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DEVELOPMENT OF ALOEVERA DRINK AND ITS EFFECT ON OSTEOARTHRITIS

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Abstract

Osteoarthritis is the degenerative disease of cartilage that led to disability which can impair the quality of life of an individual. Aloe Vera contains bradykinin, salicylate, and other natural steroids and vitamins that reduce inflammation. The benefits of using Aloe Vera for osteoarthritis are twofold, since it is an anti-inflammatory agent, and has prophylactic properties against the gastrointestinal irritant effects of non-steroidal anti-inflammatory drugs. The single blinded, randomized controlled trial with the sample consisted of 90 osteoarthritic participants (30 in each group), with age range of 45 to 65-year recruited through purposive sampling, from two public and two private hospitals of Lahore. The participants were randomly divided into three treatment groups including two experimental groups (Group A & B) and one control group (Group C). The individuals in group A were provided aloe-vera drink and group B was provided with placebo drink, the individuals of group C were not provided any drink and they were asked to continue the medical intervention provided by physician. Baseline score of outcomes variables such as pain intensity and functional status was measured through Visual Analogue Scale and Patient Specific Functional Scale respectively. The pain intensity, functional status was again assessed by the assessor at 20th day, 42th day and one month after the discontinuation of treatment. There was significant reduction in pain score and improvement in functional status among the Group A participants were observed. The mean score of pain at VAS of study participants was 5. 2 ± 2.3. There was a significant difference in mean of pain score within- group effect p=0.001 and between-group effect with p= 0.02, which represented that aloe-vera has positive effects in reducing pain score in participants with knee osteoarthritis. A statistically significant within group effect (p=0.000) and between-group effect (p= 0.015) of aloe-vera was found on physical function of participants.

Keywords
Osteoarthritis, aleovera, BMD

1.Introduction

Osteoarthritis (OA) is one of the serious, fourth foremost reason of debility in the world, affecting the middle-aged people. the degenerative disease of cartilage led to the disability which can impair the quality of life of an individual. The prevalence of OA increases with advancing age and females are most commonly affected than male (Choi, Kim, Son, Oh, & Cho, 2013; Zarrintan, Mobasseri, Zarrintan, & Ostadrahimi, 2015). The knee joint is the prime weight-bearing joint of the body. It is the most vulnerable joint to get this disorder in comparison to other joints of body, increased body weight or obesity, lack of physical exercise, drug abuse, and eating habits are the modifiable factors which can be targeted for the management of this disease (Choi et al., 2013). A long list of natural or herbal products are available to alleviate the pain symptoms and stiffness of OA. Aloe Vera is an everlasting, most frequently used herbs in alternative medication known for its therapeutic properties (Sharma, Kharkwal, Kharkwal, Abdin, & Varma, 2014). The chief constituents found in Aloe Vera consist of anthracene, anthraquinone, anthranilic acid, glucosamine and cinnamic acid (Maan *et al.,* 2018). This plant is well recognized to have anti-fungal, anti-bacterial and anti-inflammatory physiognomies. This glucosamine can treat the discomfort in addition to stiffness experienced in the arthritis condition. Research has demonstrated that Carboxypeptidase that is present in Aloe Vera, shows an anti-inflammatory outcome by inactivating bradykinins. Bradykinin produces pain associated with vasodilation in addition to its hydrolysis that produces an analgesic effect (Maan *et al*., 2018). Another active compound also presents in aloe vera, possessing an aspirin-like anti-inflammatory and antibacterial features known as salicylic acid. In an experiment conducted by researchers, it was found that, Aloe Vera shows dose-dependent inhibitory effect on reactive oxygen metabolite, it suppressed the formation of prostaglandin E2 by 30% in 1:50 ratio, but had not shown any upshot on thromboxane B2 production (Joseph & Raj, 2010). The drink made with Aloe Vera can be used to treat basic arthritis related symptoms. The gel is equally effective as it is recognized to contain plant sterols. These sterols have been speculated to have alike effect on the body as that of steroidal drugs for reducing inflammation. Moreover, unlike these steroidal drugs, the aloe extracts have no side-effect like suppressing the regeneration of tissues for restoration. On the other hand, the particles present in the gel induce revival of the injured tissues (Van Wyk & Wink, 2015). According to Natural Living Products, the presences of salicylate, bradykinin, and additional natural steroids, Aloe vera are responsible in reducing inflammation the swollen joints (Kaur, Nain, & Nain, 2012). Aloe Vera drink encompass strong anti-inflammatory properties due to the presences of anti-oxidant holding properties of vitamins like A, B, C and E. The drink reduces the degree of inflammation that is caused by arthritis through absorbing various toxins that are responsible in swelling of joints (Van Wyk & Wink, 2015). The advantages of using Aloe Vera for osteoarthritis may be multifactorial. Not only it is useful as anti-inflammatory compound, but it also possesses prophylactic characteristics (Cowan, 2010). The plant of Aloe Vera has been stated to contain

