Effect of the consumption of a fibrous extract of *Stevia rebaudiana* Bertoni Stems on glycemia

Efecto del consumo de un extracto fibroso de tallos de *stevia rebaudiana* Bertoni sobre la glicemia

Enrique Barbosa-Martin[1], Juan Eduardo Moguel-Ceballos[2], Cristina Rodriguez-Rosas[3], Dora Edih Valencia-Rivera[4], Addy Leticia Zarza -Garcia[5]

DOI: 10.19136/hs.a21n2.4707

Research article

• Received date: September 1, 2021 • Accepted date: October 29, 2021 • Online publication: April 8, 2022

Corresponding Author:

Addy Leticia Zarza Garcia. Postal Addres: Av. Central s/n Esq. Fracc. Maya world. C.P.24153. Cd Carmen, Campeche, Mexico E-mail:azazarza@pampano.unacar.mx

Abstract

Objective: To evaluate the effect of the ingestion of a fibrous extract of *Stevia rebaudiana* Bertoni stems on postprandial glycemia levels in healthy subjects.
Materials and Methods: Cross-sectional, experimental research, carried out with ethical conditions of consent and reliability, in the Laboratory for the Evaluation of Nutritional Status of the Autonomous University of Carmen. For the clinical and anthropometric assessment of the participants, a medical history and body composition scan were used, respectively. The study population consisted of 16 healthy women with normal body mass indices (20-25 kg/m^2). Instruments: a) Clinical-dietetic record and b) Biochemical data obtained from blood sampling obtained at different times. The data analysis was carried out with descriptive statistics.
Results: The results shown in the group of participants in this study, it was observed that the mean value of the area under the curve (AUC) of glucose was 709.18 ± 23.60, while that of the fibrous extract of stevia stems was 556.59 ± 50.47 .
Conclusions: *Stevia rebaudiana* stems, due to their dietary fiber content, can be an alternative for the use and revaluation of sustained waste in the circular economy in the development of functional products, giving it an added value that contributes in some way to reducing overweight and obesity, with a hypoglycemic effect in patients with type 2 diabetes mellitus (DM).

Keywords: Stevia; Plant Stems; Blood glucose

Resumen

Objetivo: Evaluar el efecto de la ingesta de un extracto fibroso de tallos de *Stevia rebaudiana* Bertoni sobre los niveles de glicemia postprandial en sujetos sanos.
Materiales y Métodos: Investigación transversal, experimental, realizada con condiciones éticas de consentimiento y confiabilidad, en el laboratorio de Evaluación del Estado Nutricional de la Universidad Autónoma del Carmen. Para la valoración clínica y antropométrica de los participantes se utilizó una historia clínica y escáner de composición corporal, respectivamente. La población de estudio fue conformada por 16 mujeres sanas con índices de masa corporal normales (20-25 kg/m^2). Instrumentos: a) Expediente clínico-dietético y b) Datos bioquímicos obtenidos de la toma sanguínea obtenidos en los diferentes tiempos. Se realizó el análisis de los datos con estadística descriptiva.
Resultados: Los resultados mostrados en el grupo de participantes en este estudio, se observó que el valor medio del área bajo la curva (AUC) de la glucosa fue de 709.18 ± 23.60, mientras que el del extracto fibroso de tallos de stevia fue de 556.59 ± 50.47.
Conclusiones: Los tallos de *Stevia rebaudiana* Bertoni. por su contenido en fibra dietética, pueden ser una alternativa para el uso y revalorización de residuos sostenidos en la economía circular en el desarrollo de productos funcionales, otorgándole un valor agregado que contribuye de alguna manera a reducir el sobrepeso y la obesidad, con efecto hipoglucemiante en pacientes con diabetes mellitus (DM) tipo 2.

Palabras clave: Stevia ; Tallos de la planta ; Glucemia

[1] Master in Food Sciences and Biotechnology. Doctoral student in Experimental Clinical Research in Health, Laboratory of Diabetes Genomics, Yucatan Academic Unit, National Autonomous University of Mexico.

[2] Master of Science in Hospitality Management. Full-time research professor PE Nutrition Autonomous University of Carmen. City of Carmen, Campeche, Mexico

[3] Master in Chemical Analysis. Head of the Food Microbiology and Toxicology Laboratory. Autonomous University of Carmen. City of Carmen, Campeche, Mexico

[4] Master in Polymer and Materials Sciences, Doctorate in Sciences. Full-time Research Professor of the PE Chemical Clinical Biologist. Affiliation Department of Chemical-Biological and Agricultural Sciences. University of Sonora, Campus Caborca, Sonora, Mexico

[5] Master of Science in Science Teaching. Doctorate in Food Sciences and Biotechnology. Full-time research professor at PE Nutrition. Autonomous University of Carmen. City of Carmen, Campeche, Mexico

