academicJournals

Vol. 14(30), pp. 2395-2399, 29 July, 2015
DOI: 10.5897/AJB2015.14766
Article Number: 88949A854465
ISSN 1684-5315

http://www.academicjournals.org/AJB

African Journal of Biotechnology

Full Length Research Paper

Assessment of the safety of aqueous extract of *Aloe vera* on haematology of Wistar rats

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Received 30 May, 2015; Accepted 20 July, 2015

***Aloe vera* is used both traditionally and packaged commercially in many regions of the world for several medicinal and or cosmetic purposes. It is claimed to have rejuvenating, moisturizing, healing or soothing properties on the skin and gastrointestinal tract. This study focused on assessment of the safety of *A. vera* on blood parameters: packed cell volume (PCV), red blood cell count (RBC), haemoglobin concentration, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, white blood cell count (WBC), its differentials neutrophils, lymphocytes and platelet counts. Thirty Wistar rats were equally and randomly divided into 3 groups and *A. vera* extract solution was administered to 2 groups for 12 or 24 h respectively, for 7 days consecutively. The third group served as control for the experiment. Blood samples were collected on day 8 to determine changes in the haemogram as a basis for toxicity. Rats administered with *A. vera* extract, particularly for 24 h showed increased levels of PCV (47.42±4.32%), RBC (9.26±0.60 X10^6/µL), WBC (12.61±0.45 X10^3/µL) and its differentials. Platelet count was also significantly increased (150.25±4.77 X10^9/L). The results from this study showed that *A. vera* stimulated increased production of all blood cell types. In conclusion, protracted consumption of the extract of *A. vera* cause stimulation of haematopoiesis which may induce or encourage the progression of haemoproliferative disorders.**

Key words: *Aloe vera*, haematology, Wistar rat.

INTRODUCTION

Aloe vera is a naturally occurring plant with succulent leaves, originating from Northern Africa (Akinyele and Odiyi, 2007). The whole leaves or juice from the leaves has been used in several cultures of the world dating back to the first century A.D. as herbal remedy for various skin conditions (Boudreau and Beland, 2006; Akinyele and Odiyi, 2007). It is being packaged and marketed alone or in combination with other substances in commercially available lotions, creams, yogurt, beverages and as desert. It is claimed to have rejuvenating, moisturezing, healing or soothing properties on the skin and gastrointestinal tract (Davies et al., 1989; Heggers et al., 1997; Vogler and Ernst, 1999; Boudreau and Beland, 2006). Preliminary reports have also been documented on its blood glucose and lipid lowering effects, suggesting possibility of its use as an anti- diabetic agent (Nassiff et

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al., 1993; Boudreau and Beland, 2006; Choudhary et al., 2014; Alinejad-Mofrad et al., 2015). Reduction of symptoms and inflammation in patients with ulcerative colitis has also been suggested amongst other medicinal uses (Langmead et al., 2004; Bottenberg et al., 2007).

Aloe vera is a stem-less or very short-stemmed succulent plant growing to 60–100 cm (24–39 in) in height and spreading by offsets. It has fleshy, thick leaves which are usually green to grey-green in colour, with some varieties showing white flecks on the upper and lower stem surfaces (Gao and Xiao, 1997; Wang et al., 2004). The margin of the leaf is serrated and has small white teeth. It has pendulous flowers which are produced in summer season and these may reach up to 90 cm (35 in) tall. The flowers have a yellow tubular corolla, 2–3 cm (0.8–1.2 in) in length. Like other *Aloe* species, *A. vera* forms arbuscular mycorrhiza, a symbiosis that allows the plant better access to mineral nutrients in soil (Gong et al., 2002).

Most evidences of the activities of *A. vera* cannot be substantiated as little scientific evidence exist on its effectiveness or safety for the medicinal or cosmetic purpose for which it is used (Cosmetic Ingredient Review Panel, 2007). The few scientific reports however, showed conflicting evidences (Vogler and Ernst, 1999; Ernst, 2000; Marshall, 2000; Boudreau and Beland, 2006). Some conflicting reports on its wound healing ability were documented by Heggars et al., (1997) and Davis et al. (1989) who reported that *A. vera* promoted wound healing, while Schmidt and Greenspoon (1991) and Kaufman et al. (1988) reported the contrary.

There are little or no reports on the effect of the plant on the blood, the vehicle of transportation of most substances. Some information of its effect on blood cells may give some insight on safety of the plant on blood cells and related organ tissues. This study was therefore designed to determine the effect of sub-chronic administration of *A. vera* on the haemogram using assessment of changes in the pack cell volume, various red and white blood cell indices and platelet counts.

MATERIALS AND METHODS

Preparation of *Aloe vera* juice

Fresh leaves of *A. vera* were plucked daily and washed. The juice was expressed by gentle milking downwards. Daily water intake of the rats was determined during the acclimatization period to be approximately 40 ml per rat per day. The fresh juice was reconstituted to 46.20 mg/ml in fresh drinking water and served to rats unprocessed. This study was carried out in September, 2012 in South West, Nigeria.

