Original article

The effects of a **Nutritional Supplement (eXfuze Seven+) on blood glucose;** a double-blind, randomized study

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ABSTRACT

This report is an analysis of a randomized, double-blind study which was conducted to determine whether eXfuze™ Seven+, a nutritional supplement, could lower the blood glucose levels. All volunteers (n = 883) from the Huntsman Senior World Games who were participants at St. George, UT, were to consume randomly, either the eXfuze™ Seven+ drink, (treatment A) or a commercially obtained grape juice (treatment B; placebo). We used Bayer's CONTOUR® blood glucose monitoring units to measure before and after blood glucose levels. All the participants voluntarily consented to be a part of the study and their ages and genders were also noted down for further analysis. A SigmaPlot11.0 ®statistical program was used to compare the treatment A (n = 496) and the placebo (n =387) by using t-tests which showed that treatment A had a blood glucose lowering trend as compared to the placebo (p-value = 0.024). Further analysis showed that gender did not affect the treatments ($\text{p-value}_{females}$ = 0.120, p-value_{males}= 0.063). Also, age did not affect the data (p-value = 0.2). When analyzing the treatment data of the individuals with a change which was greater than or equal to 0, the p-value was found to be less than 0.001, thus indicating that treatment A appeared to cause less spiking of the blood glucose than the placebo. By graphing these data, we saw a pattern where the treatment A data-points tended to aggregate closer to zero than the treatment B data-points. Therefore, this study strongly suggests that the eXfuze™ Seven+ treatment causes a downward trend in the blood glucose levels as compared to the placebo.

Background: eXfuze™ Seven+ (eXf+) is a health supplement containing various botanical fruit extracts which have purported health benefits.

Aim: To determine the effects of eXfuze™ Seven+ on the blood glucose levels.

Materials and Methods:Treatment cups (one-ounce) which were labeled as 'treatment A' (eXf+) and 'treatment B' (placebo) were given to 883 participants from the 2009 Huntsman Senior World Games which were held at St. George, Utah; each participant received a cup containing one ounce of a particular drink. The pre-treatment and post-treatment blood glucose levels of the volunteers were measured by using Bayer's blood glucose monitoring units. Furthermore, the ages, genders, sports, and before and after dosing-times of the participants were noted. All the participants voluntarily agreed to participate in the study as a part of the health screen which was provided by the Huntsman Senior World Games. The participants were asked to return within a 30-60 minute time interval to take a final glucose measurement. There was no attempt to control the participants' consumption of food or drink before the treatment, but they were encouraged to avoid simple carbohydrates after drinking the treatment or placebo. A total of 296 valid data points were collected from the individuals who consumed eXfuze™ Seven+ (treatment A), and a total of 287 valid data points were collected from those who consumed commercially the available grape juice (treatment B; placebo). SigmaPlot 11.0®was used to determine the t-tests and the homogeneity of the variance. Further analysis was done by using the statistics programme called SAS®.

Results: The p-values from both the statistical programmes showed the same levels of significance, differing only slightly due to a difference in the number of data points which were used for the analysis. An initial comparison between all the treatment A and placebo data resulted in a statistically significant difference (p=0.024). The overall mean change for treatment A was -1.77 mg% of blood glucose, whereas the mean change for treatment B was +1.88 mg% of blood glucose. Hence, treatment A, with its decreasing trend, was significantly different than the placebo's increasing trend. The analyses of gender versus treatment and age versus treatment resulted in no significant differences (p=0.9119 and p = 0.680 respectively).

Conclusions: The data clearly show that eXfuze™ Seven+ causes a significant decreasing trend in the blood glucose levels.

KEY MESSAGES

1. There was a significant decreasing trend in the blood glucose levels when one ounce of the treatment drink (eXfuze™ Seven+) was consumed.
2. Age and gender did not significantly affect the results.
3. There was an increasing trend in the blood glucose levels when one ounce of the control (grape juice) was consumed.
4. This study shows the positive short-term health effects of consuming eXfuze™ Seven+.