Introduction

The postprandial state (from Latin post-prandium) is defined as the period following the consumption of food; therefore, glycaemia and postprandial dyslipidemia refer to the variation in plasma glucose and lipid concentrations, respectively. Scientific evidence shows that there is a correlation between the abnormal postprandial state and the development of atherosclerosis[1,2]. During the postprandial metabolism of food fats, lipoproteins abundant in triglycerides of intestinal origin are generated that can interact with circulating leukocytes, with macrophages and with cells of the smooth muscle of the vascular wall. This can cause localized accumulation of lipids, as well as variations in the expression of genes related to atherosclerosis. Similarly, it has been observed that lipid deposits in the arteries are not only a consequence of the high concentration of low-density lipoproteins (LDL) in the plasma but are also the result of a normal process of absorption, transport, and deposition. serum lipids. On the other hand, experimental studies indicate that the size of the particle is a key point and determinant of atherogenicity. The size of the LDL particles (18-25 nm) and the HDL high-density lipoprotein (10-25 nm) allow them to cross the endothelium, however, their effect is opposite since LDL is atherogenic and HDL is antiatherogenic. This is due to the participation of HDL in the so-called reverse cholesterol transport[3].

Atherosclerosis is a systemic inflammatory disease with a high predisposition to trigger cardiovascular diseases, it develops gradually, its pathogenesis is multifactorial, genetic and environmental factors intercede, that is, unhealthy habits (no physical activity, non-beneficial diet rich in fat , sugars, alcohol consumption and smoking)[4], it is a process in which the arteries of medium and large caliber enlarge and become rigid, there is a distensibility of the vessel, accumulation of atheroma plaques, response of inflammatory mediators , damage to the endothelium and formation of thrombi, excess cholesterol can precipitate in the form of crystals within the macrophage (cells specialized in the localization and phagocytosis of bacteria and other organisms), that activates inflammasomes, cytoplasmic complexes with rich proteins that play a primary role in the inflammatory process (cytokine 1L1β), there is recent evidence that the NLRP3 inflammasome is a key point in the progression of atherosclerosis[5,6], without a doubt the ight inflammation is the fundamental part of many chronic diseases, it has been observed that this process is related to age, at older age there is an exponential increase in the risk of inflammation, becoming a factor in the development of cardiovascular disease (CVD), related with affections to the heart or blood vessels, the most frequent are coronary artery disease, stroke, venous thrombosis, cardiomyopathy, hypertensive heart disease, thromboembolic disease and arrhythmia[7].

Currently there are studies focused on evaluating and characterizing dietary fiber in various sources of residues of different plant species[8,9,10] considering the role and its beneficial chemical and biological attributes of its consumption in health, which is why there is interest in the food industry to use it in the manufacture of high consumption products such as bakery and pastries.

Dietary fiber is an entity made up of different compounds, in relation to its chemical structure, its physical and biological properties, it is a heterogeneous mixture of different compounds, which is why it has been the subject of controversy to define it, dietary fiber comes from various sources , like vegetables, it is considered with prebiotic effects with functional activity, this depending on the type of fiber and the microbiota of the individual, its function in health goes beyond the nutritional aspect, it is not absorbed or digested in the intestinal tract superior, reach the colon intact where they are attacked by the intestinal microbiota[11].

Dietary fiber exerts an action in the protective control against cardiovascular diseases, as well as in the decrease of the postprandial serum concentration of glucose and insulin, both in healthy individuals and in those suffering from Diabetes mellitus (DM); the mechanism is explained by the increase in the viscosity of the nutrient content in the small intestine, which delays the diffusion of glucose towards the ciliated border of the intestinal mucosa; the binding of glucose to dietary fiber (DF) and a decrease in its availability for absorption; and the inhibition of the action of α-amylase on starch[12].

There is scientific evidence on the medicinal and nutritional properties, among others, of Stevia leaves[13]; facilitates digestion, gastrointestinal functions and maintains the feeling of vitality and well-being, due to the presence of water (80% to 85%), glycosides, β-carotene, chromium, riboflavin, cobalt, magnesium, potassium, iron, phosphorus, thiamine, zinc, etc. Through various investigations it has been shown that the extracts of stevia leaves are safe for use in food and beverages for the entire population in general, without any side effects, through various investigations it has been shown that the extracts of the Stevia leaves are safe for use in food and beverages for the entire population In general, without any side effect[14], however there is little scientific literature on the physicochemical and biological properties of stevia (*Stevia rebaudiana* Bertoni) stems, these tissues are generally considered as waste, so they are little used, some reports of the literature mention about the attributes of these tissues, they constitute a good source of bioactive compounds with different mechanisms of action[15], among these compounds is dietary fiber[16] which could be used to develop functional foods for the regulation of energy intake and reduction of intestinal absorption of nutrients, improving

yes the energy available, according to the above, the intention of this study was to evaluate the effect of consumption of a fibrous extract of *Stevia rebaudiana* Bertoni on postprandial glycemia levels in healthy subjects.

Materials and Methods

Raw Materials

Stems of *Stevia rebaudiana* Bertoni, Morita II variety, provided by the Mochochá Experimental Field, National Institute of Forestry, Agricultural and Livestock Research (INIFAP), Yucatán, Mexico were used. The phenotypic traits of the selected variety are: thick-branched stems and elliptical-shaped leaves arranged in an opposite way. The samples were obtained from the first cut of the plants of the experimental plots at the age of three months and were dried for three days, from 9:00 to 12: 000, in periods of sun-shade.

