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Consumption of Aqueous Extract of Raw *Aloe Vera* Leaves: Histopathological and Biochemical Studies in Rat and Tilapia

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Abstract

Forty-five juvenile tilapia and 30 weanling albino rats exposed to water containing 50, 100 and 150ppm of aqueous extract of *Aloe vera* leaves for 96 hours and 28 days, respectively were used for this study. Fifteen tilapia and 10 rats exposed to clean water (0 ppm *A. vera*) served as controls. Clinical signs, mortality, gross and histologic organ pathology in the tilapia; weekly haematology, plasma biochemical parameters and organ pathology were monitored in the rats. Fish cultured in water containing *A. vera* exhibited erratic swimming patterns, rapid opercular movements, skin depigmentation and died within 24-96 hours. Gross and histologic tissue lesions in the test fish include skin depigmentation, pale and shriveled gills, dull, opaque and sunken eyes, stunting and clubbing of gill filaments, vacuolar degeneration and necrosis of gill epithelial cells, hyaline degeneration and necrosis of myofibrils, calcification of vasa vasori, hepatocellular vacuolar degeneration and necrosis. Haematologic and plasma biochemical changes in test rats include moderate to severe normocytic normochromic anaemia, hypoproteinaemia, increased AST levels, and decreased cholesterol and triglyceride levels. Gross and histologic tissue lesions include mild to moderate pulmonary congestion, flabbiness of the heart, hepatomegaly, mottling of kidneys, vacuolar degeneration and necrosis of hepatocytes, Kupffer cell hyperplasia, periportal fibrosis, glomerular and tubular degeneration and necrosis, matting and clubbing of small intestinal villi, catarrhal enteritis and goblet cell hyperplasia. The severity of these changes increased with increasing concentrations of *A. vera*. No mortality, gross or histologic changes were observed in both control fish and rats. Results from this study show that consumption of water containing extracts of raw *A. vera* is very toxic to fish and rats. The serious health implication for human consumption of raw *A. vera* is discussed.

Key words: *Aloe vera*, tilapia, rats, alternate medicine, human health implications

INTRODUCTION

Aloe vera (L), a member of the family *Liliaceae*, is a popular perennial succulent plant that is cactus-like in its characteristics (Tyler, 1993). The plant has a long history as a multipurpose folk remedy (Reynolds and Dweck, 1999), and has been associated with myth, magic and medicine since pre-biblical times (Balter, 1992). Historical evidence indicates that *A. vera* originated in the warm, dry climate of southern and eastern Africa, and was subsequently introduced into northern

Africa, the Arabian Peninsula, China, Gibraltar, the Mediterranean countries, and the West Indies (Haller, 1990). Hedendal (2000) described *A. vera* as one of the most talked about, yet most misunderstood plants in history. Modern clinical use of *A. vera* began in the 1920s and claims now abound, in numerous research and commercial literature in journals and on the Internet, regarding its numerous therapeutic potentials when used both topically and parenterally. It is acclaimed to cure ailments ranging from mild fever, wounds and burns, gastrointestinal disorders, diabetes, sexual

vitality and fertility problems to cancer, immune modulation and AIDS (Woo *et al.*, 1981; Sebastian and Bhandari, 1984; Agarwal, 1985; Koo, 1994; Kim and Lee, 1997; Kemper and Chiou, 1999; Kim *et al.*, 1999; Reynold and Dweck, 1999; Davis, 2001; Ritter, 2003).

In Nigeria, there is a very strong cultural belief in herbal medicare, most often due to the latter's economic advantage and easier reach compared to the high cost of orthodox medicine. This is more compounded by low literacy levels and often epileptic and grossly inefficient orthodox healthcare delivery system. Since the sudden introduction and widely acclaimed megatherapeutic potentials of *A. vera* and its products (the *cure-all* craze) in the mid 1990s, and the highly expensive "processed" *A. vera* products, it is common site to see homestead *A. vera* "plantations" at every corner in most towns and villages. This has led to unrecommended and uncontrolled consumption of raw *A. vera* leaves by the lowly and mighty in the society. Conflicting reports on the therapeutic potentials of *A. vera* (Schmidt and Greenspoon, 1993), its toxicity, especially when used parenterally (Brusick and Menge, 1997; Balter, 1992), and the fact that most advertised *A. vera* products have no specific approval for use by the Food and Drug Administration of the United States of America (FDA) (FLP, 2003; Changes International, 2004) necessitated this current research on the effects of aqueous extracts of raw *A. vera* leaves on rats and fish, as animal models. The implication of unguided human consumption of *A. vera* leaves in our healthcare system is discussed.

Materials and Methods

Preparation of Aqueous Extract of Aloe vera

Aloe vera plant was obtained from the Department of Agronomy, University of Ibadan, Ibadan, Nigeria. The leaves were washed with clean water, cut into pieces and weighed. 250gm of the cut leaves was pulverized in an electric blender (Philip Electrical, UK), soaked in 2 litres of water for 3 hours and later filtered through a 1mm mesh sieve. The filtrate was made up to 10 litres with water, making a working dilution of 25,000ppm of the water extract of *A. vera*.

