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Crude *Aloe vera* Gel Reduces Small Intestinal Transit and Increases Body Weight in Normal Albino Wistar Rats

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Authors' contributions

This work was carried out in collaboration between all authors. Author NVU designed the study, coordinated the research, and wrote the first draft of the manuscript. Author PUA managed the analysis and interpretation of data. Authors OTH and AAB wrote the protocol and managed the literature searches. Authors OEE and AAB supervised and guided the entire experimental procedure. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aims: This study was carried out to determine the effect of crude *Aloe vera* gel on blood glucose level in normal animals and to ascertain the relationship between food intake, body weight changes and intestinal transit in animals administered crude *Aloe vera* gel.
Methodology: The phyto-constituents and median lethal dose of the plant material were determined before administration. Sixteen albino wistar rats were randomly assigned one of two groups thus, control group and test group. The control group was fed with rat food and water while the test group was given a daily oral dose of crude *Aloe vera* gel (0.2ml/100g body weight) in addition to free access to food and water. Food intake, water intake, body weight and fasting blood glucose levels were measured during the research work. At the end of 21 days, intestinal transit was determined using the method described by Uwagboe and Orimilikwe [15].
Results: Intestinal transit was significantly lower (P<0.001) in the test group compared to

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control. Food intake, water intake and blood glucose level in the test group was not significantly different compared to the control group. The test group had a significantly (P<0.001) higher body weight change when compared to control.
Conclusion: Crude *Aloe vera* gel reduces small intestinal transit, thus resulting in longer periods for absorption of digested food materials and may be responsible for the increased body weight observed in the test group since food intake was not significantly increased.

Keywords: Aloe vera; blood glucose; body weight; food intake; intestinal transit.

1. INTRODUCTION

Movement of chyme through the small intestine is a factor of the intestinal smooth muscle activity. Intestinal transit (in percentage) is the length of the small intestine travelled by chyme per unit time. Bowel transit depends on the type of food consumed as well as the quantity of fluid taken [1]. Generally, consumption of fruits, vegetables and whole grains result in higher intestinal transit (lower transit time) [1]. A number of gastrointestinal hormones affect small intestinal transit by influencing gastric emptying and intestinal motility [2]. Cholecystokinin (CCK) for example, secreted by I - cells of the small intestine in response to the presence of acid rich chyme inhibits gastric motility and increases intestinal motility [2]. To this end, ingested food materials rich in fatty acids, peptides and amino acids will increase small intestinal transit. The time available for absorption of digested food materials also depends on the small intestinal muscle activity. Increased intestinal muscle activity results in increased transit (reduced transit time) at the detriment of the digested food materials. In terms of the body's energy requirements, this will imply that the body rather depends on fat deposits for energy mobilization - thus weight loss.

The use of *Aloe vera* is being promoted for a large variety of conditions. Often general practitioners seem to know less than their patients about its alleged benefits. Aloe is a cactus-like, succulent perennial plant with over 360 species, belonging to family Liliaceae (sub-family of the Asphodelaceae), native to North Africa and cultivated in warm climatic areas [3]. *Aloe vera* barbadensis is the species that is most effective [4]. Aloe can be utilized therapeutically, mainly in two basic forms – latex and gel. A third and less popular form in which *Aloe vera* is used is the leaves extract. *Aloe vera* gel is well known for its healing potentials. The latex of *Aloe vera* contains the anthraquinone glycosides aloin A and B, which are potent laxatives [5,6]. *Aloe vera* has been found helpful in the following body systems - cardiovascular system [7,8,9], endocrine system [10,11], respiratory system [6], blood and immune system [9,12].

The beneficial effects of *Aloe vera* on blood glucose and many other parameters have been widely documented, but there is paucity in scientific report on its effect on intestinal transit which is a factor that determines the magnitude of absorption of digested food materials. This study was therefore designed to elucidate the effect of crude *Aloe vera* gel on intestinal transit in normal rats and the possible implication of altered intestinal transit on body weight changes.