Once the stems were obtained, they were dried in a Fisher Scientific oven (USA) at 50° C for 24 hours, processed in a Thomas Wiley Model 4 toothed mill (USA) and finally sieved on a 2 mm mesh.

Obtaining fibrous residue

Sodium bisulfite ($NaHSO_3$) 1500 ppm [17] was used in a ratio of 1: 5 (p/v) and it was allowed to react for 30 minutes stirring constantly. Subsequently, the resulting solution was filtered using a mesh number 80 and the non-filtered material (fiber) was dried at 50° C for 24 hours in a Fisher Scientific oven (USA).

Type of study and ethical considerations

The approach of the present study is cross-sectional and experimental, carried out with ethical conditions of consent and reliability. For this, the guidelines established in the Declaration of Helsinki[18] were followed and the protocol of this project was approved by the Bioethics Committee of the Faculty of Health Sciences of UNACAR (Oficio de registro: F.C.S./I.287/19). Each participant voluntarily agreed to participate, and their signatures were collected on an informed consent letter, with a confidential nature assured.

Inclusion and exclusion criteria.

Inclusion criteria: age, normal body mass index, sex, health status.

Exclusion criteria: suffering from or having a disease, being in control with any medication, presence of pregnancy.

Anthropometric and biochemical measurements

The study population (16 women) underwent a detailed medical history in order to have family and personal history data, as well as a physical examination to determine the normal state of health of the participants. The instruments used were: a) Clinical-dietary record and b) Biochemical data derived from the blood sample at different times.

Medical records were used to assess state of health of the participants and for the analysis of body composition, a RJL brand equipment, Quantum III model, year 2009 and a Seca brand wall stadiometer, model 2006, s/a were used. For the analysis of serum glucose, a Chenwell 2910 equipment was used, which is based on the glucose oxidase method[19].

Postprandial trial

The study population was made up of 16 healthy women (without chronic degenerative diseases) and with body mass index (BMI) within the normal category. The inclusion criteria were age, normal body mass index, sex, health status, the exclusion criteria: suffering from or having a disease, being in control with any medication, presence of pregnancy.

All participants were recruited in the Laboratory for the Evaluation of Nutritional Status of the Faculty of Health Sciences of the Universidad Autónoma del Carmen, Campeche. First, there was an introductory session, where the volunteers were explained the methodology to follow; In this session, informed consent signatures and medical history data were also collected to validate their health status.

To carry out the test, the participants were instructed to have dinner the day before at 9:00 p.m. and that it consist of standardized dishes (quesadillas, sandwiches, hot cakes, etc.) that did not exceed 600 kcal. Similarly, it was confirmed that 24 hours prior to the experiment they had not drink alcohol or performed excessive physical activity. Likewise, a fast of at least 10 hours prior to the test was indicated.

The postprandial trial was carried out using three experimental phases: reception, administration of the extract and measurement of glycemia. On each day of the experimental session, the volunteers were summoned at 07:00 hours and after their arrival they were given a 10-minute rest (reception phase). After resting, the first glucose measurement was performed (Time 0') and immediately afterwards, 5 g of fibrous extract of Stevia stems (B.S.) mixed in 250 ml of water (extract administration phase) were administered orally. At 15 minutes the second blood extraction was carried out (T 15') and subsequently at 30, 45, 60, 90 and 120 minutes (T 30', T 45', T 60', T 90' and T 120', respectively); measuring the serum glucose concentration at each time (measurement

phase). During the course of the experiment, the participants could drink only 200 ml of water and could not sleep or engage in physical activity. The test was repeated seven days apart but using 75 g of anhydrous glucose dissolved in 250 ml of water as a control.

Glycemic index estimation

The glycemic index is recognized as a measure to establish the acute impact of carbohydrates in a food on blood glucose. According to the above, foods with a high glycemic index promote an increase in glycemia, and the opposite happens with those with a low glycemic index**.**

It was carried out based on a standardized methodology[19] with some modifications. Using the glycemia values of the times described in the postprandial test, the percentage of glycemia variation at the different times was estimated, as well as the area under the curve (AUC); both for the fibrous extract and for glucose. Based on the above, the glycemic index (GI) was estimated using the following formula:

$$GI = \frac{\text{AUC of fibrous extract}}{\text{AUC of glucose}} x\ 100$$

Finally, the average of the individual GIs was calculated, and this was reported as the GI of the fibrous extract.

Statistic analysis

First, the data normality test was performed using the Shapiro-Wilk test, both for the descriptive variables of the population and for the glycemia values by time. Based on the normal distribution of the data, paired T tests were used to identify differences in means.The values are reported as the mean ± standard deviation, values were considered statistically significant at $p<0.05$.

For the paired data analysis, the SPSS Version 20[20] statistical program was used, and the GraphPad Prism 7.0 program was used to calculate the areas under the curve.

Results

The evaluation was carried out in a sample of 16 young and healthy female volunteers. The population median was 22 years old, and the mean BMI was 21.6 kg / m2 ± 1.69 (Table 1). The foregoing reveals that the study population presented a normal weight, since according to the BMI criteria proposed by the World Health Organization (WHO) [21] it is categorized within the "normal" range.

