

Full Length Research Paper

Effect of Aloe vera (*Aloe barbadensis*) gel extract on repolarization state of myocardium in albino rat

Pradeep Kumar^{1*}, Sadhana Verma², Shraddha Singh¹, Sunita Tiwari¹ and M. Y. Khan²¹Department of Biotechnology, BBA University, Lucknow.²Department of Physiology, CSM Medical University, Lucknow.

Accepted 10 December, 2017

Aloe vera is a well known medicinal plant contents with over 75 different ingredients, anthraquinones, saponins, and sterols. Recent studies showed that it is a potent hypolipemic, hypoglycemic and antioxidant. In present study we investigated the dose dependent effect of aloe vera gel on repolarization state of myocardium, heart rate, QRS complex and QT interval using electrocardiograph in albino rats. A total of 24 male albino rats were divided into four groups, one control and three experimental. An aqueous solution of *Aloe barbadensis* was prepared by taking fresh leaf of aloe plant. Animals of all the groups were anesthetized and were treated (i.p.) with aloe vera gel extract in doses of 100, 200 and 300 mg/kg body weight in experimental groups I, II and III, respectively. Electrocardiograms were recorded at 0 (basal), 15 and 30 min after injection of aloe vera/ saline. Aloe vera in doses of 200 mg increases QTc from 73.10 ± 3.25 (mv) to 75.04 ± 1.93 (mv) and in 300 mg, QTc increased from 72.10 ± 1.85 to 76.10 ± 1.56 which is statistically significant ($p < 0.05$). Higher doses of aloe vera cause prolongation of QTc interval in albino rat. Therefore administration of aloe vera in higher doses may be cardio toxic.

Key words: Aloe vera, ECG, QTc prolongation.

INTRODUCTION

The Aloe vera (*Aloe barbadensis*) traditionally known as *Ghrit Kumari* belongs to the family liliaceae. It contains 99-99.5% water with an average pH of 4.5. The solid material of aloe barbadensis contains over 75 different ingredients including vitamins, enzyme, sugars, anthraquinones, lignin, saponins, sterols, amino acid and salicylic acid (Shelton, 1991). Aloe barbadensis was used by Roman, Greek, and Indian since 2100 BC for their medicinal properties (Amar and Resham, 2008). The anthraquinones present in aloe vera was used as a powerful purgative, laxative, potent antimicrobial and analgesic agent (Ishii et al., 1994; Ndhala et al., 2009). Burn and wound healing effects of aloe vera are very abundant with small quantity of solid material by providing essential micronutrients, anti-inflammatory and

antimicrobial effects (Chithra et al., 1998; Khorasani et al., 2009).

Rajasekaran et al. (2006) reported that in hyperlipidemic patients, aloe vera causes significant decrease in total cholesterol triglycerides and low density lipoprotein (LDL) (Rajasekaran et al., 2006). Other studies with high molecular weight fractions of aloe vera showed beneficial effect on lipid profile as well as serum glucose (Yongchaiyudha et al., 1996; Akira et al., 2005). Rajasekaran et al. (2005) reported that aloe has antioxidant, free radical scavenging and cardio active properties (Rajasekaran et al., 2005).

Various nutritional plants and vegetables exert cardio protective effect, reduce genotoxicity and have no toxicity to animals (Plat and Mensink, 2001; Fujii et al., 2008). On the other hand, cardio toxicity is observed with administration of Ma Huang (a source of ephedra alkaloids) and Caffeine (Dunnick et al., 2007). Multiple organ toxicity is observed with supplementation of

*Corresponding author. E-mail: jenypradeep2002@yahoo.com.

Table 1. Effect of *Aloe vera* gel extract on ECG.

