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COMPARATIVE EVALUATION OF THE ANALGESIC AND ANTIPYRETIC EFFECTS OF A RECIPE WITH TWO PLANTS: SENNA ALATA L. (FABACEAE) AND JATROPHA CURCAS L. (EUPHORBIACEAE)

Elion Itou RDG*	Laboratory of pharmacodynamics and experimental physiopathology, Faculty of Sciences and Techniques, Marien Ngouabi University, BP 69, Brazzaville-Congo, National Institute for Research in Health Sciences, Scientific City of Brazzaville (ex-ORSTOM), route de l'auberge de Gascogne château d'eau, Congo, Laboratory of Biochemistry and Pharmacology, Faculty of Health Sciences, Marien Ngouabi University, BP 69, Brazzaville-Congo, *Corresponding Author
Etou Ossibi AW	Laboratory of pharmacodynamics and experimental physiopathology, Faculty of Sciences and Techniques, Marien Ngouabi University, BP 69, Brazzaville-Congo, Laboratory of Biochemistry and Pharmacology, Faculty of Health Sciences, Marien Ngouabi University, BP 69, Brazzaville-Congo
Morabandza CJ	Laboratory of Biochemistry and Pharmacology, Faculty of Health Sciences, Marien Ngouabi University, BP 69, Brazzaville-Congo, Department of Natural Sciences, Ecole Normale Supérieure, Marien Ngouabi University, B.P 69, Brazzaville - Congo
Mbou-Mouko JDD	Laboratory of pharmacodynamics and experimental physiopathology, Faculty of Sciences and Techniques, Marien Ngouabi University, BP 69, Brazzaville-Congo
Boumba Y	Laboratory of pharmacodynamics and experimental physiopathology, Faculty of Sciences and Techniques, Marien Ngouabi University, BP 69, Brazzaville-Congo
Abena AA	Laboratory of pharmacodynamics and experimental physiopathology, Faculty of Sciences and Techniques, Marien Ngouabi University, BP 69, Brazzaville-Congo

ABSTRACT This work aimed to evaluete the acute toxicity and to compare the analgesic and antipyretic effects of a *recipe* consisting of a mixture of leaf powders from of *S. alata*, and *J.curcas* with these two plants. Acute toxicity was evalueted by oral administration of a single dose (5000 mg/kg) orally in mice according the OECD, (2001) guideline no. 423. The results obtained show that the aqueous extracts of the leaves of *S. alata*, *J.curcas* and the recipe caused a brief reduction of mobility. However, no mortality and change in general behavior were observed. Pain was induced by intraperitoneal administration of 0.6% acetic acid in mice and by 2.5% subplantar formaldehyde in rats. The results obtained show that paracetamol (standard drug, 100 mg/kg), tramadol (standard drug, 10 mg/kg), aqueous extracts of *S. alata* (250, 500 and 1000 mg/kg), *J. curcas* (250, 500 and 1000 mg/kg) and the recipe (250, 500 and 1000 mg/kg) significantly reduced ($P<0.001$) the number of abdominal writhing induced by acetic acid as well as the frequency of licking or biting of the paws induced by formaldehyde during the two phases compared to the control group. These results suggest a peripheral and central analgesic effect of the aqueous extracts with a potentiation of the effect by the *recipe*. Fever was induced by subcutaneous administration of a solution of brewer's yeast (*Saccharomyces cerevisiae*). The results obtained show that the aqueous extracts of *S. alata* (250, 500 and 1000 mg/kg), *J. curcas* (1000 mg/kg) and the *recipe* (250, 500 and 1000 mg/kg) significantly lower ($p<0.05$) the hyperthermia induced by brewers' yeast with more marked falls obtained with the *receipt* between 4 and 5 hours.