Fish Experiment

Sixty juvenile tilapia, *Oreochromis niloticus* (mean length 9.5±1.5cm; body weight 30.0±5.0g) were purchased from Tropical Aquaculture Products Limited, a commercial fish multiplication center in Ibadan, Nigeria. The fish were divided into four groups of 15 juveniles each in aerated

four 40.5 litre plastic aquaria. Each of the aquaria contained 20 litres of water to which appropriate volumes of the working stock of the aqueous extract of *A. vera* were added to make 0ppm (no *A. vera*), 50ppm, 100ppm and 150ppm. Fish in the 0ppm tank served as the controls. Water temperature, dissolved oxygen and ammonia levels were maintained at acceptable levels (Boyd, 1981; Moses, 1983). The pH value of the water in each tank was determined using a pH probe (Gallenkamp, GmBh, Germany) and recorded. The fish were fed at 5% of their body weight, daily in two equal rations, in the morning (7.00hr) and evening (18.00hr). The feed was compounded to contain 28% crude protein and 3,400 calories. Immediately after the fish were placed in the tanks, observations of clinical signs (swimming patterns and response to stimuli), skin colouration and mortality were monitored every 6 hours in a 96-hour biostatic assay.

Rat Experiment

Forty white albino rats, aged 8 weeks, purchased from the Experimental Animal Laboratory of the Faculty of Veterinary Medicine, University of Ibadan, Nigeria were used for this study. The rats were stabilized for 1 week during which they were fed commercial rat pellets (Ladokun Feeds, Ibadan, Nigeria) and clean drinking water *ad libitum*. At the commencement of the experiment, the rats were divided into four groups of 10 rats each and given drinking water containing 0ppm, 50ppm, 100ppm and 150ppm aqueous extract of *A. vera*, as described for the fish experiment. Clinical signs were monitored every 6 hours.

Two rats per group were randomly selected on days 0, 7, 14, 21 and 28 and mildly sedated in a diethyl ether fume chamber for 1-2 minutes. They were thereafter put on dorsal recumbency and the skin on the ribs and sternum was held taut using the left thumb and index fingers. Using a 22G needle attached to a 5ml syringe, 3ml of blood was aspirated from the heart into labeled tubes containing the sodium salt of ethylenediamine tetraacetic acid (Na-EDTA) anticoagulant, and gently mixed to prevent clotting. Packed cell volume (PCV), haemoglobin (Hb) concentration, erythrocyte (RBC), total leucocyte (WBC) and differential leucocyte counts, and corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC) were determined by standard techniques (Jain, 1986). After the centrifugation of the unclotted blood at 1,200g for 10 minutes, the plasma was carefully removed and used for the estimation of the

following biochemical parameters: total protein, albumin, globulin, urea and creatinine as described by Ogunsanmi *et al.* (1994). Others include activities of plasma aspartate aminotransferase (AST) and alanine aminotransferase (ALT), measured by the procedures of Reitman and Frankel (1957), alkaline phosphatase (ALP) by a modified method of Frajola *et al.* (1965) and γ -glutamyl transferase (GGT) by the method of Szas (1969). The plasma total cholesterol and triglyceride were determined as described by Toro and Ackermann (1975).

Thereafter, the rats were dissected and gross changes in the organs observed and recorded. Sections of the intestines, liver, lungs, kidney, heart and brain of each rat were harvested into labelled sample bottles containing 10% phosphate-buffered formalin fixative for 24 hours. They were thereafter, trimmed and dehydrated in graded concentrations of xylene, embedded in wax and sectioned at 5 μ and fixed on to clean, grease-free glass slides. The thin sections were stained with haematoxylin and eosin (H&E) for histologic examination under the light microscope. Photomicrographs of organ/tissue lesions were taken with Authotek Camera (Leitz GmBH, Germany), attached to the light microscope and processed routinely.

Statistical Analyses

Data obtained were subjected to statistical analysis using 2way analysis of variance (SAS, 1987), and means were compared for significant differences (if any) using the Duncan's multiple range test (Duncan, 1959).

Results

Fish Experiment

No untoward clinical changes were observed in the control tank (0ppm *A. vera*) throughout the 96 hours of the experiment. Varying degrees of changes in swimming patterns, consisting of erratic swimming and reversal movements, attempts at jumping out of water, rapid opercular movements, gasping, staying for long periods of time under water, and blanching (depigmentation) of skin were observed in fish in the test tanks. These changes were progressively more severe with increase in concentration of *A. vera* extract in tank water, that is, 50ppm, 100ppm and 150ppm, with the latter being most severe.

The pH of the stock aqueous extract of *A. vera* was 5.8, while those of the water in the aquaria are Tank 1 (0ppm *A. vera*) – pH 7.2, Tank 2 (50ppm *A. vera*) – pH 6.9, Tank 3 (100ppm *A. vera*) – pH 6.7 and Tank 4 (150ppm *A. vera*) – pH

6.6. The mortality patterns of the test fish are as shown on Table 1. None of the control fish died throughout the period of study. Similarly, no deaths were recorded in all the fish tanks within 24 hours of the experiment. The first sets of mortalities (40%) were recorded after 24 hours in the Tank 4 (150ppm *A. vera*). 100% mortality was recorded in Tank 3 (100ppm) after 48 hours, while 80% of the fish in Tank 2 (50ppm) died after 72 hours.

