A Nutraceutical Combination of Cinnamon, Purple Onion, and Tea Linked with Key Enzymes on Treatment of Type 2 Diabetes

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Abstract

Background: Diabetes mellitus (DM) is concomitant with significant morbidity and mortality and its prevalence is accumulative worldwide. The conventional antidiabetic agents are known to mitigate the symptoms of diabetes; however, they may also cause adverse effects. This study explores the efficacy of polyherbal dietary supplement cinnamon, purple onion, and tea on the mediation of postprandial hyperglycemia for in the search of combinations with a maximal response.

Materials and methods: A starch solution (3 g/kg Bwt) of oral starch tolerance test (OSTT) and glucose solution (4 g/kg Bwt) of oral glucose tolerance test (OGTT) with and without cinnamon, purple onion, tea extract (15 mg/kg Bwt), and mixture (each 5 mg/kg Bwt, 1:1:1), metformin (14 mg/kg Bwt), or acarbose (50 mg/kg Bwt) was administered to high fat plus high fructose-induced diabetic mice after an overnight fast. Postprandial plasma glucose levels were measured and incremental areas under the response curve were calculated.

Results: Compared with acarbose, the mixture of extracts (purple onion, cinnamon, and tea) indicated decreasing blood glucose in OSTT. In OGTT, the mixture of extracts showed greater efficacy for hypoglycemia when compared with metformin. The molecular docking of α -Amylase, α -Glucosidase, and AMPK confirmed the putatively acting molecules from the extracts of purple onion, cinnamon, and tea.

Conclusions: Overall, this investigation evidenced a beneficial mediation for the progression of lowering blood glucose with a combinatory extract of cinnamon, dietary onion, and tea, implicating their prospective as nutraceuticals that might ameliorate hyperglycemia in diabetes.

Introduction

Diabetes is a chronic health disease attributed to risk factors like obesity, physical inactivity, ageing, life style, and genetic predisposition. At present, the highly processed, calorie-dense, and nutrient-depleted diet favored by the current and younger generations and Western lifestyles frequently lead to exaggerated supraphysiological post-prandial spikes in blood glucose and lipids. The major contributors in the pathophysiology of Type 2 diabetes (TII DM) include resistance to insulin action, β cell dysfunction, an abnormality in glucose metabolism and storage, visceral obesity, and to some extent inflammation and oxidative stress. Insulin resistance, along with a defect in insulin secretion by the pancreatic β cells is instrumental towards progression to hyperglycemia¹. In particular, TII DM also known as non-insulin dependent diabetes mellitus (NIDDM) is a progressive metabolic disease that has affected a considerable percentage of the worldwide population and is associated with considerable morbidity and mortality of around 4.95% and 4.00%, respectively. This is due to its complications such as ketoacidosis, nephropathy, cardiovascular complication, neuropathy, retinopathy, hepatopathy, sexual dysfunction, and periodontal disease². A wide range of variation in prevalence of DM around the world and it is has affected 300 million as of 2017; with more than 425 million expected by 2030; and 642 million by 2045³, which shows a tremendous growth in immediate future. In clinical practice, a number of oral medications are

available to control blood glucose levels including herbs, folk medicine, tradition Chinese medicine, and clinical conventional medicines. There are several types of glucose-lowering drugs, including insulin and various oral anti-diabetic agents such as sulfonylureas, biguanides, Thiazolidinediones, α -Glucosidase inhibitors Meglitirides are available and these drugs are used as monotherapy or in combination to achieve better glycemic control. Commonly, α -glucosidase inhibitors like Precose® (acarbose) and Glyset® (miglitol) are used to prolong the increases in postprandial blood glucose⁴. This drug therapy results in effectively controlling blood glucose for TII DM patients. Nevertheless, these oral hypoglycemic drugs are still predisposed to various undesirable adverse effects caused by long-term administration, including cardiovascular disease, lactate acidosis, hypoglycemia, and gastrointestinal complaints^{5,6}; thus, they are limited in their overall of medical benefit for patients with diabetes. The increasing prevalence of hyperglycemia and negative clinical consequences of commercial anti-diabetic medicines have increased the demands to discover new drugs for controlling postprandial glucose levels⁷ because high blood glucose leads to the fluctuation of glycosylated hemoglobin and further induces the onset of diabetic complications.

