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Extracts of leaves from the plant Stevia rebaudiana Bertoni have been used in the traditional treatment of diabetes in Paraguay and Brazil. Recently, we demonstrated a direct insulinotropic effect in isolated mouse islets and the clonal beta cell line INS-1 of the glycoside stevioside that is present in large quantity in these leaves. Type 2 diabetes is a chronic metabolic disorder that results from defects in both insulin and glucagon secretion as well as insulin action. In the present study we wanted to unravel if stevioside in vivo exerts an antihyperglycaemic effect in a nonobese animal model of type 2 diabetes. An i.v. glucose tolerance test (IVGT) was carried out with and without stevioside in the type 2 diabetic Goto-Kakizaki (GK) rat, as well as in the normal Wistar rat. Stevioside (0.2 g/kg BW) and D-glucose (2.0 g/kg BW) were administered as i.v. bolus injections in anaesthetized rats. Stevioside significantly suppressed the glucose response to the IVGT in GK rats (incremental area under the curve (IAUC): 648 +/- 50 (stevioside) vs 958 +/- 85 mM x 120 min (control); P < 0.05) and concomitantly increased the insulin response (IAUC: 51116 +/- 10967 (stevioside) vs 21548 +/- 3101 microU x 120 min (control); P < 0.05). Interestingly, the glucagon level was suppressed by stevioside during the IVGT, (total area under the curve (TAUC): 5720 +/- 922 (stevioside) vs 8713 +/- 901 pg/ml x 120 min (control); P < 0.05). In the normal Wistar rat stevioside enhanced insulin levels above basal during the IVGT (IAUC: 79913 +/- 3107 (stevioside) vs 17347 +/- 2882 microU x 120 min (control); P < 0.001), however, without altering the blood glucose response (IAUC: 416 +/- 43 (stevioside) vs 417 +/- 47 mM x 120 min (control)) or the glucagon levels (TAUC: 5493 +/- 527 (stevioside) vs 5033 +/- 264 pg/ml x 120 min (control)). In conclusion, stevioside exerts antihyperglycaemic, insulinotropic, and glucagonostatic actions in the type 2 diabetic GK rat, and may have the potential of becoming a new antidiabetic drug for use in type 2 diabetes.

PMID: 11924770 [PubMed - indexed for MEDLINE]
• Stevioside acts directly on pancreatic beta cells to secrete insulin: actions independent of cyclic adenosine monophosphate and adenosine triphosphate-sensitive K+-channel activity.

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The natural sweetener stevioside, which is found in the plant Stevia rebaudiana Bertoni, has been used for many years in the treatment of diabetes among Indians in Paraguay and Brazil. However, the mechanism for the blood glucose-lowering effect remains unknown. To elucidate the impact of stevioside and its aglucon steviol on insulin release from normal mouse islets and the beta-cell line INS-1 were used. Both stevioside and steviol (1 nmol/L to 1 mmol/L) dose-dependently enhanced insulin secretion from incubated mouse islets in the presence of 16.7 mmol/L glucose (P < .05). The insulinotropic effects of stevioside and steviol were critically dependent on the prevailing glucose concentration, ie, stevioside (1 mmol/L) and steviol (1 micromol/L) only potentiated insulin secretion at or above 8.3 mmol/L glucose (P < .05). Interestingly, the insulinotropic effects of both stevioside and steviol were preserved in the absence of extracellular Ca2+. During perifusion of islets, stevioside (1 mmol/L) and steviol (1 micromol/L) had a long-lasting and apparently reversible insulinotropic effect in the presence of 16.7 mmol/L glucose (P < .05). To determine if stevioside and steviol act directly on beta cells, the effects on INS-1 cells were also investigated. Stevioside and steviol both potentiated insulin secretion from INS-1 cells (P < .05). Neither stevioside (1 to 100 micromol/L) nor steviol (10 nmol/L to 10 micromol/L) influenced the plasma membrane K+ adenosine triphosphate ((K+)ATP)-sensitive channel activity, nor did they alter cyclic adenosine monophosphate (cAMP) levels in islets. In conclusion, stevioside and steviol stimulate insulin secretion via a direct action on beta cells. The results indicate that the compounds may have a potential role as antihyperglycemic agents in the treatment of type 2 diabetes mellitus.

