EFFECTS OF AELO VERA EXTRACT ON BLOOD SUGAR OF RABBITS: AN ANIMAL STUDY.

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ABSTRACT

Objectives: To observe the effect of Aloe vera on Blood Sugar on Rabbits (animal models).

Main outcome measures: Level of glucose in blood of animal models in different scheduled stages of the experiment. **Materials and Methods:** This Experimental (Interventional) study was conducted at department of pharmacology Pepoles University of Medical and Health Sciences, Nawabshah (SBA) from April 2019 to September 2019, after the proper approval of Research Ethical Committee of the University. This study was carried out on healthy animal models using rabbits in animal house of Gambat Medical College at Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat District KhairpurMirs'. Adult male and female rabbits ranging from 16 months to 24 months of age. Thirty healthy adult male and female rabbits were selected fulfilling the inclusion and exclusion criteria. Subjects were divided in three groups, Group-A was control group, Group-B was study group-1, served with 200mg/kg of Aloe Vera and Group-C was study group-2 and was served with 400mg/kg of Aloe Vera. Parameters such as Blood Glucose level and feed intake were evaluated at the end of experiment. The data was documented in predesigned structured questionnaire. The data was entered and analysed by using SPSS software version 25.0. **Results:** Blood Glucose level of rabbits showed significant reduction after thirty days of intervention compared with Control Group. Group-B served with 200mg/kg of Aloe vera showed negative correlation with control group on day 30 for both (-0.212 degree of relationship) with p value (p = 0.023). Group-C served with 400mg/kg of Aloe vera also showed negative correlation with control group on day 30 for both (-0.072 degree of relationship) with p value (p = 0.000). This shows that there is statistically significant role of Aloe vera in Glycemic control. **Conclusion:** It was concluded that Aloe vera has good effects in lowering Blood Glucose level of rabbits, if used regularly. Aloe vera can be used as herbal remedy with hypoglycemic drugs in pre-diabetic and diabetic patients to control blood glucose.

Key words: An experimental study, Aloe vera leaves, Rabbits, Blood Sugar, Nawabshah.

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INTRODUCTION

Aloe Vera also known as Aloe barbabadensis Miller is a commonly used plant all over the world. Aloe vera belongs to Liliaceae family originated from South Africa. This plant can grow in dry climate also. Some species out of 400 are considered for commercial importance because is well known for its considerable use as medicine or remedy and is also most important plant in medical research field. The Aloe vera gel has complex chemical composition, it contains 75 potentially active constituents like vitamins, minerals enzymes, sugars, saponins, lignin, salicylic acids, and amino acids[1,2]. It contain vitamins A, C and E which works as antioxidents. Amylases, lipases, alkaline phophatases, cellulases, catalases and peroxidases are biochemical catalysts present in AV that help in food digestion. Many minerals like sodium, calcium, potassium, magnesium, manganese, zinc, selenium, copper, chromium and iron are found in the Aloe plant, required for various metabolic processes in the body[3,4]. Glucose and Fructose (Monosaccharide), Glucomannose and Polymannose (polysaccharide) are positioned in mucilaginous layer act as immune modulators. Glumannan used in cosmetic Products is a good moisturizer.The vinegary reddish yellow exudates anthraquinones and their derivatives are found beneath the outer green peel. Phenolic compounds conventionally known as laxatives, have a potent purgative effect when given in bulky amount. Cholesterol, Campesterol, β-Sitosterol and Lupeol present in Aloe vera have anti- inflammatory, antiseptic and analgesic properties. Auxins and gibberellins are also present in Aloe vera these hormones are helpful in healing of wound and have anti-inflammatory action. Small amounts of aspirin like compound

are found in Aloe vera that maintains anti-inflammatory and antibacterial properties. Aloe vera gel contains the small amount of amino acids, of which about twenty nonessential amino acids and eight essential amino acids. Amino acids are essential for cell repair and growth. Lignin present in AV is used in topical preparation of medicinal and cosmetic products as it enhances penetration effects of other ingredients into the skin. Saponins substance is used in preparation of soaps for cleansing and antiseptic purposes[5-8].