Paper speed 100 mm/s		Control	Group-1	Group-2	Group-3	p value
Basal	QTc ms	71.6 ± 2.24	73.3 ± 1.97	73.10 ± 3.25	72.10 ± 1.85	NS
	QRS ms	55.0 ± 10.0	60.8 ± 11.1	46.6 ± 2.58	49.1 ± 10.6	NS
	H R (bpm)	368 ± 27.6	352 ± 23.8	356 ± 19.9	358 ± 15.6	NS
After 15 min	QTc ms	72.1 ± 1.85	73.4 ± 3.13	74.11 ± 3.45	74.77 ± 2.30	0.03*cont vs gr-3
	QRS ms	55.0 ± 10.0	53.3 ± 9.83	50.8 ± 7.36	52.5 ± 10.3	NS
	H R(bpm)	374 ± 27.1	359 ± 27.7	350 ± 25.4	347 ± 10.5	NS
After 30 min	QTc ms	71.2 ± 3.64	72.7 ± 1.37	75.04 ± 1.93	76.10 ± 1.56	0.02* cont vs gr-3
	QRS ms	55.0 ± 9.17	48.3 ± 6.05	45.8 ± 2.04	50.8 ± 11.5	NS
	H R(bpm)	352 ± 15.1	378 ± 24.8	364 ± 24.2	361 ± 19.2	0.05* cont vs gr-3

anagryne and ammodendrine. *Rhazya stricta* leaves have been proved to be fatal to animal within 24 h (Na, 2008; Adam et al., 2002). Since aloe-vera has been claimed to be useful in various pathological conditions, it is very necessary to rule out the toxicity of aloe barbadensis. QTc prolongation represents the re-polarization abnormalities involving slowly activating potassium channel (Chen et al., 2000). Therefore, in present study we investigated the effect of aloe vera on re-polarization state of myocardium of albino rats.

MATERIAL AND METHODS

A total of 24 male albino rats weighing between 200-250 gm were divided into four groups, one control and three experimental of 6 animal each. Animals were housed in polypropylene cages and kept in a room that was maintained between 28-32°C. The light cycle was maintained and animals were fed with rat feed (Amrut Maharashtra), and water was given *ad libitum*. Animal experiments were conducted in accordance with the institutional ethics committee guideline for the conduct of the experiments on laboratory animals and as per guidelines of CPCSEA India, study was approved by institutional ethics committee.

Aloe vera extract

An aqueous solution of aloe barbadensis was prepared by taking 10 gm of gel from the fresh leaf of aloe plant and dissolved in 100 ml of distilled water. This solution was kept on vortex for 15 min and then solution was filtered and used for the study.

Experimental protocol

Animals of all the groups were anesthetized with Phenobarbitone (25 mg/kg body weight i.p.) and secured on animal operation table for ECG recording. Animal of experimental groups were treated (i.p.) with aloe vera gel extract in doses of 100, 200 and 300 mg/kg body weight in experimental groups I, II and III respectively. The animals of control groups were treated with 2.0 ml solution of normal saline. Electrocardiograms were recorded at 0 (basal), 15 and 30 min after injection of aloe vera/ saline.

Recording of electrocardiogram

The electrocardiogram (ECG) was taken with a paper speed of 100 mm/s at normal filtering using CHARDIART 508 BPL with digital reporting system. QRS duration was defined as the maximum QRS duration in any lead from the first to the final sharp vector crossing the isoelectric line. QT interval was measured from the lead II. QT interval was defined as the interval between the beginning of QRS complex and the end of T wave. The onset and offset of T wave were defined as the intersections of the isoelectric line and the tangent of the maximal slope on the up and down limbs of T wave, respectively. Three consecutive cycles were measured in standard lead-II, and a mean value was calculated from the three values. Rate-corrected QT values (QTc) were derived using the formula (Mitchell et al., 1998) $QTc = QT / \sqrt{RR/100}$ and these were represented as QTc.

Statistical analysis

All data are expressed as the mean ± SD; differences between groups were calculated using SPSS-13 software. The treatment and control group were compared by non parametric analysis.

RESULTS

Non mortality was observed after intraperitoneal injection of anesthesia and/aqua's solution of aloe vera gel in albino rats. Animals become conscious after 6 h of anesthesia, and survived. Electrocardiographic (ECG) parameters were recorded at 0 min (basal), 15 and 30 min after every intervention in all groups; all values of HR, QRS and QTc were shown in Table 1. No significant changes ($p > 0.05$), in base line HR, QRS and QT, were observed in animals of any group. Results suggest that there were no significant changes ($p > 0.05$) in HR, QRS and QTc in control group, at 0 min, 15 and 30 min after intraperitoneal injection of vehicle (2 ml saline).

