

Hypoglycaemic Property of Yacon (*Smallanthus sonchifolius* (Poepp. and Hendl.) H. Robinson): A Review

Neyder Contreras-Puentes^{1*}, Antistio Alvíz-Amador²

ABSTRACT

Diabetes is currently a chronically more important disease due to the high rates affecting 8.5% of the world population. The need to look for natural sources as alternative elements for the treatment of this type of diseases is of greater impetus, in which the discovery and research of new natural products has been strengthened. Currently, in integrative therapies it is common to use natural elements such as yacon, due to its extensive pharmacological properties explored as anti-oxidants, prebiotics, anti-cancer, normolipemians, cytoprotective and mainly for its greater use as a hypoglycaemic element. Thus, in this work was carried out a systematic review of the most important scientific reports on the role of yacon in hypoglycaemic activity; likewise, to develop a conceptual expansion of the metabolites and chemical composition reported that relate to their activity in the regulation of glycaemia levels and finally relating possible mechanisms related between the presence of said metabolites and hypoglycaemic activity.

Key words: *Smallanthus sonchifolius*, Hypoglycaemic, Anti-diabetic, Yacon, FOS, Polyphenols.

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INTRODUCTION

Diabetes is a group of chronic metabolic disorders at the level of macromolecules such as carbohydrates, fats and proteins.^[1,2] It is characterized by a substantial increase in blood sugar levels. It may be due to a dysfunction in the regulatory mechanisms by insulin.^[3] And it has been related as a multifactorial group of disorders that leads to progressive and chronic hyperglycaemia. Associated with the inhibition of insulin secretion by pancreatic beta cells, which induces the inadequate use of energy substrates in tissues.^[4]

Diabetes has a consistent and consistent effect on the world population. It is estimated that 8.3% of the world population (382 million) suffers from this disorder and in the projections established for 2035 it has been indicated that it will affect 10% (592 million).^[4,5] A high proportion of individuals with diabetes maintain a distribution in low and middle income countries. It is estimated that about 175 million people with this disease are not diagnosed. This disease has generated more than 5 million deaths, considering cardiovascular diseases the main cause related to diabetes and it has been indicated that more than 21 million mothers with live births were affected by the disease.^[1,6] Diabetes mellitus is one of the high frequency metabolic diseases worldwide, it has been related to another series of metabolic disorders such as hyperlipidaemias, morbid obesity and definitely having its greatest repercussions in the appearance of cardiovascular diseases, which increase

the population indices of incidence of an inadequate quality of life and deterioration of health.^[7,8]

At present, the presence of pharmacological treatments for the disease is evident; however, lately these tools have been constantly limited or have favoured the phenomena of dependence and the appearance of continuous adverse reactions by the use of these substances. However, the use of hypoglycaemic agents of natural origin are strategies that are becoming more relevant every day due to the lower generation of side effects, the ease and availability in obtaining said material, or as sources for the discovery of new molecules.

In this way, the search for these alternatives in order to achieve balance at the glycaemic level and as preventive elements of diabetic alterations, has led to the use of promising plants such as the yacon (*Smallanthus sonchifolius* (Poepp. and Hendl.) H. Robinson), which has been discovered antioxidant properties, anticancer and including antidiabetic properties.^[9] Asteraceae This plant of Andean origin has also been characterized by its applications in the gastrointestinal tract by the presence of rich oligosaccharides in fructans with prebiotic activity, improving the growth and activity of the intestinal flora.^[10] Additionally, yacon is able to provide a low caloric content that represents an important advantage in the treatment of individuals with diabetes mellitus (DM I or DM II) or alterations of the metabolic syndrome.^[11] As well as preventive

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effects for the reduction of atherosclerotic and vascular risk factors in patients with hypoglycaemic activity.^[7,12]

In this way, it will lead to the description of studies related to the hypoglycaemic activity of *Smallanthus sonchifolius* (Poepp. and Hendl.) H. Robinson as an important natural alternative in the prevention, treatment of diseases related to glycaemic imbalance.