Table 1:

Mortality patterns in the control and test tilapia exposed to varying concentrations of aqueous extract of *A. vera*

Aquaria	Concentration of <i>A. vera</i>	Mortality (n/15; %)
Between 0 – 24 hours		
Tank 1	0 ppm	0 (0%)
Tank 2	50 ppm	0 (0%)
Tank 3	100 ppm	0 (0%)
Tank 4	150 ppm	0 (0%)
24 – 48 hours		
Tank 1	0 ppm	0 (0%)
Tank 2	50 ppm	0 (0%)
Tank 3	100 ppm	0 (0%)
Tank 4	150 ppm	6 (40%)
48 – 72 hours		
Tank 1	0 ppm	0 (0%)
Tank 2	50 ppm	3 (20%)
Tank 3	100 ppm	15 (100%)
Tank 4	150 ppm	9 (60%)
72 - 96 hours		
Tank 1	0 ppm	0 (0%)
Tank 2	50 ppm	12 (80%)
Tank 3	100 ppm	-
Tank 4	150 ppm	-

No significant gross and histopathological changes were observed in the tissues and organs of control fish (0ppm *A. vera*) throughout the period of experiment. Table 2 shows the scores of gross and histologic changes in tissues/organs of the fish in the various experimental tanks. Generally, gross lesions include depigmentation of skin and pale and shriveled gills, and dull, opaque and sunken eyes. Histologic changes include varying severities and spread of stunting and clubbing of gill filaments vacuolar degeneration and necrosis of gill epithelial cells and heterophilic infiltration of the gill submucosae (Plate 1). Others include hyaline degeneration and necrosis of myofibrils and calcification of vasa vasori, vacuolar degeneration and necrosis of hepatocytes, and to a lesser degree, pancreatic cells and infiltration by melanomacrophages. There was severe villous atrophy, characterized by denudation and stunting

of villi, congestion, glandular degeneration, necrosis and lymphocytic infiltration in the submucosae of the intestines (Plate 2) and focal areas of neuronal degeneration, neuronophagia

and gliosis in the cerebrum. The most severe histologic lesions were observed in fish in the tank containing 50ppm *A. vera*.

Table 2: Pathology scores of control and test tilapia exposed to varying concentrations of aqueous extract of *A. vera*

Organ/Tissue Lesions	Tank 1 (0ppm)	Tank 2 (50ppm)	Tank 3 (100ppm)	Tank 4 (150ppm)
Skin and Eyes				
Blanched (depigmented) skin	-	+++	++	±
Sunken eyes	-	++	++	+
Gills				
Blanched and shriveled	-	++	++	±
Stunted, matted, clubbed gill filaments	-	+++	++	+
Vacuolar degeneration, necrosis of epithelia cells	-	++	++	+
Liver				
Hepatic degeneration and necrosis	-	+++	++	±
Heart				
Hyaline degeneration and necrosis of myofibrils	-	++	+	±
Calcification of vasa vasori	-	+	++	-
Small intestines				
Villous atrophy (matting and stunting)	-	+++	++	+
Goblet cell hyperplasia	±	++	++	+
Glandular degeneration and necrosis	-	+++	++	+
Brain				
Neuronal degeneration	-	++	+	±
Gliosis	-	+	++	+

Key to scores:- - = No lesions observed; ± = Mild, focal lesions; + = Mild, multifocal lesions; ++ = Moderately severe diffuse lesions; +++ = Very severe diffuse lesions

Table 3:

Haematology of rats given oral administration of the water extract of *A. vera*

Day/Rat Group	Haematological parameters/indices				
	PCV (%)	Hb conc. (g/dl)	RBC counts (x10 ⁶ /µl)	MCV (fl)	MCHC (g/dl)
0 Group 1 *	29.0±2.2 ^a	8.5±0.7 ^{ab}	4.3±0.1 ^a	67.5±1.9 ^a	29.3±2.3 ^a
Group 2	30.5±1.2 ^a	10.2±4.0 ^a	4.7±0.5 ^a	63.6±2.2 ^a	33.3±3.1 ^a
Group 3	30.0±3.1 ^a	10.3±2.3 ^a	5.0±0.3 ^a	65.6±6.7 ^a	33.5±3.9 ^a
Group 4	29.3±2.0 ^a	8.7±1.1 ^{ab}	4.5±0.2 ^a	65.2±5.1 ^a	30.2±3.0 ^a
7 Group 1	29.5±3.3 ^a	9.8±2.1 ^{ab}	4.9±0.6 ^a	60.3±3.1 ^a	33.2±2.6 ^a
Group 2	24.5±2.1 ^b	8.1±0.7 ^{ab}	3.9±0.3 ^b	62.8±1.2 ^a	33.1±2.4 ^a
Group 3	23.5±2.1 ^b	6.9±0.5 ^b	3.5±0.3 ^b	67.2±1.3 ^a	29.8±4.8 ^a
Group 4	22.6±1.3 ^b	6.7±1.1 ^b	3.6±0.5 ^b	63.1±3.2 ^a	29.7±2.6 ^a
14 Group 1	28.0±2.7 ^a	8.9±1.9 ^a	4.1±0.6 ^a	68.4±3.4 ^a	32.1±1.1 ^a
Group 2	22.5±0.7 ^b	7.5±0.2 ^{ab}	3.6±0.1 ^b	62.6±2.0 ^a	33.3±2.1 ^a
Group 3	24.0±2.8 ^b	7.9±0.9 ^{ab}	3.6±0.8 ^a	66.7±2.5 ^a	32.9±2.9 ^a
Group 4	23.1±1.4 ^b	6.8±1.1 ^b	3.4±1.3 ^b	68.6±1.1 ^a	29.8±2.0 ^a
21 Group 1	30.0±2.1 ^a	9.1±0.7 ^a	4.5±0.3 ^a	66.9±1.1 ^a	33.6±1.9 ^a
Group 2	23.6±2.3 ^b	7.2±2.1 ^{ab}	3.7±0.9 ^b	64.4±1.5 ^a	31.0±2.6 ^a
Group 3	23.2±4.2 ^b	7.4±1.4 ^{ab}	3.5±0.5 ^b	66.3±1.4 ^a	31.7±1.0 ^a
Group 4	22.4±2.2 ^b	7.1±0.9 ^{ab}	3.2±0.4 ^b	66.9±0.9 ^a	32.0±1.3 ^a
28 Group 1	31.5±0.7 ^a	10.1±0.2 ^a	4.5±0.6 ^a	70.1±3.5 ^a	32.4±3.9 ^a
Group 2	24.0±1.4 ^b	7.0±0.8 ^{ab}	3.4±0.3 ^b	68.4±2.5 ^a	29.3±2.0 ^a
Group 3	23.5±2.9 ^b	7.3±1.6 ^{ab}	3.4±0.2 ^b	69.1±1.3 ^a	31.1±1.2 ^a
Group 4	23.0±1.7 ^b	7.2±1.8 ^{ab}	3.3±0.5 ^b	69.7±2.1 ^a	31.4±2.3 ^a