Key Words: eXfuze, Blood-glucose, Fruit juice extract, Hypoglycaemia

INTRODUCTION

eXfuze™ produces a new nutritional drink (eXfuze Seven+) with an innovative blend of seven tropical fruits which are often referred to as superfoods. These superfoods include noni, gac, goji, açai, mangosteen, seabuckthorn, and brown seaweed [1]. There have been anecdotal reports that the eXfuze™ products may reduce or stabilise the blood sugar levels. Indeed, maintaining a preprandial blood glucose level at 70-130 mg/dl is important for sustaining a healthy body. Excessive or insufficient levels may lead to fatigue or other complications. Rising levels of glucose is an increasing problem in the global community today and it is becoming critical to be able to maintain a balanced diet that will not cause fluctuation of one's blood glucose levels drastically. Therefore, foods with hypoglycaemic characteristics should be beneficial to the general population. However, to date, there have been no scientific studies to test the hypothesis that eXfuze™ products can reduce blood sugar. The objective of this study was to test this hypothesis by using a double blind, randomized, experimental design.

MATERIALS AND METHODS

The participants in this study ranged from 18 to 90 years of age, with a mean age of 64.3 years. The individuals were randomly selected from the athletes who participated at the Huntsman Senior World Games at St. George, UT, in cooperation with Brigham Young University's Health Assessment Programme. The participation was completely random and so there was no attempt to exclude or include a certain subset of the athlete population. All the participants (n=883) volunteered and gave their consent to participate in the study. Each athlete was given either treatment A or treatment B. Treatment A was a commercial product, eXfuze Seven⁺, which was manufactured by exfuze™. The placebo, treatment B, was a commercially available grape juice which was chosen primarily because it was pure juice with the same colour and tasted quite similar to treatment A. The glucose levels were determined by using a Bayer's CONTOUR® hand-held glucosometer.

Cups containing either treatment A or treatment B were separated on a table in an allocated area and were labeled as either "A" or "B". The drinks were poured by a head technician who was behind a curtain and out of sight of the participants. Each athlete had his/her baseline blood glucose recorded, and was then asked to consume either treatment A (n=496) or B (n = 387). Neither the participant nor the technicians who measured the blood glucose levels had prior knowledge about the treatment details. Once all the athletes had their baseline levels measured and had also consumed their drinks, they were asked to return within a 30-60 minutes interval to allow for a final blood glucose measurement. There was no attempt to control what the participants ate or drank prior to the baseline measurement; however, after being treated, they were encouraged to refrain from consuming simple carbohydrates.

The data were entered into the SigmaPlot 11.0® statistical programme and were analysed by using an unpaired comparison t-test. A descriptive statistics software (mean and standard deviation) was used to perform the t-test for each group of data. A confirming data analysis was conducted independently by using the SAS© statistical programme, which utilized a mixed model analysis of variance. All of the data were reported by considering p values of ≤0.05 as significant and p values of ≤0.01 as highly significant.

RESULTS

The baseline measurements were successfully recorded from a total of 883 individuals who returned for a post-treatment glucose measurement; 496 individuals (53.6% males and 46.4% females) were treated with eXfuze™ Seven⁺, while 387 individuals (59.2% males and 40.8% females) were treated with the grape juice placebo. The volunteer's name, type of sport, age, gender, the time the drink was consumed, and the time he/she returned was also noted down [Table/Fig 1].

	Treatment A (eXfuze seven+)	Treatment B (placebo)	Total
Number of participants	496	387	883
Age Range	18-90	18-89	18-90
Number of males/females	266/230	229/158	495/388
Average age	64.048	64.478	64.263

[Table/Fig 1]: xxxxxx

The treatment subjects started at an average baseline glucose level of 109.65 mg%, and they decreased by -1.76 points to a value of 107.89 mg%. The control subjects had an average baseline of 108.04 mg% and they increased by a +2.12 point change to 110.12 mg%, thus creating an opposite trend from the treatment. The conclusions from both the statistical programmes were identical. The results showed that the decreasing trend of the treatment was significantly different (p = 0.0128) from the increasing trend of the placebo.

We observed that there was a 0.169 mg % increase in the blood glucose levels per year of age, meaning that in general, the older volunteers had an increasing trend of having higher glucose levels. However, there was no significant difference between age and treatment (p = 0.680). There was also no significant gender difference between the two treatments (p = 0.063) and no treatment differences with time (p = 0.457) and gender (p = 0.912). In general, males had higher blood glucose levels than females by about seven points [Table/Fig 3].