MATERIALS AND METHODS

Through the databases Google Scholar, OVID, Scielo, ScienceDirect, PubMed, the search for articles of high scientific rigor was carried out, from the years 2001 to 2019, it is used as keywords yacon, *Smallanthus sonchifolius*, antidiabetic or hypoglycaemic. The search was limited to articles in English with the following inclusion requirements: original articles with full text, studies with methodologies related to the use of yacon (*Smallanthus sonchifolius*) with hypoglycaemic or antidiabetic activity for the treatment of different metabolic diseases and diabetes.

RESULTS

In the databases consulted, a total of 838 publications were found, with the chosen keywords. Were excluded articles duplicates and with inconsistencies in title and abstract, following with the evaluation and selection of publication with insufficient data, information unavailable and reduplicate data. Which were employed for its study 31 articles with such inclusion criteria. Likewise, the relevance of the study and its strong relationship with the subject was taken into account to develop correctly the analysis of the articles concerning the use of yacon (*Smallanthus sonchifolius* (Poepp. and Hendl.) H. Robinson) and its applications as antidiabetic or hypoglycaemic agent. (Figure 1).

Yacon (*Smallanthus sonchifolius* (Poepp. and Hendl.) H. Robinson).

The yacon, also scientifically denominated like *Smallanthus sonchifolius* (Poepp. and Hendl.) H. Robinson is a perennial plant of the Asteracea family, predominant in the Andean regions of South America. Etymologically, the yacon is derived from the Quechua term “yaku”, which is translated and used worldwide as “diluted or rich in water”.^[13-15] The cultivation of this plant in other regions was also identified in New Zealand, Australia and Japan; but its cultivation was also introduced in Europe in countries such as Italy, Germany, France and some reports established at the level of the Czech Republic and the United States.^[16,17] The conditions of growth of yacon is characterized by different factors such as seasons, culture conditions, harvest, altitudes of development,

storage conditions and temperature. Yacon is highly adaptable to different climates with temperatures conditions in the ranged from 0°C to 24°C, altitudes between 800 to 2000 m above sea level and variability in type soils.^[17-19] However, the development of tuberous roots and presence of metabolites dependent of each condition of growth.

The yacon has been characterized by presenting a series of growth in the form of tuberous rhizomes capable of developing underground and generating roots of propagation (growth) and roots of storage (food source). This plant can reach heights between 1.5 and 2 m in height and phenotypically is identified by its small yellow flowers and unlike other similar plants tends to present a growth throughout the period of the year.^[17] Yacon as fresh raw material mostly contains water (> 70%) and on the other hand it can contain a remaining of components such as fructooligosaccharides (FOS); which in its dry content can be constituted between 6.4% - 70%, depending on the location and cultivation area of said plant.^[17,20]

It has been identified that yacon has a series of properties that favour the normal development of the organism, such as immunomodulatory, antioxidant, anti-carcinogenic activities, favouring processes such as bone absorption, lipid metabolism and including hypoglycaemic activity and regulation. of the levels of glucose-sensitivity to insulin.^[19-21]

Chemical components of *Smallanthus sonchifolius* (Poepp. and Hendl.) H. Robinson).

Yacon has a variety of chemical components that have been found and characterized in different parts of the plant. In general, each part of the plant has a content of macromolecules such as carbohydrates, lipids, proteins, fibers and high-water content. (Table 1). Likewise, the reports have described the presence of isolated compounds such as oxalic acid, tannins and carotenoids.^[22,23] Also, isolated terpenes (sesquiterpene lactones), catechol, flavonoids and a high content of phenolic compounds has been described in yacon leaves, in which molecules with antioxidant and antidiabetic activity are included such as gallic acid, caffeic acid, rosmarinic acid, ferulic acid, *p*-coumaric acid, chlorogenic acid, protocatechuic acid and quercetin.^[12,16,19,24-29] (Figure 2).