KEYWORDS : analgesic, antipyretic, potential effect, Senna alata, Jatropha curcas

INTRODUCTION

Pain and fever are symptoms that accompany many communicable and non-communicable diseases. They are nowadays a real public health problem. In the Republic of Congo, a study conducted on acute articular rheumatism in schools in suburban districts of Brazzaville gives a prevalence of 3.5% [1]. Joint pain is often associated with fever. However, high fevers can denature enzymes and increase oxygen requirements and the speed of cellular metabolism. Defense reactions and the repair process are thus accelerated, which causes convulsions in certain predisposed individuals [2]. Taking pain into account was one of the most decisive battles during the second half of the 20th century, after it had been somewhat neglected paradoxically in previous decades, at a time when the whole attention was paid to scientific, technical and therapeutic progress. Several effective pain and fever drugs exist on the market, but the majority have significant side effects; this is the case with morphine, which has an emetic action and can cause depression of the respiratory centers; paracetamol which can lead to bone marrow aplasia and aspirin which can cause gastritis or thrombocytopenia[3].

It is therefore necessary to search through the Congolese pharmacopoeia and traditional medicine for preparations free of adverse effects and capable of treating pain and fever. Indeed, traditional Congolese medicine, long neglected and relegated to the background, is beginning to arouse great interest in the middle and poorest social strata[4]. The virtues of medicinal plants are well established and are multiple, they find their use in different branches of the pharmaceutical industry and in traditional medicine. In addition, a scientific evaluation of the pharmacological properties of the plants of the Congolese pharmacopoeia is very important to make, in order to obtain the maximum of information relating to their pharmacological effectiveness and their toxicology, correlated with the presence of the active principles which they contain. These plants are used in association (recipe) or alone and generally in the form of decoctions or macerated. The use of the recipe leads to estimate a potentiation of the analgesic and antipyretic effects. Several studies have shown a potentiation of the pharmacological effects sought by making a recipe[5] [6] [7]. Moreover, the World Health Organization (WHO), for example, recommends artemisinin-based combination therapy (ACT) to treat uncomplicated malaria caused by *P. falciparum*, combining two active ingredients that have different modes of action. In view of all the above, it therefore seems necessary to us to estimate the toxicity and to compare the analgesic and antipyretic effects of recipe with these two plants.

I. MATERIAL AND METHODS

Plant material

The plant material consisted of the leaves of Senna alata and Jatropha curcas. These leaves were collected in Brazzaville accompanied by an informant (Texaco district for *Senna alata*; Moukondo district for *Jatropha curcas*). The identification was made by Doctor Jean Marie Moutsamboté Systematic botanist at the École Normale Supérieure d'Agronomy et de Foresterie (ENSAF) then confirmed at the Botany Laboratory of the Institute for Research in Exact and Natural Sciences

(IRSEN) of Brazzaville. After harvest, these leaves were dried at room temperature in the Laboratory of Pharmacognosy and Experimental Physiopathology of the Faculty of Science and Technology. After drying, they were pulverized using a mortar. The powder obtained was used for the preparation of the aqueous extracts.

Animal material

Male and female rats (150-200 g) and male and female albino mice (18-25 g) approximately three months old were used. These animals were provided to us by the animal facility of the Faculty of Science and Technology of Marien NGOUABI University. They were fed a standard diet with free access to tap water. They were acclimatized for one week before experimentation and kept under standard conditions (12 hours of light, 12 hours of darkness, at a temperature of 27 ± 1° C). The rules of ethics published by the International Association for the Study of Pain have been considered [8].

Extraction

The aqueous extracts and recipe used were prepared by decoction. 30g of powder of *S. alata,* 30g of powder of *J.curcas* and 30 g of the *recipe* (15 g of *S.alata* powder and 15 g of *J.curcas* powder) were mixed in 150 ml of distilled water each. The whole was boiled for 15 minutes. After cooling and then filtration with cotton wool, the decoction was concentrated using a balloon heater (70°C). The dry concentrates obtained, constituting the aqueous extract of the leaves of *S.alata* and *J.curcas* as well as that of the *recipe* were kept to evaluate the analgesic and antipyretic effects.