2. MATERIALS AND METHODS

2.1 Plant Material and Preparation of Crude *Aloe vera* Gel

Fresh, mature *Aloe vera* plant with leaves within 40 – 60 cm long was obtained from University of Calabar Botanical Garden and identified by the Chief Herbarium Officer of Botany Department of University of Calabar. *Aloe vera* plants that are more than two years old were selected for the study because they have been shown to contain more enzymes and proteins that make up the inner gel [13].

The *Aloe vera* leaf was harvested and washed clean with water. A clean, dry cloth was then used to mop up the water from the *Aloe vera* leaf. Using a knife, the leaf was sliced longitudinally. The gel (clear block) which was noticed upon slicing the leaf was gently scraped into an electric blender to shatter the block and mix thoroughly. After blending, the crude *Aloe vera* gel was administered at once. There was no form of storage. This was to ensure that the constituents of the crude *Aloe vera* gel were not compromised. Care was taken not to scrape too much into the leaf to avoid the *Aloe vera* latex which is completely different from the gel. This preparation was done daily throughout the duration of the experiment. The median lethal dose (LD_{50}) of the plant extract was determined by the method described by Lorke [14].

2.2 Animal Preparation and Protocol

Sixteen albino wistar rats were used for this study. The animals were obtained from the Animal house in the department of Pharmacology, University of Calabar, Calabar, Nigeria. Each animal was placed in its own separate metabolic cage containing its food and water. The metabolic cages were well ventilated, exposed to normal temperature and 12/12 hours light/dark cycle. After fourteen days of habituation, the animals were randomly assigned into one of two groups such that each group contained eight animals, thus, control group; given 0.2ml/100g body weight distil water orally, and the test group; treated with *Aloe vera* gel (0.2ml/100g body weight) orally. All animals had unrestricted access to food and water.

2.2.1 Crude *Aloe vera* gel administration

After fourteen days of habituation, the crude *Aloe vera* gel was orally administered to the test group at a dose of 0.2ml/100g body weight twice daily for 21 days. Administration was facilitated by the use of a syringe and orogastric tube. The experimental procedures involving the animals and their care were in line with the approved guidelines by the local research and ethical committee.

2.3 Determination of Fasting Blood Glucose Level

The blood glucose level of each animal was measured by the use of the Fine test glucose meter (manufactured by INFOMED IMPEX, INDIA). Blood used for the test was obtained by pricking the distal end of the tail and placing the drop of blood on the test strip. Fasting blood glucose levels after grouping of animals was measured and recorded. It was also measured before small intestinal transit experiment. The differences were analyzed statistically.

2.4 Determination of Food Intake

The food intake was obtained by giving a measured quantity of rat pellet each day and weighing the quantity remaining, same time the next day. The difference in quantity was recorded as the food intake. The recording was made at the same time daily to ensure consistency and accuracy.

2.5 Determination of Water Intake

Water intake was obtained using a measuring cylinder and a calibrated conical flask. The daily water intake of the animals was obtained by subtracting the volume of water remaining at the end of 24 hours of feeding from the amount initially deposited in the cylinder at the start of each day's feeding.

2.6 Determination of Body Weight Changes

The body weight of the animals were determined by using a weighing balance. The initial weight of each animal was recorded after random grouping, before commencement of administration. The rats were subsequently weighed every two days until the end of the study. The weight of the animals at the end of 21days was recorded. The difference between the initial and final weight was recorded as body weight change.