Pharmacological Properties of Aloe Vera:
AV is used in burn and wound healing, active ingredient in preparation of more than ninety five percent of the dermatology products due to its Moisturizing and anti-aging effect. Aloe vera also protects the skin against dangerous effects of radiation by generation of antioxidant properties of protein methallothionein[9]. Aloe Vera relieves pain and discomfort causes by inflammation and also accelerates the wound healing by its anti-inflammatory effects[10]. Aloe vera protects the skin against dangerous effects of Radiation by generation of antioxidant properties of protein methallothionein[11]. AV also has anti-diabetic effect, anti-mutagenic effect, immune modulatory effect and antioxidant property[12]. Gastric Ulcers are also treated with A. vera gel in human as well as animals because of its anti-inflammatory effects and rapid healing properties[13]. Presence of lectins and mucus enhance stimulatory effects and regulation of gastric secretions. Use of A. vera can help to prevent regression of arthritis and pain due to tendinitis. Aloe jel directly penetrates in to the skin at the injury site and relieves local pain by absorbing bio- active ingredients into deep tissue. Potent laxative present in Aloe Anthraquinones stimulate mucus secretion, increases intestinal water content and increases peristalsis of intestine[14].

High Blood Glucose level leading to Diabetes Mellitus is a major public health concern and this high prevalence is due to lack of public knowledge and awareness about the dangers of high carbohydrate and lipids consumption. High sugar foods intake will result in absorption of sugar by insulin-dependent cells such as muscle cells and adipose cells and will increase sugar oxidation rate. In turn, there will be increased production of hydrogen nicotinamide adenine dinucleotide (NADH) and flavin adenine dinucleotide hydrogen (FADH2). Worldwide the prevalence of diabetes all age groups was estimated 2.8 percent in 2000 and it is estimated that it will be more than 5.4 percent in 2025[15]. Pakistan is in the phase of economic and epidemiologic transitions. Rising urbanization has resulted change in life style, lack of exercise and advances food intake and stress has added to increase the prevalence of DM in Pakistan[16,17]. One of the causes of metabolic disorders in Pakistan is due to urban pollution. In Pakistan current prevalence of Diabetes Mellitus is 11.77 percent and is higher in males as compared to females. This disease is more common in urban population than rural population[18].

MATERIALS AND METHODS
The present Experimental (Interventional) study was conducted at the department of Pharmacology at Peoples University of Medical and Health Sciences, Nawabshah over 06 months duration from April 2019 to September 2019. Healthy adult male and female rabbits having ages range from 16 to 24 months and weighing 1.5kg to 2.5kg were selected for study purpose. Animal models were acquired from animal house of Gambat Medical College at Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat District Khairpur Mirs' after taking written permission from administration authorities of the concerned animal house. The animals were kept and maintained in cages especially designed for research purpose, under standard condition of well aerated room temperature of 20^0C to 30^0C with air-conditioning, light/dark cycle of 12 hours of the day under conventional laboratory conditions throughout the study period. Air conditioning was available in animal house and five rabbits were housed in each cage. Each cage was sufficient for five rabbits to live in. Animal models were allowed free access to fresh water and hay.

Thirty Rabbits were selected of 16 to 24 months of age and divided in three groups labeled A, B and C consisting 10 Rabbits in each group[19]. Group A was control group and was served with Hay and fresh water, while group B was study group 1 and was served with 200mg/kg Aloe vera extract along with Hay and fresh water and group C was served with 400mh/kg of Aloe vera with Hay and fresh water and were observed for the period of 30 days[20,21].

PREPARATION OF ALOE VERA EXTRACT: Leaves of Aloe vera were cut down by kitchen knife, than washed and weight was measured, unwrapped and the leaf pulps were scratched with table spoon / knife. Then pulps were mixed to make uniform with grinder / blender machine (Panasonic) than mixed with 0.9 % normal saline in equal quantity and again mixed and filtered with clean fabric. Prepared filtrate was kept at 4^0C in refrigerator for daily use[22,23].

