



## Effects of *Spondias mombin* Linn (Anacardiaceae) on rat parturition

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### ABSTRACT

The leaves of *Spondias mombin* Linn (Anacardiaceae) are used by traditional healers in some parts of Africa to treat dystocia and postpartum hemorrhage. All experiments are performed on albino wistar mature and immature rats. This study was undertaken to evaluate the effect of *Spondias mombin* Linn on rat parturition in order to determine its action on labor time, uterus and sex steroids organs weight and coagulation time. Hydro-ethanolic extract of *Spondias mombin* leaves were given daily by oral route to female rats from 19<sup>th</sup> day of pregnancy, at doses of 100; 250 and 500 mg/kg. The dose 250 mg/kg reduced significantly ( $P < 0,05$ ) labor time. To explore estrogenic activity of the extract, the dose of 250 mg/kg, given daily by oral route to immature female rats for 7 days, induced vaginal opening and the increase in uterus and ovarian weight. The extract at 100 mg/ml was reduced the coagulation time. These results suggest that the leaves hydro-ethanolic extract of *S. mombin* contain one or more principles which reduced labor time, induced vaginal opening, increased uterus and ovarian weight and reduced coagulation time.

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**Keywords:** *Spondias mombin*, labor time, vaginal opening, uterus, ovarian, coagulation time.

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### INTRODUCTION

Dynamic dystocia, considered as most important maternal mortality cause in maternity (Thonneau et al., 2004) in the African towns, is due to uterus abnormal contractions and bad uterus collar dilatation or most generally to uterus atony. For Bield et al. (1987), uterus atony causes frequently hemorrhage during the delivery. Thus, dystocia and post-partum hemorrhage are very serious menace to feminine population in the age of procreation. Many drugs from plants

are used as herb remedies for the parturition complications by most African people. This fact is due to people's difficulties to have access to modern therapeutic. There are *Carica papaya* and *Citrus aurantifolia* leaves decoction, dark of *Adansonia digitata*, leaves and roots of *Cleome gynandra* (Oryem-Origa et al., 2003), seeds of *Momordica charantia*, leaves of *Commelina erecta* (Kamatenesi-Mugisha et al., 2007). Togolese folk medicine uses *Spondias mombin* to treat dystocia and prevent post-partum hemorrhage (Adjanohoun

et al., 1987), but no scientific investigation has shown *S. mombin* effects on these two dysfunctions. This plant has been traditionally reported for its medicinal and food values. Kramer et al. (2006), recommend its use for pregnant woman but only after five months of pregnancy. Young leaves of the plant are cooked as greens and excessive indulgence in the fruit is said to cause dysentery (Moran, 1987).

In order to give a scientific base in dystocia and post-partum hemorrhage treatment with *S. mombin* leaves, the present study aims to investigate effects of *S. mombin* leaves on labor time, estrogenic activity and haemostatic activity.

## MATERIALS AND METHODS

### Plant material

*S. mombin*'s leaves were collected in September 2006 in Agoè nyivé village, north suburb of Lomé (Togo) and identified in Botanic Laboratory herbarium (University of Lomé, Togo) were a voucher specimen is deposited.

### Preparation of extract

Leaves were washed, dried under air conditioning and were ground. This powder was used to prepare the extract by maceration, using water/ethanol 95 °C mixture (1:1) for 72 h. After filtration, solvent was evaporated and we obtained an hydro-alcohol extract yield of approximately 21,7% from original fresh leaves.

### Animals

Albino wistar mature male and female rats weighing 110-180 g and immature female rats weighing 35-45 g were used. They were obtained from the animal of the Physiology Department (University of Lomé, Togo) housed under standard conditions of light (12 h cycles), temperature and tap water ad libitum.

### Effect on labor time until 19<sup>th</sup> day of pregnancy

Male and female rats were caged together at the estrous day which was marked by the vaginal orifice redness and the increased of body temperature. The following day, males were taken out from cages and this day was the first day of pregnancy. And then, on 19<sup>th</sup> day, all female rats which weren't pregnant were removed from cages. Three groups of five pregnant rats were given orally extract at doses 100; 250 and 500 mg/kg BW respectively from 19<sup>th</sup> day and five other rats considered as control were given by the same way with distilled water.

### Estrogenic activity

Immature female rats weighing 35-45 g were used and divided into three groups. The first group as control received distilled water, the second group was given 250 mg/kg BW of extract and the third received 2 mg/kg of 17 $\beta$ -estradiol (climen®) as reference drug. Generally, six rats were used in each group and treatments were performed on 7 days along by gavages. The following days after the last treatment, all the rats were euthanized and uteri, ovarian, surreal glands were dissected and weighed. All organs were dried for 24 hours at 100 °C and weighed again. Studied parameters are body weigh, vaginal opening and uterus, ovarian, surreal glands weights.