PID: 10690946 [PubMed - indexed for MEDLINE]
• **Effect of Stevia rebaudiana on glucose tolerance in normal adult humans.**

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The effect of aqueous extracts of Stevia rebaudiana leaves on a glucose tolerance test was investigated in 16 normal volunteers. Aqueous extracts of 5 grams of leaves were administered to volunteers at regular 6-h intervals for 3 days. Glucose tolerance tests were performed before and after extract administration. A second group of 6 normal volunteers who ingested an aqueous arabinose solution was also studied to eliminate possible stress effects. The extract of Stevia rebaudiana increased glucose tolerance. The extract significantly decreased plasma glucose levels during the test and after overnight fasting in all volunteers.

PMID: 3651629 [PubMed - indexed for MEDLINE]
• Oral use of a topical preparation containing an extract of Stevia rebaudiana and the chrysanthemum flower in the management of hyperglycemia.

White JR Jr, Kramer J, Campbell RK, Bernstein R.

Publication Types:
• Comment
• Letter

PMID: 7956646 [PubMed - indexed for MEDLINE]
• Traditional plant medicines as treatments for diabetes.

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More than 400 traditional plant treatments for diabetes mellitus have been recorded, but only a small number of these have received scientific and medical evaluation to assess their efficacy. Traditional treatments have mostly disappeared in occidental societies, but some are prescribed by practitioners of alternative medicine or taken by patients as supplements to conventional therapy. However, plant remedies are the mainstay of treatment in underdeveloped regions. A hypoglycemic action from some treatments has been confirmed in animal models and non-insulin-dependent diabetic patients, and various hypoglycemic compounds have been identified. A botanical substitute for insulin seems unlikely, but traditional treatments may provide valuable clues for the development of new oral hypoglycemic agents and simple dietary adjuncts.

Publication Types: Review, Review, Tutorial

PMID: 2673695 [PubMed - indexed for MEDLINE]
• The effect of stevioside on blood pressure and plasma catecholamines in spontaneously hypertensive rats.

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Stevioside is a sweet-tasting glycoside, composed of stevia, a diterpenic carboxylic alcohol with three glucose molecules, mainly used as a substitute for non-alcoholic sweetener. It has previously been shown to reduce blood pressure in studies in animals and human. The effect of intravenous stevioside on the blood pressure was studied in spontaneously hypertensive rats (SHR). The hypotensive effect on both systolic and diastolic blood pressure was dose-dependent for intravenous doses of 50, 100 and 200 mg/kg in conscious SHR. The maximum reductions in systolic and diastolic blood pressure were 31.4 +/- 4.2% and 40.8 +/- 5.6% (mean +/- SEM) respectively and the hypotensive effect lasted for more than 60 min with a dose of 200 mg/kg. Serum dopamine, norepinephrine and epinephrine levels were not changed significantly 60 min after intravenous injection of stevioside 100 mg/kg in anesthetized SHR. The present data show that stevioside given intravenously to conscious SHR was effective in blood pressure reduction and there was no change in serum catecholamines in anaesthetized animals with this natural compound.

PMID: 9806223 [PubMed - indexed for MEDLINE]
Stevioside effect on renal function of normal and hypertensive rats.

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Physiological and pharmacological experiments have suggested that stevioside from the leaves of Stevia rebaudiana acts as a typical systemic vasodilator. The effect of stevioside on renal function in both normal and with experimental renal hypertension rats (GII) was evaluated using clearance techniques. Stevioside provoked hypotension, diuresis and natriuresis in both the normal and hypertensive rats. Normal rats presented an increase in renal plasma flow (RPF) and glomerular filtration rate (GFR) constant following stevioside administration. The last effect is in part due to vasodilation of both the afferent and efferent arterioles. Moreover, stevioside infusion in hypertensive rats caused an increase in RPF and GFR. These data are consistent with impairment of a renal autoregulation mechanism in this experimental hypertensive model.