Effects of aloe vera on Heart rate

In group-I (aloe vera 100 mg/kg body weight) the heart

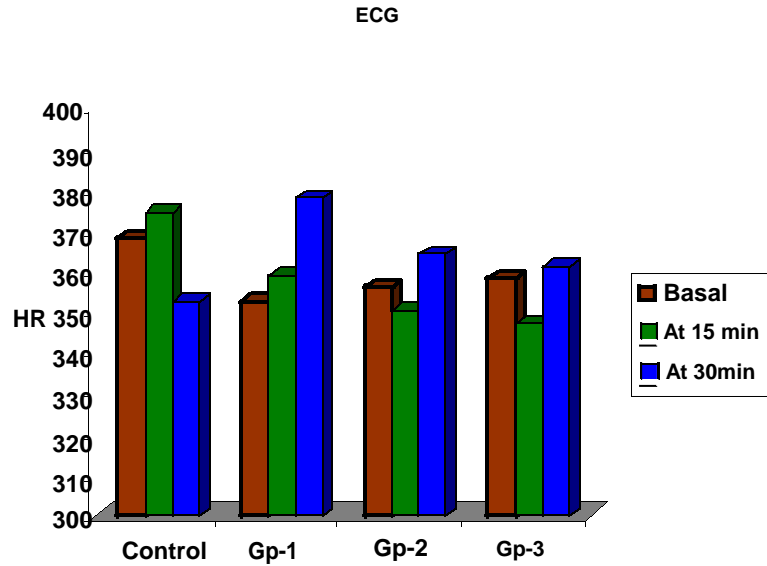


Figure 1. Effect of aloe vera gel on HR.

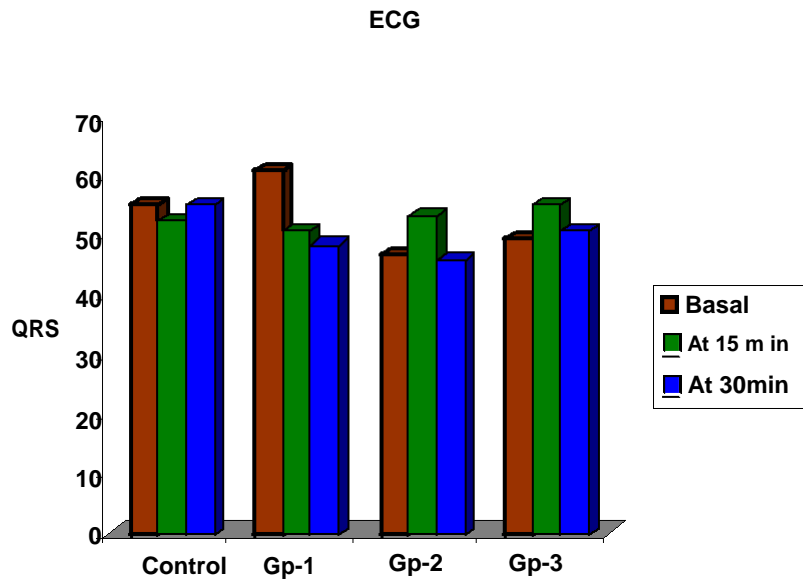


Figure 2. Effect of aloe vera gel on QRS.

rate increases (insignificant $p > 0.05$) from 352 ± 23.8 to 378 ± 24.8 bpm (basal vs. 30 min) after intraperitoneal injection of aloe vera gel. While in groups II and III (aloe vera 200 and 300 mg/kg body wt) the increase of heart rate was also not significant (Figure 1).

Effects on QRS

No significant difference was observed in QRS in vehicle injected animal (control) after 15/ 30 min. In group-I (100

mg aloe vera treated) the aloe vera fails to show any effect after 15 min, but after 30 min non significant reduction is observed in QRS duration. In groups II and III the change in QRS was not significant (Figure 2).