On the other hand, the composition of flavonoid-like molecules and substances related to sesquiterpene lactones have been described, which have been related to a protective role for defense of plant, resistance to invading insects and from the medicinal point of view these compounds may be related to the hypoglycemic effect.^[30,31] Likewise, phytochemical studies in yacon have shown the presence of a large number of sesquiterpene lactones such as uvedalin, polymatin A/B, sonchifolin and enhydrin (Figure 3), which is also isolated from other congener species such as *Smallanthus* sp. (*S. uvedalia*, *S. fruticosus* and *S. maculata*).^[13,14]

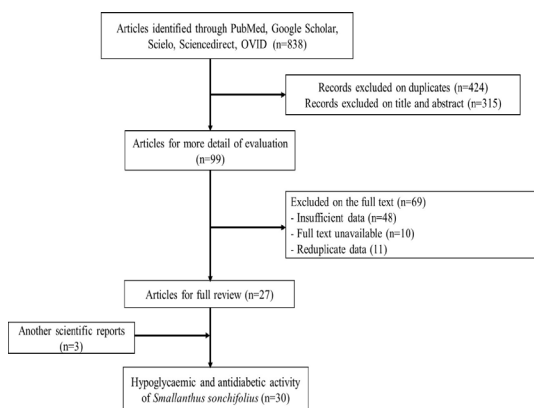


Figure 1: Flowchart of the study selection process of antidiabetic and hypoglycaemic activity of *Smallanthus sonchifolius* (Poepp. and Hendl.) H. Robinson).

Table 1: Chemical composition of different parts of the yacon (*Smallanthus sonchifolius* (Poepp. and Hendl.) H. Robinson).

Component (%)	Roots Tubers			
	Fresh	Dry	Leaves (Fresh)	Stems (Fresh)
Water	> 70	-	> 60	> 80
Proteins	0,3 – 3	2 – 8	17	11
Lipids	0,3 – 1	< 1	< 5	< 1
Fiber	0,5 – 7	3 – 7	< 3	< 2
Saccharides	>10	> 60	< 2	10
Minerals and microelements	<1	<1	<1	<1

For another hand, it has been established that within the content of yacon a series of phenolic and flavonoids compounds that constitute secondary metabolites, responsible for a series of physiological activities already corroborated as antioxidant activity, cytoprotective and hypoglycaemic effects.^[9,16] Such metabolites have been isolated and identified in different studies and associated with response regulatory of blood glucose or related with hypoglycaemic activity. These structures as enhydrin, *o*-quinone derivatives, smallanthaditerpenic acids A, B, C and D (Figure 4, A-D), 5,7-dihydroxy-4'-methoxyflavonol, 5,7,3'-trihydroxy-4'-methoxyflavonol, 7,4'-dihydroxy-3,5'-dimethoxyflavone (Figure 4, E-G), *ent*-kaurenoic acid, *ent*-kaurane-3 β ,16 β ,17,19-tertol, *ent*-kaurane-16 β ,17,18,19-tertol (Figure 4, H and I) and 4,5-di-*o*-CQA, 3,5-di-*o*-CQA (Figure 3, J-K).^[21,32-34]

For another hand, the tuber of the plant contains in its composition between 0.3-3.7% of proteins and 70-80% of the dry material may contain saccharides, primarily fructooligosaccharides; Likewise, contain 60% inulin or β -(2 \rightarrow 1) oligofructans with reports the main fructooligosaccharides as 1-kestose and nystose (Figure 5).^[13,17,21] Hermann *et al.* has shown the presence of varying amounts of fructose (3-22%, in dry material) and glucose (2-5%, dry material).^[35,36]

In general, the caloric contribution presented by yacon used as food has been between 600 - 900 KJ/Kg of fresh material, demonstrating a low caloric power and its use dietary fiber.^[18] Likewise, has been described in content of microelements and mineral salts as calcium, phosphorus, potassium, magnesium, sulphur, copper, manganese, zinc and iron.^[23,37,38]