Treatment		Blood glucose (mg %)	Change in blood glucose levels (mg%)	p - value
eXfuze Seven +	Before	109.65	Δ -1.76	
	After	107.89		
Placebo	Before	108.04	Δ + 2.12	0.0128
	After	110.12		

[Table/Fig 3]: xxxxxx

DISCUSSION

eXfuze Seven7⁺ (eXf+) has a unique blend of fruits that uses a proprietary method to extract and fuse the fruits together. This particular blend of fruits may be the key to its overall effect in lowering the blood glucose levels. Although there are extensive literature reports on the health effects of some components of eXfuze Seven7+ (eXf+ such as seabuckthorn and brown seaweed), there are only a few studies which have reported on a mixture of multiple fruits and none on eXf+ [2], [3].

Torronenet al. [4] and Baechler et al. [5] studied a mixed berry puree and a multi-phytonutrient supplement. Their first experiment showed that berries which were rich in polyphenols can lower the postprandial plasma glucose levels. They showed further, that a liquid multi-phytonutrient supplement has DNA protective qualities. Similarly, eXf+ includes a berry which is known as the seabuckthorn, a fruit which was originally found in Eurasia. Its seed and leaf extracts seem to have significant antioxidant properties. It appears that the supplementation of the seabuckthorn seed residues might be a helpful in preventing hyperlipidaemia and oxidative stress [6], [7]. Seabuckthorn leaf extracts apparently have cytoprotective properties which can help in modulating chromium induced oxidative stress injuries. In addition, the cytoprotective properties of the seabuckthorn flavones have been attributed to their antioxidant activities [8]. A recent study on seabuckthorn shows that it has stabilizing effects on insulin and glucose levels after a high glucose meal [9]. Evidently, seabuckthorn has significant hypoglycaemic effects, which may make it one of the main contributors of eXf+'s overall hypoglycaemic effect.

Noni (*Morindacitrifolia*), a traditional Tahitian medicinal fruit, has conflicting data which is relative to its possible role in reducing the blood glucose levels. For example, Soon and Tan showed that the dried roots of *Morindaofficinalis* have hypoglycaemic, hyperglycaemic, and antioxidant properties. Furthermore, its antioxidant properties can be traced to two specific chemical constituents: neolignan and americanin (Su et al. [10]). Other studies suggest that noni reduces oxidative stress by decreasing the superoxide anion radicals and the lipid hydroperoxides which contribute to hypoglycaemia [11]. However, Sabitha et al. [12] reported that the postprandial blood glucose levels across the placebo and the treatment group were statistically significant, although comparisons within the separate groups were insignificant.Thus, they concluded that noni's effect on the glucose levels and on the plasma lipid levels were inconclusive.

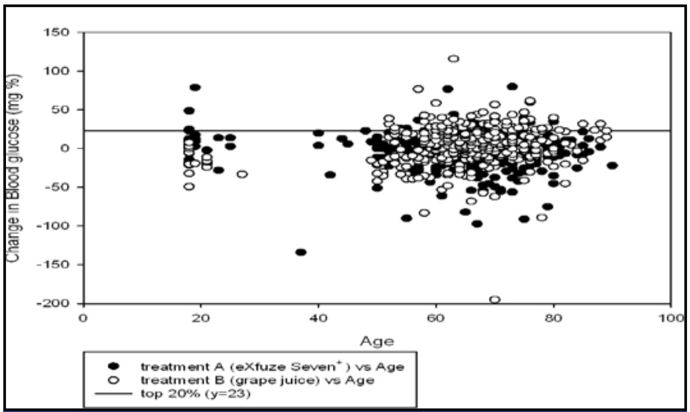
Goji (*Lyciumbarbarum*) has also been shown to have some antioxidant properties. Amagaseet al. [13] showed that the use of a *Lyciumbarbarum* preparation beyond 30 days reduced the free radicals. Also, when an extracted polysaccharide from goji was tested on DNA-damaged rats with non-insulin dependent diabetes mellitus (NIDDM), it was found to significantly decrease the blood glucose levels. Wu H et al. [14] showed that NIDDM rats who were tagged with superoxidedismutase and malondialdehyde oxidative stress markers controlled the blood glucose levels and modulated glucose metabolism—thus significantly improving these stress markers. Wu SJ et al. [15] concluded that *Lyciumbarbarum* could be an excellent dietary supplement for those who needed a good source of antioxidants and that it may help in reducing oxidative stress and inalleviating some hypoglycaemic complications. By the inclusion of this fruit the drink, it may be a possible link to the drink's hypoglycaemic activity.

