the dry aqueous extracts at a dose of 2000 mg / kg of the leaves or stems of *Flueggea virosa* showed no signs of toxicity or mortality after 14 days.

3.3.2. Analgesic Activity

The results of the analgesic activity of the 10% extemporaneous and dry aqueous extracts of the leaves and stems of *Flueggea virosa* on the pain caused by acetic acid are reported in Table 3. Overall, all the extracts tested showed the analgesic activity. However, it was the dry extract of the stems that led to the best activity with 64.82% inhibition of pain.

Table 3. *Analgesic activity of extemporaneous and dry aqueous extracts of the leaves and stems of Flueggea virosa on pain caused by acetic acid.*

Treatments (doses/kg)	Number of contorsions (M ± SD)	% Inhibition
Distilled Water (20 ml/kg)	61.40 ± 01.14	----
10% Leaf Extemporaneous Decoction (20 ml/kg)	37.00±05.61**	39.73
Dry Leaf Decoction Extract (250 mg/kg)	18.80±08,10**	69.38
10% Stem Extemporaneous Decoction (20 ml/kg)	30.60±09.23**	50.16
Dry Stem Decoction Extract (100 mg/kg)	21.60±06.02**	64.82
Paracetamol (100 mg/kg)	13.00±05.91**	82.98

M=Mean from six mice; SD=Standard Deviation, t-Student *significant when p<0.05; **Highly significant with p<0.01 compared to negative control group treated with distilled water

3.3.3. Anti-inflammatory Activity

The data on the anti-inflammatory effects of the aqueous extracts (extemporaneous and dry) of the leaves and stems of *F. virosa* are shown in Tables 4-7 below.

Effects of extemporaneous extracts

Carrageenan caused significant inflammation to the paw of the animals (Table 4). The extracts acted better on inflammation in related time with better activity observed at the fifth hour by the extract from the stems with 54.57% inhibition of inflammation (Table 5).

Table 4. *Effects of extemporaneous extracts on œdema induced by injection of carrageenan in mice.*

Treatments (doses/kg)	Swelling Degree of paw (M ± SD) in mn over the time					
	E0	E1	E2	E3	E4	E5
Distilled Water (20 ml/kg)	0.76±0.2	1.95±0.2	2.08±0.3	2.03±0.2	2.18±0.2	2.15±0.5
Leaf Extract (20 ml/kg)	0.68±0.2	1,96±0.3	1.66±0.2	2.05±0.3	2.06±0.3	1.80±0.4
Stem Extract (20 ml/kg)	1.39±0.2	1,85±0.3	1.89±0.3	1.76±0.2	1.96±0.3	1.89±0.3

M=Mean from 5 mice; DS=Standard Deviation; E=Œdema over the time

Table 5. *Percentage inhibition of œdema by extemporaneous extracts according to negative control.*

Treatments (doses/kg)	% Inhibition of Œdema					
	0h	1h	2h	3h	4h	5h
Distilled Water (20 ml/kg)	-	-	-	-	-	-
Leaf Extract (20 ml/kg)	-	AI	17.15*	23.22*	34.60*	48.52**
Stem Extract (20 ml/kg)	-	14.65*	34.30*	40.71**	47.28**	54.57**

E=Œdema over the time; *Significant when p<0.05; **Highly significant when p<0.01 compared to negative control group treated with distilled water. AI=Absence of inhibition.

Effects of dry aqueous extracts

The activity was organ and dose dependent according to the swelling degree (Table 6). From the third hour we saw good anti-inflammatory activity with the dry stem extract which was 59.07% inhibition even exceeding that of indomethacin used at 10 mg / kg (Table 7).

Table 6. *Effects of dry extracts on œdema induced by injection of carrageenan in mice.*

Treatments (doses/kg)	Swelling Degree of paw (M ± SD) in mm over the time			
	E0	E1	E2	E3
Distilled Water (20 ml/kg)	1.34±0.1	2.27±0.3	2.6±0.5	2.31±0.4
Leaf Extract (250 mg/kg)	1.33±0.1	2.13±0.2	2.64±0.1	2.29±0.2
Stem Extract (100 mg/kg)	1.24±0.1	2.11±0.2	2.23±0.4	2.09±0.2

M=Mean from 5 mice; DS=Standard Deviation; E=Œdema over the time

Table 7. *Percentage inhibition of œdema by the dry extracts and the reference drug according to the negative control.*

Treatments (doses/kg)	% Inhibition of Œdema			
	0h	1h	2h	3h
Distilled Water (20 ml/kg)	-	-	-	-
Leaf Extract (250 mg/kg)	-	AI	AI	12.04*
Stem Extract (100 mg/kg)	-	32.40*	54.60**	59.07**
Indomethacin (10mg/kg)	-	6.14*	24.40*	26.31*

*Significant with p<0.05; **Highly significant with p < 0.01 compared to negative control group treated with distilled Water. AI=Absence of Inhibition.

4. Discussion

Flueggea virosa is a plant whose roots are used in traditional medicine in men with benign prostatic hyperplasia, but the stems and leaves were chosen in order to keep the plant alive.

The leaf extracts were greenish in colour and sticky in consistency while the stem extracts were yellowish and less sticky. The yields obtained for the leaves were much higher than those for the stems. This would probably be related to a rapid release of the polar constituents from the leaves when they are in contact with the polar solvents.

The leaves and stems were rich in secondary metabolites such as flavonoids, tannins, sterols and triterpenes, leucoanthocyanins but with traces of saponins. Tube reactions do not revealed the presence of alkaloids in the two samples.