2.7 Intestinal Transit Measurement

Intestinal transit was measured using the method described by Uwagboe and Orimilique [15] with slight modification. The rats in the different groups studied were deprived of food for 24 hours but were allowed access to water. This was to make sure the bowel was cleared of all food materials. 10g of activated charcoal was thoroughly mixed with 1g gum Arabic in 100ml of distil water to serve as the marker substance. Each rat was fed with 2ml of this marker substance orally using a metallic (8cm long) intubating syringe. The animals were timed for 60min each. At the expiration of each 60min, the rats were introduced into a confined chamber with 30% of the chamber's volume containing CO_2 from a compressed gas cylinder (CO_2 - euthanesia). As soon as loss of righting reflex was observed for $\geq$ 30 seconds, the animal was removed from the chamber and cervical decapitation was then employed to ensure death [16]. The abdomen was immediately cut open through the linea alba. The duodenum was then identified as the continuation of the pyloric sphincter while the ileocecal sphincter was also prominent at the cecal end. The duodenum was cut away from the pyloric sphincter and the ileum was also cut at the ileocecal sphincter. The small intestine was immediately stretched and the location of the marker (a black stain) was clearly visible along the small intestine. A thread was used to tie the intestine at the point where the marker stopped. Using a measuring tape, the total length of the intestine was measured and recorded. The measuring tape was also used to measure the length travelled by the marker from the pyloric sphincter.

The intestinal transit was calculated as:

$$\frac{\text{Length travelled by black marker substance}}{\text{Total length of intestine}} \times 100$$

The values were recorded and differences analyzed statistically.

2.8 Statistical Analysis

All results are presented as mean ± standard error of mean. Student's t - test was used to analyze the data collected. $P<0.05$ was considered significant. Computer software SPSS version 17.0 (*SPSS* Inc., Chicago, Illinois, U.S.A) and Excel Analyzer version 2010 (Microsoft Inc.) were used for the analysis.

3. RESULTS

3.1 Determination of Fasting Blood Glucose Level after Grouping

The fasting blood glucose level of animals in the control group and test group after grouping was 63 ± 2.7 mg/dl and 63 ± 1.4 mg/dl respectively. There was no significant difference in the fasting blood glucose levels of the animals in the various groups prior to crude *Aloe vera* gel administration (Fig. 1).

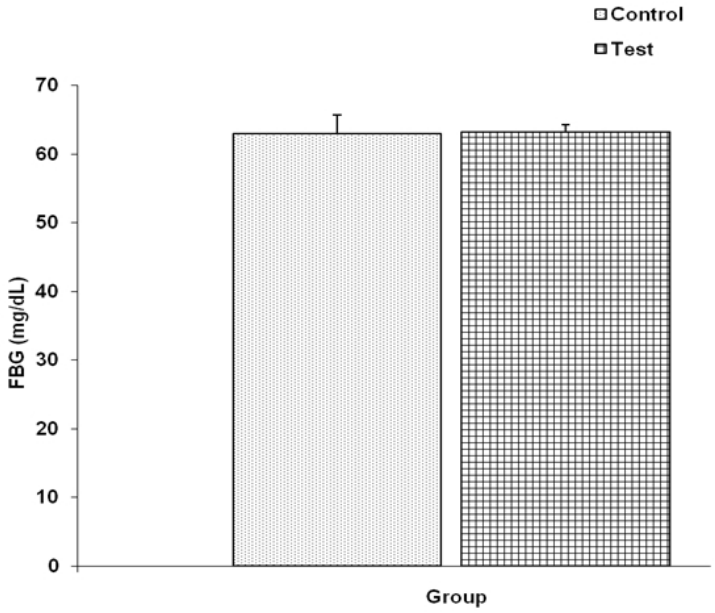

Fig. 1. Comparison of fasting blood glucose (FBG) of the different groups after grouping

Values are mean ± SEM, n = 8.

3.2 Fasting Blood Glucose Level before Intestinal Transit Experiment

The fasting blood glucose level of animals in the control and test groups prior to small intestinal transit experiment was 72 ± 0.7 mg/dl and 74 ± 1.0 mg/dl respectively. There was no significant difference in the fasting blood glucose levels of the animals in the various groups before intestinal transit measurement (Fig. 2).

