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Hematological evaluation of *aloe vera* (L.) burm.f and vitamin E

Nuzhat Sultana[1]*, Rahila Najam[2]

[1]Department of Pharmacology, Faculty of Pharmacy, University of Karachi, Karachi-75270, Pakistan.
[2]Department of Pharmacology, Faculty of Pharmacy, University of Karachi, Karachi-75270, Pakistan.

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Abstract

Aloe vera and vitamin E (natural antioxidants) are traditional medicine used to treat various disorders. The purpose of the study was to evaluate the hematological profile of herbal drugs. Drugs were showing the significant increase in hemoglobin concentration and erythrocyte count. In addition, *Aloe vera* and vitamin E (alpha-tocopherol) reduced the platelets count at long-term administration and increase in the bleeding time. Herbal drugs take part in the prevention of free radical formation and reduced the production of reactive oxygen specie by NADPH Oxidase and then prevent the rupture of erythrocytes by free radicals, thus improve the integrity of erythrocyte by decreasing the fragility of erythrocytes and maintain erythrocyte count and hemoglobin level. It suggested that pretreatment of *Aloe vera* and vitamin E have protective role in anemia against oxidative stress and have free radical scavenging activity after long- term administration.

INTRODUCTION

About 400 species of *Aloe vera* (L.) Burm.f (Aloe barbadensis Mill) or Lily of Desert, family *Liliacea* are found but few of them are used for the prevention and treatment of diseases [1-2] and has medicinal value [3]. It is a succulent plant [4] with total solid ranges 0.5 1.5%. Inner and outer portion of *Aloe vera* contains various constituents such as flavonoids, aloe-emodin. Inner portion of *Aloe vera* contained gel or mucilage which is a clear, tasteless and thin substance [5] and outer portion under the green rind is bitter and pale yellow latex is present [6].

Aloe vera contains at least 75 bioactive constituents [7-8] few are polysaccharides, glycoprotein [9], flavonoids [10], Aloesin [11], saponins [12], antioxidant Vitamins A, B_2, B_{12}, C and E [13] and amino acids [14]. *Aloe vera* mucilage consists 22 amino acids in which eight are essential amino acids and body cannot synthesize these amino acids [15].

Aloe vera helps in chronic wound healing [16], use as an anticancer agent [17]. Acemannan is a polysaccharide found in *Aloe vera* and acts as an immune stimulant against psoriasis vulgaris [5]. Aloin or barbaloin obtained from *Aloe vera* is a bitter, yellow-brown colored crystalline compound. It increases peristaltic movement by preventing the re-absorption of water and produces laxative effect [18].

Anthraquinone has free radical scavenging activity [19] Aloe emodin is responsible for the strong laxative action and found in adult plant not in natal plant [20] but removed during processing because of its laxative effect [21]. Furthermore, Anthronol, Barbaloin, Isobarbaloin are also found in large quantities in *Aloe vera* [22].

In addition, *Aloe vera* gel provides cellulose, hemicelluloses and mannans for skin growth and repair [23]. For anti-inflammatory effect, carboxypeptidase is responsible to inactivate the bradykinin found in *Aloe vera.* Sistosterol, Campesterol are the derivatives of Sterol found in *Aloe vera* and involved in reduction of edema [24]. Plant has analgesic activity [25]. In addition, *Aloe vera* helpful against allergic reaction and itching.

Aloe vera provides antimicrobial [26-27], hypoglycemic effect [28], antioxidative [29], stimulates uterine contraction [2] and anti-pruritic activities [30].

Natural antioxidant vitamin E found in some food, added to others, and available as a dietary supplement. Vitamin E is a group of fat-soluble vitamin exists in eight chemical forms (alpha-, beta-, gamma-, and delta- tocopherol and alpha-, beta-, gamma-, and delta- tocotrienol) that have varying levels of biological activity. Alpha-tocopherol is the most prevalent [31], responsible to stops the reactive oxygen production [32] and protect the cell membranes from oxidative damage has neurological functions as well [33], acts as an antioxidant [34]. In addition, vitamin E is a platelets aggregation inhibitor [35].

MATERIALS AND METHOD

Selection of Animals

Long-term administration of *Aloe vera* and vitamin E carried out on rabbits and the average weight of animals ranging from 1000-1790 gm with equal sex distribution. All rabbits were randomly assign into three groups each containing ten animals, one group of animals served as control group, while other two groups of animal served as treated group as *Aloe vera* and vitamin E groups. All procedures and protocols were follow in accordance with guiding principles in the care and use of animals, Helsinki declaration, 1964 [36].