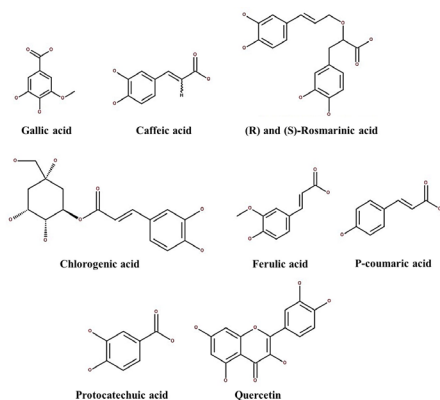


Figure 2: Major chemical constituents present in yacon with antioxidant activity related to hypoglycaemic effect.

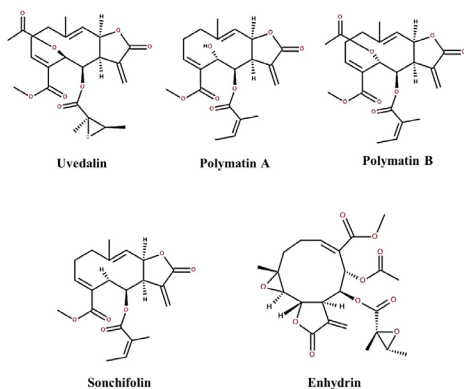


Figure 3: Sesquiterpene lactones present in yacon related to the hypoglycaemic effect.

Equally, have been determined the presence of antioxidants, Vitamins (A, E, C and beta-carotene).^[38]

Hypoglycaemic activity of *Smalanthus sonchifolius* (Poepp. and Hendl.) H. Robinson

For many years, numerous plants have offered reports of antidiabetic activity or hypoglycaemic effects that have been considered as alternatives for the treatment of diseases of great relevance such as diabetes or disorders in the blood glucose level and even associated with metabolic syndrome. One of these plants that have shown this activity is yacon; that for some years have been used traditionally for the treatment of these manifestations of the disease and other related problems.

In this review we have framed a complete study of historical and current aspects that demonstrate the hypoglycaemic activity of yacon, as a natural source and pharmacological action with future tool for the treatment related to the process of syndromes metabolic. As described in the Table 2.

In Latin America and other populations such as Japan, the leaves of the plant have been used for the preparation of infusions for the extraction of its metabolites with important pharmacological properties.^[43] Previously, scientists had discovered the first indications of the antidiabetic activity of yacon and until now with the implementation of the animal models to which the disorder was induced by streptozotocin (STZ), it was quantitatively proved the effectiveness of the plant on these organisms.^[8,14]

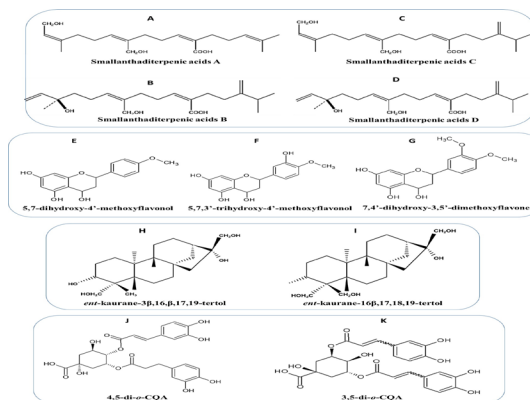


Figure 4: Compounds isolates of *Smalanthus sonchifolius* related with hypoglycaemic activity. CQA: (Caffeoylquinic acid).

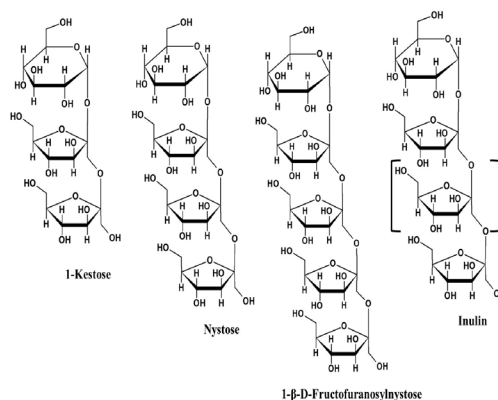


Figure 5: Fructooligosaccharides (FOS) compounds majorly founded in yacon and related with hypoglycaemic effect.