glucosamine which is also found in the cartilage of the joints. This glucosamine can treat the discomfort in addition to stiffness experienced in the arthritis condition. The beneficial drink also holds some minerals which generate certain enzyme reactions in the affected joints. These enzyme reactions speed up the curing process in the joints and slow down the development of distortion (Amin, Ozgen, & Selamoglu, 2018; Surjushe, Vasani, & Saple, 2008). A study published in the Paper of the American Podiatric Medical Association in 1994 stated that Aloe Vera has the capacity to reduce arthritis associated complication of joints. Study also states that it also has advantageous properties in autoimmune disorders analogous to rheumatoid arthritis. (Javed, 2014) Another research described reduction in the degree of swelling by 79.7% percent, whereas alternative stated reduced inflammation upto 67.3%. Consuming aloe vera 30 minutes prior to main meals including breakfast, lunch, and dinner. Initially starting with minor dosage and progressively intensify up to 2 tablespoons, three times a day (Cowan, 2010). Globally most common form of arthritis affecting individuals is Osteoarthritis. The prevalence of knee osteoarthritis in Pakistan is quite high as compared to neighboring countries (Baqai, Khanam, & Parveen, 2010). The poor socio-economic status in our country demands cost effective treatment. In Pakistan, 25% women are affected by arthritis which result in pain, functional disability in addition to poor quality of life. (Aga Khan University Karachi 2013 Report). Review of Literature demonstrates that aloe Vera usage reduces inflammatory levels in arthritis individuals as much as eighty-nine percent and hence improves the pain and functional status. It is easily available in Pakistan and of low cost. There is limited data available or published on determination of effects of aloe vera on individuals with knee arthritis in Pakistan. Keeping in mind aforementioned facts, the current study was carried out to develop formulation for Aloe-vera drink and evaluate its organoleptic properties also determine its effects in managing osteoarthritis

2. Materials and Methods

Current research was a single blinded, randomized controlled trial (RCT). The research was conducted in six months from July 2019 to January 2020. The present study intended to find out effects related to aloe-vera on participants with knee osteoarthritis. The participants with musculoskeletal conditions seek treatment from orthopedic or rheumatology departments of primary and tertiary care hospitals. In order to meet the desired population with disease of interest, two public and private hospitals of Lahore were selected respectively. the research was conducted and participants were screened for selection criteria. Purposive sampling method was used to enroll the participants in research. The sample size of 90 participants (30 in each group) was estimated by using 28% prevalence of disease, with the given formula through a sample size calculator (n4Studies) app.

$$n = \frac{z^2_{1-\frac{\alpha}{2}} p(1-p)}{d^2}$$

p = 0.28

Delta = 0.07

Alpha = 0.05,

Z (0.975) = 1.959964

The "p" in formula represents the prevalence of disease, alpha is the level of significance, delta is the margin of error. Sample selection is a crucial part of study. In spick and span to get the answer of research question also to meet the objective of study, the sample should have particular characteristics and variable of interest. So, a selection criterion was developed to include the participants in the study. Participants who were fulfilling the inclusion and exclusion criteria were enrolled in the research: There were three treatment groups in this study. The participants were randomly divided into these three treatment groups including 2 experimental groups (Group A & B) and 1 control group (Group C). The three groups along with the description of treatment given to them is summarized in the table below.