Acute toxicity

Acute toxicity was estimated according with OECD Guideline No. 423 (2001) [9]. The mice were fasted for 24 hours before oral administration of the differents aqueous extract. Six groups of 3 mice each were formed and treated as follows: group 1, control treated with distilled water (0.5 mL/100g); groups 2, 3 and 4 treated with aqueous extracts at a dose of 5000 mg/kg of *S. alata*, *J. curcas* and the recipe (association). Observations were made every thirty minutes for 4 hours to assess the general condition of the animals : They focused on piloerection, aggression, mobility, alertness, stool status, vomiting and mortality. Mortality was evaluated for 48 hours after oral administration of the products.

Acetic acid-induced abdominal writhing in mice

The method described by Koster was used (Koster, 1959) [10]. The administration of 0.6% acetic acid intraperitoneally to mice causes a pain syndrome. The pain syndrome is characterized by stretching movements of the hind legs and twisting of the dorsal-abdominal musculature. An analgesic would act by reducing the number of abdominal writhes compared to the control. Eleven groups of 5 mice each fasted for 24 hours were formed. The different doses of aqueous extracts of *S.alata* (250, 500 and 1000 mg/kg), *J. curcas* (250, 500 and 1000 mg/kg), recipe (250, 500 and 1000 mg/kg), physiological water (control group, 0.5 ml/100 g) and paracetamol (standard group, 100 mg/kg) were administered orally, 1 hour before intraperitoneal administration of 0.6% acetic acid solution to the animals. 5 minutes after the injection of acetic acid, the number of abdominal writhes developed by the animals was counted for 20 minutes [11].

Formaldehyde-induced paw liking

Subplantar administration of a 2.5% formaldehyde solution induces neurogenic pain and inflammatory pain. The pain syndrome is characterized by licking or biting the paw. A central analgesic would inhibit both phases equally, while a peripheral analgesic would inhibit only the second phase[12]. Eleven groups of 5 rats each fasted for 24 hours were formed. The different doses of aqueous extracts of *S.alata* (250, 500 and 1000 mg/kg), *J. curcas* (250, 500 and 1000 mg/kg), recipe (250, 500 and 1000 mg/kg), physiological water (control group; 0.5 ml/100g) and tramadol (standard group, 10 mg/kg) were administered orally, 1 hour before plantar administration of the 2.5% formaldehyde solution (0.2 ml/rat). Then the animals were placed in different cages to observe the nociceptive effects. The number of times (frequency) that the animal licks or bites its paw (see appendix) was counted between zero and 10 minutes to assess neurogenic pain response, between 10 and 30 minutes to assess inflammatory pain response.

Brewer's yeast pyrexia test

Subcutaneous administration of 20% brewer's yeast induces hyperthermia 24 hours after. An antipyretic would act by reducing this hyperthermia. Before constituting the different batches to evaluate the antipyretic activity of the diffents aqueous extract, we proceeded to the selection of the animals. For this, the normal rectal temperature of each rat was measured using a digital thermometer. Fever was induced in all animals by subcutaneous administration of a 20% solution of brewer's yeast (*Saccharomyces cerevisiae*) 10 ml/kg [13]. 24 hours later, the rectal temperature of the animals was measured again. All the animals that did not show an increase in their rectal temperature of 0.5°C were excluded from the experiment (Muhammad et al., 2012). The animals selected were divided into group of 5 rats each and treated orally with different doses of aqueous extracts of *S.alata* (250, 500 and 1000 mg/kg), *J. curcas* (250, 500 and 1000 mg/kg), *recipe* (250, 500 and 1000 mg/kg), physiological water (control batch; 0.5 ml/100g) and paracetamol (reference group, 100 mg/kg). The rectal temperature was measured 1, 2, 3, 4 and 5 hours after administration of the products.

Chemical screening

The various secondary metabolites contained in the leaves of Senna alata, Jatropha curcas and the Recipe were determined using the tube reaction method[4]

Statistical analysis

All values were expressed as mean ± standard error of mean (SEM). Analysis of variance followed by Student-Fischer t test "t" was performed. The significance level was set at $p<0.05$

II. RESULTS

Acute toxicity of aqueous extracts of *Senna alata* leaves, *Jatropha curcas* and the *recipe*

The mice that received the aqueous extracts of the leaves of *S.alata, J.curcas* and the recipe at a dose of 5000 mg/kg showed a brief reduction of mobility after administration of the products. Changes in piloerection, aggression, alertness, stool status, vomiting and mortality were not observed.