Table 2: Studies relevant of antidiabetic or hypoglycaemic activity of *Smallanthus sonchifolius* (Poepp. and Hendl.) H. Robinson).

Countries	Part of plant	Samples	Outcomes	Metabolites	References
Argentina	Leaves	Male Sprague–Dawley rats (weight)	↑ Plasma insulin, control of blood glucose	NR	[39]
Brazil	Leaves	Male Wistar rats	↓ Glycaemia in diabetic and non-diabetic. Restored plasmatic enzymes	NR	[40]
Brazil	Leaves	Male Wistar rats	↓ Glycaemia in diabetic rats Restored G6PD and AST activity ↓ Glycogen content in the liver and skeletal muscle	Kaurenoic and 15- α -angeloyloxy-kaur-16-en-19-oic acids	[41]
Brazil	Leaves	Males Wistar rats	↓ Blood glucose levels ↓ Body weight Regulation liver enzymes	caffeic acid, chlorogenic acid, ferulic acid and gallic acid	[24]
Brazil	Leaves	Male Wistar rats	↓ Glycaemia values ↑ antioxidants activity	Ferulic acid, p-coumaric acid, caffeic acid, chlorogenic acid, protocatechuic acid, quercetin	[25]
Brazil	Leaf	Male Wistar rats	↓ Glycaemia values ↑ Insulin concentration ↓ Serum triacylglycerol and fatty acid contents	Phenolic compounds	[42]
Brazil	Tuberous roots	Male Wistar rats	↓ Glucose levels ↑ Catalase activity	Polyphenols and fructooligosaccharides	[43]
China		Males mices	↓ Serum glucose levels	<i>ent</i> -kaurane-3 β ,16 β ,17,19-tetrol and <i>ent</i> -kaurane-16 β ,17,18,19-tetrol	[32]
Indonesia	Leaves	Male Wistar rats	↓ Blood glucose	Polyphenols and chlorogenic acid	[8]
Argentina	Leaves	Males mices	↓ post-prandial glucose (0.8 mg/kg body weight)	Enhydrin, uvedalin, fluctuanin, polymatin B, sonchifolin and minor lactones.	[44]
Argentina	Roots	Adult male Wistar rats	↓ Plasma triacylglycerol and LDL levels ↓ Postprandial peak glucose ↑ Insulin-positive pancreatic cell	Saccharides and FOS	[37]
Argentina	Roots	Adult male Wistar rats	↓ Glucose levels ↓ Malondialdehyde levels ↑ Glutathione peroxidase and glutathione levels in liver and kidney	FOS	[45]
Argentina	Leaves	Male adult Wistar rats	↓ high blood glucose level in diabetic rats	NR	[14]
Ukraine	Leaves and roots tubers	Male Wistar rats	↑ Antioxidants activity ↓ Serum glucose	<i>o</i> -quinone derivatives Phenolic compounds Flavonoids: 5,7-dihydroxy-4'-methoxyflavonol, 5,7,3'-trihydroxy-4'-methoxyflavonol, 5-hydroxy-4'-methoxy-7-O-glycosilflavone and 7,4'-dihydroxy-3,5'-dimethoxyflavone	[46]
Ukraine	Leaves and roots tubers	Male Wistar rats	↓ Glucose levels	Caffeic, chlorogenic, ferulic and protocatechuic acids, enhydrin, sesquiterpene lactone, FOS.	[47]
Brazil	Roots	Male Wistar rats	Stabilization of lipid and glycaemic profile ↓ Weight gain ↑ Antioxidant defenses	Flavonoids and phenolic acids. FOS	[12]
Japan	Leaf	KK-Ay rats	↓ Blood glucose ↓ Cholesterol	NR	[48]
Brazil	Roots	Males mices (11 groups)	Improvement glycaemic and lipid profile ↑ CAT, SOD, GPx, GSH, vitamin C, polyphenols	Phenolic compounds	[49]

