

# TERATOGENIC EFFECT OF MATERNAL ADMINISTRATION OF ALOE VERA EXTRACT ON FOETAL MORPHOLOGY AND THE HISTOLOGY OF THE FOETAL KIDNEY

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## ABSTRACT

Aloe Vera has been regarded as the miraculous healing plant. On this assumption, aloe has been greatly misused by the populace. This study is to find the probable teratogenic effect of Aloe vera extract on the morphological and histological features of the fetal kidney. Twenty female rats weighing between 180 – 200g were used for this study. Twenty adult female rats were caged with sexually matured male rats overnight. The presence of tailed structures in the vagina smear obtained the following morning confirmed coitus and the sperm positive day was designated as day zero of pregnancy. Oral doses of 1ml, 2ml and 3ml doses of Aloe vera extract was administered respectively from 4<sup>th</sup> to 15<sup>th</sup> day of gestation. On the 21<sup>st</sup> day of gestation, the rats were sacrificed and the fetuses examined for gross anomalies. Parameters such as foetal body weight (FW), crown rump length (CRL), and tail length (TL), were measured. Result obtained showed significant reduction in all the parameters ( FW, CRL, TL) measured when compared with the control group ( $p < 0.05$ ). Histological observations of the foetal kidney showed marked distortion of normal kidney architecture in the treated groups, particularly those whose mothers received 3ml of the extract. Our results suggest that high doses of Aloe vera extract may cause intrauterine growth retardation and may be nephrotoxic to the developing rat's kidney.

**KEYWORDS:** Aloe Vera extract, Foetal morphology, Kidney histology.

## INTRODUCTION

Aloe, a popular house plant, has a long history as a multipurpose folk remedy. Commonly known as Aloe vera, the plant can be separated into two basic products: gel and latex (Tyler, 1993). Although Aloe vera is a member of the lily family, it is very cactus-like in its characteristic. This unique plant also belongs to a larger plant family called "xeroids". (Anon, 1996). Of the 250 species of aloé, four are recognized as having nutritional and medicinal values with *Aloe barbadensis* miller leading the group. *Aloe barbadensis* miller is the type of Aloe used in most commercial products with aloe content available today (Tyler, 1993).

Chemical assays of Aloe Vera show that the plant is 96 percent water and the rest of the plant is formed by a complex mixture of more than 20 substances, such as: anthraquinone glycosides, resin, salicylates, glucomannan, enzymes, minerals, acemannan (Rowe et al, 1941) sterols and glycoproteins (Anon, 1996). It also contains 8 out of the 13 recognized vitamins, such as vitamin A, C, E, vitamin B1, B2, B5, B6 and B12 (Pierce, 1993). Acemannan is a complex carbohydrate isolated from Aloe leaves and has been shown to accelerate wound healing and reduce radiation-induced skin reaction (Roberts et al, 1995). Aloe latex contains the anthraquinone glycosides, Aloin A and B, which are potent laxatives (Tyler, 1994). The anthraquinones and anthrone in the aloe latex probably

produce their laxative effect by increasing colon peristalsis and increasing the intestinal water content by opening chloride channels of the colon membrane to cause a net reduction of liquid absorption of the colon (Brusick et al, 1997).

False advertising claims for Aloe Vera are very common especially on the internet, some web pages are making bold claims and using testimonials promoting it for treating AIDS virus, arthritis or other chronic and debilitating conditions. Most of these claims have not been substantiated with scientific studies (Grindlay et al, 1986).

The application of traditional herbal remedies is common in Nigeria and pregnant women are very vulnerable to herbal remedies as most of them frequent herbal homes. This study was undertaken to investigate the probable morphological and histological alteration of the fetal kidney induced by Aloe Vera extract.