Sr.No	Treatment Groups	Intervention
1	T-1- Experimental Group/Group A	Aloe-vera drink along with conventional medical management
2	T-2 Experimental Group / Group B	Placebo drink/honey & lemon drink along with conventional medical management
3	T-3 Control Group/ Group C	Convention medical management for knee osteoarthritis

Convention medical management for knee osteoarthritis The participants were randomly allocated to research/treatment group via block random sampling. The description of treatment is as follows: Treatment A (Aloe-vera Drink): Aloe-vera drink was given to participants in experimental group A in addition with conservation medical treatment. Development of aloe-vera drink was prepared via following these steps Procurement of raw materials (aloe-vera, honey, lemon juice, salt and water). Extraction of aloe-vera gel, Preparation of aloe-vera drink with standardized recipe, Sensory Evaluation of Aloe-vera Drink for acceptance of Taste & Smell. It was advised to consume 1 glass (240ml) of placebo drink with empty stomach, 30 mins before breakfast daily up to 42 days. Treatment B (Placebo Drink):Placebo drink was given in combination with conservative medical management to participants in experimental group B. The placebo drink was prepared my mixing the honey, lemon juice and salt into water. It was advised to consume 1 glass (240ml) of placebo drink with empty stomach, 30 mins before breakfast daily up to 42 days. The data from the participants was collected through the following step by step procedures: Total 120 participants were screened for eligibility criteria and 90 participants were recruited on basis of selection criteria. Informed consent was sought from them. The research protocols and objectives were explained to them. It was ensured that research will pose no harm to any of them. They were ensured that confidentiality and anonymity will be maintained along with the right to draw back from research when one will. Nutraceutical drink and placebo drink were formulated according to given composition. Then, Sensory evaluation of the drinks for acceptance of taste and smell was done by sensory evaluation panel. A panel of three experts was formed and 9-point hedonic scale was used for evaluation of taste and smell of aloe-vera juice and

honey water juice. According to expert, drink made up of honey water was most liked by all the panelist on both categories i.e. taste and smell whereas aloe-vera containing drink was least preferred. Firstly, demographic data, medical and family history was obtained and BMI was calculated through measuring height and weight of individuals. Baseline score of outcomes variables such as severity of pain and functional status were evaluated through Visual Analogue Scale and Patient Specific Functional Scale respectively. Biochemical test including fasting plasma glucose level and hemoglobin level were also monitored through their test reports. Bone Mineral Density score and its levels were also observed and documented in questionnaire. The individuals were allocated to treatment groups through block randomization technique. The individuals in experimental group A were provided aloe-vera drink and experimental group B was provided with honey water drink respectively to consume one glass daily. It was advised to take the drink at least 30 minutes before breakfast for 42 days while continuing the medical intervention provided to them. They were provided a record book to mark a tick after taking the drink. The individuals of group C were not provided any drink and they were asked to continue the medical intervention provided by physician. The pain intensity, functional status, BMI, were again assessed by the accessor at 20th day, 42th day and one month after the discontinuation of treatment. The assessor was kept blind of the treatment group. The dependent variables were measured through following outcome measure tools: Pain score was measured through Visual Analogue Scale (VAS) to measure intensity of pain. (Gupta et al., 2011) Patient Specific Functional Scale (PSFS) was also used to check the functional status of the participant. (Mannberg Bäckman, Stråt, Ahlström, & Brodin, 2016). 9-Point Hedonic Scale was used to measure the acceptability of food (Lim, 2011). Statistics were analyzed by means of Statistical Package for Social Sciences (SPSS) version 21. Quantitative data including age, score of pain intensity & functional status was presented in terms of mean and standard deviation. Categorical data i.e. gender, socio-economic status, family history of drug, life style habits etc. was expressed in form of frequency charts and appropriate graph. Mixed design analysis of Variance (ANOVA), also known as Split design ANOVA, used to evaluate the station of independent variables on dependent variables (between-group difference) also to observed independent variables effects over the time period (within-group difference). Statistical significance established at $p<0.05$

3. Ethical Consideration

All Rights for anonymity and confidentiality were reserved.

3.1 RESULTS

The study was a single blinded, randomized controlled trial with the sample size of 90 participants, having mean age of 54.42 ± 4.62 years.