Analgesic effect of aqueous extracts of *Senna alata, Jatropha curcas* and *recipe* on pain induced by acetic acid

Intraperitoneal administration of acetic acid to mice causes abdominal writhes (Table 1). Paracetamol (100 mg/kg), aqueous extracts of *S.alata*, *J.curcas* and the recipe at the doses used significantly reduced ($P<0.001$) the number of abdominal writhes developed by the mice compared to the control group (water distilled). These results also show that the reduction in abdominal cramps is not dose-dependent with the aqueous extracts of S. alata and J. curcas. However, this trend is reversed with the *recipe* where the reduction is dose-dependent. The number of abdominal writhes developed by the control mice is 68.45±0.99; 46.20±2.03 ($p<0.001$) for mice treated with paracetamol (100 mg/kg); 61.40±0.74, 53.80±1.06 and 53.40±00.60 ($p<0.001$) for the *S.alata* extract at doses of 250, 500 and 1000 mg/kg respectively. For the aqueous extract of *J. curcas* (250, 500 and 100 mg/kg) the number of writhes developed by the mice at the respective doses is 56.4 ± 2.33, 48.2 ± 1.52 and 47.60±1.12 ($p<0.001$). This number is 44.25±2.4, 37.55±2.41 and 34.84±1.63 ($p<0.001$) for the recipe at doses of 250, 500 and 1000 mg/kg respectively. Furthermore, it is noted that the strongest inhibitions are obtained with doses of 500 mg/kg for each aqueous extract used (25.08 % for *S.alata* and 30.46% for *J.curcas*) contrary to the recipe where it is 49.10%) with the dose of 1000 mg/kg.

Table n°1: Effect of aqueous extract of *S.alata, J.curcas* and *recipe* on abdominal writhes induced by 0.6 % acetic acid in mice

Treatment	Doses	Number of abdominal writhes	Inhibition (%)
Control group	0.5 ml/100g	68.50±0.99	/
Paracétamol	100 mg/kg	46.20±2.03***	32.50
Senna alata	250 mg/kg	61.40±0.74***	10.88
	500 mg/kg	53.80±1.06***	21.40
	1000 mg/kg	53.40±00.60***	21.98
Jatropha curcas	250 mg/kg	56.40±2.33**	17.60
	500 mg/kg	48.20±1.52***	29.58
	1000 mg/kg	47.60±1.12**	30.46
Recipe	250 mg/kg	44.25±2.48***	35.35
	500 mg/kg	37.55±2.41***	45.14
	1000 mg/kg	34.84±1.63***	49.10

Each value represents the mean ± ESM. ***$p<0.001$ Significant different (Student t-test) versus control group

Analgesic effect of aqueous extracts of *Senna alata*, *Jatropha curcas* and the *recipe* on pain induced by formaldehyde