Table 1. General characteristics of the studied population

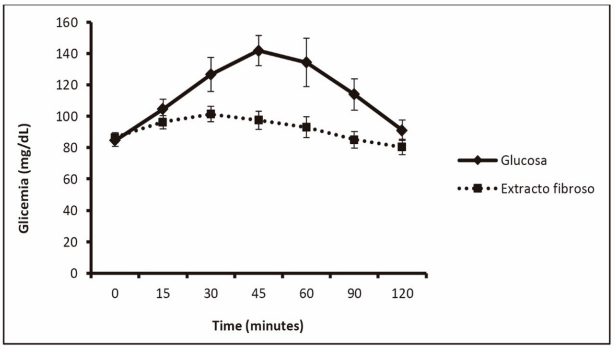
Variable	Results
Age (years)	22 (22, 23)
Weight (kg)	54.26 ± 6.85
Height (cm)	157.93 ± 6.03
BMI (kg/m^2)	21.68 ± 1.69

Source: elaboration from own data

Considering that time 0 (T 0') of the postprandial test corresponds to fasting glycemia, it was observed that no participant showed altered glucose levels, according to the diagnostic criteria of the American Diabetes Association[22]. In this same sense, no statistical differences were observed between the means of the T 0' glycemia of the test with the fibrous extract and the control test with glucose (86.50 ± 6.40 mg / dL and 84.62 ± 7.42, respectively; $p = 0.225$) (Figure 1).

When comparing between the different times, it was observed that there were statistical differences in the times T 15', T 30', T 45', T 60' T 90' and T 120', between the glycemia of the test with the fibrous extract and of the control test with glucose ($p <0.05$). At these same times, significantly lower glycemic values were observed in the test with the fibrous extract ($p<0.05$)(Figure1).

Figure 1. Glycemic response to treatments. * $p <0.05$, ** $p <0.001$. Paired T-Student test

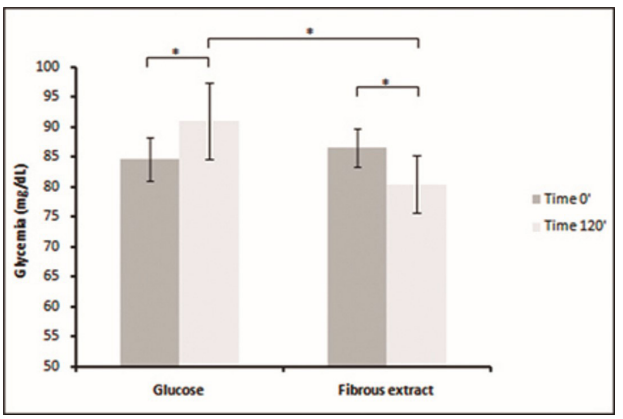


Source: elaboration from own data

Another relevant aspect is that when comparing T 0' and T 120' in the control test with glucose, it was observed that the glycemia at the end time (91 ± 12.89 mg / dL) was significantly higher than the baseline glycemia (84.62 ± 7.42 mg / dL) ($p = 0.029$). This shows that, in the study population, 120 minutes after ingesting a glucose load is not enough to recover baseline blood glucose levels. This was a contrary condition to that observed in the treatment with the fibrous extract, since after 120 minutes of ingestion

of this, the glycemia was significantly lower than the basal glycemia (80.4 ± 9.69 and 86.5 ± 6.4, respectively; p = 0.006). Statistical differences were even observed between the glycemia in T 120' of the control group and the fibrous extract (p = 0.001). No statistical differences were observed between the glycemia at T 0' of the control group and the treatment group (p = 0.225) (Figure 2).

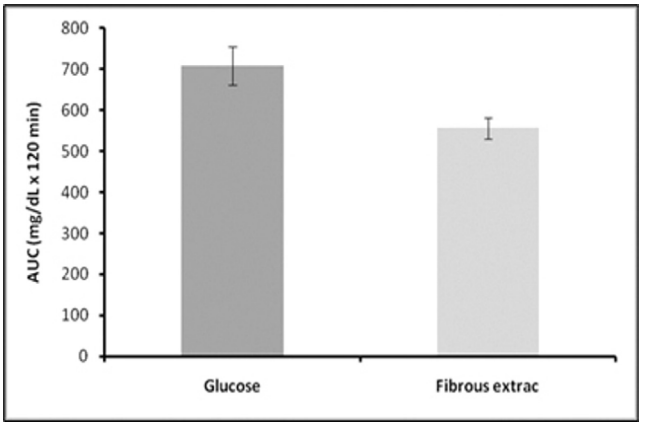
Figure 2. Glycemic response to treatments at times 0' and 120'. *p <0.05. Paired T-student test.



Source: elaboration from own data

The average value of the area under the curve (AUC) of glucose was 709.18 ± 23.60, while that of the fibrous extract of stevia stems was 556.59 ± 50.47 (figure3).Statistical analysis revealed that the AUC of glucose was statistically higher than that of fiber extract (p = 0.0001). Based on these data, it was estimated that the glycemic index of the fibrous extract was 79.2%, which makes it similar to foods such as whole wheat bread[23].