17 % of the participants were male and 83% were females. According to the standard Asian classification of BMI, 41 % of the participants were overweight, 14% were found to be obese, and 45% were of normal weight. None of the study participant was underweight. Out of 90 study participants, 53%

had a previous family history of knee osteoarthritis whereas, and 47 % participants did not have any previous history of knee osteoarthritis. Figure 1: The bone mineral density of participants was determined through DEXA scan and T-sore was calculated. The mean score of BMD in experimental group A was -1.73 ± 0.45, in experimental group B was -1.92 ± 0.55, in control group was -1.99 ± 0.59. The value of T-score in three study groups represented that the study participants were having osteopenia. Mixed design ANOVA was applied to find mean difference of pain score between the three study groups (between-subject effects) and the mean difference in pain score from baseline to one-month follow-up after the termination of treatment (within-subject effects) and to find the statistical significance. The pain score in experimental group A was decreased by a mean of 2.35 ± 1.06 from 1st day at the start of study till one-month follow-up period. In experimental group, a mean reduction of 1.14 ± 0.75 in pain score was observed whereas in control group C, the pain was reduced by mean of 1.55 ± 0.69 from day 1st to one-month follow-up. The reduction of pain score was observed highest in participants of experimental group A having aloe- vera dink.

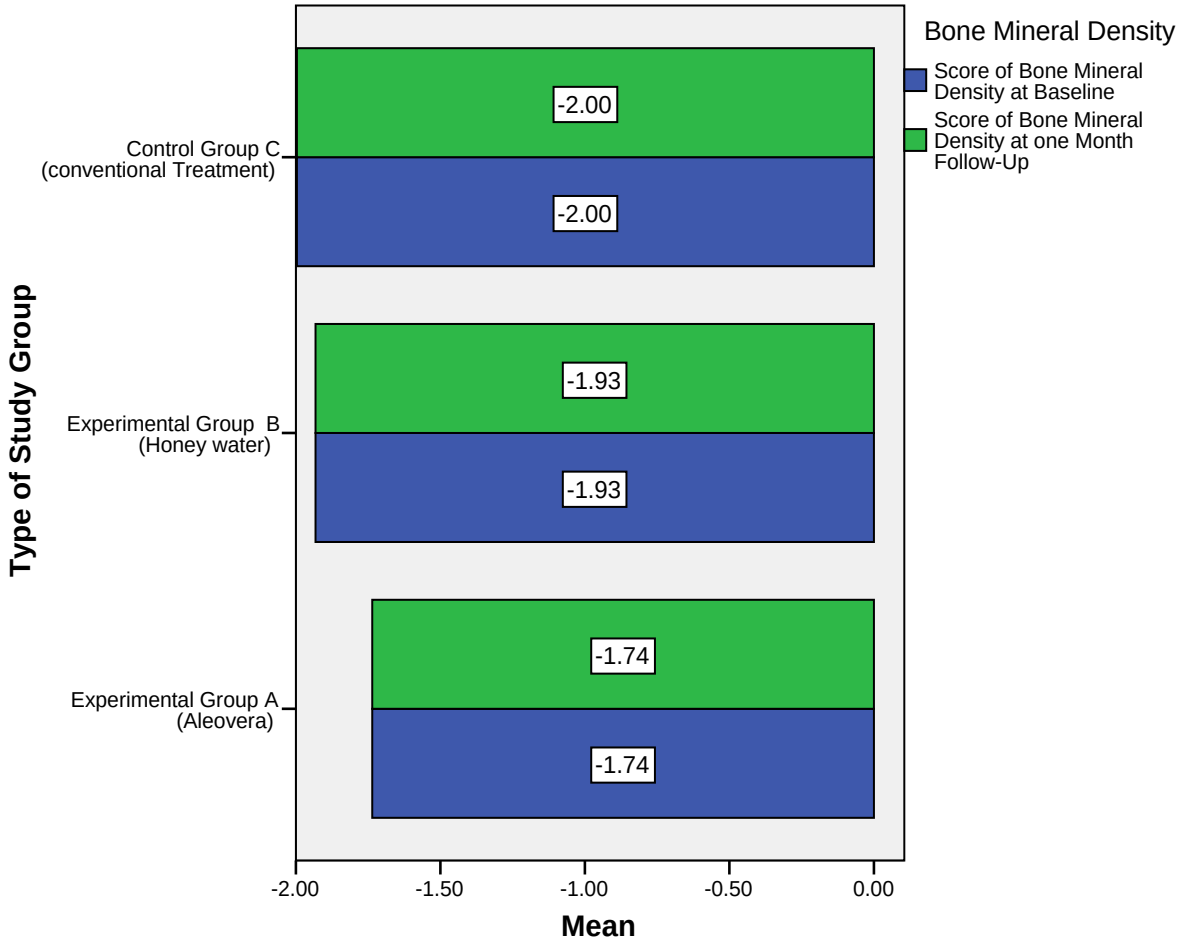

Figure 1: Bone Mineral Density (BMD) of Participants:

