

Evaluation of a Plants Decoction in the Treatment of Female Infertility

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Abstract According to the WHO infertility an inability for a heterosexual couple to conceive after of regular unprotected sex, would affect about 17,5 % of the population. This highlights the extent of the problem of infertility on a global. Moreover, the female infertility rate is becoming increasingly worrying. Furthermore, limits to several was signaled medical treatments. The use of medicinal plants appears as an appropriate alternative. This study is to verify the therapeutic virtues of a decoction of *Adenia lobata*, *Costus afer* and *Baphia nitida* leaves traditionally used for female infertility by traditional practitioners (Côte d'Ivoire). The mixture of the aqueous decoction from these 3 plant species were tested by gavage on female rats for 30 days at different doses of 400 mg/mL and 200 mg/mL. A phytochemical containing mancozeb was used as a competitive product to prevent fertility at concentrations of 500 and 250 mg/mL. Then a combination of this decoction and the chemical was also tested in the respective order of combination of 250-200 mg/mL and 250-400 mg/mL. The results revealed that this decoction showed a very interesting hormonal activity in the rabbits. It stimulates the production of hormones in the female (Estradiol and FSH) at a concentration of 200 mg/mL. This extract would be non-toxic on the vital organs at these doses. This decoction presents a better hormonal activity at the dose of 200 mg/mL and is not toxic to vital organs.

Keywords: Female infertility, plant extract, stimulation, female hormon

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1. Introduction

Infertility described as a couple's failure to conceive, despite having engaged in regular, and unprotected intercourse for a year, has become an increasing lyre cursive biological phenomenon [1]. It affects 10-15 % of couples worldwide [2]. In sub-Saharan Africa, according to the work, the infertility rate among women is about 30 % [3,4].

Several factors are responsible for this and the most common are stress, poor diet and pollution. Furthermore, due to the quantity of pollutants present in our daily environment, to which we are exposed, the proper functioning of our hormonal system is hindered and may increase the risk of infertility, which today constitutes a real public health problem, especially in Africa [5,6]. Indeed, most populations are exposed to these pollutants such as pesticides, which are increasingly used instead of mechanical tools for fieldwork [7].

Thus, to solve this public health problem, several medical treatments are recommended by modern medicine, including ovulation stimulation with drugs and medically assisted procreation, in particular artificial insemination

and in vitro fecundation. These treatments remain expensive, sometimes have many side effects and are inaccessible to populations, especially in Africa. In addition, hospital facilities capable of offering such treatments are few in number and are generally far away from rural areas [8].

Thus, one of the means available to the population and to which about 80 % of them remain attached is traditional medicine [9,10]. Indeed, the use of medicinal plants appears today to be an appropriate alternative to solve this infertility problem [11,12]. Several studies have shown the involvement of many secondary metabolites from medicinal plants in the treatment of various pathologies including the regulation of reproductive functions [13].

From these studies, others reveal that plant species used in the treatment of female infertility include *Baphia nitida*, *Costus afer* and *Adenia lobata* [14,15]. They are used as an aqueous decoction in the Moronou region (Côte d'Ivoire) by traditional practitioners. Furthermore, given that we are exposed to chemicals and especially pesticides in an increasingly polluted environment that can cause infertility in humans, it would be wise to check the therapeutic virtues of this leaf decoction and to lay the scientific basis for its use.

2. Material and Methods

2.1. Materiel

The substance used is a powder obtained from dried leaves of *Baphia nitida*, *Adenia lobata* and *Costus afer* whose specimens were identified by the Botanical Laboratory of the Jean Lorougnon Guédé University. A phytosanitary product (Manco 80WP) based on Mancozeb 80 % (active molecule) supplied by HEBEI RUNXUCHEN TRADING CO. LTD., was used as a control. The animals used for this study were 35 female Wistar (*Rattus norvegicus*) aged between 45-65 days.