## MATERIALS AND METHODS

### Preparation of Aloe Vera extract

Aloe vera plant was bought from a herbal shop located at Mayne Avenue, off Edgerly Road, Calabar and was taken to the Botany Department, University of Calabar, for identification of the Aloe species. The plant was identified to be *Aloe barbadensis* miller. Fresh medium sized leaves were plucked, washed and cut into small sizes and blended into juice form to obtain the

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Aloe vera extract for the experiment. The Aloe extract was prepared on daily basis

### Procedures

Twenty adult female wistar rats weighing about 180-200g were used in this study. The female rats were divided into four groups labelled A, B, C and D, with each group consisting of 5 rats. Group A was the control group, groups B, C and D were the experimental groups. The female rats of proven fertility determined by daily vaginal lavage were caged overnight with sexually matured male rats of the same strain. The following morning, vaginal smear was done to check the presence of sperm in the female tract. The presence of tailed structures (spermatozoa) signified day zero of pregnancy. Groups B, C and D rats were given 1ml, 2ml and 3ml of the Aloe extract on the 4<sup>th</sup> through 15<sup>th</sup> day of gestation through an oral route with the aid of orogastric tube. The control group A animals received corresponding volumes of distilled water on the corresponding days of gestation. Pregnancy was terminated on the 20<sup>th</sup> day of gestation and the fetuses collected by uterectomy. The fetuses were blotted dry and examined for gross malformations. Fetuses were weighed on LibrorEB-330H balance. Crown rump length, as well as tail length were measured using venier caliper. The kidneys were dissected out and were fixed in Bouin's fluid for haematoxylin and eosin staining method of Drury and Wallington (1973).

Statistical analysis was performed using analysis of variance and student's t-tests. Experimental data was presented as mean  $\pm$  standard error of mean (SEM). Values of ( $p < 0.05$ ) were taken to be statistically significant.

## RESULTS

### Morphological Changes

The results are presented in Table 1, which showed that the fetuses from rats that were given 2ml and 3ml of Aloe extract indicated significant ( $p < 0.05$ ) reduction in all parameters measured when compared to

Table 1: Effect of maternal administration of Aloe vera extract on days 4-15th of gestation on the fetal body weight, crown rump length and tail length.

Parameters	Control Group A	Treated Groups and Doses		
		B (1ml)	C (2ml)	D (3ml)
Foetal body weight (g)	5.82	4.88	4.50	4.37
Mean SEM	$\pm$ 0.09	$\pm$ 0.11	$\pm$ 0.04	$\pm$ 0.01
Crown rump length (cm)	4.63	4.52	4.37	4.25
Mean SEM	$\pm$ 0.09	$\pm$ 0.07	$\pm$ 0.04	$\pm$ 0.02
Tail length (cm)	1.62	1.51	1.39	1.34
Mean SEM	$\pm$ 0.03	$\pm$ 0.03	$\pm$ 0.02	$\pm$ 0.02

( $p < 0.05$ )

fetuses from rats in the control. The foetal weight was ( $4.50 \pm 0.04$ ), crown rump length ( $4.37 \pm 0.04$ ), tail length ( $1.39 \pm 0.02$ ) in the group given 2ml of Aloe vera extract and the foetal weight ( $4.37 \pm 0.01$ ), crown rump length ( $4.25 \pm 0.02$ ) and tail length ( $1.34 \pm 0.02$ ) in the group given 3ml of Aloe vera extract were significantly ( $p < 0.05$ ) lower than the corresponding values of foetal weight ( $5.82 \pm 0.09$ ), crown rump length ( $4.63 \pm 0.09$ ), and tail length ( $1.62 \pm 0.03$ ) in the control group.

### Histological Changes

Histological study of the kidney using haematoxylin and eosin staining method showed in the control group A, the renal corpuscles made up of glomeruli and bowmans capsules. Also seen were proximal and distal convoluted tubules. (Plate 1)

Shrunken tubules, mild degeneration of glomeruli, narrowing of the capsular spaces were seen in the group B and C which received 1ml and 2ml of Aloe extract (Plate 2, 3), with the effect being more severe in group C. The kidneys of group D animals that received 3ml of the extract showed severe acute tubular necrosis and a total distortion of the renal structural detail (Plate 4).

## DISCUSSION

Body weight (Ordy et al, 1963, Davies, 1968), crown rump length (Goldman and Yakovac, 1965), tail length and trans umbilical distance (Singh and Padmanabhan, 1978; Campbell, 1974) have been commonly used as indices of fetal growth and growth retardation in experimental animals. In this study, body weight, crown rump length and tail length were used to assess growth retardation. Doses of 1ml, 2ml and 3ml of Aloe extract administered on 4<sup>th</sup> through 15<sup>th</sup> day of gestation induced statically significant ( $p < 0.05$ ) intrauterine foetal growth retardation as evidenced from the reduction in fetal weight, crown rump length and tail length when compared with the control.