Figure 2: The analysis related to Between-Subjects Effects of pain intensity score revealed that there was a significant main effect of type of group with F (2, 80) = 3.910, p=0.024 which is less than 0.05. This effect showed that if all the other variable were ignored then the three group i.e. aloe-vera group, honey water group and control groups were significantly different in terms of reduction in pain intensity.

Table 2: Tests of Between-Subjects Effects of Pain

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Type_of_Group	18.689	2	9.345	3.910	.024	.089
Error	191.196	80	2.390			

Figure 3; The effect of treatment group on functional status of participants at patient specific functional scale (PSFS) was determined through Mixed design ANOVA. The mean difference of functional status score from 1st day at the start of study till one-month follow-up was -2.17 ± 0.94 in experimental group A, -0.89 ± 0.68 in experimental group B, and -1.55 ± 0.69 in control group C which showed that maximum improvement in functional status was in participants of experimental group A having aloe-vera drink.

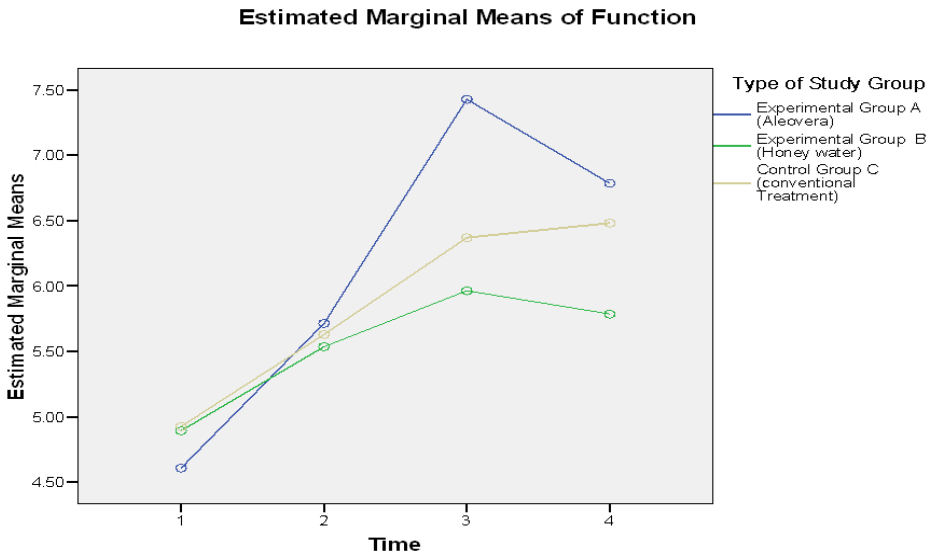

Figure 3: Graph Representing Changes in Mean Score of Functional Status

with respect to Treatment Groups and Follow-up Time Period Figure 4: Tests of Between-Subjects Effects of functional status score revealed that there was a significant main effect of type of treatment group with F (2, 80) = 4.450, p=0.015, which is surely less than 0.05. This main effect of functional status between-group showed that if other test variables were ignored then the three treatment groups i.e., aloe-vera group, honey water group and control groups were having statistically significant

difference with regard to improvement in functional status

Table 4: Tests of Between-Subjects Effects of Functional Status Score

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Type of Group	19.458	2	9.729	4.450	.015
Error	174.897	80	2.186		