2.2. Methods

2.2.1. Conditioning of Animals

On arrival, the rats were weighed and placed in cages lined with litter, which is renewed twice a week. They were acclimatized to room temperature for a fortnight and had free access to food (pellets for rodent feeding) and water.

2.2.2. Preparation of the Aqueous Extract

After identification of the species, the treated and dried leaves were sprayed. The powders from these 3 species were put to get her taking into account a mass proportionality (1-1-1) and used to prepare the aqueous extract. In fact, 100 g of this set of powders were macerated in 1 L of distilled water using a magnetic stirrer for 24 hours. The homogenate obtained was wrung out with a clean fabric and the solution collected was filtered successively two (2) times on hydrophilic cotton and then two (2) times on Whatman 3 mm filter paper. The filtrate was dried in the oven at 60°C for 12 days. The resulting dry aqueous extract was preserved for the various tests.

2.2.3. Treatment of Animals

The animals were divided into seven (7) lots of five (5). Treatments were administered by gavage once a day at the same time for thirty (30) days using a volume of 1 mL of each prepared solution. Thus, lot 1 received only distilled water, lots 2 and 3 received solutions of the phytosanitary product (500 mg/mL and 250 mg/mL respectively) and lots 4 and 5 were force-fed with the plant extract solution (400 mg/mL and 200 mg/mL respectively). Lots 6 and 7 are treated with an association of solutions (1/2 - 1/2) of the plant protection product and plant extract at 250-200 mg/mL and 250-400 mg/mL respectively.

2.2.4. Determination of Rat's Body Weight

The animals are weighed very two days using a precisions scale at fixed times before each feeding for the duration of the experiment (30 days).

2.2.5. Blood Sampling and Analysis

At the end of the experiment, the rats were weighed and according to the recommendations of the Federal office for food Safety and Veterinary affairs, the animals were sacrificed and blood samples (2-2.5 mL) were taken immediately and collected in labelled tubes (dry tubes and tubes containing EDTA). These tubes were centrifuged at 3000 rpm for 3 min. Sera were collected in Eppendorf tubes and stored at -20 °C for analysis. Thus the analyses included the determination of Estradiol and FSH at the Architect Abbott automaton and creatinine, urea and transaminases (ALT, AST) at the Cobas C311 automaton.

2.2.6. Organ Removal and Determination of Absolute and Relative Weights

Organs including liver, ovary, kidney and spleen were removed and immediately put into a physiological solution of NaCl 9 ‰. These organs were then weighed (absolute weight). In addition, the relative weight of these organs was also determined by the formula:

$$\text{Relative weight} = \frac{\text{Absolute weight of the organ}}{\text{Live weight of the animal}} \times 100$$

2.2.7. Statistical Analysis

The statistical analysis of the data was carried out using Grap Pad Prism 7.00 software. The comparison between the dose effect and the experimental duration was carried out using the ANOVA variance analysis method. For a value of $P \leq 0.05$, the difference is considered to be significant.

3. Results

3.1. Change in Body Weight

The results obtained show a steady body weight gain (positive r) in control rats ($r = 0.9816$), rats given the plant extract solution at a dose of 400 mg/mL ($r = 0.9979$) and 200 mg/mL ($r = 0.9894$) and those given the combination of chemical and plant extract (250-400 mg/mL and 250-200 mg/mL) with r values of 0.5215 and 0.9677 respectively. Rats receiving only the chemical solution showed a significant body weight loss of -0.953 (500 mg/mL) and -0.9963 (250 mg/mL) at the end of the experiment. The best weight gain was observed in rats from batch 5 with an extract dose of 200 mg/mL, followed by batch 6 (combined dose 250-200 mg/mL of chemical and plant extract respectively).

There was also a significant difference between the dose administered and the duration of the experiment. It is highly significant ($p < 0.0001$) for batches 2, 3, 4, 5 and 7, while for batch 6 (chemical/plant extract at 250-200 mg/mL), the difference is significant with a p value < 0.0383 (Figure 1).