Importantly, it has been postulated that herbal medicines and alternative medications have decreased or fewer severe adverse effects⁸. Thus, seeking natural compounds as new anti-diabetic agents with less or no adverse effects becomes an urgent issue. Spices and herbs are known for their tastes, aromas and flavors, as well as for their medical properties and value that have been applied for centuries in traditional medical systems to treat various kinds of illnesses such as the common cold, diabetes, cough, and cancer. *Allium cepa*, a spice plant, is commonly known as an onion and belongs to the family liliaceae. Among its various activities is the regulation of hypoglycemic activity, which is considered an important effect in DM⁹. There is substantial epidemiological evidence that a diet high in polyphenol-rich fruit, vegetables, cocoa, tea, and coffee protects against chronic diseases including TII DM. *Cinnamomum cassia* (cassia or Chinese cinnamon, the most common commercial type) bark is the outer skin of an evergreen tall tree belonging to the family Lauraceae and possesses various biological functions including acting as an anti-oxidant, anti-microbial, anti-inflammation, anti-diabetic, and shows anti-tumor activity¹⁰. Tea (*Camellia sinensis*) has been extensively studied in recent decades for its beneficial health effects in the prevention of obesity, metabolic syndrome, diabetes, cancer, and other diseases¹¹. However, evidence is limited regarding the efficacy of individual herbs for glycemic control particularly polyherbal dietary supplement. In this study, the optimal of combinatorial extract of cinnamon, purple onion, and tea was evaluated to achieve a maximal response in anti-hyperglycemia in diabetic mice.

Materials And Methods

Plant source and reagents

The cinnamon (*Cinnamomum cassia*) bark, dietary purple onion (*Allium cepa*), and tea (*Camellia sinensis*, Da Hong Pao, black tea) were purchased from the store of Xiamen (Fujian, China). Glucose, acarbose, metformin, and vildagliptin were obtained from Sigma-Aldrich (St. Louis, Missouri, USA).

Extracts preparation

Firstly, the fresh onion was dried in air-driven oven at 40°C for 3 days. Then dried onion was cut into segments and ground into powder. The dried powder (2 kg) was extracted with 10 L 50% ethanol (v/v) in brown glass bottle at room temperature for 3 days with shaking. The collected cinnamon bark (1 kg) and tea leaves (1 kg) were washed with tap water and then soaked in 50% ethanol (1 g/5 mL) and shook for 72 h, respectively. Each supernatant was collected and the residue was extracted for another two times. All of the supernatant was combined and centrifuged at 4,000 g for 20 min. Then the supernatant was evaporated at 42°C with an evaporator. and these concentrated syrups (onion) and layers (cinnamon bark and tea) were stored in a refrigerator at -20°C before experimental use. The syrups (onion) and layers (cinnamon bark and tea) syrup and layers were suspended in H₂O for tests. The extracted yield of Cinnamon, Da Hong Pao tea, and Purple onion was 12%, 4%, and 11%, respectively. Based on the metabolic rate of mouse is approximate 10 fold difference in that of human, mixed extracts (each 5 mg/kg Bwt,1:1;1) in animal use was converted into the human being as a functional food or nutraceutical (50 mg/60 kg Bwt each).

Diet-induced diabetic model preparation

Animal care and diet-induced obese (DIO) induction

All the experimental procedures were done in accordance with guidelines published by the National Institutes of Health (Guide for the Care and Use of Laboratory Animals, 8th edition) and fulfilled the ARRIVE guidelines.

Animal experiments were approved by the Xiamen Medical College Animal Ethics Committee and the “Guide for the Care and Use of Laboratory Animals” of Xiamen Medical College was followed.