### Haemostatic activity

To assess haemostatic activity of the extract, we used Lee-White method. Two series of experiments were performed. In the first, tubes were used to determine coagulation time and second, lames were used. For that, 10; 25; 50 and 100  $\mu$ l of 100 mg/ml extract were deposited in tubes and on lames containing respectively 0,5 ml and a drop of blood.

### Statistical analysis

All the data obtained were expressed as mean  $\pm$  SEM. SYSTAT 5.0 was used to determine the differences of means. These means were all analyzed statistically using Student's *t*-test. Values of  $P < 0,05$  were taken to imply statistical significance.

## RESULTS

### Labor time, body weight and vaginal orifice opening

Table 1 shows hydroethanolic extract of *S. mombin* effect on labor time, on fetuses number and their weight. There was significance ( $P < 0,05$ ) reduce of labor time with 250 mg/kg extract when compared with control. But no treatment didn't influence the number and the weight of fetuses.

The body weight and vaginal orifice opening of immature female rats treated for 7 days with a dose of 250 mg/kg of extract and 17 $\beta$ -estradiol at 2 mg/kg BW are shown in Table 2. No significant variation is observed

between body weights after 7 days of treatment. But the extract and 17 $\beta$ -estradiol are induced 33,33% and 100% vaginal orifice opening respectively compared to the control.

### Uterus, ovarian and surreal glands weights

The uterus, ovarian and surreal glands weights of immature rats treated for 7 days with the extract and 17 $\beta$ -estradiol are shown in Table 3. A significant increase ( $p < 0,05$ ) of uterus and ovarian weights, 318,1% and 213,3% respectively were observed after treatment with 250 mg/kg. No significant increase of surreal glands weight ( $p > 0,05$ ) is observed at this dose.

### Coagulation time

Coagulation time is reduced, compared to control, by 10 and 25  $\mu$ l of extract. Effect of *S. mombin* on coagulation time is shown in Table 4.

**Table 1:** Effect of *S. mombin* hydroethanolic extracts on labor time, on fetuses number and the weight.

Treatment	Labor time (hours)	Fetuses number	Fetuses weight (g)
Control	68,6 $\pm$ 0,51	5,6 $\pm$ 0,40	4,6 $\pm$ 0,24
100 mg/kg	67,2 $\pm$ 1,11	5,2 $\pm$ 0,37	4,8 $\pm$ 0,20
250 mg/kg	57,6 $\pm$ 2,78*	5,6 $\pm$ 0,40	4,8 $\pm$ 0,20
500 mg/kg	70,8 $\pm$ 2,28	5,8 $\pm$ 0,37	4,6 $\pm$ 0,24

Values are given as mean  $\pm$  SEM for 6 rats in each group. \*  $P < 0,05$  compared to the mean of control group (Student *t*-test).

**Table 2:** Body weight and vaginal orifice opening of immature female rats treated for 7 days.

Treatment	Body weight (g)		Increase percentage (%)	Vaginal opening percentage (%)
	Pre-treatment period	Post-treatment period		
Control	39,7 $\pm$ 2,1	44,8 $\pm$ 2,4	11,6 $\pm$ 2,3	0
250 mg/kg	40,3 $\pm$ 3,8	45,5 $\pm$ 4,0	11,4 $\pm$ 6,2	33,33
Estradiol	39,8 $\pm$ 3,0	44,6 $\pm$ 4,3	10,8 $\pm$ 3,0	100

Values are given as mean  $\pm$  SEM for 6 rats in each group.

**Table 3:** Increase percentage of uterus, ovarian and surreal glands weights after treatment.

Treatment	Uterus weight (percentage)	Ovarian weight (percentage)	Surreal glands weight (percentage)
Control	199,7 ± 28,1	121,0 ± 14,9	199,9 ± 15,5
250 mg/kg	318,1 ± 21,4*	213,3 ± 26,8*	223,6 ± 28,4
Estradiol	382,4 ± 31,6**	241,6 ± 31,4*	229,1 ± 42,4

Values are given as mean ± SEM for 6 rats in each group. \* P < 0,05 ; \*\* P < 0,001 compared to the mean of control group (Student *t*-test).