4. Discussion

Knee osteoarthritis is one of the major musculoskeletal problems causing pain, and functional limitations leading to disability among elderly population. It mainly affects the population above 40 years of age and females are most common victim of this disease. Besides advancing age and female gender, obesity and life style habits are the common cause which makes this disease more debilitating and also effects the quality of life of individuals. A diverse list of pharmacological agents has been used as a therapy to reduce pain and stiffness associated with knee osteoarthritis. Despite the relief in severity of symptoms, it has been found that a number of associated adverse effects ranging from mild to severe that possibly develop with the prolong use of these drugs. Yet, these drugs does not reverse the process of degeneration in the joint (Zhang, Robertson, Zhao, Chen, & Xu, 2019). In comparison to pharmacological drugs, a number of nutraceutical or herbal agents were identified in literature to had anti-inflammatory, and bone remodeling with collagen regenerative properties (Kaur *et al*., 2012). In the list of herbal and plant-based agents for treatment of knee arthritis, Aloe-Vera was found to have multiple therapeutic effects on various systems of body. In this study the effects of aloe-vera juice were compared with the participants to whom honey lemon juice was given and with the participants of control group to whom nothing was given besides the conservative medical management. The results shown that aloe-vera has potent role in pain management also improving functional limitation in participants having osteoarthritis of knees. Moreover, in contrast to this aloe-vera does not shown any effect on improving BMD of participants. The mean age of participants in this study was 51.03 ± 5.43 as the knee osteoarthritis is more common in advance age. The findings of this study showed that there was significant reduction in pain score and improvement in functional status among the participants of the age range from 45-65 years with addition of aloe-vera juice. These results were similar with the findings of study conducted in 2015 by Yagi A. who reported that aloe-vera is effective in age related disorders of bone and other systems of body. It includes acemannan which had bone and collagen (in tendon & ligament) regeneration and remodeling properties (Yagi, 2015). The aloe-vera juice was introduced to experimental group A participant for a period of 42 days and its effects of severity of symptoms due to knee osteoarthritis and on other comorbidities were observed. The literature supported the long-term

usage of aloe-vera on age related disorders without any harmful effects. The result of a study conducted by Ikeno Y in 2002 represented that ingestion of aloe-vera for long periods of duration rather had beneficial effects on age related disorders with no obvious harmful and destructive effects (Ikeno, Hubbard, Lee, Yu, & Herlihy, 2002). In the current study, the composition of aloe-vera drink had lemon juice as well which is not only a rich source of Vit. C but also enhances the taste of the juice. The combination of aloe-vera and Vit. C had added effects on decreasing the degenerative process of OA as supported by the study of Toliopoulos I *et, al.* in 2012. They reported that this combination of aloe-vera and Vit. C stimulates the proliferation of Natural Killer Cells (NKCs) that serve to enhance the immunity against inflammatory process in the joint (Toliopoulos, Simos, Verginadis, Oikonomidis, & Karkabounas, 2012). In present research study, the aloe-vera formulation has been administered orally to participants with knee OA for 42 days and it was found effective on pain reduction and improvement of functional limitation. Likewise, the study by Vigneshwari EK *et, al*. in 2020 supported the oral intake of aloe-vera for alleviating the painful symptoms of knee OA. The results reported by the study of Banasova M. *et, al*. in 2013 were also in favor the oral intake of aloe-vera drink. In addition to relieving arthritic symptoms, they found that it had anti-diabetic properties as well. Pain is one of the medical emergencies and a major symptom which require the medical or surgical management. Participants with knee osteoarthritis grade I & II experience mild to moderate pain at rest or usually in a transition from sitting to standing, at walking, stair climbing and descending. The mean score of pain at VAS of study participants was 5. 2 ± 2.3. The results presented with consequential difference in average pain score within- group effect p=0.000 and between-group effect with p= 0.02 representing aloe-vera has positive effects in reducing pain score in participants having osteoarthritis of knees. The results of current study were similar to the findings of a study conducted by Balan in 2014 and Gupta in 2011 on clinical properties of aloe-vera gel and capsule related to knee osteoarthritis, who determined that usage of aloe-vera given as gel and capsule has significant effect on reducing knee pain with p=0.001. (Bałan *et al*., 2014; Gupta *et al.*, 2011) The participants with knee osteoarthritis found difficulty in standing or weight-bearing after the rest period and reported pain in stair climbing especially ascending the stairs. The outcome of this research revealed, the use of aloe-vera improves functional status of participants suffering from knee osteoarthritis. The results showed statistically significant within group effect (p=0.000) and between-group effect (p= 0.015) of aloe-vera on physical function of participants. The same results were produced in a research done by KMFR Siddiqui and his fellows, in 2017 who reported that use of aloe-vera increased the functional status of participants with frozen shoulder on SPADI scale with $p < 0.001$ (Siddiqui *et al*, 2017) One of the limitations of the current study is that it did not focus on the adverse properties of aloe-vera drink on the study participants also the interaction of aloe-vera juice and honey water drink on already prescribed medicines.