DOSAGE ADMINISTRATION: Handling with care in the aseptic atmosphere with all precautions of any chance of biting from rabbit already weighted leaf extract filtrate of 200mg/kg and 400mg/kg was mixed with tap water in equal quantity. Oral cavity of the rabbits was examined for any infection or ulcer than Group A was served with 200mg/kg and Group B was served with 400mg/kg of Aloe vera filtrate and administered directly into the oral cavity of rabbit by help of feeding syringe and oral cavity was examined for deglutition[19].

BLOOD EXTRACTION: Total of 02cc blood sample was drawn through clear venipuncture from rabbit ear, using the large veins because veins in ear are more prominent and visible. 02cc blood drawn with the help of butterfly needle and syringe and was collected in Vacutainer blood collection tube already labeled with identification code of the subjects and was

immediately carried to Diagnostic Laboratory at Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat District Khairpur Mirs' for the test of Blood Sugar level. Reports were collected from Diagnostic Laboratory and results were recorded on the already designed form.

DATA ANALYSIS PROCEDURE

After collecting laboratory investigation reports from Diagnostic Laboratory in Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat District Khairpur Mirs', the data was processed by hand sorting techniques, calculator, Microsoft office and using statistical program for social sciences (SPSS Version 25).
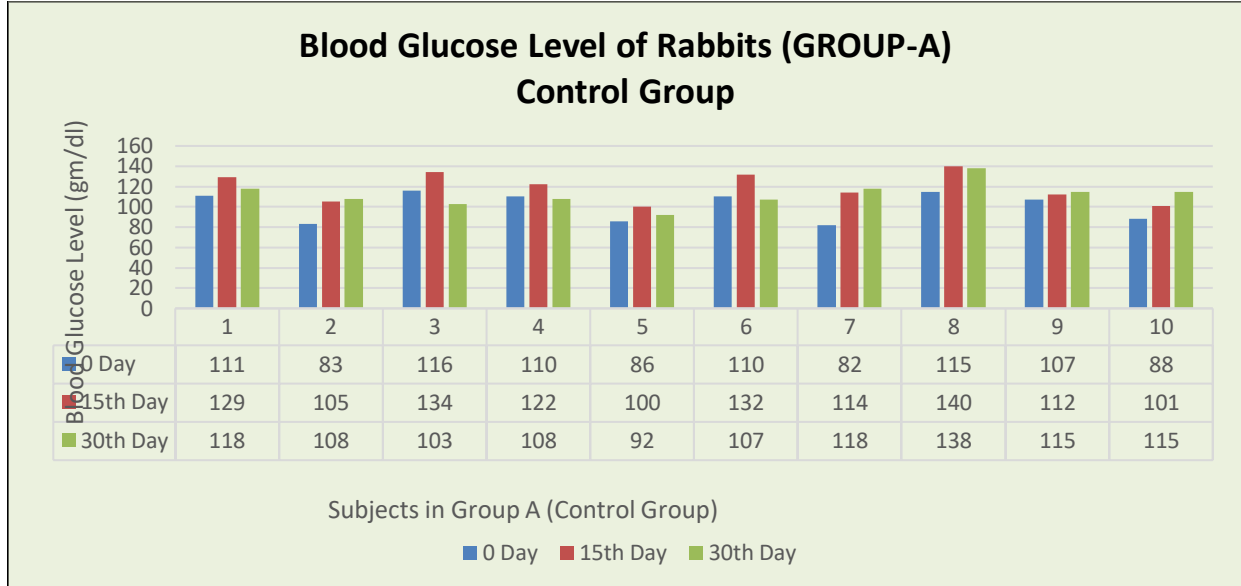
RESULTS

This experimental study was conducted on thirty healthy adult rabbits to observe the effect of Aloe vera on Blood Sugar. Base line data was collected at day regarding age, weight and Blood Sugar level. The prepared Aloe vera extract was given to the experimental groups in quantity 200mg/kg to Group-B and 400mg/kg to Group-C as per schedule. The periodic blood sample was drawn for measurement of Blood Glucose level and weight was measured on three occasions (Day 0, 15 and 30). Data was collected and analyzed by using statistical software SPSS version 25.0.