Housing

Rabbits were maintain in 22±1 °C room temperature with twelve-twelve hours light and dark cycle i.e. light on from 07.00 a.m to 07.00 p.m at the Department of Pharmacology, University of Karachi and had access to water and food *ad labitum. They were housed two per cage in under standard environmental conditions and kept at least one week before start of experiments.*

Experimental Protocol

Aloe vera and vitamin E were purchase from the market in the form of capsule. Hematological study of *Aloe vera* (500 mg-orally) [37] and vitamin E (400IU, orally) [38] done daily for a period of 30 days according to the body weight of animals. The

control group received 0.01 ml saline (0.9% NaCl) by the same route as the treated groups.

Hematological study

Blood samples were collected at 7th , 15th and 30th day of dosing of *Aloe vera* in vacuum blood collection tubes i.e Ethylene-Diamine-Tetra-Acetic acid vacuette (EDTA.K3) for hematological examination and tested hemoglobin concentration , erythrocyte count, hematocrit (*HCT*) or packed cell volume (*PCV*), mean corpuscular volume (MCV), *mean corpuscular hemoglobin* (MCH), *mean corpuscular hemoglobin concentration* (MCHC), leukocyte and platelet count by automatic Humacount plus (3 part differential with histogram, Hematology analyzer. model # 6400/S, Human Germany).

Statistical Analysis

All results were express as average value ±standard deviation (St.Dev). Newman [39] and Keuls [40] Test determined the significance of difference between averages. The data obtained from present study was analyze for P-value < 0.01 was considered significant and P-value < 0.001 was considered highly significant, following the one way ANOVA.

RESULTS

Effect on Haemoglobin

Post-hoc analysis by Newman Keuls test shows that animals at 15 days of dosing of *Aloe vera* showed highly significant increase in haemoglobin (12±0.04 g/dl) and animals at 07 and 30 days of dosing of *Aloe vera* showed non - significant increase in haemoglobin (9±1.2 and 10±1.9 g/dl respectively) whereas vitamin E animals group showed highly significant increase in Hemoglobin (9.68±0.007 g/dl) in comparison to control animals group (8.0±0.04 g/dl - Figure 1)

Effect on Erythrocytes count

Post-hoc analysis by Newman Keuls test shows that animals at 15 days of dosing of *Aloe vera* showed highly significant increase in erythrocytes count (5.6±0.03 million/µl) and animals at 07 and 30 days non - significant increase in erythrocytes count (4.42±0.6 and 4.7±0.9 million/µl respectively) whereas vitamin E animals group showed highly significant increase in erythrocytes count (5.6±0.07 million/µl) in comparison to control animals group (3.94±0.005 million/µl - Figure 2).

Effect on Hematocrit (HCT/PCV)

Post-hoc analysis by Newman Keuls test shows that animals at 15 days of dosing of *Aloe vera* showed highly significant increase in hematocrit (36±0.2 %) and animals at 07 and 30 days of dosing of *Aloe vera* showed non - significant increase in hematocrit (26±2.6 and 29±5.3 % respectively) in comparison to control animals group (25±0.04 % - Figure 3).

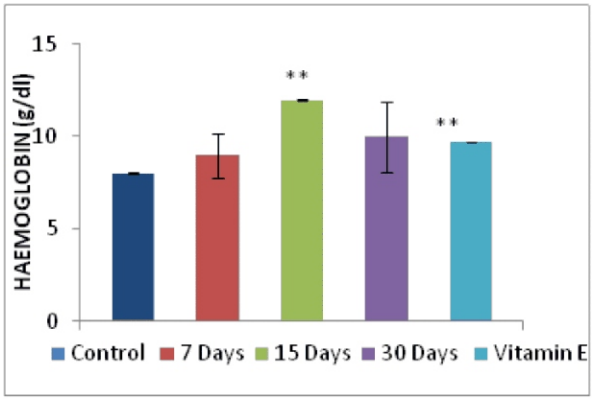
Effect on MCV

Post-hoc analysis by Newman Keuls test shows that at 07 and 30 days of dosing of *Aloe vera* showed significant decrease in MCV (60±2.2 and 61±1.4 fl respectively) and at 15 days of dosing of *Aloe vera* showed non - significant decrease in MCV (63±0.1 fl) in comparison to control animals group (64±0.04 fl- Figure 4).