Eighty male ICR mice with 6-week-old were obtained from Wu’s laboratory animals (Fujian, China) and kept at controlled environmental conditions with room temperature (22 ± 2°C) and humidity (50 ± 10%). The 12/12 h light/dark (6 am–6 pm) cycle was maintained throughout the study. Mice had free access to food and water and maintained on a standard laboratory diet. In the induction of obese-induced diabetes, mice were fed a high-fat diet (150 g lard·kg⁻¹ commercial lab diet) and 60% (v/v) fructose *ad libitum* for 14 weeks. Once mice were heavier than 40 g, they were defined as diet-induced obese (DIO) mice and further glucose tolerance and insulin response was carried out. Animal welfare was evaluated according to Laboratory animal–Guideline for ethical review of animal welfare (GB/T 35892 – 2018).

Insulin intolerance test (IGT) and determination of diabetic mice

The protocol of OGTT and glucose tolerance (GT) were followed as in our previous study¹². First, DIO mice fasted for 10 h prior to oral gavaged 4 g/kg Bwt glucose solution. At the beginning of the test, mice were bled from the tail vein and measured by an Accu-Chek blood glucose analyzer (Hoffmann-La Roche AG, Basel, Switzerland) for a fasting blood glucose level. In 120 min, blood glucose levels were consecutively detected every 30 min via sampling from the tail vein and measured blood glucose levels. In IGT, 0.8 IU/kg Bwt of insulin (Novo Nordisk A/S, Kalundborg, Denmark) was subcutaneously (s.c.) injected after glucose administration. As 120 min post-prandial blood glucose level was higher than 6

mmol/L and failure rescued from hyperglycemia by insulin, and consequently fifty-six mice were defined as DIO diabetic mice and used for experiments later.

Oral Glucose tolerance test (OGTT)

The procedure of OGTT was similar to the way of delimited diabetic mice with slight modification. Forty-eight DIO diabetic mice were divided into 6 groups ($n = 8$), including the Control (water); positive control (clinical medication with Metformin (14 mg/kg Bwt); Cinnamon (15 mg/kg Bwt), Da Hong Pao tea (15 mg/kg Bwt), Purple onion (15 mg/kg Bwt), and mixed extracts (each 5 mg/kg Bwt, 1:1:1). Each group animals received oral gavaged with drug and herbal supplements prior to glucose solution (4 g/kg Bwt, fresh preparation) and blood glucose of mouse was measured by an Accu-Chek for every 30 min until 120 min. All data in each group were collected and plotted with gavaging time to calculate the area under the curve (AUC) to determine hypoglycemic efficacy.

Oral starch tolerance test (OSTT)

Fifty-six DIO diabetic mice were divided into 7 groups ($n = 8$), and the protocol of OSTT was the same as OGTT with three modifications: (a) the control group animals gagaved with 4 g/kg Bwt of glucose was replaced with 3 g/kg Bwt of corn starch solution (fresh preparation); (b). two positive control groups as Acarbose (50 mg/kg), Vildagliptin (5 mg/kg Bwt) plus Metformin (85 mg/kg Bwt), and (c). The monitoring period of blood sugar levels was extended to 180 min.

Molecule docking

Molecule docking is a potential approach to search the interaction of a small molecule with target protein virtually via computational biology and can be used to screen the binding affinity of compounds and proteins, which subsequently find the rank of the docking results¹³. In the previous literature, the virtual screening of natural compounds has been reported for diabetes therapy¹⁴ and the selected natural compounds were also chosen based on our previous study^{15,16}. The structures of all tested targets are available in Protein Data Bank (PDB website; α -Amylase 1: 3BLP; α -Amylase 2: 5U3A; α -Glucosidase: 3TOP; AMPK1: 4RER; AMPK2: 5ISO) that were downloaded from the RCSB repository. In each protein structures, we selected the key residues to constitute the putative binding pocket (α -Amylase 1: Asp212, Phe248; α -Amylase 2: Asp212, Phe248; α -Glucosidase: Asp1420, Glu1423, Asp1526; AMPK1: ASP 150; AMPK2: ASP 139). The setup of the model was GA run 10, GA search efficiency 200%, and removal of water and adding hydrogen with the GOLD program (Cambridge Crystallographic Data Centre, Cambridge, United Kingdom).