Subplantar administration of formaldehyde to rats caused neurogenic pain and inflammatory pain that was manifested by licking or chewing the paws (Table 2). Tramadol (10 mg/kg), aqueous extracts *of S.alata*, of *J.curcas* and the *recipe* at the doses used significantly reduced (P<0.001) the frequency of licking or biting the paws during the two phases by compared to the control group (distilled water). These results also show that during the neurogenic phase, the frequency of licking or biting the paws decreases as the doses of the aqueous extracts of *S.alata*, of *J.curcas* and the *recipe* increase. However, this evolution is not observed during the inflammatory response phase of pain. With regard to neurogenic pain, these frequencies are 16 ± 1.14 for the controls; 10.33 ± 1.07 (p<0.001) for rats treated with tramadol (10 mg/kg); 8.6±0.50; 7.68±0.70 and 7.49±1.19 (p<0.001) for the *S.alata* extract at doses of 250, 500 and 1000 mg/kg respectively. For the aqueous extract of *J. curcas* (250, 500 and 100 mg/kg) at the respective doses, these frequencies are 7.6 ± 0.40; 7.61±0.51 and 7.36±0.49 (p<0.001). For the *recipe*, these frequencies are 7.8±0.58; 7.54±0.71 and 7.35±0.85 (p<0.001) at doses of 250, 500 and 1000 mg/kg respectively. With regard to inflammatory pain, the frequencies of licking or biting the paws are 66 ± 1.67 for the controls; 38.80 ± 2.62 (p<0.001) for rats treated with tramadol (10 mg/kg); 41.6±2.31; 38.00±2.28 and 37.20±2.65 (p<0.001) for *S. alata* extract at doses of 250, 500 and 1000 mg/kg respectively. For the aqueous extract of *J.curcas* (250, 500 and 100 mg/kg) at the respective doses, they are 48.92±2.50; 35.40±1.98 and 35.00±2.42 (p<0.001). For the *recipe*, these frequencies are 36.06±0.58; 33.40±1.88 and 32.40±0.81 (p<0.001) at doses of 250, 500 and 1000 mg/kg respectively.

Tableau n°2 : Effect of Covid-Organics on neurogenic and inflammatory pain response induced by formaldehyde in rat

Treatment	Doses	Neurogenic pain response (0-10 Min)		Inflammatory pain response (10-30 Min)	
		Frequency of legs licking and of biting	Inhibition (%)	Frequency of legs licking and of biting	Inhibition (%)
Control group	0.5 ml/100g	16±1.14	/	66±1.67	/
Tramadol	10 mg/kg	10.33 ±1.07***	35.43	38.8 ±2.62***	41.21
Senna alata	250 mg/kg	8.60±0.50***	46.25	41.60±2.31***	36.96
	500 mg/kg	7.68±0.70***	52	38.00±2.28***	42.42
	1000 mg/kg	7.49±1.19***	53.18	37.20±2.65***	43.63
Jatropha curcas	250 mg/kg	7.6±0.40***	52.50	48.92±2.50***	25.87
	500 mg/kg	7.61±0.51***	52.43	35.40±1.98***	46.36
	1000 mg/kg	7.36±0.49***	54	35.00±2.42***	46.96
Recipe	250 mg	7.8±0.58***	51.25	36.06±0.58***	45.36
	500 mg	7.54±0.71***	52.87	33.40±1.88***	49.39
	1000 mg	7.35±0.85***	54.06	32.40±0.81***	50.90

***p<0.001; (Student t-test). Each value represents the mean ± ESM; versus control group

Effect of aqueous extracts of *Senna alata, Jatropha curcas* and *recipe* on hyperthermia induced by brewer's yeast 20% in rats

The results of the effect of the aqueous extracts of *S.alata, of J.curcas* and the *recipe* on hyperthermia induced by brewer's yeast in rats are presented in Table 3. They show that the aqueous extracts of *S.alata, J.curcas* and the *recipe* do not significantly (p>0.05) reduce the hyperthermia induced by brewer's yeast, unlike paracetamol used as standard drug two (02) hours after administration of these products. However, 3 hours after administration of the test products, the aqueous extracts of *S.alata* (250, 500 and 1000 mg/kg), *J.curcas* (1000 mg/kg) and the *recipe* (250, 500 and 1000 mg/kg) drop significantly (p<0.05; p<0.01) hyperthermia induced by brewer's yeast. The maximum decreases in hyperthermia are obtained at 3 hours for paracetamol (35.72 ±0.35; p<0.05), at 5 hours for the aqueous extract of *S. alata* at a dose of 1000 mg/kg (36.06±0.49; p<0.001); at 4 hours for *J.curcas* of 36.36±0.31(250 mg/kg; p<0.001), 36.36±0.21 (500 mg/kg; p<0.001) and 36.28±0, 40 (1000mg/kg; p<0.001); at 5 hours for the recipe 500 mg/kg (35.3±0.02; p<0.001) and 1000 mg/kg (35.2±0.2 ; P<0.001). By generally comparing the decreases in hyperthermia of each aqueous extract with the recipe, we note that the inhibition increases over time by both extracts.