Figure 3. Area under the curve of treatments.



Source: elaboration from own data.

Discussion

According to analyzed data in this study, the glycemic response with the fibrous extract was significantly lower than with the glucose control; It can be seen that before consumption the mean of the reference food was 89mg / DL at minute 15; with the fibrous extract it was reduced (84.62 mg / DL), and at 120 minutes it was 129mg / DL (reference food), and 97mg / DL (fibrous extract); the results shown were similar to the trial reported in another study[24] .

In a report with extracts from *Stevia* leaves[25] the results were optimal at minute 20 after stevia overload; In a different trial to measure and compare the postprandial effect of dietary fiber with other digestible carbohydrates[26] it was observed that at minute 30 the postprandial effect was lower with dietary fiber than in the samples of digestible carbohydrates, the evidence shows that there is a notable decrease of glucose; Scientific evidence about dietary fiber demonstrates its favorable effects on health, such as the benefit in the absorption and regulation of blood sugar levels, promote the health of the intestinal microbiome, help control healthy weight, inducing satiety, promote digestive health, stimulate the reduction of total cholesterol in the blood, decrease the risk of developing cancer, among others[27]. In the different studies, there are positive results that indicate that stevia extract can be used as an additive into food. In the aforementioned study[24] 3 different formulations were used: 25%, 50% and 75% of the stevia extract, in our study 5 grams of extract were used and similar results were obtained, reducing blood glucose in the study subjects. However, for Antón[25] study, the formulation of stevia used to make his product is not shown. Specific studies by administering 6 g of partially hydrolyzed gum agar (soluble fiber) at each meal for twelve months, it was observed that postprandial plasma glucose levels and triglycerides were significantly reduced; the American Diabetes Association recommends the consumption of 20 to 25 g / day in healthy people and up to 50g / day in people with Diabetes; However, the amounts present limitations in palatability and secondary gastrointestinal problems[28] in Mexico there are not complete tables of fiber content in foods, The tables recording the fiber content refer to tables from other (foreign) countries, which do not refer to the type of chemical analysis to calculate it[29], considering that each food has different types of fiber, so it can be over or underestimated in For each food, it is admitted that the population living in the field consumes a greater amount of fiber, this population ingests significant amounts of fruits, vegetables, greens, cereals and legumes where fiber is present, a report from ENSANUT 2012 shows the lack in fiber consumption from an early age[30], and the results of the mid-way survey of ENSANUT 2016 show data of lack of fiber consumption in children with food insecurity from 24 to 59 months, in adolescents (men:

23.7 g, and women 21.2 g), observing lower consumption in older adults (men: 20.2, and women: 17.9g)[31], according to this report, rural localities in Mexico are going through a change in their eating habits, they are substituting natural to processed foods, due to the accessibility of this type of food. products, observing a preference for foods and beverages sweetened with refined sugars and high in saturated fats, and a significant decrease in the consumption of natural foods, a source of vitamins, minerals, and fibers, this is influencing the increase in overweight and obesity, diseases related to chronic degenerative diseases such as diabetes mellitus (DM), hypertension, among others.

Advances in food and nutrition technology have contributed to the design and development of an extensive range of foods rich in dietary fiber based on their technological properties that have been accepted by consumers interested in maintaining healthy diets, with respect to this type. food. products, in Mexico there are a series of complementary laws and official standards (NOM) that must comply with the labels of all industrialized products to guide the consumer[32], among these is the Official Mexican Standard NOM-043-SSA2-200533[33], Basic services of health. Promotion and education for health in alimentary matters. Criteria for providing guidance; NOM-051-SCFI / SSA1-2010[34], among the general labeling specifications for prepackaged foods and non-alcoholic beverages -Commercial and health information, establishes that in the declaration of the nutritional properties of an industrialized food it is necessary to provide information to the consumer about the amount and type of dietary fiber (polymers of natural carbohydrates, those obtained from food raw materials by physical, enzymatic or chemical and synthetic means with beneficial effects on health) of the product in question in the nutritional tables, in the modification of this standard (NOM-051-SCFI / SSA1-201034)[35] the front labeling system of products is established, to guide the consumer in the nutritional criteria on the content of excess energy, critical nutrients and ingredients that represent excessively a health risk.

Considering the chemical characteristics of *Stevia rebaudiana*, classified as a 100% natural non-toxic[36] species, supported by various scientific studies that have been carried out on leaves and stems, have shown its safety, most of these studies have focused on its sweetening power , especially from the leaves, without caloric intake when metabolized, is antacid, cardiotonic, does not cause tooth decay when fermented by oral bacteria, with microbiological activity, improves hypertension, among others, so through this study they are provided interesting data regarding the impact of the beneficial effects of *Stevia rebaudiana* fibers on health.