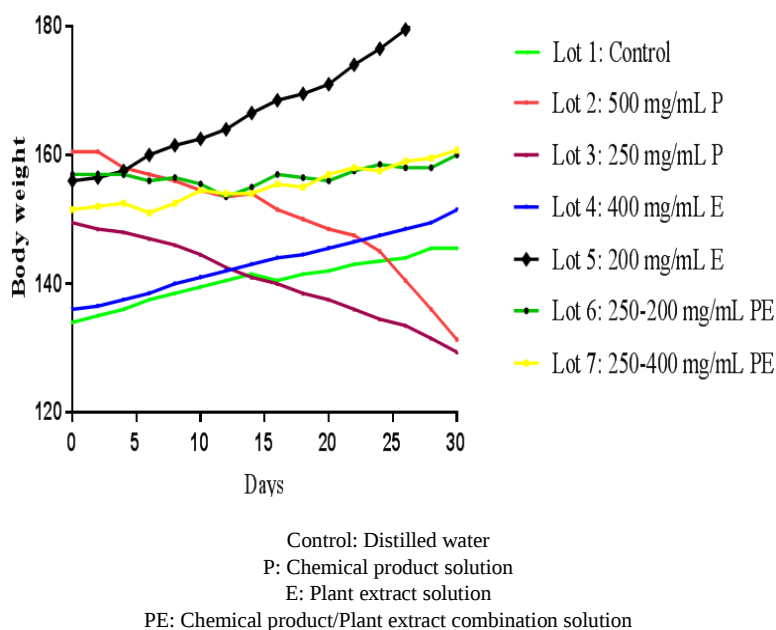


Figure 1. Curves of changes in rats body weight as a function of doses administered for 30 days

3.2. Variation in Absolute and Relative Organ Weights

The absolute weights of liver, kidney, ovary and spleen showed no significant difference ($p > 0.05$) between the control lot and the lots treated with the plant extract, the chemical and the chemical/plant extract combination. However, compared with the control batch, organ weights were highest in rats treated with 500 mg/mL and 250 mg/mL of the chemical. Plant extract at 200 mg/mL, 400 mg/mL and the chemical/plant extract combination (250-200 mg/mL) showed the lowest values. These values are statistically close to those of the control batch. The best value is for the 200 mg/mL dose. The same applies to the relative weight of these same organs (Table 1).

3.3. Dosing of the Parameters

The results of the estradiol assay show that animals treated at the 200 mg/mL dose of the plant extract have a higher level of estradiol than the control lot. For rats treated with 400 mg/mL of the plant extract and 250-200 mg/mL of the combination of the chemical and the plant extract, the estradiol levels found were lower than those of the control lot. On the other hand, at 500 and 250 mg/mL of the chemical and 250-400 mg/mL of the combination of chemical product and plant extract administered to rats, there is a considerable decrease in estradiol levels (Table 2).

The FSH values are twice as high in animals treated with 400 and 200 mg/mL of the plant extract and 250-200 mg/mL of the chemical product/plant extract combination compared to the control. While this rate in rats treated with 500 and 250 mg/mL of the chemical product and 250-400 mg/mL of the chemical product/plant extract combination was lower than the control (Table 2).

The results also show that the highest levels of urea and creatinine are observed in rats fed 500 mg/mL of the chemical. The best results, close to those of the control, were found in animals treated with the 200 mg/mL plant extract dose and the combined chemical/plant extract dose

(250-200 mg/mL). In addition, for the chemical (250 mg/mL), the plant extract (400 mg/mL) and chemical product/plant extract combination (250-400 mg/mL), the levels obtained are moderately high (Table 2).

Furthermore, the transaminase values (AST and ALT) obtained at the 200 mg/mL dose of the plant extract are statistically comparable to those of the controls. The highest values are observed in rats force-fed at 500 mg/mL of the chemical followed by those force-fed at 250 mg/mL. In addition, at the dose of 400 mg/mL (plant extract) and 250-200 mg/mL and 250-400 mg/mL (chemical product/plant extract combination), the transaminase values are higher than those of the control lot (Table 2).