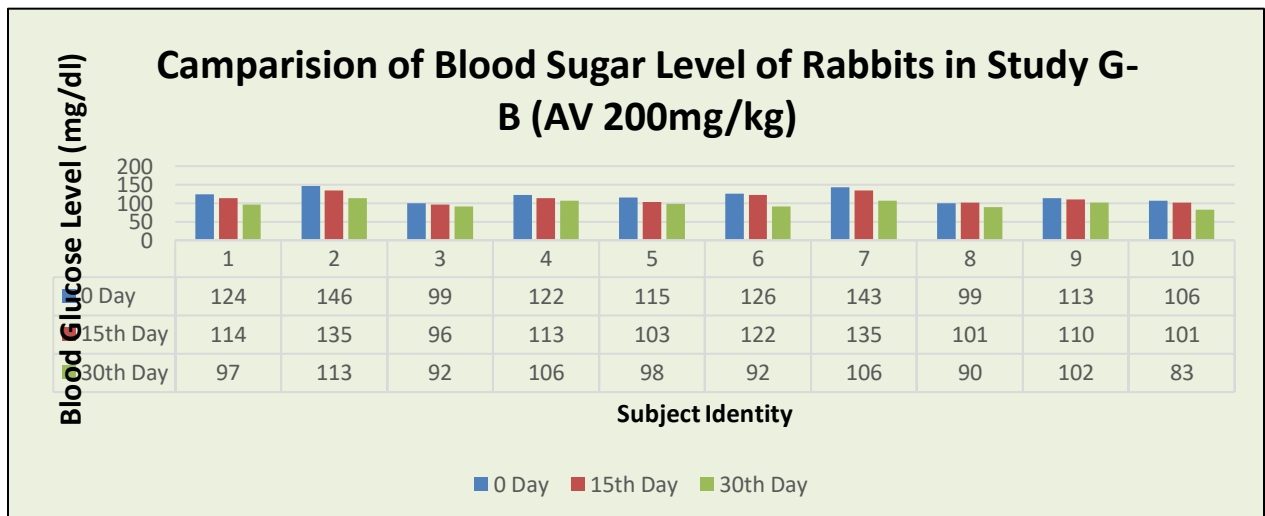|						
Table 01: Baseline data of All Subjects (Rabbits) included in the Study.						
Sr. No.	**Sample Name**	**Group**	**Age (In Months)**	**Data collection days**	**Site of Blood Extraction**	**Any Side Effect**
1	A-1		16	0, 15, 30		No
2	A-2		18	0, 15, 30		No
3	A-3		16	0, 15, 30		No
4	A-4		19	0, 15, 30		No
5	A-5		17	0, 15, 30		No
6	A-6		18	0, 15, 30		No
7	A-7		19	0, 15, 30		No
8	A-8		16	0, 15, 30		No
9	A-9	A	21	0, 15, 30	Ear	No
10	A-10		16	0, 15, 30		No
11	B-1		18	0, 15, 30		No
12	B-2		21	0, 15, 30		No
13	B-3		20	0, 15, 30		No
14	B-4		18	0, 15, 30		No
15	B-5		18	0, 15, 30		Yes
16	B-6		18	0, 15, 30		No
17	B-7		18	0, 15, 30		No
18	B-8		16	0, 15, 30		No
19	B-9	B	18	0, 15, 30	Ear	No
20	B-10		17	0, 15, 30		No
21	C-1		18	0, 15, 30		No
22	C-2		16	0, 15, 30		No
23	C-3		16	0, 15, 30		No
24	C-4		17	0, 15, 30		No
25	C-5		20	0, 15, 30		No
26	C-6		18	0, 15, 30		No
27	C-7		18	0, 15, 30		No
28	C-8		17	0, 15, 30		No
29	C-9	C	16	0, 15, 30	Ear	No
30	C-10		18	0, 15, 30		No