* Rats in Groups 1, 2, 3 and 4 received 0, 50, 100 and 150ppm aqueous extract of *A. vera*, respectively

Table 4:

Plasma proteins and enzyme activities of rats given oral administration of the water extract of *A. vera*

Day/Rat Group	Total protein (g/dl)	Albumin (g/dl)	Globulin (g/dl)	ALP (IU/l)	ALT (IU/l)	AST (IU/l)
0 Group 1*	6.6±0.3 ^a	3.1±0.1 ^a	3.5±0.3 ^a	177.5±11.8 ^b	38.5±2.8 ^a	22.0±1.0 ^e
Group 2	6.4±0.3 ^a	3.2±0.1 ^a	3.2±0.1 ^a	145.0±7.7 ^c	35.0±9.9 ^a	23.5±1.2 ^e
Group 3	6.4±0.2 ^a	3.3±0.2 ^a	3.1±0.2 ^a	159.0±10.1 ^c	34.0±1.4 ^a	23.0±1.4 ^e
Group 4	6.6±0.3 ^a	3.3±0.2 ^a	3.3±0.3 ^a	166.3±9.6 ^b	39.0±2.3 ^a	22.3±2.0 ^e
7 Group 1	6.6±0.2 ^a	3.1±0.2 ^a	3.5±0.2 ^a	191.0±12.7 ^a	27.0±1.2 ^b	23.0±1.0 ^e
Group 2	6.1±0.2 ^b	2.5±0.3 ^b	3.6±0.3 ^a	146.0±8.4 ^c	28.5±4.9 ^{ab}	26.9±2.4 ^d
Group 3	6.0±0.1 ^b	2.6±0.1 ^b	3.4±0.2 ^a	167.0±7.7 ^b	26.5±3.5 ^b	28.0±2.1 ^d
Group 4	5.9±0.1 ^b	2.4±0.2 ^b	3.5±0.1 ^a	155.9±8.6 ^c	30.1±3.3 ^a	26.9±2.2 ^d
14 Group 1	6.5±0.1 ^c	3.2±0.3 ^a	3.3±0.1 ^a	220.0±14.4 ^a	30.0±2.8 ^a	20.0±1.4 ^e
Group 2	5.6±0.1 ^c	2.2±0.1 ^b	3.4±0.2 ^a	179.0±4.2 ^{ab}	27.0±4.4 ^b	40.0±2.7 ^c
Group 3	5.7±0.2 ^c	2.4±0.1 ^b	3.3±0.2 ^a	145.0±7.7 ^c	30.3±2.3 ^a	38.0±1.9 ^c
Group 4	5.4±0.3 ^c	2.2±0.2 ^b	3.2±0.1 ^a	201.2±3.3 ^a	37.2±3.0 ^a	52.3±6.3 ^b
21 Group 1	6.6±0.1 ^a	3.3±0.2 ^a	3.3±0.0 ^a	215.5±18.7 ^a	38.0±2.3 ^a	22.0±1.5 ^e
Group 2	5.6±0.0 ^c	2.2±0.1 ^b	3.4±0.0 ^a	168.0±4.4 ^b	29.0±1.4 ^a	59.0±4.1 ^a
Group 3	5.5±0.1 ^c	2.3±0.2 ^b	3.2±0.1 ^a	137.0±7.8 ^c	35.0±4.2 ^a	63.0±6.2 ^a
Group 4	5.6±0.2 ^c	2.1±0.2 ^b	3.4±0.2 ^a	166.7±10.3 ^b	29.6±4.5 ^a	60.5±3.5 ^a
28 Group 1	6.7±0.2 ^a	3.5±0.1 ^a	3.2±0.1 ^a	187.5±10.6 ^{ab}	34.5±3.9 ^a	25.0±2.4 ^e
Group 2	5.3±0.1 ^c	2.1±0.0 ^b	3.2±0.2 ^a	222.0±16.7 ^a	28.5±2.7 ^{ab}	61.0±4.4 ^a
Group 3	5.5±0.0 ^c	2.3±0.0 ^b	3.2±0.0 ^a	149.0±8.4 ^c	27.0±2.0 ^b	67.5±3.5 ^a
Group 4	5.4±0.1 ^c	2.2±0.1 ^b	3.2±0.1 ^a	200.9±6.7 ^a	31.2±2.2 ^a	68.3±3.8 ^a