Statistical analysis

Data were expressed as means $\pm$ SEM for *in vivo* results and means $\pm$ SD for the resting part. Statistical comparisons of the results were carried out using one-way analysis of variance (ANOVA). Means within each column followed by the different letters are significantly different at $p < 0.05$ by using the post-hoc Tukey's test.

Results

The mediating carbohydrates digestion of the extract of cinnamon, dietary onion, and tea; and the combinatorial of three mixtures in OSTT

After fasting overnight, DOI mice were administrated with the extract of cinnamon, onion or tea alone, and the combinatorial extract of three mixtures; and then given 3 g/kg of starch by oral gavage. In non-diabetic mice (normal mice), the data revealed the mixed extract of cinnamon, onion, and tea did not cause the hypoglycemia to even slightly improve carbohydrate digestion (Fig. 1a). When compared with acarbose, the data showed that the combinatorial extract of three mixtures had the greatest efficacy in decreasing blood glucose from the response of each 30 min interval for a total of 180 min, which was the test period (Fig. 1b). Interestingly, the result of the AUC calculation further confirmed the mixed extract of cinnamon, onion, and tea had more potential for controlling carbohydrates digestion (Fig. 1b).

The regulating blood glucose of the extract of cinnamon, dietary onion, tea and the combinatorial of three mixtures in OGTT

After fasting overnight, DOI mice were administrated with the extract of cinnamon, onion, or tea alone, and the combinatorial extract of three mixtures; and then given 4 g/kg of glucose by oral gavage. In non-diabetic mice (normal mice), the data revealed the mixed extract of cinnamon, onion, and tea did not cause the hypoglycemia even to slightly improve glucose absorption (Fig. 2a). When compared with metformin, the results showed that the combinatorial extract of three mixtures had the greatest efficacy of decreasing blood glucose from the response of each 30 min interval for a total of 120 min (Fig. 2b). Additionally, the result of AUC calculation further confirmed the mixed extract of cinnamon, onion, and tea (Fig. 2b). This result reveals that cinnamon, onion, and tea might moderately mediate AMPK to mitigate hyperglycemia as metformin does.

The putative acting target of anti-hyperglycemia in the extract of cinnamon, dietary onion, tea and the combinatorial of three mixtures via molecular docking

Of note, the major components of diallyl disulfide and quercetin (onion); cinnamic acid, cinnamic alcohol, and cinnamic aldehyde (cinnamon); and catechin and epigallocatechin (tea). The main acting molecules of clinical reference for the drug acarbose are α -amylase and α -glucosidase, which, therefore, act as moderators on these two molecular targets for cinnamon, onion, and tea particular cinnamic alcohol (cinnamon), quercetin (onion), catechin, and epigallocatechin gallate (tea) with α -amylase, α -glucosidase, and AMPK (Table 1; Fig. 3). Moreover, when compared with metformin (AMPK acting molecule), the result illustrates that all components from three test materials seem to have higher binding (Figs. 1, 2 and 3; Table 1).

Table 1
The virtual screening of molecular targets related to diabetics.

Name (CID, M.W.*)	CHEM PLP				
	α-Amylase1	α-Amylase2	α-Glucosidase	AMPK1	AMPK2
Diallyl disulfide (16590, 146.3)	37.14	-	-	-	-
Quercetin (5280343, 302.238)	48.93	-	54.78	49.54	44.30
Catechin (9064, 290.27)	49.04	46.76	56.10	44.89	45.96
Epigallocatechin gallate (65064, 458.4)	52.59	41.51	54.03	56.54	56.97
Cinnamic acid (444539, 148.16)	35.09	-	32.07	36.79	44.05
Cinnamic alcohol (5315892, 134.17)	40.23	40.83	-	-	-
Cinnamic aldehyde (637511, 132.16)	37.37	-	-	34.85	42.25
Metformin# (4091, 129.167)	-	-	-	20.35	31.45
Acarbose# (122172882, 645.608)	50.43	39.96	17.46	-	-
* : g/mol;-: Non-binding; #: Reference drug					
α-Amylase1: 3BLP; α-Amylase2: 5U3A; α-Glucosidase: 3TOP; AMPK1: 4RER; AMPK2: 5ISO					