Republic of Korea	Yacon tuber	Male Sprague-Dawley rats were	↓ Plasma glucose ↓ Total cholesterol (TC) and triglyceride (TG) concentrations	Chlorogenic acid (CGA)	[50]
Philippines	Leaf tea	Male albino mice (<i>Mus musculus</i> L.)	↓ Blood glucose into 1-2 h	<i>ent</i> -kaurenoic acid	[51]
Brazil	Roots tuber Yellow yacon	Male Wistar rats	Not reduce blood glucose ↓ Triglycerides levels and HDL-cholesterol	NR	[52]
Czech Republic Italy Portugal	Leaf		Good α -amylase and α -glucosidase inhibition	4,5-di-O-caffeoylquinic acid (CQA) and 3,5-di-O-CQA	[53]
Japan	Roots Tubers	Male Zucker fa/fa rats	↓ Blood glucose Effects on hepatic insulin sensitivity	NR	[54]
Argentina	Leaves	Adult male Wistar rats	↓ Blood glucose levels in diabetic rats	Enhydrin Phenolic compounds	[55]
Czech Republic	Leaves and tubers	ND	ND	Chlorogenic, caffeic and ferulic acid	[56]
Peru	Leaves	Males mices	↓ Glycaemia levels	NR	[57]
Czech Republic	Leaves	Rat hepatocyte primary cultures Rat	↓ Glucose production	Phenolic compounds	[58]
China	Leaves	NR	Produced inhibitory effect of α -glucosidase.	Smallanthaditerpenic acids A, B, C and D	[28]
Peru	Roots tubers	Males albino mices	↓ Glycaemia levels	FOS	[59]
Argentina	Roots	Adult male Wistar rats	↓ fasting glucose levels, improved glucose tolerance	NR	[60]

AST: Glutamate Aspartate Aminotransferase; CGA: Chlorogenic acid; CQA: caffeoylquinic acid; G6PD: Glucose-6-phosphate dehydrogenase; FOS: Fructooligosaccharides; ND: No determined; NR: Non-reported; (↓): Decreased; (↑): Increased.

The induction of type I diabetes mellitus in rat models with STZ use has shown the disease to appear progressively dose-dependent; as well as the appearance of a series of manifestations such as glycosuria, hyperglycemia, polyphagia and gradual decrease in body weight compared to healthy controls. However, treatments with yacon tea extracts in percentages from 2 - 10% have caused a significant decrease in STZ-induced hyperglycaemia. Also, the measurement functional parameters (creatinine and albumin) of the exposed individuals allowed assuring the regulation of the levels of each one and achieving an improvement in lipid profiles.^[61] Thus, in similar reports of hypoglycaemic and lipid-lowering activity have been demonstrated that extracts of yacon roots and a diet rich in roots of the plant, induce large reduction glycaemia, total cholesterol, LDL, VLDL and triacylglycerides levels in comparison with the control groups employed.^[62] Additionally, it is established a mechanism of action related with function of diet-rich in inulin increases excretion of cholesterol and bile acids, which has a direct impact in the decrease of cholesterol and LDL cholesterol levels.^[34,63,64] In addition, showed that a diet rich in fructans affects the triacylglycerides concentration and the reduction of lipids.^[17]

Likewise, in studies have determinate components of the yacon as β -(2 \rightarrow 1) fructooligosaccharides (FOS), that have shown important role in the biological activity of the plant.^[35,65] Primarily, it does not undergo any process of digestion in the upper part of the gastrointestinal tract and therefore are fermented by intestinal bacteria, which use it as a substrate, as well as generating in the organism a mutual benefit of promoting the growth of bacterial species such as *Lactobacillus* and *Bifidobacterium*, which develop remarkable physiological effects in the organism.^[8,19,66] However, it has been ensured that the tuber of the yacon is functionally used as a food or supplement for individuals suffering from metabolic disorders at the level of glucose metabolism, due to the low content of