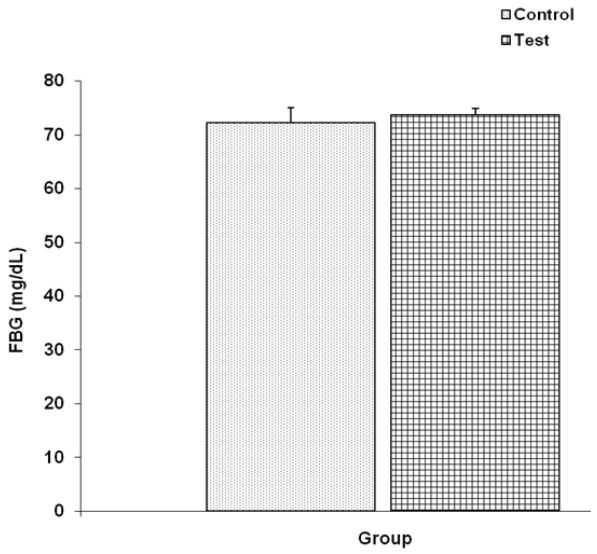

Fig. 2. Comparison of fasting blood glucose (FBG) of the different groups just before transit time estimation

Values are mean ± SEM, n = 8.

3.3 Mean Daily Food Intake

The mean daily food intake of animals in the control and test group was 23.6 ± 0.4311g and 24.6 ± 0.5766g respectively. There was no significant difference in the Mean food intake between the two groups (Fig. 3).

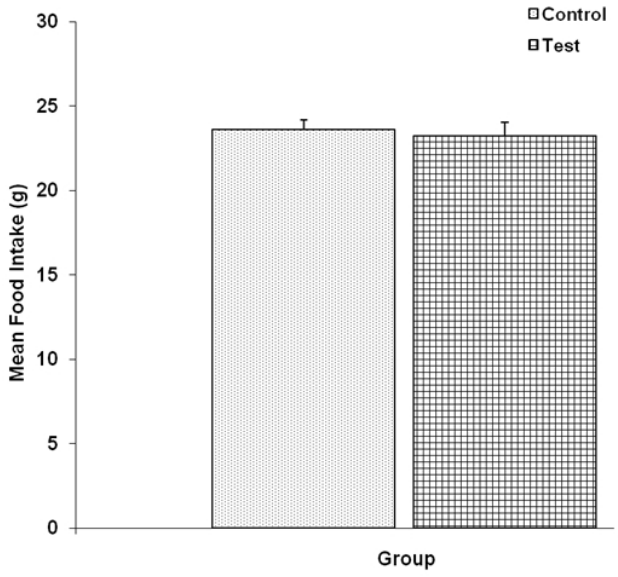

Fig. 3. Comparison of mean food intake of the different experimental groups

Values are mean ± SEM, n = 8.

3.4 Mean Daily Water Intake

The mean daily water intake of animals in the control and test group was 25.3 ± 0.2701ml and 22.9 ± 0.3922ml respectively. There was no significant difference in the mean daily water intake between the two groups (Fig. 4).