The leaves were rich in coumarins, carotenoids and mucilages which on the other hand, were absent in the stems [23]. The colour and precipitation reactions used in this present work failed to demonstrate alkaloids in the investigated samples. However, they have been demonstrated in leaf extracts by thin layer chromatography using Dragendorff's reagent [23]. This result goes in the same direction like the one obtained by recent work carried out at DMT on leafy stems of *Flueggea virosa* [24]. In Nigeria the presence of alkaloids, tannins and flavonoids in the organs of *Flueggea virosa* has been revealed in methanolic extracts from the roots and leaves of *Flueggea virosa* [25, 26]. Also in Nigeria, scientists have found in addition alkaloids, saponins, flavonoids, anthraquinones and steroids in the leaf methanolic extract of the plant [27].

Extracts from the leaves and stems showed the presence of anti-free radicals by scavenging the DPPH radical. However, these anti-free radicals were more pronounced with the hydroalcoholic extracts of the leaves. The presence of anti-free radical substances could be explained by the richness of the organs analysed in polyphenolic compounds. Numerous studies have shown the anti-free radical activity of extracts or isolated molecules of *Flueggea virosa* [28-30].

Based on the current experimental conditions, the 20% extemporaneous decoction extracts and the dry 10% aqueous extracts at 2000 mg / kg showed no signs of toxicity after 14 days. Many studies have shown the low toxicity of *Flueggea virosa*. In 2008 Magaji and his team found some LD_{50} of 774.6 mg / kg and greater than 5000 mg / kg after respective administration of root methanolic extracts intraperitoneally and orally in mice [25]. Other previous authors found some LD_{50} of 1265 mg / kg and 1264.9 mg / kg, respectively, after intraperitoneally administration of leaf methanolic extract, respectively in mice and rats [26, 27]. The toxicity mentioned in Kheraro (1974) and reported by Paris et al., 1955 at doses of 2.5 to 5 g / kg in mice could depend on the source of their sample [16]. In Mali Traoré et al. found that the toxicity dose of leafy stems of *F. virosa* was greater than 2000 mg / kg [24].

Regarding analgesic and anti-inflammatory activities, we found that most of the extracts exhibited analgesic and anti-inflammatory activities, but the best activities were those of the dry stem aqueous extract at 100 mg / kg per oral route with 64.82% as the percentage inhibition of pain and 59.07% against inflammation. These effects could be due to the presence of saponins. Indeed, according to Catier and Roux, 2007, some saponins are endowed with analgesic and anti-inflammatory properties [31].

The current results confirmed those of Magaji and coworkers who showed that the root methanolic extract (6.25; 12.5 and 25 mg / kg) administered intraperitoneally inhibited the acetic acid-induced pain in a dose-dependent manner but the strong activity was exhibited by the dose of 25 mg / kg, alleviating the pain induced by formalin. It increased significantly ($P < 0.01$) the latency time for hot plate-induced pain and inhibited carrageenan-induced inflammation ($P < 0.05$) in mice [25]. In Nigeria, researchers found similar results with leaf methanolic extract (25, 50 and 100 mg / kg) administered intraperitoneally in mice [26]. In 2012 Ezeonwumelu and his colleagues found analgesic activity with root extracts at doses of 200 and 400 mg / kg administered orally in rats [32]. Recent work carried out in Mali has shown that the leafy branches of *F. virosa* exhibited analgesic effects and remarkable anti-inflammatory activities at 100 and 200 mg / kg [24].

The major goal of all drugs used against BPH is to reduce the number of symptoms associated with this condition in order to improve the patient's quality of life. The imbalance between oxidative stress and antioxidants plays an important role in the development of benign prostatic hyperplasia [33]. Although the mechanism by which oxidative stress causes inflammation remains unclear, it is clear that oxidative stress is associated with many chronic inflammatory diseases. A general consensus shows that polyphenols are powerful anti-inflammatory and antioxidant factors through complex mechanisms. *In vitro* studies on BPH cell lines as well as several *in vivo* works using animal models have shown antioxidant and anti-inflammatory effects [34]. Furthermore, all pain has an inflammatory profile made up of inflammation mediators present in this pain syndrome [35]. The late diffuse pain induced in mice by intraperitoneally administration of acetic acid was manifested by stretching movement of the hind paw and torsions of the dorso-abdominal musculature. Prior studies on medicinal plants from two different countries found that many African people used medicinal plants to treat pain [36, 37]. In addition a pharmacological investigation confirmed the analgesic activity against acetic acid induced-pain in mice of aqueous extracts from four medicinal plants used in Mali and Togo [38]. Elsewhere the extracts of *F. virosa* tested on this pain significantly reduced its symptoms. Authors have reported that the reduction in pain induced by acetic acid in mice may be due to the presence of polyphenols such as flavonoids [39]. Thus present extracts, all rich in polyphenols with antioxidant, anti-inflammatory and analgesic properties,

could act on the functional component of the prostate by reducing its volume and the pressure exerted by its muscles on the urethra. This could explain how extracts of *Flueggea virosa* may have a beneficial effect in the medical management of BPH.

5. Conclusion

This work aimed to validate and justify the traditional use of the leaves and stems of *Flueggea virosa* in the management of benign prostatic hyperplasia. Indeed, these samples contain polyphenolic compounds (flavonoids, tannins, etc.) with anti-free radical properties.

The dry extract of the stems (100 mg / kg) demonstrated the best analgesic and anti-inflammatory activities. The results of acute toxicity support the safety of the aqueous (extemporaneous and dry) extracts used at the therapeutic dose in the management of benign prostatic hyperplasia. These effects may therefore be beneficial in the medical management of BPH. This work will contribute to the development of a new improved traditional medicine (ITM) based on the stems of *Flueggea virosa*.

Conflict of Interest

All the authors do not have any possible conflicts of interest.

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