Phytochemical profile of aqueous extracts of *Senna alata, Jatropha curcas* and *recipe*

The phytochemical profile of the extracts and the *recipe* are shown in Table 4. It shows that alkaloids, tannins Flavons, Flavonols, anthraquinons were highlighted plant extracts and recipe. Saponosides were only highlighted in the aqueous extract of *J.curcas* and the *Recipe*. However, flavonones were not highlighted in the herbal extracts and the *recipe*.

Tableau n°4: Phytochemical compound of *S.alata, J.curcas* and recipe (association)

Compounds	Senna alata	Jatropha curcas	Recipe
Alkaloïds	++	+	+
Tannins	+	+	+
Flavons	+	+	+
Flavanons	-	-	-
Flavanols	+	+	+
Anthraquinons	+	+	+
Saponosids	-	+	+

Meaning of symbols: Low presence "+"; Moderate presence "+ +"; Absence "-"

Tableau n°3 : Effect of Covid organics on pyrexia induced by the Brewer's yeast (Saccharomyces cerevisiae) in rat

Treatment	Doses	T0 normal	Temperature(T°) after pyrexia induced					
			0h	1h	2h	3h	4h	5h
Control group	(0.5 ml/100 g)	36.06±0.34	36.50±0. 20	37.10 ±0.25 ns	37.32 ±0,19 ns	37.66 ±0.13	37.42 ±0.04 4	37.10 ±0.04
Paracetamol	(100 mg/kg)	35.34±0.22	36.20±0.22	35.74 ±0.32 ns	35.72 ±0.35 *	35.60 ±0.23 **	35.36 ±0.19 *	35.22 ±0.20 *
Senna alata	(250 mg/kg)	35.84±0.32	36.74±0.24	36.74 ±0.22 ns	36.74 ±0.22 ns	36.70 ±0.30 *	36.40 ±0.21 **	36.36 ±0.29 *
	(500 mg/kg)	36.12±0.26	36.84±0.14	36.84 ±0.13 ns	36.74 ±0.31 ns	36.54 ±0.33 *	36.28 ±0.42 **	36.24 ± 0.30*
	1000 mg	35.90±0.33	36.96±0.32	36.96 ±0.90 ns	36.72 ±0.92 ns	36.24 ±0.78 **	36.20 ±0.7* *	36.06 ±0.49 ***
Jatropha curcas	250 mg	36.36±0.13	37.14±0.17	37.78 ±0.94 ns	36.26 ±0.39 ns	36.54 ±0.40 ns	36.36 ±0.31 **	36.30 ±0.20 *
	500 mg	35.54±0.23	36.90±0.21	36.74 ±0.31 ns	36.6± 0.28n s	36.5± 0.27n s	36.36 ±0.21 **	36.26 ±0.10 *
	1000 mg	36.20±0.30	36.92±0.23	37.7± 0.18n s	36.94 ±0.43 ns	36.42 ±0.42 *	36.28 ±0.40 **	36.22 ±0.19 **
Recette	250 mg	36.16±0.24	37.68±0.18	36.52 ±0.23 ns	36.82 ±0.36 ns	36.26 ±0.27 *	36.32 ±0.25 **	35.80 ±0.32 **
	500 mg	35.7±0.28	36.52±0.28	36.44 ±0.23 ns	36.26 ±0.36 ns	36.22 ±0.34 *	36.28 ±0.25 **	35.30 ±0.02 ***
	1000 mg	35.9±0.57	36.46±0.50	36.52 ±0.52 ns	36.52 ±0.55 ns	36.42 ±0.48 *	36.34 ±0.68 **	35.20 ±0.20 ***