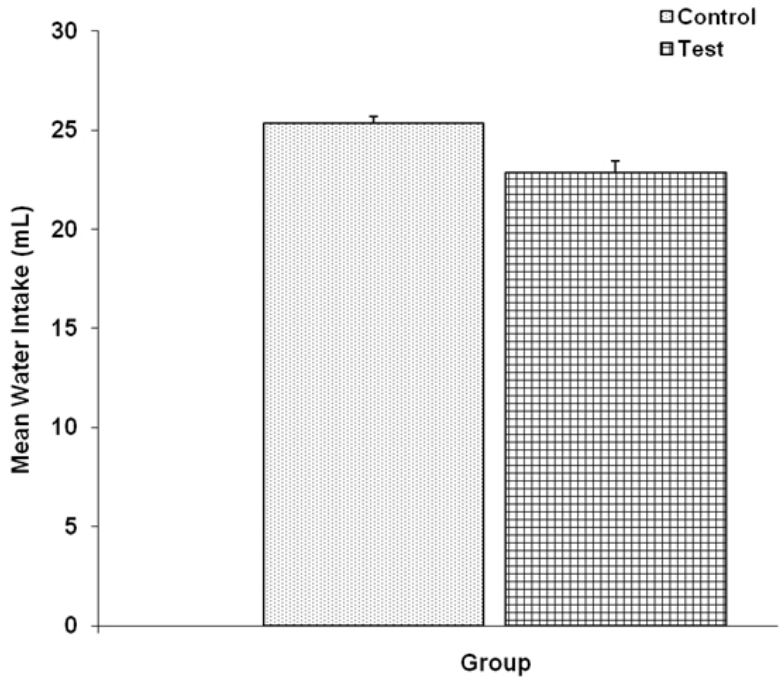

Fig. 4. Comparison of mean water intake of the different experimental groups
Values are mean ± SEM, n = 8.

3.5 Body Weight Change

The initial body weight of animals in the control and test group was 197.50 ± 2.5g and 201.25 ± 3.0g respectively. There was no significant difference in the initial body weight of animals after grouping (Fig. 5a). The final body weight of animals in the test group was 232.50 ± 2.5g, significantly higher (P<0.001) compared to control which was 206.25 ± 4.6g (Fig. 5a). Consequently, the body weight change in the test group was 31.25 ± 2.3g, significantly higher (P<0.001) compared to control which was 8.75 ± 3.0g (Fig. 5b).

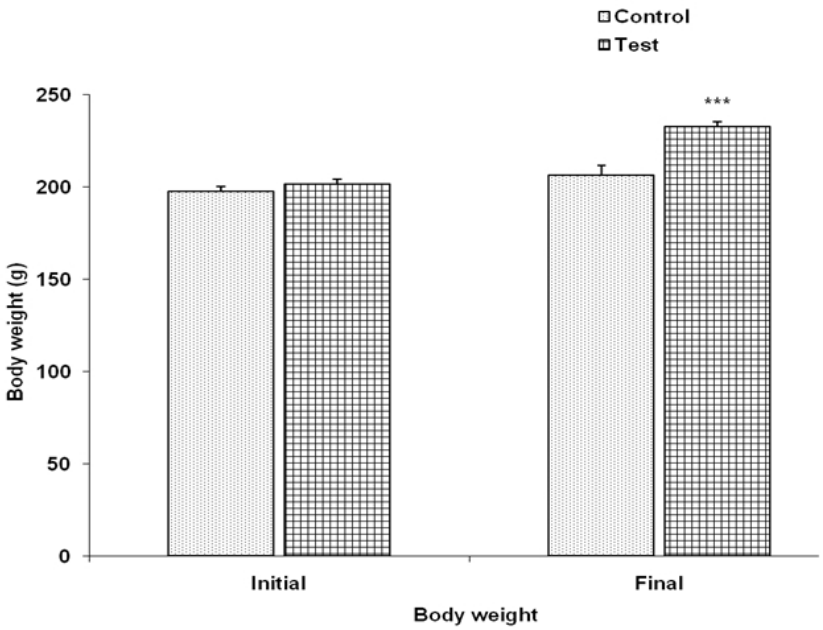

Fig. 5a. Comparison of initial and final body weights of the different experimental groups