Effect on MCH

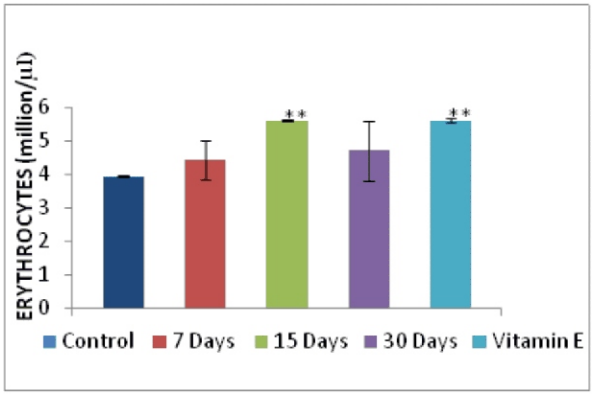
Post-hoc analysis by Newman Keuls test shows that animals at 15 days of dosing of *Aloe vera* showed highly significant increase in MCH (22±0.004 pg) and at 07 and 30 days of dosing of

Figure 1 : Effect of Aloe vera and vitamin E on Hemoglobin in different days of dosing



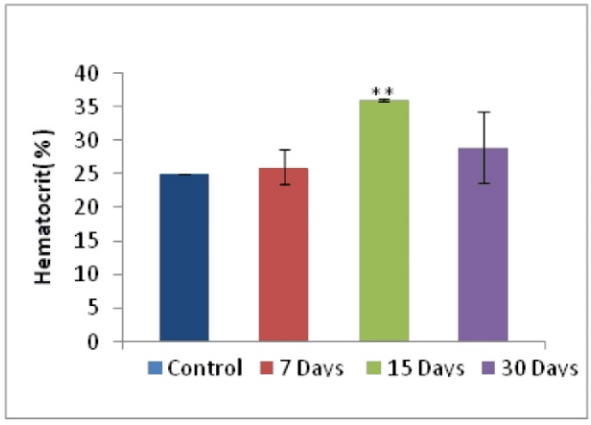
n = 10, Average value ± St. Dev
Significant difference by Newman Keuls test
**p < 0.001 as compared to control rabbits, following one way ANOVA

Figure 2 : Effect of Aloe vera and vitamin E on Erythrocytes count in different days of dosing



n = 10, Average value ± St. Dev
Significant difference by Newman Keuls test
**p < 0.001 as compared to control rabbits, following one way ANOVA

Figure 3 : Effect of Aloe vera on Hematocrit (HCT/PCV) in different days of dosing



n = 10, Average value ± St. Dev
Significant difference by Newman Keuls test
**p < 0.001 as compared to control rabbits, following one way ANOVA

Aloe vera showed highly significant decrease in MCH (20±0.1 and 20±0.2 pg respectively) in comparison to control animals group (20±0.04 pg - Figure 5).

Effect on MCHC

Post-hoc analysis by Newman Keuls test shows that animals at 15 and 30 days of dosing of *Aloe vera* showed highly significant increase in MCHC (34±0.1 and 33±0.3 g/dl respectively) and at 7 days of dosing of *Aloe vera* showed significant increase in MCHC (33±1.1 g/dl) in comparison to control animals group (32±0.04 g/dl - Figure 6).

Effect on Leukocytes count

Post-hoc analysis by Newman Keuls test shows that animals at 07 days of dosing of *Aloe vera* showed highly significant decrease in leukocytes count [2.6±0.05 (10^9/l)] and at 15 and 30 days of dosing of *Aloe vera* showed non - significant decrease in leukocytes count [4.0±0.6 and 4.1±0.6 (10^9/l) respectively] whereas vitamin E animals group showed non - significant decrease in leukocytes count [4.87±0.007 (10^9/l)] in comparison to control animals group [4.8±0.05 (10^9/) Figure 7].

Effect on Platelets count

Post-hoc analysis by Newman Keuls test shows that animals at 15 days of dosing of *Aloe vera* showed highly significant increase in platelets count [656±28 (10^9/l)] , at 30 days of dosing showed highly significant decrease in platelets count [250±0.7 (10^9/l)] and at 07 days of dosing of *Aloe vera* showed significant decrease in platelets count [305±57.0 (10^9/l)] whereas vitamin E animals group showed significant decrease in platelets count [396.6±0.01 (10^9/l)] in comparison to control animals group [416±0.04 (10^9/l) Figure 8] .