Each value represents the mean ± ESM of temperature. *p<0.05, **p <0.01 and ***p<0.001 significant different (Student t-test) versus

control group. ns= no significant value p>0.05

III. DISCUSSION

The objective of this work was to compare the potential analgesic and antipyretic effects of aqueous extracts of *S. alata*, *J.curcas* and a recipe composed of the powder of the leaves of these two plants. Before evaluating the analgesic and antipyretic effects, we had evaluated their acute toxicity in mice in order to determine the LD50 and the therapeutic doses. Acute toxicity was assessed by administering a dose of 5000 mg/kg of each extract and recipe to mice. This choice is justified by the fact that these two plants used are the subject of traditional use in the treatment of several pathologies such as: constipation ascites or generalized edema, external otitis [5]. It appears from this study that the aqueous extracts of the leaves of Senna alata, of Jatropha curcas and the recipe at the dose used did not modify the general condition of the animals. This result suggests that the aqueous extracts and the recipe would not be toxic and that the toxic doses would be higher than the dose of 5000 mg/kg. According to the globally harmonized classification system, *S.alata, J.curcas* and the recipe would be classified in category 5 of plants or preparations not presenting a danger to the organism (OECD, 2001)[9]. Thus the doses of 250, 500 1000 mg / kg corresponding to 1/20th, 1/10th and 1/5th of the dose of 5000mg/kg were retained as therapeutic doses to evaluate the analgesic and antipyretic effects of aqueous extracts of *S.alata, J.curcas* and that of the *recipe.*

In this study, two methods were used to evaluate the analgesic effect of aqueous extracts from the leaves of Senna alata, Jatropha curcas and the recipe. These methods were chosen to highlight peripheral and central type pain. Acetic acid induces abdominal cramps which generally reflect visceral pain, the nociceptive effect of the peripheral type and the formaldehyde test induces both types of pain [15]. In addition, the brewer's yeast test was used to induce fever (hyperthermia). Pain was induced by 0.6% acetic acid in mice. This method has already been used by several authors[16] [13]. Acetic acid is a sensory irritant which induces peripheral and central type pain [10]. Acetic acid pain induction is a well-recommended protocol for evaluating the medicinal properties of medicinal agents. This method is widely used to assess peripheral analgesic activity due to its sensitivity [16]. Pain induction is caused by the release of endogenous substances as well as some other pain mediators, such as arachidonic acid via cyclooxygenase and prostaglandin biosynthesis. Stimulation of the local peritoneal receptor could be the cause of abdominal cramps. By producing a localized inflammatory response due to the release of arachidonic acid from tissue phospholipids via cyclooxygenase (COX), and by producing specific prostaglandins such as PGE2 and PGF2α as well as lipooxygenase products, acetic acid can also increase peritoneal fluids by inducing capillary permeability [17]. These products, prostaglandin and lipooxygenase cause inflammation and pain by increasing capillary permeability. In this study, the results obtained showed that the aqueous extracts of *S.alata*, *J.curcas* and the recipe significantly inhibited abdominal writhes caused by the administration of acetic acid. These results suggest an analgesic effect of these extracts which could go through an interference with one of the mechanisms of pain induction by acetic acid. Other authors have already shown the analgesic effect of plant extracts on pain induced by acetic acid [13] [18]. Furthermore, it was found that the reduction in abdominal writhes is not dose-dependent with the aqueous extracts of *S.alata and J.curcas*. However with the recipe, this reduction is dose-dependent. This finding suggests a synergistic effect of the action of the two plants. The combination of several plants for the sole purpose of amplifying or potentiating the effect to solve a pathological problem is demonstrated in improved traditional medicines, such is the case of Tetra * (congolese improved traditional medicine) which contains about twenty plants ; as well as for modern medicines. For example, therapy for type 2 diabetes has expanded dramatically over the past decade. Indeed, two therapeutic groups of antidiabetics, analogs of GLP-1 (glucagon-like peptide-1) and SGLT2 (sodium-glucose cotransporter-2) inhibitors have shown efficacy not only on glycemic control but also on weight and on other clinical and biological parameters. The combination of these two therapeutic classes offers a logical solution due to their different mechanisms of action [19].