4. Discussion

Weight gain in batches treated with the plant extract (400 mg/mL, 200 mg/mL) and those treated with the combination of chemical product and the plant extract (250-200 mg/mL and 250-400 mg/mL) observed reveals that plant extract has a positive effect on the organism. While in animals treated with the chemical, weight loss and slower growth were observed. This weight loss is explained by the fact that these rats ate little due to the chemical effect. Indeed, when a living being is exposed in the long term to certain doses of the chemical, this usually causes a loss of appetite and weight and generally leads to a malfunction of the systems including the reproductive system [16,17].

Furthermore, since there is no significant difference between the absolute and relative weights of the noble organs such as liver, ovaries, kidneys and spleen to the plant extract, this would be due to the non-toxicity of the plant decoction on these vital organs at these doses. However, the chemical acts negatively on these organs [18]. Moreover, a dose of 200 mg/mL of plant extract would be the best dose.

The reason for the considerably lower estrogen and

FSH levels in animals treated with the chemical alone and at the combined dose of 250-400 mg/mL is that the chemical being an endocrine disruptor, it interferes the action or irreversibly inhibits the synthesis of natural hormones. This is the case with sex hormones such as estradiol and FSH at certain doses. This will have the effect of preventing follicle maturation and ovulation in rats, especially at uncontrolled and long-term doses [19,20,21]. Unlike the high levels of these hormones at the dose of 200 and 400 mg/mL of the plant extract would be explained by the fact that the aqueous extract would contain hormonal activating properties. Indeed, the FSH hormone stimulates follicle growth and maturation and also promotes the synthesis of estrogen by these follicles. Once the threshold is reached, estrogens exert a positive feedback control on the hypothalamus by inducing the pituitary release of the LH (Luteinizing Hormone) responsible for ovulation at its peak. The effect of this extract would make it possible to stimulate the synthesis of FSH and then estradiol [22,23,24].

With regard to urea and creatinine as significant markers of kidney function, analysis of the results shows that the chemical product (500 mg/mL and 250 mg/mL), the plant extract (400 mg/mL) and the combination of the chemical product and the plant extract (250-400 mg/mL) have a toxic effect on kidney and reproductive functions. The same applies to transaminases; aspartate

aminotransferase (AST) and alanine aminotransferase (ALT) which are markers of liver dysfunction. Their blood levels also increase to 500 and 250 mg/mL of the chemical product, the plant extract (400 mg/mL) and the combination of the chemical product and the plant extract (250-400 mg/mL). This could indicate liver damage [25,26,27]. However, at the combined dose of chemical product/aqueous extract (250-200 mg/mL), the values of these kidney and hepatic parameters seem to be close to those of the control.

In addition, at a dose of 200 mg/mL of plant extract, the enzyme values (AST and ALT) and those of urea and creatinine are substantially equal to those of the controls. It could be said that the aqueous extract at this dose would have no noticeable effect on kidney and hepatic functions and would be the dose to be administered to have the expected effects [28,29,30].

These results also show that the molecules activating the reproductive function contained in the plant decoction would act positively by competing for action with that of the chemical product. This would reduce their destructive action on the renal, hepatic and reproductive levels. This is justified by the attenuated action when the plant extract is combined with the chemical product at the dose of 200-250 mg/mL. This decoction could be an alternative treatment for female sterility at 200 mg/mL.