DISCUSSION

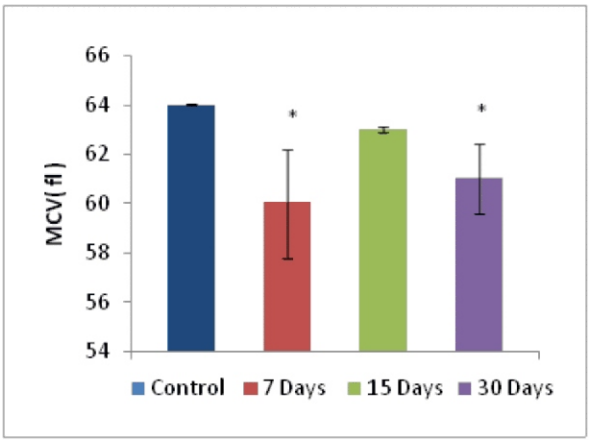
Currently investigated plant showed highly significant increase in haemoglobin concentration and erythrocytes count and these results are similar to the results of vitamin E, which is a known natural antioxidant [41]. *Aloe vera* and vitamin E take part in the prevention of free radical formation and reduced the production of reactive oxygen specie by NADPH Oxidase (nicotinamide adenine dinucleotide phosphate-oxidase) [42] and then prevent the rupture of erythrocytes by free radicals, thus improves the integrity of erythrocyte by decreasing the fragility of erythrocytes and maintain erythrocyte count and hemoglobin level.

Aloe vera has protective effect against systemic toxicity induced by sulfur mustard, prevents the formation of reactive oxygen specie and free radical, and maintains the level of haemoglobin and erythrocytes [43]. Increase concentration of hemoglobin and number of erythrocyte count may be due to reduction in rouleaux formation by *Aloe vera* and vitamin E that reduces the blood viscosity and finally helps in increases the concentration of haemoglobin and number of erythrocyte count.

It could be due to the carbohydrates found in *Aloe vera* such as polysaccharide e.g polymannans and glucomannan and monosaccharide e.g. fructose and glucose [44] and some other carbohydrates such as hemicelluloses [23] have stimulatory effects on hematopoietic system [44].

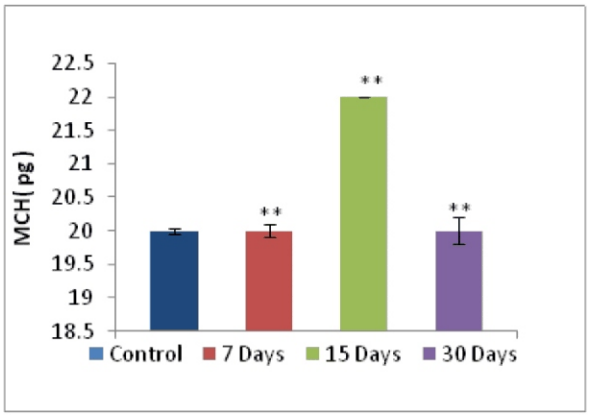
Hematocrit or packed cell volume (HCT/PCV) is the volume of erythrocytes in blood that is normally about 40 - 45% and it is elevated in polycythemia vera in which production of red blood cells increased by bone marrow, also increases in dengue fever or

Figure 4 : Effect of Aloe vera on MCV in different days of dosing



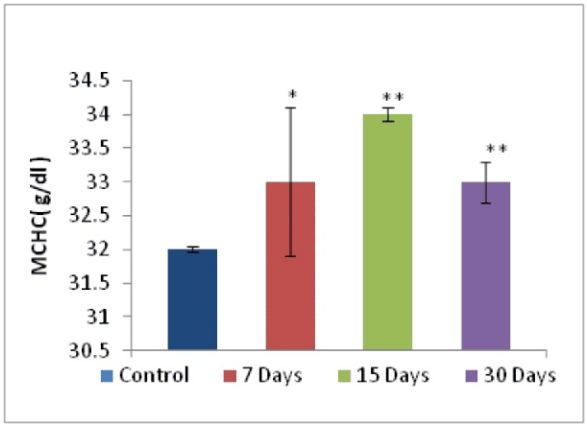
n = 10, Average value ± St. Dev
Significant difference by Newman Keuls test
*p < 0.01 as compared to control rabbits, following one way ANOVA

Figure 5 : Effect of Aloe vera on MCH in different days of dosing



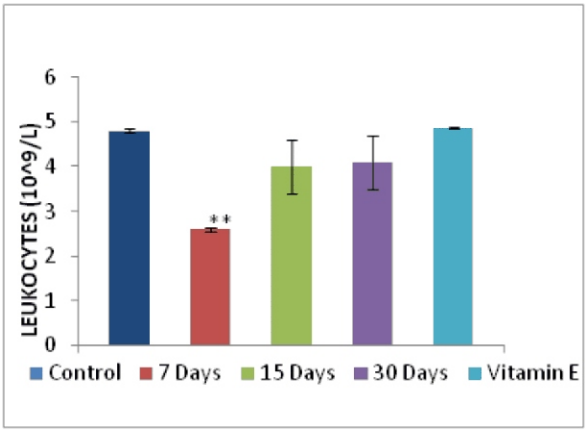
n = 10, Average value ± St. Dev
Significant difference by Newman Keuls test
**p < 0.001 as compared to control rabbits, following one way ANOVA