PMID: 1434679 [PubMed - indexed for MEDLINE]
Absorption and metabolism of glycosidic sweeteners of stevia mixture and their aglycone, steviol, in rats and humans.

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Stevia mixture, sweeteners extracted from the leaves of Stevia rebaudiana Bertoni, consists mainly of the glycosides of the diterpene derivative steviol. The aims of this study were to investigate the absorption (in rats) and the hepatic metabolism (in rats and humans) of both stevia mixture and steviol. Absorption was investigated both in vivo and ex vivo. In ex vivo experiments using the rat everted sac method, no absorption of stevia mixture was observed, but significant absorption of steviol was noted (equivalent to approximately 70% of the absorption reference- salicylic acid- value). In the in vivo experiment, rats received a single oral administration of either steviol or stevia mixture; a peak steviol concentration in plasma was observed 15 min after its oral administration, demonstrating rapid absorption. However, after oral administration of stevia mixture, the steviol concentration in plasma increased steadily over 8 h, suggesting that stevia mixture components are first degraded and then absorbed as steviol in the rat intestine. Steviol metabolism in humans and rats was examined by incubating steviol with liver microsomes from the two species. Oxidative (monohydroxy and dihydroxy) metabolites of steviol were observed by LC-ESI/MS after incubation with both human and rat liver microsomes. The intrinsic clearance of steviol in human liver microsomes was 4-times lower than that found in rat liver microsomes. In conclusion, this study suggests that there are no major species differences in steviol hepatic metabolism between rats and humans. Absorption from the human intestine can be predicted to occur in an analogous manner to that from the rat intestine.

PMID: 12738193 [PubMed - in process]
Stevia Medical Studies

- Antihyperglycemic and blood pressure-reducing effects of stevioside in the diabetic Goto-Kakizaki rat.

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Stevioside, a glycoside present in the leaves of the plant, Stevia rebaudiana Bertoni (SrB), has acute insulinotropic effects in vitro. Its potential antihyperglycemic and blood pressure-lowering effects were examined in a long-term study in the type 2 diabetic Goto-Kakizaki (GK) rat. Rats were fed 0.025 g x kg(-1) x d(-1) of stevioside (purity > 99.6%) for 6 weeks. An intra-arterial catheter was inserted into the rats after 5 weeks, and conscious rats were subjected to arterial glucose tolerance test (2.0 g x kg(-1)) during week 6. Stevioside had an antihyperglycemic effect (incremental area under the glucose response curve [IAUC]): 985 +/- 20 (stevioside) versus 1,575 +/- 21 (control) mmol/L x 180 minutes, (P <.05), it enhanced the first-phase insulin response (IAUC: 343 +/- 33 [stevioside] v 136 +/- 24 [control] microU/mL insulin x 30 minutes, P <.05) and concomitantly suppressed the glucagon levels (total AUC: 2,026 +/- 234 [stevioside] v 3,535 +/- 282 [control] pg/mL x 180 minutes, P <.05). In addition, stevioside caused a pronounced suppression of both the systolic (135 +/- 2 v 153 +/- 5 mm Hg; P <.001) and the diastolic blood pressure (74 +/- 1 v 83 +/- 1 mm Hg; P <.001). Bolus injections of stevioside (0.025 g x kg(-1)) did not induce hypoglycemia. Stevioside augmented the insulin content in the beta-cell line, INS-1. Stevioside may increase the insulin secretion, in part, by induction of genes involved in glycolysis. It may also improve the nutrient-sensing mechanisms, increase cytosolic long-chain fatty acyl-coenzyme A (CoA), and downregulate phosphodiesterase 1 (PDE1) estimated by the microarray gene chip technology. In conclusion, stevioside enjoys a dual positive effect by acting as an antihyperglycemic and a blood pressure-lowering substance; effects that may have therapeutic potential in the treatment of type 2 diabetes and the metabolic syndrome. Copyright 2003, Elsevier Science (USA). All rights reserved.