Effects on QTc

The aloe vera gel in concentration of 100 mg/kg body weight does not cause significant changes in QTc. While in doses of 200 mg QTc increases from 73.10 ± 3.25 (mv)

ECG

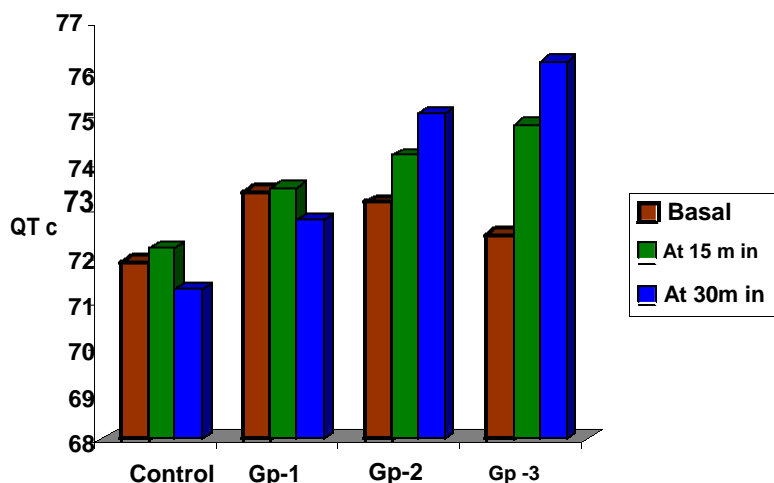


Figure 3. Effect of aloe vera gel on QTc.

to 75.04 ± 1.93 (mv) and in 300 mg QTc increases from 72.10 ± 1.85 to 76.10 ± 1.56 which is statistically significant ($p < 0.05$) (Figure 3).

DISCUSSION

Various studies with oral administration and local application of aloe vera extract/gel and along with other herbs have shown that it has potential role in correction of hyperglycemia, burn injury and ulcers. It also acts as anti inflammatory as well as antioxidant (Ndhlala et al., 2009; Khorasani et al., 2009).

The effects of aloe vera have not been tried in evaluation of electro cardio graphical parameters either in human or in animals. Current study has been planned with objective to elucidate the influence of fresh aloe vera gel on re-polarization state of myocardium in albino rats. Various substances cause re-polarization abnormalities by involving slowly activating potassium channel (Chen et al., 2000). Beta adrenergic stimulation in cardiomyocyte enhances the phosphorylation of K^+ channel via protein kinase (Abriel et al., 2004). Aloe Vera has been proved to stimulate beta receptor in langendorff perfused isolated heart (kumar et al., 2007).

In present study aloe vera gel, in different doses, given to albino rats and its effects on re-polarization state of myocardium was assessed. Corrected QT interval (Qtc) is a marker for re-polarization characteristics of myocardium. Potassium channel sets the membrane potential as well as the excitability of most living cells. The K^+ ions are predominantly responsible for the prolongation of QTc (Finlayson et al., 2004).

In our study low doses of aloe vera does not produce any changes in either in depolarization or re-polarization state of myocardium but in high doses of 300 mg/kg body weight, QTc increases significantly. It showed that aloe vera gel has ability to modulate the activity of K^+ channel either via stimulating the adrenergic receptor or protein kinase, because K^+ channels are responsible for re-polarization. The exact mechanism responsible for QTc prolongation, in high dose of aloe vera gel treated rats, can not be explained with this preliminary study and need further research. But it can be speculated that aloe vera increases QTc via adrenergic stimulation. QTc prolongation is reported to be associated with arrhythmia and sudden cardiac death (Chih- Sheng et al., 2007; Gamal et al., 1995; Carella et al., 1996). Therefore, in high doses aloe vera may be cardio toxic.

REFERENCES

- Abriel H, Schlapfer J, Keller D, Gavillet B, Buclin T, Biollaz J (2004). Molecular and clinical determinants of drug-induced long QT syndrome: an iatrogenic channelopathy. *Swiss Med. Wkly.*, 134: 685–694.
- Adam SE, Al-Yahya MA, Al-Farhan AH (2002). Toxicity of Nerium oleander and Rhazya stricta in Najdi sheep: hematologic and clinicopathologic alterations. *Am. J. Chin. Med.*, 30(2-3): 255-262.
- Akira Yogi, Sahar Consolini AE, Migliori GN (2005). Cardiovascular effects of the South American medicinal plant *Ceerochia pachystachya* (ambay) on rats. *J. Ethnopharmacol.*, 96(3): 417-422.
- Amar S, Resham V, Suple DG (2008). Aloe vera a short review. *Ind. J. Dermatol.*, 3(4): 163-166.
- Carella MJ, Mantz SL, Rovner DR, Willis PW 3rd, Gossain VV, Bouknight RR (1996). Obesity, adiposity, and lengthening of the QT interval: improvement after weight loss. *Int. J. Obes. Relat. Metab. Disord.*, 20: 938-942.
- Chen CC, Lin YC, Chen SA (2000). Shortening of cardiac action