* Rats in Groups 1, 2, 3 and 4 received 0, 50, 100 and 150ppm aqueous extract of *A. vera*, respectively

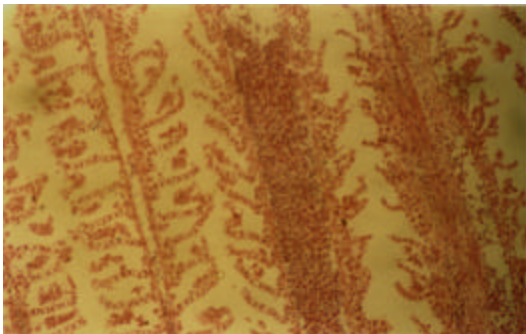


Plate 1:

Photomicrograph of the gills of test fish in 50 ppm *Aloe vera* showing widespread vacuolar degeneration and necrosis of epithelia cells, haemorrhages and heterophilic infiltration. H & E. x600.

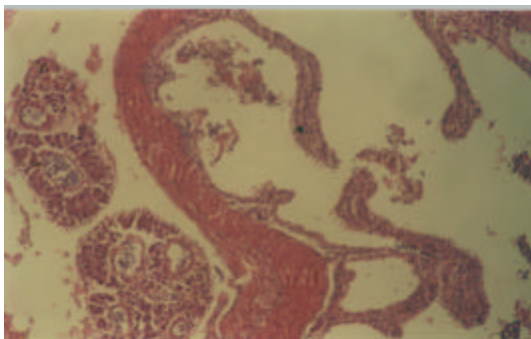


Plate 2:

Photomicrograph of the intestine of test fish in 50 ppm *Aloe vera* showing severe haemorrhage, stunting and denudation of villi and glandular degeneration. H & E. x450

Rat Experiment

Rats in Groups 2, 3 and 4 developed moderately severe normocytic normochromic anaemia ($p < 0.05$) from day 7 onwards, while the control rats (Group 1; 0ppm *A. vera*) were not anaemic throughout the 28-day experimental period (Table 3). There were no notable changes in the leucogram of all the rats throughout the experiment (data not shown). Hypoproteinaemia, characterized by hypoalbuminaemia ($p < 0.05$) developed in rats of Groups 2, 3 and 4, from day 7 onwards, with the latter being most severe (Table 4). Of the plasma enzymes, only AST increased considerably ($p < 0.05$) in rats of Groups 3 and 4 from day 14 onwards. ALP and ALT levels showed inconsistent changes in the experimental rats throughout the experiment. Both cholesterol and triglyceride levels decreased ($p < 0.05$) after day 7 onwards; while there were no significant changes ($p > 0.05$) in plasma creatinine levels, changes in plasma urea levels were inconsistent (Table 5).

Table 6 shows the scores of gross and histologic changes in tissues/organs of the experimental rats. Apart from slightly congested lungs in one of rats on day 14 of the experiment, no observable gross lesions were observed in all the organs of the control rats (0ppm *A. vera*) throughout the 28-day period of the study.

Table 5: Plasma lipids and metabolites (mg/dl) of rats given oral administration of aqueous extract of *A. vera*