Discussion

Growing evidence to demonstrate the majority of herbal products and secondary metabolites used in treating DM, the acting mechanisms are involved in the regulation of insulin signaling pathways, translocation of glucose transporter 4 (GLUT-4) transporter and/or activation the peroxisome proliferator-

activated receptor γ (PPAR γ). Several flavonoids suppress glucose absorption by inhibiting intestinal α -amylase and α -glucosidase¹⁷. Dietary polyphenols may impede α -amylase and α -glucosidase, hinder glucose absorption in the intestine by sodium-dependent glucose transporter 1 (SGLT1), stimulate insulin secretion and reduce hepatic glucose output. Furthermore, polyphenols may also activate insulin-dependent glucose uptake, activate 5' adenosine monophosphate-activated protein kinase (AMPK)¹⁸. AMPK would decrease gluconeogenesis and fatty acid synthesis and enhance catabolism, leading to body weight reduction and metabolic syndrome alleviation¹⁹.

Interestingly, a possible mechanism by which garlic, white onion, and purple onion exerts antidiabetic properties could be through the inhibitory effect on α -amylase and α -glucosidase coupled with their ability to prevent lipid peroxidation in the pancreas and heart, which validate their strong antioxidant properties²⁰. Sulfur compounds including S-methylcysteine and flavonoids such as quercetin are mainly responsible for the hypoglycemic activity of *A. cepa* helping to decrease the levels of blood glucose, serum lipids, oxidative stress, and lipid peroxidation, as well as increasing antioxidant enzyme activity and insulin secretion⁹. Extracts of onion have been shown to have hypoglycemic and hypolipidemic effects by normalizing the activities of liver hexokinase, glucose 6-phosphatase, and HMG coenzyme-A reductase⁹. In preliminary clinical trials, patients with diabetes safely consumed slices of *A. cepa*, exhibiting sufficient hypoglycemic activity. In the future, further studies need to investigate and seek to confirm the hypoglycemic activities of *A. cepa* and its constituents and/or their synthetic analogs.

On the other side, while blood sugar levels are not adequately lowered, the medication metformin is typically recommended²¹. Metformin's efficacy reflects activation of AMP-activated kinase, which shows preliminary evidence that certain compounds in our study have similar activities but without the side effects associated with metformin. Other natural agents with the potential to treat and possibly prevent DM include extracts of bitter melon and cinnamon. Nutraceuticals featuring meaningful doses of combinations of these agents would likely have substantial diabetes-preventive efficacy, and presumably could be marketed legally as aids to good glucose tolerance and insulin sensitive²².

Crude extract of cinnamon showed the strongest anti-amylase activities that provide a prospective therapeutic approach for the management of DM²³. Cinnamon contains derivatives, such as cinnamaldehyde, cinnamic acid, cinnamate, and numerous other components such as polyphenols and antioxidant, anti-inflammatory, antidiabetic, antimicrobial, and anticancer effects. Experimental studies have confirmed that *C. cassia* contains terpenoids, phenylpropanoids, glycosides etc. and many medicinal values including antitumor, anti-inflammatory, analgesic, anti-diabetic, anti-obesity, antibacterial, antiviral, cardiovascular protective, cytoprotective, neuroprotective, immunoregulatory effects, and anti-tyrosinase activity²⁴. All cinnamon types showed potent species-specific effects on starch digestion enzyme activity inhibition. *C. cassia* was most effective against α -amylase and all tests strongly inhibited α -glucosidase when compared to acarbose²⁵. Natural agents that slow carbohydrate absorption may mimic the protective effect of acarbose. Recently, many trials have investigated the beneficial effects of cinnamon for Alzheimer's disease, diabetes, arthritis, and arteriosclerosis.