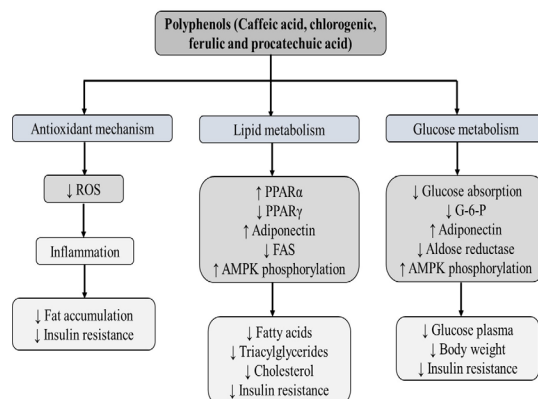


Figure 6: Mechanism hypoglycaemic associated with FOS and others metabolites hypoglycaemic activity. FOS: Fructooligosaccharides. Adapted of Meng *et al.* 2013.

glucose and high content of β -(2 \rightarrow 1)fructooligosaccharides that have related their activity.^[16] (Figure 6).

Habib *et al.* have evaluated the properties of the fructooligosaccharides (FOS) in the roots of yacon, which were used as supplements in the diet of Wistar rats with diabetes induced by STZ.^[15] The authors corroborated that the administration of yacon rich in FOS in rats, produced a significant decrease in plasma triacylglycerides and VLDL levels.^[63] The treatment protects diabetic rats from postprandial peak and accumulation of triacylglycerides. Researchers in their study additionally discovered that was greater stimulation in the growth of pancreatic cells with insulin-positive effect in small portions of cells of the exocrine parenchyma

and a slight increase in plasma insulin was observed in the fasting period.^[45,67]

For another hand, in the investigations that have led to the evaluation of the appearance of adverse effects, it has indicated that symptomatology is very unlikely using the therapeutic quantities that some studies have established. Valentová *et al.* have indicated that the toxicity of yacon in rats are tolerable and there are no elevated effects of glucose levels after 120 days of the investigation, using doses between 340–6.800 mg of FOS/Kg of weight body/day. Likewise, the results obtained provide safety for products containing yacon when daily doses higher to 2 g were used in patients with metabolic syndrome risk.^[68] Similarly, Oliveira *et al.* in the evaluation of hypoglycaemic, hypolipidemic and antioxidant effects, described that yacon supplementation did not induce hepatotoxic or nephrotoxic processes but it did favour the improvement of glycaemic index values and an acceptable response in lipid profiles.^[49]

Equally, induction of diabetogenic effects in rats has been reported employed extracts from yacon leaves. In the study, were evaluated different days, showed that only on the seventh day there were significant differences between the groups treated with the yacon leaves compared with the control groups; however, in relation to the groups treated with the extracts of the plant and to which insulin was administered, they did not show significant differences in hypoglycaemic activity.^[8] Evidence of a reduction in the blood glucose level and a potential use as a replacement for insulin, an activity that is possibly related to the content of polyphenols in yacon leaves that contain chlorogenic acid.^[8,44] Alike, Valentová *et al.* demonstrated effects of yacon by extract leaves from the plant, supplying it to rats, evidencing positive effects at the level of glucose metabolism, functioning of hepatocytes and avoiding oxidative damage. Hypoglycaemic activity that have been related with mechanisms de activation of PPAR γ to hepatic level that stimuli phenomena's as glycogen synthesis and decrease of gluconeogenesis generating finally in hepatic glucose output.^[69,70] Confirming therefore the presence of antioxidant activity, cytoprotective and remarkably anti-hyperglycaemic properties.^[58]