Group-A was control group and was served with Hay and fresh water. Samples were taken on Day 0, Day 15 and Day 30 and Blood Glucose level measured and data was recorded. Mean Blood Glucose level on day 0 was 100.8 gm/dl, on day 15 was 118.9 gm/dl and on day 30 was 112.2gm/dl. Below graph shows blood Glucose level of each subject.

Graph 01: Showing Blood Glucose Level of Rabbits in Group-A (Control Group) taken on Day 0, 15 and 30.

Blood Glucose Level of Rabbits (GROUP-A) Control Group

	1	2	3	4	5	6	7	8	9	10
0 Day	111	83	116	110	86	110	82	115	107	88
15th Day	129	105	134	122	100	132	114	140	112	101
30th Day	118	108	103	108	92	107	118	138	115	115

Subjects in Group A (Control Group)
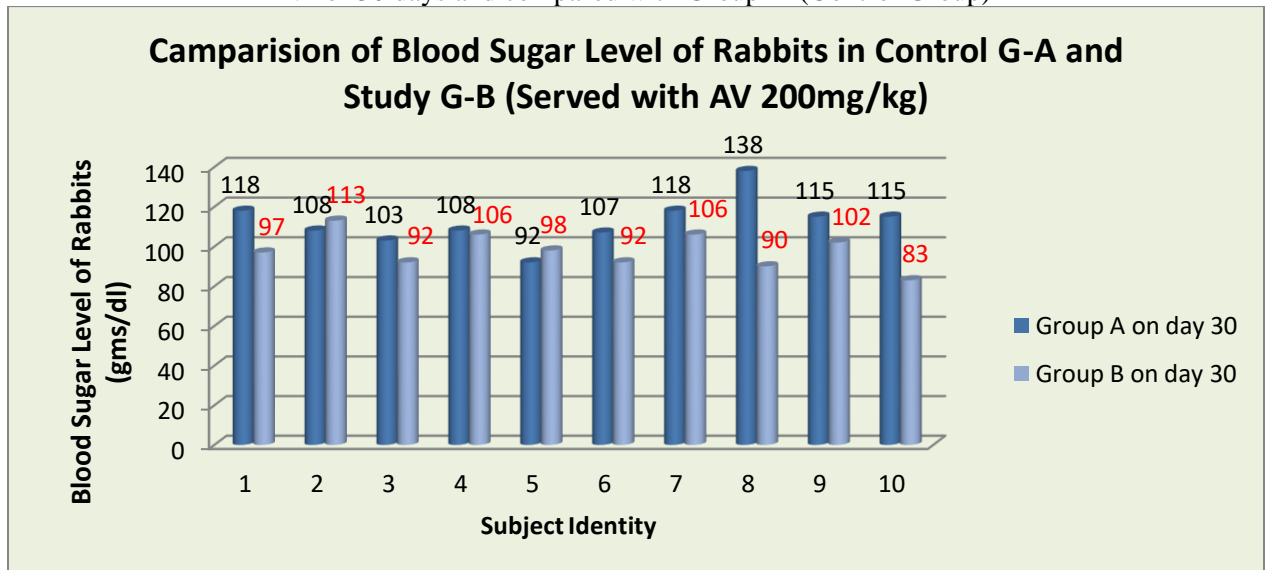
■ 0 Day ■ 15th Day ■ 30th Day

Group-B was study group and was served with 200mg/kg of Aloe vera along with Hay and fresh water Samples were taken on Day 0, Day 15 and Day 30 and Blood Glucose level measured and data was recorded. Mean Blood Glucose level on day 0 was 119.3 gm/dl, on day 15 was 113.0 gm/dl and on day 30 was 97.9gm/dl. Paired sample T-Test was applied and results were analyzed. There is Negative correlation within the Group-B on day 0 and day 30 (0.773 degree of relationship) with p value (p = 0.000).