Brown seaweed (*Laminaria japonica*) is another ingredient that contains antioxidants such as pigments and polyphenols. These components apparently inhibit lipid peroxidation and scavenging reactive oxygen radicals, thus making brown seaweed a potential candidate for lowering the blood glucose levels in vivo16. Experimental studies on diabetic rats showed a decrease in the blood glucose levels when the *Laminaria japonica* extract was given to the animals [17]. Thus, the current studies demonstrate that brown seaweed may also be a contributing factor in lowering hyperglycaemia and in preventing possible vascular complications [17]. Other researchers have suggested that fucoidan (a component of brown seaweed) is a good antioxidant [18]. However, unpublished data from our laboratory suggest that the antioxidant level of brown seaweed (9300 µmol TE/ 100g) is the lowest among the seven tropical fruits which are found in eXf+. Hence, the antioxidant/hypoglycaemic value of brown seaweed is still open to questions. Some studies have shown that certain isolated compounds from Laminaria japonica inhibit free radical chain reactions. This was concluded by Zhao et al [19] in their study, about a low molecular weight sulfated polysaccharide which was extracted from *Laminaria japonica*.

Research on the açai berry has shown that it has significant antioxidant levels in human healthy volunteers [20], but that there are no significant publications on its effects on the blood glucose levels. There are also no well-defined research articles on the effects of mangosteen on the blood glucose levels.

Considering this discussion, it is not surprising to find that a mixture of these foods in eXf+ causes a decreasing trend in the blood glucose levels, since some of the individual components have been shown to contribute to hypoglycaemia. It was however unexpected that this nutritional supplement caused a glucose lowering trend within just one hour post-treatment. In Table/Fig 2, we can see that the plot of all the data may at first glance, seem to be simply a cluster of insignificant data points. However, when we take the top 20% of both the treatments and count as to how many individuals had a change of blood glucose levels of 23 mg% or higher, we can see that there are twice as many in the placebo group (treatment B, 64 individuals) than in the eXf+ treatment group (treatment A, 31 individuals). These data support the analysis and the conclusion of the treatment A data by showing a significant decreasing trend of -1.76 mg%.

Often, health professionals will recommend the control the blood glucose levels through diet and exercise before prescribing drugs to treat severe hyperglycaemia. For example, the American Diabetes Association3 recommends that the normal blood glucose levels by using the AIC test (the average glucose for the past 2-3 months) must be less than 7.0% and that the preprandial plasma glucose levels (before a meal) must be 70-130 mg/dl (5.0-7.2 µmol/L). In addition, it recommends that the postprandial plasma glucose (after a meal) must be less than 180 mg/dl (<10.0 µmol/L). The signs of hyperglycaemia include a blood glucose level over 240 mg/dl and the presence of ketones in the urine. Therefore, if this dietary supplement has a blood glucose lowering effect, many people who struggle with hyperglycaemia could benefit by adding this nutritional supplement to their diet. Still, there is much that we don't understand about the precise mechanisms of how these fruit-derived, anti-hyperglycaemic chemicals work. [Table/Fig 2]



[Table/Fig 2]: Summary of the change in blood glucose (mg %) followed as a function of age for both treatment A (eXfuze Seven+, dark circles) and treatment B (grape juice, open circles). There were 64 individuals from treatment B who had a blood glucose change of 23 mg% or higher, while there were 31 individuals in treatment A, with a blood glucose change of 23 mg% or higher.

Investigations are continuing in our laboratory on these mechanisms, while we are also trying to determine whether there is any synergistic hypoglycaemic activity when the fruits are mixed together, one at a time, in an appropriate experimental design.

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