Table 1. Absolute weight and Relative weight of rat organs

Organs Concentration (mg/mL)		Absolute weight			
		Liver	Ovary	Kidney	Spleen
Batche 1 : Control		4.61 ± 0.28	0.03 ± 0.01	0.39 ± 0.01	0.35 ± 0.07
P	Batche 2 : 500	5.98 ± 1.44	0.05 ± 0.01	0.43 ± 0.13	0.45 ± 0.04
	Batche 3 : 250	5.71 ± 0.14	0.04 ± 0.01	0.47 ± 0.02	0.52 ± 0.10
E	Batche 4 : 400	4.68 ± 1.31	0.03 ± 0.01	0.34 ± 0.07	0.43 ± 0.06
	Batche 5 : 200	4.39 ± 0.12	0.03 ± 0.01	0.40 ± 0.02	0.37 ± 0.06
PE	Batche 6 : 250-200	4.38 ± 0.04	0.03 ± 0.01	0.41 ± 0.17	0.43 ± 0.04
	Batche 7 : 250-400	6.04 ± 0.51	0.04 ± 0.03	0.42 ± 0.02	0.46 ± 0.01
P-value		0.17	0.56	0.47	0.27
		Absolute weight			
Batche 1 : Control		3.21 ± 0.10	0.02 ± 0.00	0.27 ± 0.00	0.24 ± 0.05
P	Batche 2 : 500	4.86 ± 1.50	0.33 ± 0.00	0.33 ± 0.06	0.36 ± 0.06
	Batche 3 : 250	3.65 ± 1.08	0.02 ± 0.01	0.28 ± 0.12	0.28 ± 0.04
E	Batche 4 : 400	3.09 ± 0.26	0.01 ± 0.00	0.30 ± 0.00	0.28 ± 0.03
	Batche 5 : 200	2.89 ± 0.05	0.02 ± 0.00	0.27 ± 0.01	0.28 ± 0.03
PE	Batche 6 : 250-200	2.71 ± 0.00	0.01 ± 0.00	0.26 ± 0.01	0.28 ± 0.00
	Batche 7 : 250-400	3.79 ± 0.08	0.02 ± 0.01	0.25 ± 0.07	0.27 ± 0.04
P-value		0.18	0.32	0.81	0.33

Control : Distilled water

P: Chemical product solution

E: Plant extract solution

PE: Chemical product/Plant extract combination solution

Table 2. Hormonal and Biochemical dosage

Beatches Concentrations (mg/mL)		Hormonal dosage		Biochemical dosage			
		Estrad pg/mL	FSH mUI/mL	Urea g/L	Creat mg/mL	AST UI/L	ALT UI/L
1 : Control		366	0.05	1.38	4	299.6	210.4
P	2 : 500	48	0.02	2.31	13	538.0	425.1
	3 : 250	73	0.02	1.98	10	467.4	301.5
E	4 : 400	102	0.10	1.81	8	391.1	261.6
	5 : 200	494	0.10	1.50	3	302.4	215.4
PE	6 : 250-200	194	0.10	1.53	5	357.0	234.8
	7 : 250-400	70	0.03	1.89	8	445.8	277.2

Estrad: Estradiol

Creat: Creatinine

FSH: Follicle Stimulating Hormone

AST: Aspartate Transaminase

ALT: Alanine Transaminase

5. Conclusion

This study investigated the therapeutic virtues of combining the aqueous extract of *Bahia nitida*, *Adenia lobata* and *Costus afer* leaves. The results show that this aqueous decoction has a highly interesting hormone-producing activity (FSH and estrogen) in rats at a dose of 200 mg/mL. It is also non-toxic to liver and kidney cells at this dose. The molecule(s) contained in this decoction interfere with the action of the chemical product (pesticide).

The estrogenic and follicle-stimulating activity of this decoction plays an important role in the regulation of reproductive hormones. These results confirm its use in traditional medicine for fertility control, even in the presence of chemicals from environmental pollution, and in the fight against abortion.

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Statement of Competing Interests

We have no competing interests

List of Abbreviations

Control: Distilled water

P: Chemical product solution

E: Plant extract solution

PE: Chemical product/Plant extract combination solution

Estrad: Estradiol

Creat: Creatinine

FSH: Follicle Stimulating Hormone

AST: Aspartate Transaminase

ALT: Alanine Transaminase

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