Graph 02: Showing blood Glucose Level of Rabbits in Group-B (Study group) served with 200mg/kg of AV for 30 days.

Camparision of Blood Sugar Level of Rabbits in Study G-B (AV 200mg/kg)

	1	2	3	4	5	6	7	8	9	10
0 Day	124	146	99	122	115	126	143	99	113	106
15th Day	114	135	96	113	103	122	135	101	110	101
30th Day	97	113	92	106	98	92	106	90	102	83

Subject Identity

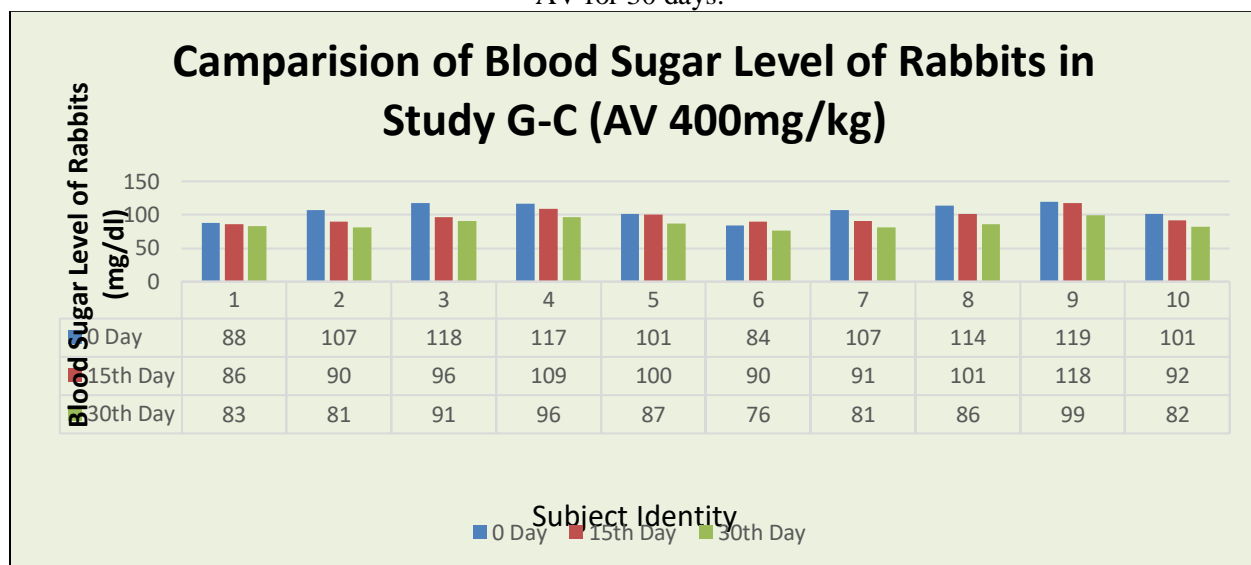■ 0 Day ■ 15th Day ■ 30th Day

Graph 03: Showing Blood Glucose Level of Rabbits in Group-B (Study group) served with 200mg/kg of AV for 30 days and compared with Group-A (Control Group)

Camparision of Blood Sugar Level of Rabbits in Control G-A and Study G-B (Served with AV 200mg/kg)

■ Group A on day 30 ■ Group B on day 30

Subject Identity

Above graph showing the Blood Glucose level of Rabbits in Group B served with 200mg/kg of Aloe vera that compared with Control Group-A. Paired sample T-Test was applied and results were analyzed. There is Negative correlation with control group on day 30 for both (-0.212 degree of relationship) with p value (p = 0.023).