PMID: 12647278 [PubMed - indexed for MEDLINE]
The genotoxicity of steviol, a metabolite of stevia extract, was evaluated for its genotoxic potential using the comet assay. In an in vitro study, steviol at 62.5, 125, 250, and 500 micrograms/ml did not damage the nuclear DNA of TK6 and WTK1 cells in the presence and absence of S9 mix. In vivo studies of steviol were conducted by two independent organizations. Mice were sacrificed 3 and 24 hr after one oral administration of steviol at 250, 500, 1000, and 2000 mg/kg. DNA damage in multiple mouse organs was measured by the comet assay as modified by us. After oral treatment, stomach, colon, liver, kidney and testis DNA were not damaged. The in vivo genotoxicity of stevia extract was also evaluated for its genotoxic potential using the comet assay. Mice were sacrificed 3 and 24 hr after oral administration of stevia extract at 250, 500, 1000, and 2000 mg/kg. Stomach, colon and liver DNA were not damaged. As all studies showed negative responses, stevia extract and steviol are concluded to not have DNA-damaging activity in cultured cells and mouse organs.

PMID: 12533916 [PubMed - in process]
In vitro metabolism of the glycosidic sweeteners, stevia mixture and enzymatically modified stevia in human intestinal microflora.

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Stevia mixture, sweeteners extracted from the leaves of Stevia rebaudiana Bertoni, consists mainly of stevioside and rebaudioside A (glycosides of the diterpene derivative steviol). The aim of this study was to investigate human intestinal metabolism of stevia mixture and its alpha-glucose derivative (known in Japan as enzymatically modified stevia) by LC/MS/ESI analysis. Degradation was examined by incubating stevia mixture, enzymatically modified stevia, stevioside, rebaudioside A, alpha-monoglucosylstevioside, alpha-monoglucosylrebaudioside A and the aglycone, steviol with pooled human faecal homogenates (obtained from five healthy volunteers) for 0, 8 and 24 h under anaerobic conditions. Stevia mixture, enzymatically modified stevia, stevioside and rebaudioside A (0.2 mg/ml) were completely eliminated within 24 h, whereas no degradation of steviol (0.08 and 0.2 mg/ml) appeared to be found during the incubation period. Stevia mixture, stevioside and rebaudioside A appeared to be hydrolyzed to steviol by human intestinal microflora: this observation is consistent with previous rat metabolism studies. Similarly, enzymatically modified stevia appeared to be metabolized via stevia components and, finally, to steviol. This study suggests that there are apparently no species differences in intestinal metabolism of stevia mixture between rats and humans.

PMID: 12504168 [PubMed - indexed for MEDLINE]
Inhibitory effect of stevioside on tumor promotion by 12-O-tetradecanoylphorbol-13-acetate in two-stage carcinogenesis in mouse skin.

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Four steviol (ent-kaurene-type diterpenoid) glycosides, stevioside, rebaudiosides A and C, and dulcoside A, have been isolated from Stevia rebaudiana BERTONI. These compounds showed strong inhibitory activity against 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation in mice. The 50% inhibitory dose of these compounds for TPA-induced inflammation was 54.1-291.6 micro g/ear. Furthermore, at 1.0 and 0.1 mg/mouse of stevioside mixture, the mixture of these compounds markedly inhibited the promoting effect of TPA (1 micro g/mouse) on skin tumor formation initiated with 7,12-dimethylbenz[a]anthracene (50 micro g/mouse).

PMID: 12419967 [PubMed - indexed for MEDLINE]
Mechanism of the antihypertensive effect of stevioside in anesthetized dogs.