Day/ Rat Group	Cholesterol	Triglyceride	Creatinine	Urea
0 Group 1	128.0±4.3 ^a	110.0±4.7 ^a	1.0±0.0 ^a	21.0±1.4 ^b
Group 2	124.5±4.9 ^a	109.0±5.5 ^a	1.1±0.2 ^a	22.5±1.1 ^b
Group 3	128.5±2.1 ^a	110.5±7.5 ^a	0.9±0.3 ^a	20.0±3.5 ^b
Group 4	126.5±2.3 ^a	108.9±6.6 ^a	1.0±0.2 ^a	23.1±1.5 ^b
7 Group 1	129.0±2.4 ^a	109.5±2.0 ^a	1.0±0.1 ^a	22.5±0.7 ^b
Group 2	105.0±2.6 ^b	95.0±1.2 ^b	1.3±0.2 ^a	27.0±1.9 ^a
Group 3	110.0±4.4 ^b	99.0±4.2 ^b	1.2±0.3 ^a	21.0±1.4 ^b
Group 4	113.5±3.6 ^b	98.6±3.5 ^b	0.8±0.2 ^a	25.3±2.1 ^{ab}
14 Group 1	125.0±1.7 ^a	111.0±2.0 ^a	1.1±0.1 ^a	21.0±1.6 ^b
Group 2	101.0±5.5 ^b	96.0±1.8 ^b	0.8±0.1 ^a	16.5±2.1 ^c
Group 3	88.5±2.2 ^c	77.0±0.0 ^c	0.7±0.2 ^a	25.0±2.4 ^{ab}
Group 4	100.2±3.1 ^b	80.1±5.2 ^c	1.2±0.3 ^a	22.3±1.8 ^b
21 Group 1	124.0±2.7 ^a	108.0±1.7 ^a	1.5±0.5 ^a	29.0±1.4 ^a
Group 2	107.5±1.1 ^b	80.0±2.8 ^c	0.9±0.1 ^a	26.5±2.1 ^a
Group 3	90.0±2.8 ^c	80.1±0.7 ^c	1.0±0.2 ^a	22.0±1.4 ^b
Group 4	91.3±1.2 ^c	78.8±1.1 ^c	1.3±0.0 ^a	22.5±1.6 ^b
28 Group 1	127.5±2.5 ^a	109.0±2.2 ^a	0.9±0.3 ^a	21.0±4.1 ^{ab}
Group 2	92.5±2.2 ^c	81.5±3.5 ^c	1.5±0.3 ^a	20.0±2.8 ^b
Group 3	77.5±3.5 ^d	65.0±1.3 ^d	0.9±0.2 ^a	26.5±2.2 ^a
Group 4	78.3±2.2 ^d	63.8±3.2 ^d	0.8±0.2 ^a	26.1±3.1 ^a

* Rats in Groups 1, 2, 3 and 4 received 0, 50, 100 and 150ppm aqueous extract of *A. vera*, respectively

Table 6: Pathology scores of rats given oral administration of varying concentrations of the aqueous extract of *A. vera*

Organ/Tissue Lesions	Group 1 (0ppm)	Group 2 (50ppm)	Group 3 (100ppm)	Group 4 (150ppm)
Lungs				
Pulmonary congestion	-	++	++	++
Thickened peribronchiolar and perivascular lymphocytic cuffs	±	+	++	++
Liver				
Hepatomegaly	-	+	++	+++
Hepatic degeneration and necrosis	-	+	+++	+++
Kupffer cell hyperplasia	-	±	++	++
Periportal fibrosis	-	-	±	+
Heart				
Flabbiness	-	+	+	++
Hyaline degeneration and necrosis of myofibrils	-	+	++	++
Mononuclear cellular infiltration	-	±	±	+
Kidney				
Mottling	-	+	++	++
Glomerular and tubular degeneration and necrosis	-	++	++	++
Small Intestine				
Congestion and haemorrhage	±	+	++	+++
Villous atrophy (matting and clubbing)	-	++	++	+++
Catarrhal enteritis	-	++	++	++
Glandular degeneration and necrosis	-	+	++	++
Brain				
Meningeal congestion and haemorrhage	-	±	+	+
Perivascular oedema	-	±	+	+
Neuronal degeneration and gliosis	-	+	+	++

Key to scores:-
 - = No lesions observed; ± = Mild, focal lesions
 + = Mild, multifocal lesions; ++ = Moderately severe diffuse lesions
 +++ = Very severe diffuse lesions

Similarly, no gross lesions were observed on the lungs, hearts, brain, intestines, spleen and kidneys of Groups 2 and 3 rats up till 14 days of the study. However, there was a progressive increase in the paleness and sizes of the livers of the rats in Groups 2, 3 and 4 from day 7 of the study onwards. Hepatomegaly was most severe in the rats in Groups 3 on day 14. There was a moderate flabbiness of the heart and increasing mottling of the kidneys of rats in Groups 3 and 4. These were most severe in rats of Group 4 on the 28th day. No gross lesions were observed on the brains and intestines, except that the intestinal contents became progressively pasty and later watery in of all the rats of Groups 2, 3 and 4 from day 7 till the end of the study.

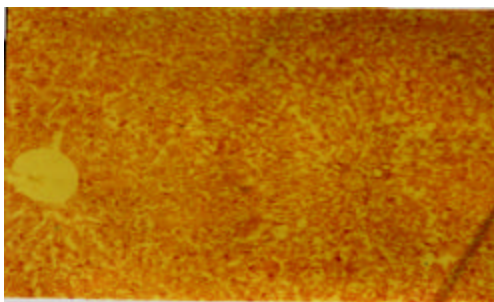


Plate 3: Photomicrograph of the liver of a Group 4 rat (150 ppm *Aloe*) on day 7 showing diffuse periportal and centrilobular vacuolar degeneration of hepatocytes H & E. x450.

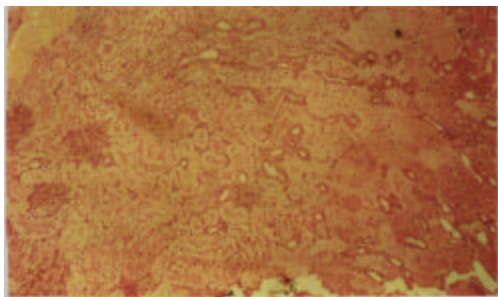


Plate 4: Photomicrograph of the cortex of the kidney of a Group 2 rat (50 ppm *Aloe*) on day 14 showing severe degeneration and necrosis of glomeruli and tubules H & E. x600.