Group-C was also study group and was served with 400mg/kg of Aloe vera along with Hay and fresh water Samples were taken on Day 0, Day 15 and Day 30 and Blood Glucose level measured and data was recorded. Mean Blood Glucose level on day 0 was 105.6 gm/dl, on day 15 was 97.3 gm/dl and on day 30 was 86.2 gm/dl. Paired sample T-Test was applied and results were analyzed. There is statistically insignificant correlation within the Group C on day 0 and day 30 (0.775 degree of relationship) with p value (p = 0.000).

Graph 04: Showing Blood Glucose Level of Rabbits in Group-C (Study group) served with 400mg/kg of AV for 30 days.

Camparision of Blood Sugar Level of Rabbits in Study G-C (AV 400mg/kg)

	1	2	3	4	5	6	7	8	9	10
0 Day	88	107	118	117	101	84	107	114	119	101
15th Day	86	90	96	109	100	90	91	101	118	92
30th Day	83	81	91	96	87	76	81	86	99	82

Subject Identity

Graph 05: Showing Blood Glucose Level of Rabbits in Group-C (Study group) served with 400mg/kg of AV for 30 days and compared with Group-A (Control Group)

Camparision of Blood Sugar Level of Rabbits in Control G-A and Study G-C (Served with AV 400mg/kg)
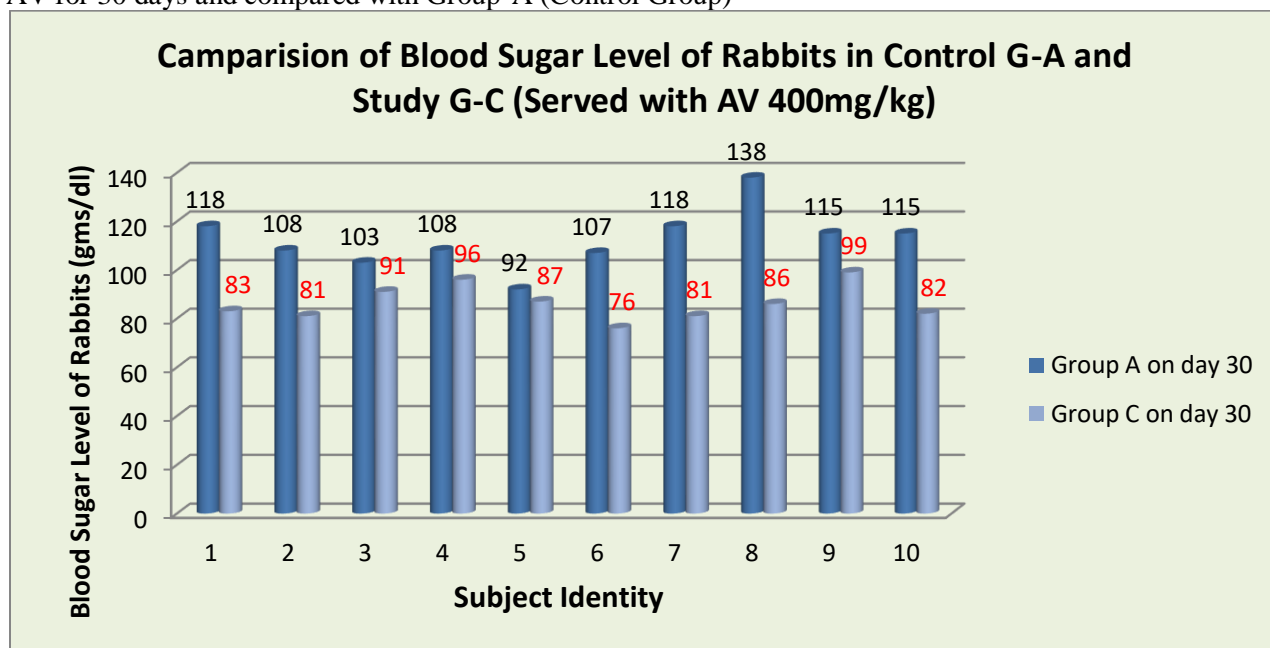
Above graph shows the level of blood glucose of Rabbits in Group C served with 400mg/kg of Aloe vera that compared with Control Group-A. Paired sample T-Test was applied and results were analyzed. There is Negative correlation with control group on day 30 for both (-0.072 degree of relationship) with p value (p = 0.000).