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Stevioside is a sweet-tasting glycoside isolated from the leaves of Stevia rebaudiana. It has been used as a noncaloric sugar substitute in Japan and Brazil for decades. Previous studies have shown that it lowered blood pressure in spontaneously hypertensive rats by intravenous injection. This study was designed to evaluate the hypotensive effect of stevioside in dogs and to define the underlying mechanism. After nasogastric administration of stevioside powder (200 mg/kg), the blood pressure of healthy mongrel dogs began to significantly decrease at 60 min and returned to baseline level at 180 min. The reduction of blood pressure was more rapid (at 5-10 min) and effective after intravenous injection. However, no significant change of blood pressure was noted after injection through left vertebral artery, implicating that the hypotensive effect is not related to the central nervous system. Stevioside also showed significant hypotensive effects in renal hypertensive dogs, in a dose-dependent manner. In cultured rat aortic smooth muscle cells (A7r5 cell line), stevioside can dose-dependently inhibit the stimulatory effects of vasopressin and phenylephrine on intracellular Ca(2+) in a calcium-containing medium. However, no intracellular Ca(2+) inhibitory effect was observed in calcium-free medium, implicating that stevioside may inhibit the Ca(2+) influx from extracellular fluid. Our present data show that stevioside did not influence the calcium ionophore (A23187) induced Ca(2+) influx, indicating that the antagonistic effect was through Ca(2+) channels. This study confirmed that stevioside is an effective antihypertensive natural product, and its hypotensive mechanism may be probably due to inhibition of the Ca(2+) influx.

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PMID: 12444299 [PubMed - in process]
• Quirogane, prenopsane, and patzcuaran skeletons obtained by photochemically induced molecular rearrangements of longipinene derivatives.

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Ultraviolet irradiation of (1R,3S,4S,5S,10R,11R)-1-acetyloxy-7-oxolongip-8-ene (6), prepared from longipinene diesters isolated from Stevia salicifolia, afforded the new quirogane (7) and prenopsane (8) derivatives, as the major products, together with the minor secondary photoproduct (1R,3R,5R,8S,11S)-1-acetyloxy-7-oxopatzcuar-9-ene (9), which possesses a novel tricyclic sesquiterpene skeleton. The stereostructures of the new compounds 7-9 were mainly determined by NMR techniques including COSY, HSQC, HMBC, and NOESY in combination with molecular modeling obtained by density functional theory calculations. A reaction mechanism accounting for the observed transformations is proposed.

PMID: 12398534 [PubMed - indexed for MEDLINE]
• Leaf ESTs from Stevia rebaudiana: a resource for gene discovery in diterpene synthesis.

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Expressed sequence tags (ESTs) are providing a new approach to gene discovery in plant secondary metabolism. Stevia rebaudiana Bert. leaves produce high concentrations of diterpene steviol glycosides and should be a rich source of transcripts involved in diterpene synthesis. In order to create a resource for gene discovery and increase our understanding of steviol glycoside biosynthesis, we sequenced 5,548 ESTs from a _S. rebaudiana_ leaf cDNA library. The EST collection was fully annotated based on database search results. ESTs involved in diterpene synthesis were identified using published sequences as electronic probes, by keyword searches of search results, and by differential representation. A significant portion of the ESTs were specific for standard leaf metabolic pathways; energy and primary metabolism represented 17.6% and 13.1% of total transcripts respectively. Diterpene metabolism in _S. rebaudiana_ represented 1.1% of total transcripts. This study identified candidate genes for 70% of the known steps in the steviol glycoside pathway. One candidate, kaurene oxidase, was the 8th most abundant EST in the collection. Identification of many candidate genes specific to the I-deoxyxylulose 5-phosphate pathway suggests that the primary source of isopentenyl diphosphate, a precursor of geranylgeranyl diphosphate, is via the non-mevalonic acid pathway. The use of ESTs has greatly facilitated the identification of candidate genes and increased our understanding of diterpene metabolism.

PMID: 12374295 [PubMed - indexed for MEDLINE]
Antihypertensive effect of stevioside in different strains of hypertensive rats.