Histopathological changes include very mild to moderate pulmonary congestion, mild peribronchiolar and perivascular lymphocytic cuffings and thickened interalveolar septa in the lungs, varying severities of vacuolar degeneration and necrosis of hepatocytes. (Plate 3), Kupffer cell hyperplasia and mild periportal fibrosis, especially on day 28 in rats of Group 4. There was moderate to severe glomerular and tubular degeneration and necrosis (Plate 4). Intestinal lesions include matting and clubbing of villi (Plate 5), catarrhal

enteritis and goblet cell hyperplasia. There were focal areas of hyaline degeneration and necrosis of myofibrils and mononuclear cellular infiltration in rats of Groups 3 and 4 on day 28. Brain lesions include meningeal congestion and haemorrhages, perivascular oedema, neuronal degeneration and moderate gliosis.

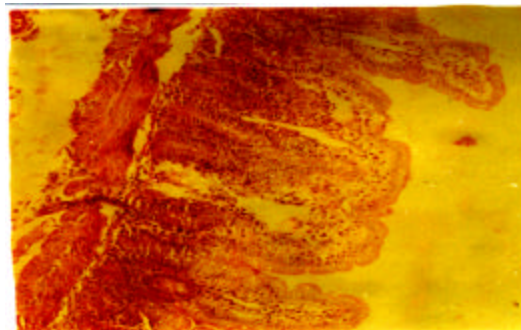


Plate 5: Photomicrograph of the small intestine of a Group 3 rat (150 ppm *Aloe*) on day 7 showing matting and stunting of villi H & E. x450.

DISCUSSION AND CONCLUSIONS

Essentially two products can be extracted from *A. vera* leaves; the clear gel that forms naturally in the leaf's hollow interior is used to treat skin irritation, and it is an active ingredient in hundreds of skin lotions, toilet soaps, sun blocks and cosmetics (Grindlay and Reynolds, 1986; Kemper and Chiou, 1999; Foster, 2004; Moody *et al.*, 2004). The resin canal cells found in thick leaf epidermis produce a yellow juice (latex) that is used as a laxative and disinfectant (Tyler, 1993; Ghazanfar, 1994; Foster, 2004), and in experimental and folklore medicine for liver complaints, piles, emetic, anti-pyretic, enlarged spleen, cooling agent, skin diseases, tuberculosis, fungal diseases, peptic ulcers, reduction of blood glucose levels, asthma, AIDS, anti-cancer, and as an immunomodulator (Shah *et al.*, 1989; Kemper and Chiou, 1999; Reynolds and Dweck, 1999; Hedendal, 2000). In fact the list is endless. The terms "gel" and "juice" are not clearly defined by manufacturers and often are confused by consumers. The mechanical separation process is not always complete, so *A. vera* latex can be found in some *A. vera* gels; hence it is desirable to make the gels as pure as possible, because *A. vera* latex contains the anthraquinone glycosides - aloin A and B, which are potent laxatives (Tyler, 1994).

The results obtained in this study have shown the water extract of *A. vera* as a very potent toxic

substance to fish and rats when consumed. It is especially lethal to fish at as low as 50ppm in water causing 100% mortality within 96 hours. There was severe depigmentation, destruction of the gills, intestines, liver and less so the kidneys and brain, with the worst organ damage occurring in fish with longer exposure of the *A. vera* extract (50ppm) over 96 hours. The organ and tissue damage in the experimental fish may be due to the direct toxicity of the *A. vera* extract on organs such as the gills, intestines, liver and heart. Damage, especially to the gills, will affect oxygen exchange and tissue respiration, culminating in organ and tissue hypoxia, degeneration and necrosis. The pH of the various concentrations of the water with *A. vera* extract in the aquaria are slightly in the acidic range (pH 6.6 – 6.9). *A. vera* gel is 99% water with a pH of 4.5 (Kemper and Chiou, 1999).

Even though, no mortality was recorded in the experimental rats in this study, diarrhoea, catarrhal enteritis, villous atrophy, liver, kidney and heart damage were the hallmarks of the intoxication of rats with *A. vera* extract, and these were more severe as the concentration of the extract increased. The normocytic normochromic anaemia and significantly increased plasma activity of AST in the experimental are the direct consequences of several organ damage, especially of the liver, heart and kidneys (Jubb *et al.*, 1995). The hypoalbuminaemia may be related to the profuse diarrhoea and protein-losing gastroenteropathy, as well as hepatic damage (Jubb *et al.*, 1995). One interesting finding however is the lowering of plasma lipids in rats that consumed the aqueous extract of *A. vera*. This could be interpreted to mean that *A. vera* may be useful for treating arteriosclerotic problems and reduction of plasma lipids. This claim however, needs to be further examined.