Conclusions

The fibrous extract of *Stevia rebaudiana* stems has a high fiber content; The results obtained in this study provide and contribute with scientific information about the physiological effect and health benefit in the consumption of dietary fiber in the diet, considering the amount, its ingestion favors the glycemic response in healthy patients, compared to reference foods. In summary, *Stevia rebaudiana* stems, due to their dietary fiber content, can be an alternative for the use and revaluation of waste sustained in the circular economy for the development of functional products, giving it an added value that contributes in some way to reducing overweight and obesity, with a hypoglycemic effect in patients with type 2 diabetes mellitus (DM), because it benefits the decrease in postprandial glycemia, improving the insulin resistance of these patients, in addition to that this fiber would grant qualities by improving the texture an+d palatability of foods allowing to partially replace sugars and fats, reducing the calorie content of the products in which they are incorporated.

Conflict of interests

The authors declare that they have no conflict of interest in this research.

Acknowledgements

To the Health Sciences Department at the Universidad Autónoma del Carmen, to the coordinator of the Educational Program of nutrition, Dr. Ángel Esteban Torres Zapata, for all the facilities granted to carry out this research in the Nutritional Status Evaluation laboratory.

Authors' contribution

Conceptualization and design: A.L.Z.G., E.B.M., C.R.R; Methods: A.L.Z.G.,E.M.B..,C.R.R.,J.E.M.C; Data collection and software: C.R.R., D.E.V.R.,J.E.M.C; Data analysis: A.L.Z.G.., C.R.R.,E.B.M..; Principal Investigator: A.L.Z.G.; Research: A.L.Z.G., E.B.M., C.R.R.,J.E.M.C.,D.E.V.R ; Manuscript preparation: A.L.Z.G., E.B.M.,D.E.V.R.; Manuscript revision and editing, A.L.Z.G.,E.B.M.,C.R.R.,,D .E.V.R.; Visualization;J.E.M.C., CRR. D.E.V.R; Translation; J.E.M.C., A.L.Z.G. Supervision: A.L.Z.G., E.B.M., J.E.M.C..; Financing ALZG. , J.E.M.C., CRR.

References

1.Gerstein HC, Yusuf S. Dysglycaemia and risk of cardiovascular disease. Lancet. [Internet]. 1996 [Citado 11 mayo 2021]; 6(347):949-50. doi: 10.1016/s0140-6736(96)91420-8. PMID: 8598762.

2.Zilversmit DB, Atherogenesis a postprandial phenomenon; Circulation[Internet].1979[Citado 20 mayo 2021]; 60: 473-485 DOI: 10.1161 / 01.cir.60.3.473.

3. Borén J, Matikainen N, Adiels M, Taskinen MR. Postprandial hypertriglyceridemia as coronary risk factor. Clin Chim Acta [Internet].2014[Citado 26 junio 2021]; 431:131-142. DOI: 10.1016 / j.cca.2014.01.015

4. Attaye, I., Pinto-Sietsma, S, Herrema ., Nieuwdorp, M. Un papel crucial de la dieta en la relación entre la microbiota intestinal y la enfermedad cardiometabólica. Annu. Rev. Med. [Internet].2020 [Citado 10 julio 2021]; 71: 149–161. https://doi.org/10.1146/annurev-med-062218-023720

5. Fatkhullina, AR, Peshkova, IO, Koltsova, EK. The Role of cytokines in the development of atherosclerosis. Biochemistry (Moscow). [Internet].2016 [Citado 20 julio 2021]; 81 (11): 1358-1370. https://doi.org/10.1134/S0006297916110134

6. Karasawa, T., Takahashi, M. Role of NLRP3 inflammasome in aterosclerosis. J. Atherosclerosis Thromb. [Internet].2017[Citado 03 agosto 2021]; 24:443-451. DOI https://doi.org/10.5551/jat.RV17001

7. Gerdes V, Guiemonde, M, Pajunen, L, Nieuwdorp, M, Laitinen, K. How strong is the evidence that gut microbiota composition can be influenced by lifestyle interventions in a cardio-protective way? Atherosclerosis. [Internet].2020 [Citado 25 julio 2021]; Vol. 311: 124-142. doi.org/10.1016/j.atherosclerosis.2020.08.028

8. Torres-Zapata, AE, Aparicio-Trápala M.A, Blé- Castillo JL, Corzo-Sosa, CA. Respuesta Glucémica e Insulínica de Pacientes con Diabetes Tipo 2 al consumo de Sopa de Calabaza Criolla (*Cucúrbita Pepo L*.) Enriquecida con Almidón de Banano. Inf. tecnol.[Internet].2012 [Citado 17 julio 2021]; 23(2): 71-86. doi.org/10.4067/S0718-07642012000200009

9. Barbosa-Martín E, Chel-Guerrero L, González-Mondragón E, Betancur-Ancona, D. Chemical and technological properties of avocado (P*ersea americana Mill*.) seed fibrous residues. Food and bioproducts processing [Internet]2016[Citado 25 julio 2021]; 100:457–463. http://dx.doi.org /10.1016/j.fbp .2016.09.006096 0-3 08