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BACKGROUND: Stevioside is a natural sweet-tasting glycoside isolated from the herb Stevia rebaudiana, composed of stevia, a diterpenic carboxylic alcohol with three glucose molecules, mainly used commercially as sugar substitute. Previous study has shown that it can lower blood pressure in anesthetized spontaneously hypertensive rats (SHR). This study was undertaken to evaluate the antihypertensive effect of stevioside in different strains of hypertensive rats and to observe whether there is difference in blood pressure lowering effect. METHODS: Noninvasive tail-cuff method was employed to measure blood pressure. Stevioside at the concentrations of 50, 100 and 200 mg/kg were administered intraperitoneally (ip) to normotensive Wistar-Kyoto rats (NTR), SHR, deoxycorticosterone acetate-salt (DOCA-NaCl) sensitive hypertensive rats (DHR) and renal hypertensive rats (RHR). RESULTS: Significant hypotensive effect of stevioside administered ip was noted in different strains of rats at the dose of 50 mg/kg. When stevioside was increased to the concentrations of 100 and 200 mg/kg, ip, it also caused slow and persistent lowering of blood pressure in SHR and NTR. Data also showed that stevioside given at the concentrations of 100, 200 and 400 mg/kg ip resulted in lowering of blood pressure in SHR dose-dependently. Blood pressure returned to previous levels after the drug was discontinued for 2-3 days. Drinking of 0.1% stevioside solution in mature SHR could have antihypertensive effect and also prevented hypertension in immature SHR. CONCLUSIONS: This study reconfirmed stevioside has hypotensive effect and the effect is more prominent in hypertensive rats.

PMID: 11939668 [PubMed - indexed for MEDLINE]
Stevia Medical Studies

• Stevioside induces antihyperglycaemic, insulinotropic and glucagonostatic effects in vivo: studies in the diabetic Goto-Kakizaki (GK) rats.

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Extracts of leaves from the plant Stevia rebaudiana Bertoni have been used in the traditional treatment of diabetes in Paraguay and Brazil. Recently, we demonstrated a direct insulinotropic effect in isolated mouse islets and the clonal beta cell line INS-1 of the glycoside stevioside that is present in large quantity in these leaves. Type 2 diabetes is a chronic metabolic disorder that results from defects in both insulin and glucagon secretion as well as insulin action. In the present study we wanted to unravel if stevioside in vivo exerts an antihyperglycaemic effect in a nonobese animal model of type 2 diabetes. An i.v. glucose tolerance test (IVGT) was carried out with and without stevioside in the type 2 diabetic Goto-Kakizaki (GK) rat, as well as in the normal Wistar rat. Stevioside (0.2 g/kg BW) and D-glucose (2.0 g/kg BW) were administered as i.v. bolus injections in anaesthetized rats. Stevioside significantly suppressed the glucose response to the IVGT in GK rats (incremental area under the curve (IAUC): 648 +/- 50 (stevioside) vs 958 +/- 85 mM x 120 min (control); P < 0.05) and concomitantly increased the insulin response (IAUC: 51116 +/- 10967 (stevioside) vs 21548 +/- 3101 microU x 120 min (control); P < 0.05). Interestingly, the glucagon level was suppressed by stevioside during the IVGT, (total area under the curve (TAUC): 5720 +/- 922 (stevioside) vs 8713 +/- 901 pg/ml x 120 min (control); P < 0.05). In the normal Wistar rat stevioside enhanced insulin levels above basal during the IVGT (IAUC: 79913 +/- 3107 (stevioside) vs 17347 +/- 2882 microU x 120 min (control); P < 0.001), however, without altering the blood glucose response (IAUC: 416 +/- 43 (stevioside) vs 417 +/- 47 mM x 120 min (control)) or the glucagon levels (TAUC: 5493 +/- 527 (stevioside) vs 5033 +/- 264 pg/ml x 120 min (control)). In conclusion, stevioside exerts antihyperglycaemic, insulinotropic, and glucagonostatic actions in the type 2 diabetic GK rat, and may have the potential of becoming a new antidiabetic drug for use in type 2 diabetes.