- potentials in endotoxic shock in guinea pigs is caused by an increase in nitric oxide activity and activation of the adenosine triphosphate-sensitive potassium channel. *Crit. Care Med.*, 28: 1713-1720.
- Chih-Sheng C, Kun-Tai L, Shuo-Tsan L (2007). Effects of atorvastatin on ventricular late potentials and repolarization dispersion in patients with hypercholesterolemia. *Kaohsiung J. Med. Sci.*, 23: 217-224.
- Chithra R, Sajithlal GB, Chandrakasan G (1998). Influence of aloe vera on collagen characteristics in healing dermal wounds in rats. *Mol. Cell Biochem.*, 181: 71-76.
- Dunnick JK, Kissling G, Gerken DK, Vallant MA, Nyska A (2007). Cardiotoxicity of Ma Huang/caffeine or ephedrine/caffeine in a rodent model system. *Toxicity Pathol.*, 35(5): 657-664.
- Finlayson K, Witche HJ, McCulloch J, Sharkey J (2004). Acquired QT interval prolongation and HERG: implications for drug discovery and development. *Eur. J. Pharmacol.*, 500: 129-112.
- Fujii H, Nishioka H, Wakame Magnuson BA, Robertes A (2008). Acute, subchronic and genotoxicity studies conducted with Oligonol, anoligomerized polyphenol formulated from lychee and green tea extracts. *Food Chem. Toxicol.*, 46(12): 3553-3562.
- Gamal A, Gallagher D, Nawras A, Gandhi P, Gomez J, Allison DB (1995). Effects of obesity on QT, RR, and QTc intervals. *Am. J. Cardiol.*, 75: 956-959.
- Ishii Y, Tanizawa H, Takino Y (1994). Studies of aloe. V: Mechanism of cathartic effect. *Biol. Pharm. Bull.*, 17: 651-653.
- Khorasani G, Hosseinimehr SJ, Azadbakht M, Zamani A, Mahdavi MR (2009). Aloe versus silver sulfadiazine creams for second-degree burns: a randomized controlled study. *Surg. Today*, 39(7): 587-591.
- Kumar P, Goyal M, Tiwari S (2007). Positive inotropic and chronotropic effect of aloe vera gel on isolated rat heart. *Ind. J. Pharmacol.*, 39: 249-220.
- Mitchell GF, Jeron A, Koren G (1998). Measurement of heart rate and Q-T interval in the conscious mouse. *Am. J. Physiol.*, 274: 47-51.
- Na EM, Vi O, De H, Oe O (2008). Multiple organs toxicity of a Nigerian herbal supplement (U & D Sweet bitter) in male albino rats. *Pak. J. Pharm. Sci.*, 21(4): 426-429.
- Ndhkala AR, Amoo SO, Stafford GI, Finnie JF, Van Staden J (2009). Antimicrobial, anti-inflammatory and mutagenic investigation of the South African tree aloe (*Aloe barberae*). *J. Ethnopharmacol.*, 124(3): 404-408.
- Plat J, Mensink RP (2001). Effects of plant sterols and stanols on lipid metabolism and cardiovascular risk. *Nutr Metab Cardiovasc Dis.*, 11(1): 31-40.
- Rajasekaran S, Ravi K, Sivagnanam K, Subramanian S (2006). Beneficial effect of Aloe vera leaf gel extract on lipid profile status in rat with streptozocine induced diabetes. *Clin. Exp. Pharmacol. Physiol.*, 33: 232-237.
- Rajasekaran S, sivagnanam K, Subramanian S (2005). Antioxidant effect of aloe of aloe vera gel extract in streptozotocin-induced diabetes in rat. *Pharmacol. Rep.*, 57: 90-96.
- Shelton M (1991). Aloe vera, its chemical and therapeutic properties. *Int. J. Dermatol.*, 30: 679-683.
- Yongchaiyudha S, Rungpitarangs V, Bunyapraphatsara N, Chokeychajaroenporn O (1996). Antidiabetic activity of Aloe vera L. juice I. Clinical trial in new cases of diabetes mellitus. *Phytomedicine*, 3(3): 241-243.