10. Zarza -García, AL, Moo-Huchín, VM., Toledo-López, VM, Godoy-Hernandez G, Rivera-Cabrera, F, Clarenc-Aarland R, Sauri-Duch Enrique, Mendoza-Espinoza, JA. Chemical, nutritional, and biological composition of three seed morphotypes of *Bixa Orellana* L. bixaceae (achiote) in the Yucatán Peninsula, México. Pak. J. Bot. [Internet].2021[Citado 27 julio 2021]; 53(6): 1-7. DOI: 10.30848 / PJB2021-6 (12)

11. Carlson JL, Erickson JM, Hess JM, Gould TJ, Slavin JL. Prebiotic Dietary Fiber and Gut Health: Comparing the in Vitro Fermentations of Beta-Glucan, Inulin and Xylooligosaccharide.Nutrients. [Internet].2017 [Citado 29 julio 2021]: 9(12):1361. DOI: 10.3390 / nu9121361

12. Higgins JA. Resistant starch metabolic effects and potential health benefits. J. AOAC Int. [Internet].2004[Citado 30 julio 2021]; 87(3):761-768. DOI: 10.1093 / jaoac / 87.3.761

13. Gupta E, Porwar S, Sundaram S. & Raig Gk. Nutritional and Therapeutic values of *Stevia rebaudiana*: A review. J. Med. Plants. Rest. [Internet]. 2013 [Citado 22 julio 2021]: 7(46) 3343-3353. DOI: 10.5897/JMPR2013.5276

14.Global Stevia Institute (GSI). Estudio de la seguridad de la *stevia* [Internet]. 2013[Citado 30 julio 2021]; disponible en: www.Globalsteviainstitute.com

15. Mendoza-Isaza NA, Hoyos-Arbeláez JA, Peláez-Jaramillo, CA. Capacidad antioxidante y contenido de polifenoles totales de extractos de tallo de *Stevia rebaudiana* en varios modelos *in vitro*. Revista EIA. [Internet].2020[Citado 12 agosto 2021]; 17(34). https://revistas.eia.edu.co/index.php/reveia/article/view/1282

16. Quirós Sauceda, AE, Palafox H., Robles Sánchez RM y González Aguilar, G. Phenolic compounds, and dietary fiber interaction: antioxidant capacity and bioavailability: BIOtecnia. [Internet].2011[Citado 9 agosto 2021]; XIII (3): 3-1. DOI: https://doi.org/10.18633/bt.v13i3.91

17. Moguel-Ordoñez Y, Betancur AD. y Chel, GL. Aprovechamiento integral del grano de Canavalia ensiformis: extracción de proteína y almidón. Tecnología de Alimentos. extracción de proteína y almidón. Tecnología de Alimentos[Internet].1996 [Consultado 15 septiembre 2020]; 31 (1): .11-16. Disponible en: https://www.scirp.org/(S(351jmbntvnsjt1aadkposzje))/reference/ReferencesPapers.aspx?ReferenceID=1330216

18. Declaración de Helsinki de la Asociación médica mundial. Principios éticos para la investigación médica en seres humanos. [Internet].2013:310(20) Disponible en: https://www.wma.net/es/policies-post/declaracion-de-helsinki-de-la- amm-principios-eticos-para-las-investigaciones-medicas-en-seres-humanos/ doi: 10.1001 / jama.2013.281053

19. Granfeldt Y, Björck I, Hagander B. On the importance of processing conditions, product thickness and egg addition for the glycaemic and hormonal responses to pasta: a comparison with bread made from "pasta ingredients". Eur J Clin Nutr. [Internet].1991[Consultado 15 mayo 2020]; 45(10):489-99. Disponible en: https://pubmed.ncbi.nlm.nih.gov/1782920/

20. Startical product and service solutions. Programa estadístico SPSS Versión 20

21. Organización Mundial de la Salud. Obesidad y Sobrepeso: OMS; 2020. Nota Descriptiva. Retrieved from: https://www.who.int/es/news-room/fact-sheets/detail/obesity-and-overweight

22. American Diabetes Association. Resumen de clasificación y diagnóstico de la diabetes; 2020. Sinapsisimex.files.wordpress.com https://sinapsismex.files.wordpress.com/2020/02/resumen-de-clasificacic3b3n-y-diagnc3b3stico-de-la-diabetes-american-diabetes-association- 2020.pdf

23. Arteaga Llona A. El Índice glicémico: Una controversia actual. Nutr. Hosp. 21 (Suppl2) [Internet].2006 [citado 13 jul 2021]; 55-60. Disponible en: http://scielo.isciii.es/scielo.php?script=sci_artte=S0212-16112006000500006&lng=es.