*Values are mean ± SEM, n = 8; ***P<0.001 vs control*

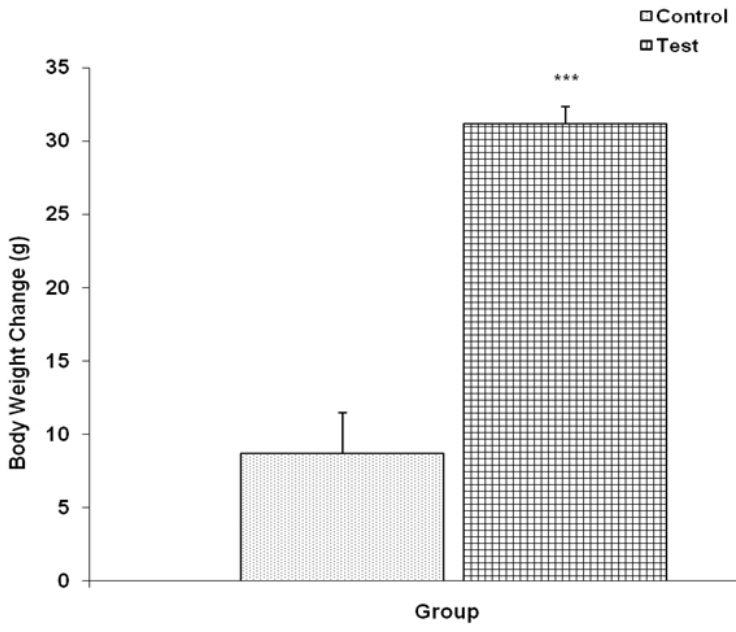

Fig. 5b. Comparison of body weight change of the different experimental groups

*Values are mean ± SEM, n =8; ***P<0.001 vs control*

3.6 Intestinal Transit

The percentage transit in the test group (45.6 ± 3.3276%) was significantly lower (P<0.001) compared to control which was 68.4 ± 5.0109% (Fig. 6).

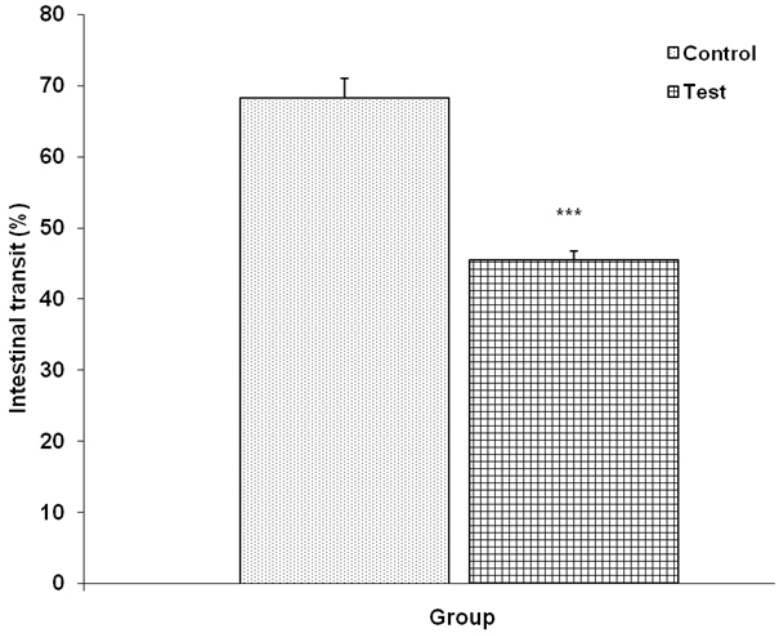

Fig. 6. Comparison of intestinal transit (percent) of the different experimental groups
*Values are mean ± SEM, n = 8; ***P<0.001 vs control*

4. DISCUSSION

Diabetes mellitus, a group of metabolic disorder with multiple etiology, is characterized by chronic hyperglycemia with disturbances in carbohydrate, fat and protein metabolism due to defect in insulin secretion, insulin action or both [17]. A number of plants have been reported to exhibit glycemic control by stimulating insulin release [18]. Although *Aloe vera* leaf extract has been found to be significantly effective in lowering blood glucose in experimental diabetics [19,20,21,22], it had no significant effect on fasting blood glucose levels in normal animals observed in this study (Fig. 2), suggesting that crude *Aloe vera* gel may be acting through a negative feedback mechanism that ensures that the beta cells of the pancreas are not excessively stimulated to produce or release insulin in normal animals.