Baroni *et al.* in studies published of antidiabetic properties of yacon have shown that extracts administered orally at doses close to 400 mg/Kg/day for 14 days, have favoured the reduction of the glucose levels of diabetic rats.^[71] The authors also indicate decrease blood glucose levels during tolerance tests in oral and intravenous glucose administration.^[24,40] Which, conclude that the effect of the extracts supplied to the rats does not induce significant changes in body weight, liver enzymes or

mortality.^[41] Likewise, reinforce the hypoglycaemic action of yacon is Khokhla *et al.* who establish that extracts obtained from roots as leaves of the plant have generated a remarkable hypoglycaemic effect by providing suspensions to rats. The authors established that administration doses of 0.5 g/Kg of the suspension induced a marked decrease in the glucose level measured in the blood serum of the study subjects. Baroni *et al.* have indicated that possibly the effect of the extracts of the yacon leaves is attributed to substances such as caffeic acid, chlorogenic, ferulic and procatechuic acid. Additionally, have evidenced a possibly mechanism associated with polyphenols effects that may be inhibit α -amylase and sucrase, depressing the supply of glucose to the cells of the gastrointestinal tract by inhibiting the sodium-glucose transporter I and II (S-GLUT1 and 2) (Figure 7).^[26,70,72]

CONCLUSION

The applicability of natural products in the search for new tools for the achievement of treatments of diseases. Currently, natural materials such as yacon is of vital importance due to its multiple applications in empirical therapeutics and in the treatment of structured research for many years. The wide range of biological activities attributed to yacon promising model for technical development and research development with potential applications in industrial production at the pharmaceutical and research level. The interest for the study of the potential chemical constituents has strengthened the orientation to the complete development of the phytochemical profiles and understanding of the possible biological activities with respect to the active metabolites commonly related.

The study of metabolic problems such as diabetes has been necessary due to the search for alternative and easily accessible sources for the treatment of the manifestations of the disease. Thus, natural sources such as yacon are elements that acquire greater relevance in studies and application at treatment of hyperglycaemic and lipid alterations that trigger an unhealthy lifestyle. Currently, yacon is one of the plants included in natural therapeutic recipes and bibliographical bases that support this effect on human health and especially because all parties provide contributions of highly established antidiabetic and hypoglycaemic activity.

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CONFLICT OF INTEREST

The authors declare none.

ABBREVIATIONS

AMPK: AMP-activated protein kinase; **AST:** Glutamate Aspartate Aminotransferase; **CGA:** Chlorogenic acid; **CQA:** Caffeoylquinic acid; **EAS:** Fatty Acid Synthase; **FOS:** Fructooligosaccharides; **G6PD:** Glucose-6-phosphate dehydrogenase; **ND:** No determined; **NR:** Non-reported; (\downarrow): Decreased; (\uparrow): Increased. **PPAR:** Peroxisome proliferator-activated receptors α y γ . **ROS:** Radical Oxygen Species.

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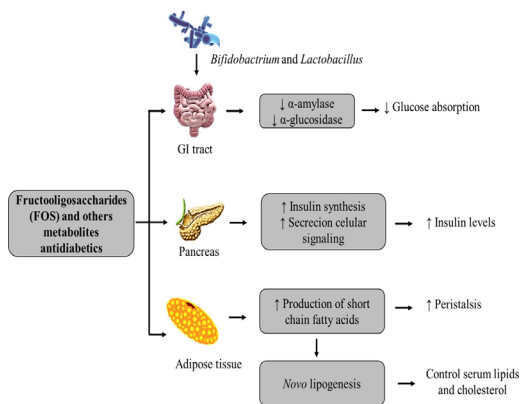


Figure 7: Mechanism hypoglycaemic associated with polyphenols activity. AMPK: AMP-activated protein kinase. FAS: Fatty Acid Synthase. PPAR: Peroxisome proliferator-activated receptors α y γ . ROS: Radical Oxygen Species. Adapted of Santana-Gálvez *et al.* 2017.

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