24. Ruiz JC, Moguel YB., Matus, AJ, y Segura MR. Antidiabetic and antioxidant activity of *Stevia rebaudiana* extracts (Var. Morita) and their incorporation into a potential functional bread J Food Scie Technol [Internet]. 2015 [Citado 9 agosto 2021]; 52(12), 7894- 7903. DOI https://doi.org/10.1007/s13197-015-1883-3

25. Anton SD, Martin CK, Han H, Coulon S, Cefalu WT, Geiselman P. y Williamson DA. Behavior of plasma insulin and glycemia when delivered breakfast with two different types of carbohydrates and dietary fiber digestible. Appetite [Internet].2010 [Citado 30 julio 2021]; 55(1), 37-43. https://doi.org/10.1016/j.appet.2010.03.009

26. Reyna N, Mendoza L, Urdaneta A, Añez R, Parra K, Reyna E, Valmore V. Behavior of plasma insulin and glycemia when delivered breakfast with two different types of carbohydrates and dietary fiber digestible. Rev. Latinoam. Hipertens [Internet].2013[Citado 22 agosto 2021]; 8(4): 90-94. Disponible en: https://www.redalyc.org/articulo.oa?id=170231793002

27. Maira Segura-Campos, Enrique Barbosa-Martín, Ángel Matus-Basto, Diana Cabrera-Amaro , María Murguía-Olmedo, Yolanda Moguel-Ordoñez, David Betancur-Ancona. Comparison of Chemical and Functional Properties of *Stevia rebaudiana* (Bertoni) Varieties Cultivated in Mexican Southeast. American. J. of Plant Scienses. [Internet]2014[Citado 3 octubre 2021];5,286-293(http://www.scirp.org/journal/ajps) http://dx.doi.org/10.4236/ajps.2014.53039

28. Vilcanqui-Pérez F. y Vilchez-Perales, C. Fibra dietaria: nuevas definiciones, propiedades funcionales y beneficios para la salud. Revisión. ALAN [Internet].2017[Citado 22 agosto 2021]; 67(2):146-156. Disponible en: https://www.alanrevista.org/ediciones/2017/2/art-10/

29. Abreu y Abreu AT, Milke-García MP, Argüello-Arévalo GA, Calderón-dela Barca AM., Carmona-Sánchez RI, Consuelo-Sánchez A, Coss-Adame E, García-Cedillo MF, Hernández-Rosiles V, Icaza- Chávez ME. Martínez-Medina, JN, Morán-Ramos S, Ochoa-Ortiz E, Reyes-Apodaca M, Rivera- Flores RL, Zamarripa-Dorsey F, Zárate-Mondragón F, Vásquez-Frias R. Fibra Dietaria y microbiota. Revisión narrativa de un grupo de expertos de la Asociación Mexicana de Gastroenterología. Rev de Gastroentrol Mex. [Internet].2021[Citado 18 agosto 2021]; 86(3) :287-304. https://doi.org/10.1016/j.rgmx.2021.02.004

30. Romero-Martínez M, Shamah-Levy T, Franco-Núñez A, Villalpando S, Cuevas-Nasu, L, Gutiérrez JP, Rivera-Dommarco, JA. Encuesta Nacional de Salud y Nutrición 2012: diseño y cobertura. Salud Pública de México [Internet]. 2013 [Consultado 22 agosto 2021]; Vol.55 suplemento 2: 332: 340. Disponible en: https://www.redalyc.org/articulo.oa?id=10628331033

31. Shamah-Levy T, Cuevas-Nasu L, Gaona-Pineda LM, Gómez-Acosta LM, Morales-Ruán MC, Hernández-Ávila M, Rivera-Dommar JA. Sobrepeso y obesidad en niños y adolescentes en México, actualización de la Encuesta Nacional de Salud y Nutrición de Medio Camino 2016. Salud Pública de México[Internet] 2018 [consultado 20 agosto 2021]; 60(3): 244-253. Disponible en: DOI: https://doi.org/10.21149/8815

32. Lizbeth Tolentino-Mayo, Sofía Rincón-Gallardo Patiño, Liliana Bahena-Espina, Víctor Ríos, Simón Barquera. Conocimiento y uso del etiquetado nutrimental de alimentos y bebidas industrializados en México. Salud Pública de México [Internet].2018[Citado 3 octubre 2021]; vol. 60, no. 3, 328-337 Disponible en: DOI: https://doi.org/10.21149/8825

33. Norma Oficial Mexicana NOM-043-SSA2-2005, Servicios básicos de salud. Promoción y Educación para la Salud en Materia Alimentaria. Criterios para brindar orientación. Diario oficial de la Federación. 28 de mayo de 2012. [Consultado el 02 octubre 2021]. Disponible en http://www.dof.gob.mx/nota_detalle.php?codigo=5285372&fecha=22/01/2013

34. NOM-051-SCFI/SSA1-2010, Especificaciones generales de etiquetado para alimentos y bebidas no alcohólicas preenvasados-Información comercial y sanitaria. Diario Oficial de la Federación. 18 de febrero de 2010. [Consultado el 02 octubre 2021]. Disponible en https://www.dof.gob.mx/normasOficiales/4010/seeco11_C/seeco11_C.htm

35 MODIFICACIÓN a la Norma Oficial Mexicana NOM-051-SCFI/SSA1-2010, Especificaciones generales de etiquetado para alimentos y bebidas no alcohólicas preenvasados-Información comercial y sanitaria. 27 de marzo de 2020. [Consultado el 02 octubre 2021]. Disponible https://www.dof.gob.mx/2020/SEECO/NOM_051.pdf

36. Aranda-González I, Barbosa-Martín E, Toraya-Avilés R, Segura-Campos M. Evaluación de seguridad de *Stevia rebaudiana* Bertoni cultivada en el sureste de México como edulcorante alimentario. Nutr Ho