Bunyapraphatsara et al. [23] showed that diabetes mellitus was associated with increased food intake (polyphagia) and water intake (polydipsia) and that *Aloe vera* gel reversed these symptoms. Crude *Aloe* vera gel however did not significantly alter food and water intake in our study on normal animals (Figs. 3 & 4). It is possible that a negative feedback mechanism checks this acclaimed attributes of *Aloe vera.*

Intestinal transit which is a function of the rate and force of smooth muscular contraction of the gut was significantly reduced (P<0.001) in the test group compared to control (Fig. 6).

Crude *Aloe vera* gel's effect on intestinal transit may be traced to its phyto-constituents which include monosaccharide, polysaccharide, lipids and proteins [24,25,26]. These components stimulate the release of cholecystokinin (CCK), a gastrointestinal hormone which reduces gastric acid secretion, lowers gastric emptying, stimulate the release of digestive enzymes and lowers intestinal transit [2,27].

There was no significant difference in body weight in the different groups prior to experiment, (Fig. 5a). Before sacrifice however, the test group showed a significant increase (P<0.001) in body weight compared to control. (Fig. 5a). The crude *Aloe vera* gel treated group showed an increased change in body weight, significantly different (P<0.001) compared to control. (Fig. 5b).

Relationship exists between food intake and body weight, lesions in the lateral hypothalamus (hunger center) leads to anorexia and loss of body weight while lesions in the ventromedial hypothalamus (satiety center) leads to overeating and obesity, therefore the amount of food eaten affects body weight. In this study, the increased body weight in the test group was not dependent on food intake (Figs. 3, 5a & 5b). This shows that crude *Aloe vera* gel influenced the body weight through a mechanism other than food intake. Increased body weight in the test group may be traced to the decreased intestinal transit caused by the crude *Aloe vera* gel, (Fig. 6). This effect may be attributed to the presence of monosaccharides and polysaccharides in *Aloe* vera gel. The polysaccharides make up approximately 20 percent of the solid content of the *Aloe vera* gel and comprise mostly a mixture of polysaccharides of a linear, highly acetylated β1-4 Mannan, branched dextrans, pectic acids and other polysaccharides with negative charge [28,29]. It is well known that polysaccharides of natural origin such as chitosan are capable of enhancing the intestinal absorption of co-administered compounds by means of a transient opening of the tight junctions between adjacent epithelial cells to allow for paracellular transport across the intestinal epithelium [25,26]. Hamman & Viljoen, and Chen [30,31] in a recent *in vitro* study showed that *Aloe vera* gel decreased the transepithelial electrical resistance of intestinal epithelial cell monolayers, thereby indicating opening of the tight junctions between adjacent epithelial cells. The *Aloe vera* gel was also able to significantly increase the transport of the macromolecular peptide drug, insulin, across the intestinal epithelial cell monolayers. These findings support the fact that decreased intestinal transit favours absorption of digested food materials thus resulting in weight gain in the crude *Aloe vera* gel group.

Presence of glucose rich chyme in the duodenum triggers the release of gastric inhibitory peptide (GIP) which belongs to a group of gastrointestinal hormones called incretins [23,32,33]. This hormone potentiates the effect of CCK in slowing gastric emptying and lowering intestinal transit, consequently allowing more time (increased transit time) for absorption of digested food materials to meet the body's need, such that the excesses are converted into fatty acids and subsequently transported into the adipocytes where they are converted to triglycerides and stored in these cells, thus weight gain.

5. CONCLUSION

Crude Aloe vera gel reduces small intestinal transit, consequently resulting in longer periods for absorption of digested food materials and may therefore be responsible for the increased body weight observed in the test group since food intake was not significantly increased.

CONSENT

Not applicable.

ETHICAL APPROVAL

All authors hereby declare that all experiments were examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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