**Table 4:** Effect of the extract on coagulation time.

Treatment	Coagulation time (seconds)							
	10 µl		25 µl		50 µl		100 µl	
	Tube	Strip	Tube	Strip	Tube	Strip	Tube	Strip
Control	317	325	305	357	339	398	375	415
Extract (100 mg/ml)	232	260	260	280	359	402	>1200	470

## DISCUSSION

Medicinal plants used to speed birth are usually taken towards the end of gestation period or at the onset of labor pains (Kamatenesi-Mugisha et al., 2007). The hydroethanolic extract of *S. mombin* leaves managed from 19<sup>th</sup> day of gestation reduced labor time of female rats which received 250 mg/kg extract. Then, the extract could be used to speed parturition and remove placenta. Offiah et al. (1989) have shown the abortive properties of aqueous extract of *S. mombin* leaves on rats.

Oxytocin and his receptors synthesis is stimulated by estrogens (Bryan et al., 1998). Oxytocin receptors concentration is lowed by low and high concentrations of estrogens (Maggi et al., 1992). Our study revealed that the dose of 500 mg/kg rise slightly labor time compared to control. Sex steroids also influence the growth, differentiaton and function of female reproductive organs such as the uterus and vagina, making them susceptible to endocrine disruption (Andrade et al., 2010).

Estrogenic activity result in morphological, histological and biochemical changes of uterus (Diel et al., 2002). Duquesnoy (2005) showed that estrogenic

impregnation widened ovaries, uterus, induced follicle maturation and endometrial glandular proliferation. The increase of uterus wet and dry weight as well as animals vaginal opening number are ways to explore estrogenic activity of *S. mombin* hydroethanolic extract on immature rats. Our results are in accordance with those of Bayala (2005) reported, who observed an increase of uterus wet and dry weight as well as animal vaginal opening with *Holarrhena floribunda* leaves aqueous macerate. The administration of *S. mombin* leaves extract at the dose of 250 mg/kg and 17- β estradiol at 2 mg/kg to immature female rats shows light increase in the surreal glands weight. Indeed, surreal glands secrete estrogens but this secretion is too weak to show morphological, histological and biochemical changes in rats. Moreover, the presence of ovaries decreased greatly estrogens production by surreal glands. Researchers (Cassidy et al., 2000) suggested that phytoestrogens are selective modulators of estrogens receptors. Two types of estrogens receptors are known: α receptors (ER α) (Green et al., 1986) and β receptors (ER β) (Kuiper et al., 1996). In mice uterus, ovaries, lungs and neurons, β receptors have a great expression, but α receptors are abundant and

were more expressed in all tissues except ovaries (Couse et al., 1997). *S. mombin* leaves could contain phytoestrogens which acted as natural estrogens and as estrogens receptors ligand.

Our previous phytochemical studies on the leaf extract of *S. mombin*, revealed the presence of tannins, flavonoids, saponins and alkaloids. These results were the same with those that Njoku et al. (2007) found. Vaya et al. (2004) described flavonoids as estrogenic activity substances. The effect of *S. mombin* leaves on parturition could be due to these components.

The new concepts of coagulation are developed by Hoffman et al. (1998). Coagulation time is one of the methods used to explore haemostatic function. Coagulation time is reduced with 10 and 25 µl of extract as well as tubes or lames. But this time is, on the contrary, risen by 50 and 100 µl compared to control. This effect should be caused by coagulation factors dilution. We can say that hydroethanolic extract of *S. mombin* might have a haemostatic activity on blood. This confirms Kone-Bamba (1987) works on medicinal plants including *Spondias mombin* recognize as haemostatic.

Acute toxicity study allowed to observe that the extract has no lethal or behavior toxic effect on animals. Raji et al. (2006) have shown that *Spondias mombin* aqueous extract has no effect on male rat's body weight or organs weight but slightly increase liver weight after four weeks treatment.

### Conclusion

Our study first, aimed at determining the effect of hydroethanolic extract of *S. mombin* leaves on the last gestational period from 19<sup>th</sup> day of gestation. Second, we assessed its estrogenic properties on young immature female rats. Third, we evaluated the effect of the extract on coagulation time.

The results of this study indicate that the extract of *S. mombin* leaves reduced significantly labor time. Tests got on estrogenic activities showed that the extract induced vaginal opening, significantly increased uterus and ovarian weight and not

significantly surreal glands weight. The reduced of coagulation time is observed at low volumes. Other studies are necessary for confirming this activity.

All these results partially show, the traditional use of this plant to speed up parturition and manage postpartum hemorrhage.

More pharmacological and toxicological assess, isolation and testing of active principles are necessary to explore the mechanism of action of *S. mombin* extract. Moreover, *in vitro* studies such as isolated uterine preparations are required to determine the exact mechanism of action of this extract on the uterine smooth muscle.

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