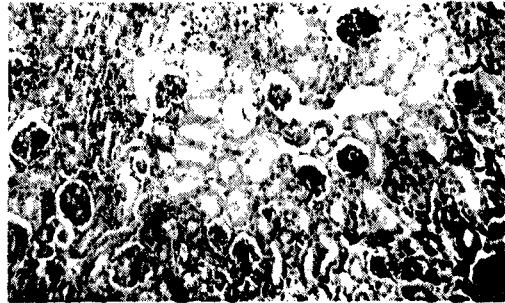
Histologically, shrunken tubules, mild and severe degeneration of glomeruli and severe acute tubular necrosis were observed within the sections of animals treated with high dose of Aloe extract. This effects may be due to the salicylates and anthraquinone content of the Aloe. Salicylic acids (aspirin), phenytoin (dilantin) have been include among the classic teratogen that causes intrauterine growth retardation (Robbins et al, 2005). This corresponds with the publication that large dose of aspirin (salicylates) ingested during pregnancy may harm the developing offspring (Corby, 1978). Anthraquinone is not excreted by the kidney, or resorption stimulates calcium binding proteins in the kidney to bind calcium. This therefore deposits calcium in the renal interstitium causing lithiasis. Lithiasis destroyed the interstitium, blood vessels and nephrons (Robbins et al, 2005). Thus in this study the severe acute tubular necrosis and total distortion of the renal structural detail can be attributed to anthraquinone component of the Aloe extract.

Plate 1



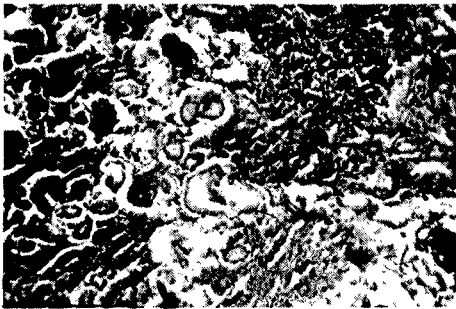
Photomicrograph showing the effects on the kidney section of group A (control), showing normal renal architecture: Renal corpuscles consisting of glomeruli and Bowman's capsule distinct.

Plate 2



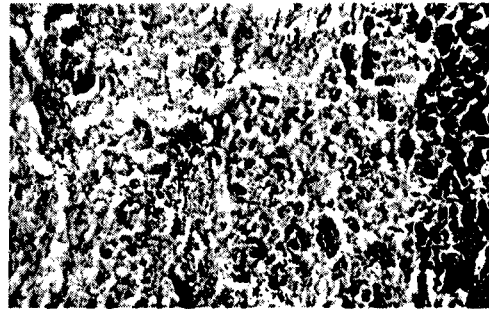
Photomicrograph showing effects on the kidney section of group B that received 1ml of the extract: showing mild degeneration of glomeruli and narrowing of the capsular spaces.

Plate 3:



Photomicrograph showing the effects on the kidney section of group C that received 2ml of the extract: showing severe degeneration of the glomeruli and Acute Tubular Necrosis (ATN)

Plate 4



Photomicrograph showing the effects on the kidney section of group D that received 3ml of the extract: showing a severe Acute Tubular Necrosis and a total disorganization of the renal structural detail.

**PLATE 1-4: PHOTOMICROGRAPHS SHOWING THE EFFECTS OF THE MATERNAL ADMINISTRATION OF ALOE VERA EXTRACT ON THE FETAL KIDNEY SECTIONS.**

The use of herbal remedies is common in Africa and many patients who visit traditional healers do not need to resort to Western medicine. Traditional remedies rarely have been analyzed and little is known about their nephrotoxicity.(Luyckx et al, 2002). Acute renal failure is one of the most serious complication resulting from the use of traditional remedies, which accounts for 35% of all case of acute renal failure in Africa.(Luyckx et al, 2002).

It is concluded from the result of this study that administering of Aloe Vera extract on 4<sup>th</sup> through 15<sup>th</sup> day of gestation causes intrauterine growth retardation and may be nephrotoxic to the developing kidney of wistar rats.

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