The formaldehyde test is a very important model used to highlight not only the analgesic effect but also to clarify the mechanisms of analgesic action. It has already been used by several authors[13][20]. Intra-plantar injection of formaldehyde in rats induces pain which is distinguished by two phases. The first phase, called neurogenic pain, is explained by direct activation of peripheral afferent fibers C and Aδ, which translates central type pain regulated by the release of substance P [21]. The second phase called inflammatory pain is explained by the continuous stimulation of nociceptors by inflammatory mediators (serotonin, histamine, bradykinin, NO and prostaglandins) released from damaged tissue, resulting in activity-dependent sensitization of CNS neurons in the dorsal horn [20]. Local anesthetics and morphine inhibit the first phase, while NSAIDs inhibit the second inflammatory phase. In this study, the results obtained show that tramadol (10 mg/kg) used as a reference analgesic of the central type, the aqueous extracts of *S.alata,* of *J.curcas* as well as the *recipe* at the doses used reduce significantly (P< 0.001) the frequency of paw licking or biting during the two phases compared to the control group (distilled water). This suggests that the extracts and the recipe would act like tramadol used as a central reference analgesic. Inflammatory pain is often associated with fever, which is why the evaluation of the antipyretic effect is necessary.

Subcutaneous administration of brewer's yeast (*Saccharomyces cerevisi*ae) caused hyperthermia (pathogenic fever) in rats 24 hours later. It is recognized that the mechanism of induction of hyperthermia by brewer's yeast involves the release of cytokines (TNFα, IL1β, and IL6) which, having reached the blood vessels, stimulate the biosynthesis of prostaglandins (PGE2) around the center thermoregulatory hypothalamic [22] [23]. In this study, the aqueous extracts of *S.alata*, *J.curcas* and the *recipe* significantly reduced hyperthermia induced by brewer's yeast like paracetamol used as reference antipyretic. Indeed, paracetamol is an effective analgesic and antipyretic. The origin of these effects is almost superimposable to that of aspirin and NSAIDs. Paracetamol reversibly blocks cyclo-oxygenase and therefore prevents the production of prostaglandins responsible for fever (central antipyretic effect) and sensitization of peripheral nociceptors (peripheral analgesic effect). The effects of the extracts and the recipe observed could be due to the presence of pharmacologically active metabolites which could interfere with the mechanism of prostaglandin production. However, it is noted that several biochemical events occur during the production of prostaglandins. It would therefore be interesting to clarify these mechanisms of action. Moreover, in this study, the results obtained also show that the decreases in hyperthermia between 3 and 5 hours by the recipe are more pronounced than those of the aqueous extracts of *S.alata* and *J.curcas*. This finding suggests a synergistic effect of the recipe; which effect would be very interesting.

The results of the phytochemical study showed the presence of alkaloids, tannins, Flavones, Flavonols, anthraquinones in the plant extracts and the recipe. The presence of these secondary metabolites in the extracts of the two plants had already been demonstrated by other authors [24] [25]. Saponosides were only highlighted in the aqueous extract of *J.curcas* and the *Recipe*. This finding suggests that these saponosides present in the recipe come from the *J. curcas* powder constituting the recipe, which could justify the amplification of the effects observed with the racette compared to the aqueous extract of Senna alata and Jatropha curcas leaves. Nevertheless, the presence of alkaloids, tannins and flavonoids could explain the analgesic and antipyretic effects observed (Elion Itou et al., 2018).

CONCLUSION

This work aimed to compare the analgesic and antipyretic effects of the avcec recipe compared to the two plants which are *S.alata* and *J.curcas*. To do this, we were first interested in studying the acute toxicity of these extracts. It follows from this work that at a dose of 5000 mg/kg these three extracts (*S.alata, J.curcas* and from the *recipe*) are not toxic (LD50 > 5000 mg/kg). The study of analgesic and antipyretic activities showed that all the extracts used have analgesic and antipyretic properties, and these effe ;cts are potentiated with the recipe. The chemical screening allowed us to identify several secondary metabolites that could justify the pharmacological effects obtained. The results obtained during this study would be of great benefit in encouraging the use of recipes to optimize the desired effects.

Conflict of interests

The authors declare that they have no conflict of interest

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