PMID: 11924770 [PubMed - indexed for MEDLINE]
**Inhibitory effect of stevioside on calcium influx to produce antihypertension.**

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Stevioside is a sweet-tasting glycoside occurring abundantly in the leaves of Stevia rebaudiana (Compositae). It has been used popularly in Japan and Brazil as a sugar substitute for decades. Previous study has shown that it lowered blood pressure in spontaneously hypertensive rats (SHRs) when administered intravenously. This study shows that intraperitoneal injection of stevioside 25 mg/kg also has antihypertensive effect in SHRs. In isolated aortic rings from normal rats, stevioside could dose-dependently relax the vasopressin-induced vasoconstriction in both the presence and absence of endothelium. However, stevioside had no effect on phenylephrine- and KCl-induced phasic vasoconstriction. In addition, stevioside lost its influence on vasopressin-induced vasoconstriction in Ca(2+)-free medium. The results indicate that stevioside caused vasorelaxation via an inhibition of Ca(2+) influx into the blood vessel. This phenomenon was further confirmed in cultured aortic smooth muscle cells (A7r5). Using 10(-5) M methylene blue for 15 min, stevioside could still relax 10(-8) M vasopressin-induced vasoconstriction in isolated rat aortic rings, showing that this vasorelaxation effect was not related to nitric oxide. The present data show that the vasorelexation effect of stevioside was mediated mainly through Ca(2+) influx inhibition.

PMID: 11745013 [PubMed - indexed for MEDLINE]
• A crude extract of Stevia rebaudiana increases the renal plasma flow of normal and hypertensive rats.

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The effect of S. rebaudiana extract on renal function was evaluated in normotensive and in experimental renal hypertensive rats (GII) using clearance techniques. Experiments were performed on male Wistar rats weighing 300-330 g (10 animals per group). Goldblatt GII experimental hypertension was induced by placing a silver clip with an internal gap of 0.25 mm around the left renal artery under ether anesthesia. The contralateral kidney was left untouched. Stevia was administered 10-12 weeks after clipping. Oral administration of Stevia extract, corresponding to 2.67 g dry leaves/day for 30 days, resulted in a significant decrease in mean arterial pressure in both the normo-(N) and hypertensive rats (H) (N rats: 113 +/- 3.0 mmHg in the control (C) group vs 69.5 +/- 4.0 mmHg in the Stevia (S) group; H rats: 155 +/- 3.0 mmHg in C vs 108 +/- 4.0 mmHg in S; P < 0.05). Glomerular filtration rate was constant in the N rats and increased significantly in the H rats after Stevia treatment 16.47 +/- 1.29 vs 14.2 +/- 1.33 ml min-1 kg-1 in the C and S groups, respectively, P < 0.05). Normo- and hypertensive rats presented an increase in renal plasma flow following oral Stevia administration (N rats: 16.4 +/- 3.10 ml min-1 kg-1 in the C group vs 33.3 +/- 3.20 ml min-1 kg-1 in the S group. P < 0.05; H rats: 19.30 +/- 2.45 ml min-1 kg-1 in the C group vs 37.0 +/- 3.93 ml min-1 kg-1 in the S group, P < 0.05). Stevia administration provoked an increase in urinary flow in both N and H animals (1.37 +/- 0.08% vs 2.32 +/- 0.11%, P < 0.05 and 1.47 +/- 0.07% vs 2.96 +/- 0.13%, P < 0.05 in N and H rats, respectively). Sodium excretion increased in N and H animals after Stevia treatment (N rats: 0.61 +/- 0.07% in the C group vs 1.55 +/- 0.20% in the S group, P < 0.05; H rats: 0.70 +/- 0.10% in the C group vs 2.22 +/- 0.45% in the S group, P < 0.05). These results are consistent with impairment of a renal autoregulation mechanism in this hypertensive model after Stevia administration. In conclusion, it was shown that Stevia extract, at doses higher than used for sweetening purposes, is a vasodilator agent in normo- and hypertensive animals.

PMID: 9033821 [PubMed - indexed for MEDLINE]