Experimental animals

Thirty male Wistar rats (140 – 160g) were obtained from the Experimental Animal Unit of the Faculty of Veterinary Medicine. The animals were housed in 12 h light: dark condition and maintained on standard rat diet. Clean water was provided *ad libitum*. The animals were stabilized for 4 weeks before commencement of the experiment. All the rats were humanely managed and the study protocols were in compliance with the Faculty of Veterinary Medicine guidelines for the use of laboratory animals.

Experimental protocol

Thirty rats were randomly and equally divided into 3 groups of one control and two treatment groups. The rats in the control group were allowed free access to clean water throughout the course of the experiment. Clean water was withdrawn from rats in treatment groups 1 and 2, and replaced with the *A. vera* solution for 12 and 24 h respectively, for 7 days consecutively. For the 12 h exposure group, half of the daily water requirement was reconstituted with *A. vera* and offered for 12 h , while fresh clean drinking water was offered for the remaining 12 h.

Sample collection

On day 8, the rats were anaesthetized using anaesthetic ether and blood samples were collected from each rat via the retro-orbital sinus. About 3 ml of blood was collected into Lithium heparinized bottles for haematological analysis by Cole's method (Cole, 1986).

Statistical analysis

All values are expressed as mean ± S.E.M. Data obtained were analyzed using one-way analysis of variance (ANOVA), followed by Tukey post-test. Differences between means were considered significantly different when values $p<0.05$ were obtained using Graph-Pad Prism software Version 5 (2007).

RESULTS

Packed cell volume (PCV)

An increase in the PCV of rats administered with the extract of *A. vera* was observed with a significant ($p<0.05$) increase in rats administered with the extract for 24 h (47.42±4.32%) when compared to the control rats (41.75±2.17%) (Table 1).

Red blood cell indices

Red blood cell count (RBC) of rats administered with the extract increased from $8.22±1.57 \times 10^6$/µL observed in the control rats to 8.97±0.16 and $9.26±0.60 \times 10^6$/µL observed in rats administered with the extract for 12 and 24 h respectively. Increases were also observed in the haemoglobin concentration of the treated rats with a significant ($p<0.05$) increase in rats treated for 24 h (16.31±0.68 g/dl) compared to the control rats (13.88±0.89 g/dl). Other red cell indices also increased accordingly (Table 1).

White blood cell indices

White blood cell count (WBC) and the differential cell

Table 1. Packed cell volume and red blood cell indices obtained from rats administered with *Aloe vera* for 12 or 24 h of seven consecutive days.

Haematological parameters	Control	12 h	24 h
PCV (%)	41.75±2.17	43.30±1.43	47.42±4.32*
RBC (X10^6/µL)	8.22±1.57	8.97±0.16	9.26±0.60
Hb (g/dl)	13.88±0.89	14.25±0.41	16.31±0.68*
MCV (*f*l)	50.79±4.05	48.27±2.00*	51.21±1.21
MCH (ρg)	16.89±0.65	16.38±0.34	17.61±0.29
MCHC (g/dl)	33.25±0.41	30.39±0.26	34.39±0.22

*Significant ($p<0.05$) difference compared to control value.

Table 2. White blood cell indices and platelet count of rats administered with *Aloe vera* for 12 or 24 h of seven consecutive days.

Haematological parameters	Control	12 h	24 h
WBC (X10^3/µL)	8.70±0.27	9.48±0.67*	12.61±0.45*
Lymphocytes (X10^3/µL)	4.77±0.49	5.53±0.31	8.35±0.12*
Neutrophils (X10^3/µL)	2.23±0.25	2.93±0.14	4.34±0.13*
Eosinophils (X10^3/µL)	0.13±0.01	0.19±0.05	0.28±0.05*
Neutrophil/ Lymphocte ratio	0.47±0.01	0.53±0.05	0.52±0.02

*Significant ($p<0.05$) difference compared to control value.