Figure 6 : Effect of Aloe vera on MCHC in different days of dosing



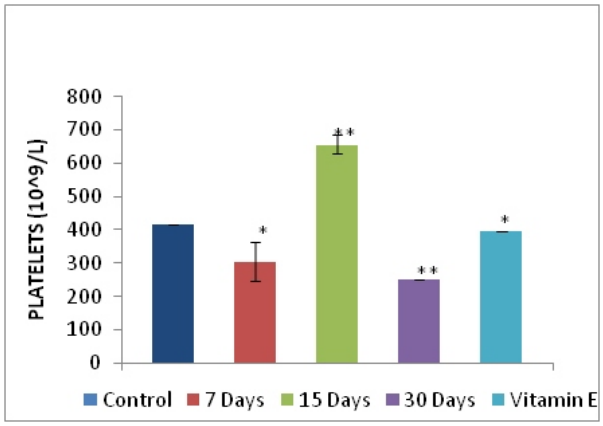
n = 10, Average value ± St. Dev
Significant difference by Newman Keuls test
*p < 0.01 as compared to control
**p < 0.001 as compared to control rabbits, following one way ANOVA

Figure 7 : Effect of Aloe vera and vitamin E on Leukocytes count in different days of dosing



n = 10, Average value ± St. Dev
Significant difference by Newman Keuls test
**p < 0.001 as compared to control rabbits, following one way ANOVA

Figure 8 : Effect of Aloe vera and vitamin E on Platelets count in different days of dosing



n = 10, Average value ± St. Dev
Significant difference by Newman Keuls test
*p < 0.01 as compared to control
**p < 0.001 as compared to control rabbits, following one way ANOVA

if a person dehydrated but chances of hemorrhage will be increased at low level. In *Aloe vera* showed no change in hematocrit or HCT/PCV as compared to the control. *Aloe vera* restores the HCT/PCV value and provides protection in oxidative stress [45].

Average red blood corpuscles volume measurement is the mean cell volume based on the cell size (MCV). In hemolytic anemia, increase number of reticulocytes indicates the elevated MCV. Hence higher MCV than normal is macrocytic anemia, if below than normal is microcytic anemia, and on the normal range is normocytic anemia. Elevated MCV has been associated with folic acid or vitamin B_{12} deficiency and liver enzymes where as low MCV has been associated with inadequate dietary iron intake or GI blood loss.

Investigated plant showed no change in MCV after hematological analysis at long term administration as compared to the control. *Aloe vera* showed protective effect against arsenic induced oxidative stress by restoration of MCV value and responsible for free radical scavenging activity [41]. Some phytochemicals such as triterpenoids, steroids and flavonoids could be involved in antioxidative activity.

The amount of hemoglobin in a red blood cell is MCH, a diagnostic test indicates cause of anemia, if higher MCH than normal is hyperchromic anemia, if below than normal is hypochromic anemia, and on the normal range is normochromic anemia. *Aloe vera* slightly decreases the MCH after 30 days dosing. No significant change occurs on MCH.

Investigated plant showed increase level of MCHC as compared to the control .It could be due to the increase level of hemoglobin and RBC count because *Aloe vera* promotes the hemopoietic system [46]. MCHC or mean cell hemoglobin concentration in packed RBC volume is elevated in sickle cell anemia and spherocytosis.

In current study, *Aloe vera* and vitamin E reduced the platelets count at long-term administration and increase in the bleeding time [11]. Aloesin found in *Aloe vera* inhibits the cycloxygenase (COX_2) and thromboxane (TXA_2) synthase. Both of these enzymes blocked by the action of aloesin skeleton groups known as feruloyl and pcoumaroyl ester groups. Hence, inhibition of these two enzymes result the platelets disaggregation and thus prolong the bleeding [42]. Vitamin E also reduces platelets thromboxane production [47].

CONCLUSION

It concluded that *Aloe vera* and vitamin E have free radical scavenging activity after long- term administration, in addition to increase the hemoglobin concentration and erythrocyte count have protective role in anemia against oxidative stress.

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