The major objective of this research was to investigate the effect of unguided and often unrecommended oral administration of *A. vera* leaves in human, using the tilapia and rats as animal models. This is very important because of the current craze, in Nigeria, by middle and low income, literate, and especially illiterate, old and young men and women who consume often large amounts of raw *A. vera* leaves due to spurious advertisements and belief in the plant as a “cure all” and “magic” plant, all in the name of “naturopathy” and “alternate” health methods. It is to be noted that most advertisers and users of this plant (and probably so for numerous other herbs) are oblivious of the fact that the parenteral administration of raw *A. vera* plant is not approved by the FDA (Smith and Struck, 1997; FLP, 2003;

Changes International, 2004). Death has been reported of four cancer patients who were treated with *A. vera* intravenously by a physician whose license was subsequently revoked after investigation and trial by the Maryland Police (Smith, 1997a; Smith and Bloom, 1997; Smith and Lipton, 1997; Smith and Struck, 1997). Brusick and Menge (1997) expressed concern over the safety of *A. vera* stating that genotoxicity studies showed that *A. vera*-containing laxatives pose cancer risks to human when used as directed. Acute toxicity with *A. vera* gel caused severe cramping, diarrhoea and nausea, while long-term ingestion has been reported to lead to potassium deficiency, muscle weakness and cardiac arrhythmias (Kemper and Chiou, 1999). Some of the known contraindications of products containing *A. vera* include intestinal obstruction or stenosis, atony, severe dehydration with electrolyte depletion, chronic constipation inflammatory intestinal diseases, cardiovascular diseases, pregnancy or lactation, in patients with cramps, colic, haemorrhoids, nephritis, or any undiagnosed abdominal symptoms such as pain, nausea, or vomiting (Hedendal, 2000).

While folk medicine has its roots in the very annals of human history, caution must be exercised in the use of some of these herbs, and that claims such as have been attributed to *A. vera* must be backed by unequivocal scientific evidence. There are many areas of contradictions in most of the advertised therapeutic potentials of *A. vera*, especially when used parenterally. A few of the notable contradictions include: its use as an emmenagogue and abortifacient (Saha *et al.*, 1961; Singh *et al.*, 1979; Nath *et al.*, 1992) vis-à-vis its use for the prevention of miscarriage (Bhattharai, 1992) and its anti-oxytotic activity (Andrade *et al.*, 1996); the use of *A. vera* gel in the treatment of peptic ulcers (Blitz *et al.*, 1963) vis-à-vis the ineffectiveness of both the exudate and gel components of *A. vera* in the treatment of gastric and duodenal ulcers experimentally induced in rats (Parmar *et al.*, 1986); and its acclaimed use in lowering blood glucose level in diabetics (Ghannam *et al.*, 1986; Ajabnoor, 1990; Yongchaiyudha *et al.*, 1996), contradicted by Koo (1994) who reported not only the ineffectiveness of the *A. vera* gel in lowering blood glucose levels of alloxan-treated rats, but that it actually seemed to have caused an increase.

Most of the Nigerians who consume raw *A. vera* leaves have very strong belief in its alleged megatherapeutic efficacy (personal communication), but are unable to purchase the numerous commercially available “processed”

products because of their prohibitive costs, as they belong to the low income group. They then resort to the unguided and continuous consumption of the raw leaves, oblivious of its implications on their health and productivity, not only in the short, but long term. There is no unified recommended dosage information for most *A. vera* products, whether raw or "processed", and provision of dosage information by most marketers and advertisers of *aloe* products does not constitute a recommendation or endorsement (Kemper and Chiou, 1999). Avila *et al.* (1997) confirmed that aloin and a low molecular weight fraction of the *A. vera* leaf (*Aloe-emodin*) are cytotoxic, and should be removed from products processed for commercial use. A high molecular weight fraction of *A. vera* was shown to deplete complement, while the low molecular weight fraction interfered with processes in activated polymorphonuclear leukocytes, leading to the production of oxygen free radicals and subsequent cytotoxicity (t'Hart *et al.*, 1988, 1990). Very many undiagnosed illnesses, inexplicable deaths and conditions in humans, especially in the under-developed and developing economies of the world, may be related to the consumption of unapproved herbal preparations or products such as from *A. vera*.

While discussing the need for alternative medical practitioners to give evidence for their acclaimed "alternative" health methods, Smith (1997b) stated that the scientific approach to drug or medicant testing is designed to weed out ideas that users wish were true, but most often are not, or in most cases unproved. Herbalists, naturopaths and even drug companies want their products used and sold, but they have to prove that these drugs work and are safe enough (Smith, 1997b). Skeptics may not be willing to accept the plausibility of most paranormal claims, especially in the case being discussed here, unless the evidence is extremely strong, hence the saying that "extraordinary claims demand extraordinary proof" (Gracely, 1998) is justifiable.

In conclusion, the oral consumption of raw *A. vera* leaves, especially when unrecommended, should be discouraged (or at best handled with utmost caution) because of its potential deleterious effects on human and animal health and productivity. It is therefore recommended that the appropriate Food and Drug Regulatory bodies in the country should closely monitor and regulate the administration of *A. vera*, in any form. The dumping into our land and water bodies of *A. vera* "wastes" by those who cultivate and "process" the plant should be discouraged in order to prevent the bioaccumulation and magnification along food

chains of *A. vera*'s toxic constituents, and hence cause mass mortality and morbidities in man and animals. Mass education and the provision of adequate and accessible basic medicare to the people are also very imperative. It is to be noted that the areas (or situations) where alternative therapies seem to have most appeal is in the very ones where conventional therapies are either not available, or are not able to satisfy the expectations of the consumer (Alcock, 2001). Even when available, it may be too expensive and unaffordable by the less privileged.

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