5.Conclusion:

It was determined from the findings that aloe vera drink has potential role in managing pain, and improving functional status of participants having knee osteoarthritis. It also decreases body weight and systolic blood pressure. However, it has no effect on fasting blood sugar level.

5.1 Recommendations

It is recommended for future researchers that more work should be conducted on finding the adverse responses of aloe-vera on participants along with any possible interaction with the allopathic medications.

Table 5: Summary of Group wise Comparison of Mean of Study Outcomes Variables from Baseline to One Moth Follow-Up

Variables	Time	Group A (Aloe-Vera Group) Mean ± S.D (N)	Group B (Honey Water Group) Mean ± S.D (N)	Group C (Control Group) Mean ± S.D (N)
Pain Score at VAS	At Baseline	1.39 ± 1.17 (30)	5.10 ± 0.99 (30)	5.11± 0.75 (30)
	At 20th Day	3.8 ± 0.97 (30)	4.36 ± 1.03 (30)	4.22 ± 0.85 (30)
	At 42nd Day	2.32 ± 0.67 (28)	3.75 ± 1.14 (28)	3.44 ± 0.58 (27)
	At One Month Follow-up	3.03 ± 0.43 (28)	3.96 ± 1.04 (28)	3.56 ± 0.64 (27)
Functional Status at PSFS	At Baseline	4.61 ± 1.17 (30)	4.89 ±0.99 (30)	4.92 ± 0.68 (30)
	At 20th Day	5.71 ± 0.97 (30)	5.54 ± 0.92 (30)	5.62 ± 0.56 (30)
	At 42nd Day	7.42 ± 0.74 (28)	5.96 ± 0.88 (28)	6.37 ± 0.56 (27)
	At one Month Follow-up	6.78 ± 0.78 (28)	5.79 ± 1.11 (28)	6.48 ± 0.51 (27)
BMI of Participants	At Baseline	26.35 ± 4.28 (30)	27.17 ± 3.18 (30)	24.08 ± 4.61 (30)
	At 20th Day	24.86 ± 4.40 (30)	26.96 ± 3.10 (30)	24.42 ± 4.59 (30)
	At 42th Day	23.28 ± 4.21 (28)	26.59 ± 3.12 (28)	24.72 ± 4.61 (27)
	At one Month Follow-up	23.82 ± 4.12 (28)	26.80 ± 3.11 (28)	25.08 ± 4.62 (28)
Systolic BP In mmHg	At Baseline	123.39 ± 10.98 (30)	127.68 ± 9.08 (30)	126.67 ± 8.32 (30)
	At 20th Day	117.14 ± 9.37 (30)	122.32 8.44 (30)	125.74 6.61 (30)
	At 42nd Day	113.93 ± 4.97 (28)	119.29 ± 7.16 (28)	126.89 ± 8.23 (27)
	At one Month Follow-up	120.00 ± 8.16 (28)	127.14 ± 9.37 (28)	127.78 ± 8.01 (27)

Fasting BSL in gm. /dl	At Baseline	120.64 ± 17.91 (30)	118.92 ± 19.54 (30)	119.44 ± 11.12 (30)
	At 20th Day	112.50 ± 17.50 (30)	117.10 ± 18.91 (30)	118.51 ± 10.54 (30)
	At 42nd Day	105.32 ± 16.37 (28)	115.92 ± 18.47 (28)	118.51 ± 10.17 (27)
	At one Month Follow-up	114.10 ± 13.67 (28)	119.46 ± 18.01 (28)	117.77 ± 12.19 (27)

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