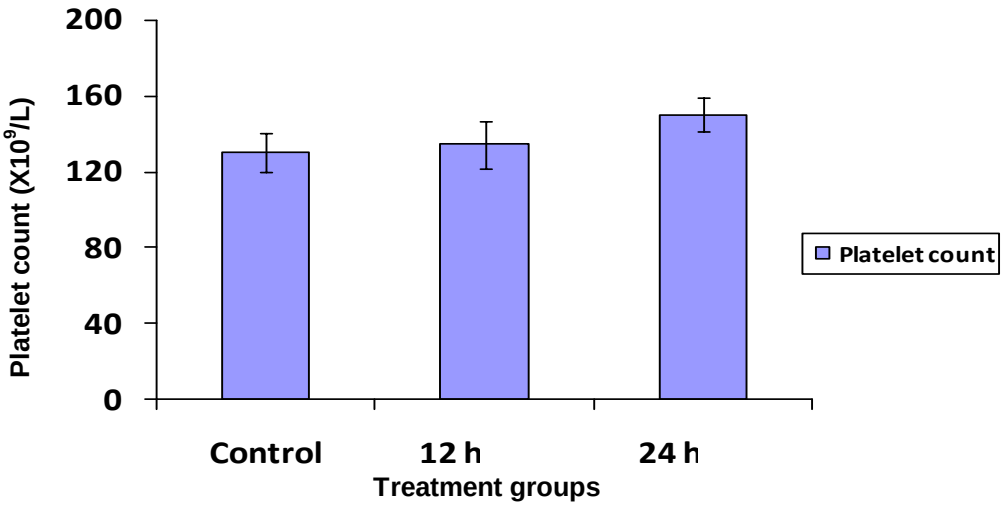

Figure 1. Mean platelet count of rats administered with aqueous extract of *Aloe vera* for a 12 or 24 h period of 7 consecutive days.

count of rats administered with *A. vera* extract increased compared to those of the control rats. Notably, WBC in rats treated for the 24 h period (12.61±0.45 ×10^3/µL) was significantly ($p<0.05$) higher than that of control rats (8.70±0.27 ×10^3/µL). The same significant ($p<0.05$) pattern was observed for the differential cell count of these rats treated for 24 h (Table 2).

Platelet count

Platelet counts were non-significantly ($p>0.05$) increased in the rats treated for 12 h (134.2±1.24 × 10^9/L) but significantly ($p<0.05$) increased in rats treated for 24 hours (150.25±4.77 × 10^9/L) compared to the control rats (130.01±2.31 × 10^9/L) (Figure 1).

DISCUSSION

In this study, rats administered with the aqueous extract of *A. vera* had increased values of the packed cell volume (PCV), red blood cell counts and other red cell indices. A significant ($p<0.05$) increase in PCV was observed in rats administered with the extract for the period of 24 h. This increase in PCV was not due to haemoconcentration because there was a generalized increase in red and white blood cells, but can be attributed to stimulation of haematopoiesis. This can further be related to the result of the red cell indices; increased MCV, MCH and MCHC, which showed that immature red cells were present in circulation, indicative of stimulation of production of immature erythrocytes, also known as reticulocytes. Morphologically, reticulocytes are characterised by increases in the size of red cells in circulation and it is usually observed as the initial response to stimulation of the haematopoietic system during active blood regeneration (Saba et al., 2009). *Telfaria occidentalis* leaves which are consumed in soups in several regions of West Africa had also been reported to have haematopoietic stimulatory ability and it is used traditional for treatment of anaemia (Alada, 2000; Dina et al., 2000).

White blood cells on the other hand showed significant ($p<0.05$) increases, particularly in rats administered with the extract for 24 h. About 2-fold increment in lymphocyte and neutrophil counts were observed in these rats. Lymphocytosis may be associated with increased immunological response to an antigenic stimulation, while the neutrophilia may be traced to increased inflammatory response in the body (Guyton and Hall, 2006a, b). Increased circulating neutrophils are usually as a result of mobilization of neutrophils into circulation in response to an antigenic stimulation. Such stimulants include trauma and bacteria endotoxins (Zekonis and Zekonis, 2004; Tang et al., 2010), of which the extract is neither. From the result obtained for this study, it can be postulated that *A. vera* may contain bioactive substances which are capable of mobilizing all blood cell types into circulation, and or stimulate haematopoiesis resulting in increased production/ release of blood cells into circulation. Our argument favours the haemopoietic theory more, considering the fact that neutrophil: lymphocyte ratios, a marker of subclinical inflammation, were approximately 0.5 in control and test groups, which were clinically and statistically non-significantly different (Sen et al., 2013; Wang, 2014).

Platelet counts were non-significantly ($p>0.05$) increased in the rats administered with the extract for 12 h, but a significant ($p<0.05$) increase was observed in rats administered the extract for the 24 h period. Thus, it can be inferred that blood clotting mechanisms may not be affected by *A. vera* extract, but this corroborates our theory in favour of indiscriminate stimulation of blood cell production.

Administration of the extract for the 12 h period showed minimal haemopoietic ability compared to rats administered with the extract for the 24 h period. A cumulative dose-dependent pattern was established from this study which discourages the continuous consumption of the extract as it is administered for certain traditional uses. The indiscriminate stimulation of blood cells may be detrimental to the body with depletion of haemopoietic stem cells in bone marrow and may eventually trigger or encourage uncontrolled stimulation of haemopoiesis which can be seen in cases of myeloproliferative disorders (Tefferi and Vainchenker, 2011; Barbui et al., 2013).

Conflict of Interest

The authors disclose that they do not have any conflict of interest.

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