DISCUSSION

Aloe vera is a succulent plant belonging to the family of Liliaceal having more than 360 species. From the inner jel of Aloe vera more than 200 medically important active ingredients have been isolated. AV is rich in different vitamins, minerals, enzymes, amino acids, anthraquinones, fatty acids and natural sugars. It has been from many centuries as Herbal product for a range of conditions/disorders such as healing of wounds especially due to burns, various skin disorders, mild fever, diabetes mellitus, gastrointestinal disorders, cancer, sexual vitality, fertility, immunity modulation, AIDS. Numerous studies have appraised and correlated the effects of Aloe vera in reducing the Blood glucose level in animal models and human studies after the treatment with Aloe vera. The demonstrated hypoglycemic effects in human are consistent with the results in animal studies. Peniati E. et al[24] conducted an experimental study on rats who were made diabetic by induction of drugs for experiment and results showed that Blood glucose level was high in control group as compared with study group who were treated with Aloe vera for 28 days and concluded that orally administration of AV is associated with lowering Blood Glucose level in animals. Our study also showed significant reduction in the level of blood glucose of rabbits after 30 days use of Aloe vera. This is in accordance with that study as well.

An experimental study conducted by Soni Y. et al[15] to see the effects of Aloe vera in elevated level of blood glucose in diabetic and pre

diabetic patients. The results of their study were statistically significant in lowering the blood glucose level. The p-value show highly significant < 0.001 in normal control groups after thirty days consumption of AV and highly significant in diabetic study group p = 0.01 after 60 ml consumption of Aloe vera for thirty days. Significant reductions of Blood glucose level were also observed in our study after consumption of Aloe vera for thirty days.

Another experimental study was conducted by Alinejad-Mofrad S. et al[25] to study the effects of Aloe vera in if improving Blood Glucose and Lipid level in pre-diabetic subjects. This study was double blind randomized clinical trial on human using different doses of Aloe vera 300mg and 500mg in two groups. The results of this study showed statistically significant decrease in fourth week after the intervention compared with control in the same time p-value were highly significant (p = 0.001), Glycosylated hemoglobin (HbA1C) in this group was also decreased and statistically significant (p = 0.042). The level of Cholesterol was also significantly decreased in this group. The study concluded that use of Aloe vera as herbs could revert impaired blood glucose level within four weeks of continuous use. This is also in accordance with this study as well.

Many researchers have claimed the anti-diabetic effects of Aloe vera. Such another study conducted by Cardenas-Ibarra L. at al[26] to establish the relationship of effects of Aloe vera on Blood Glucose level. The study was randomized double blind crossover trial and was conducted on female having early metabolic syndrome. The subjects were given Aloe vera (AG) gel and infusion of Cnidoscolus chayamansa (CC), the effects were observed for four, one, four weeks respectively. The outcome was measured by the level of decrease of Glycosylated Hemoglobin level and results were statistically significant. Mild abdominal pain was noted in subjects after the use of double dose of Aloe vera. From the study data there was significant reduction in Blood Glucose level with the use of Aloe vera juice for four weeks. This is also in accordance with our study as well.

CONCLUSION: Aloe vera is succulent plant found all over the world and traditionally used as herbal remedy for the management of many diseases due to its ethno botanical and pharmacological properties. Based on our research it was concluded that Aloe vera extract have excellent effects in lowering Blood Glucose level of rabbits. Aloe vera can be used as herbal remedy in addition to hypoglycemic drugs in pre-diabetic and diabetic patients. Because of no or few side effects Aloe vera safely can be used for the treatment and control of diabetes with other hypoglycemic drugs.

ETHICS APPROVAL: The ERC gave ethical review approval

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin

AUTHORS' CONTRIBUTIONS: All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST: No competing interest declared.

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