Accumulatively experimental studies have demonstrated that tea has protective effects against DM and its complications via several underlined mechanisms, including augmenting insulin action, ameliorating insulin resistance, triggering insulin signaling pathway, protecting islet β -cells, scavenging free radicals, and diminishing inflammation²⁶. Teas has polyphenols called catechins and the most abundant being the (-) epigallocatechin gallate and also contain other phenolic compounds such as gallic, caffeic, chlorogenic or cinnamic acids, quercetin, and proanthocyanidols²⁷. Generally, tea is classified into six categories: white, green, yellow, oolong, black, and dark teas based on the process of fermentation degree²⁸. In the present results exhibited Da Hong Pao tea, black tea had greater efficacy of anti-hyperglycemia. Remarkably, black tea has thousands of various biological compounds such as flavonoids (Thearubigins (TRs) and theaflavins (TFs) and catechins), phenolic acids (caffeic acid (CA), gallic acid (GA), chlorogenic acids (CGA) and cauramic acid (CA) that illustrated many promising pharmacological effects regarded as growth promoter, cardio-protector, potent cholesterol-lowering effect, and has antioxidant and antimicrobial effects, etc.²⁹.

The previous literature has reported that natural compounds isolated from medical plants or Chinese herbs that reduce hyperglycemia in animals. Interestingly, they have some biological activities, which can treat or ameliorate diabetes *e.g.* catechin³⁰ and quercetin³¹. Accordingly, these compounds could inhibit the activities of α -amylase and α -glucosidase and delay carbohydrate digestion. In docking results, we have shown that some of the chemical compounds isolated from cinnamon, purple onion, and tea had a better effect on the inhibition of α -amylase and α -glucosidase than that of the clinic drug. This *in silico* evidence is associated with *in vivo* diabetic mice tests. Interestingly, there are a large number of aforementioned phytochemicals with good pharmacological activity in the natural plants as the extract of onion, cinnamon, and tea mixture that can be applied to treat human diseases because of their anti-oxidation and anti-inflammation properties particularly for metabolic syndromes.

Some of oral anti-hyperglycemic drugs have been obtained from plants or have a microbial origin, such as galegine isolated from *Galega officinalis*, which has a great similarity to the antidiabetic drug metformin. Picnogenol, acarbose, miglitol, and voglibose are other antidiabetic products of natural origin³². A variety of herbs has been used in traditional medicine for the treatment of diabetes. Nevertheless, the natural compounds are more stable and have less side effects when compared to clinic drug³³. Diet and plant derived products have also been tested in a number of preclinical and clinical trials^{34, 35}. Since herbal medicine has been chosen as a monotherapy or an adjuvant to conventional therapeutics, thorough clinical trials and standardized herbal preparations are required to evaluate their efficacy, safety, tolerability, and underlined clinical recommendations^{3, 36–38}.

The inhibitory activities of α -amylase and α -glucosidase; anti-hyperglycemia of purple onion, cinnamon, and tea mixture extracts when compared to the acarbose and metformin in OSTT and OGTT. A mixture extract (purple onion, cinnamon, and tea) has demonstrated remarkable antidiabetic activities and is further confirmed that they could preserve the active component in the regulation of AMPK, α -amylase, and α -glucosidase. Several compounds (Diallyl disulfide, Quercetin, Cinnamic acid, Cinnamic alcohol,

Cinnamic aldehyde, Catechin, and Epigallocatechin gallate) in extracts of purple onion, cinnamon, and tea mixture have a notably inhibitory effect of diabetic molecules when compared with clinical drugs (acarbose, anti- α -amylase) and metformin, AMPK) via virtual screen.

Conclusion

The present study illustrates that the extract of onion, cinnamon, and tea mixture has potential therapeutic value for the treatment of diabetes in human clinical trials. Moreover, finding active ingredients from these plants for understanding the action mechanism via molecular docking is an important approach to the drug discovery and development in new anti-diabetic drugs (Fig. 4).

List Of Abbreviations

AMPK: 5' adenosine monophosphate-activated protein kinase

ANOVA: one-way analysis of variance

DIO: diet-induced obese

DM: Diabetes mellitus

GLUT-4: glucose transporter 4

GT: glucose tolerance

IGT: insulin glucose intolerance test

NIDDM: non-insulin dependent diabetes mellitus

OGTT: oral glucose tolerance test

OSTT: oral starch tolerance test

PPAR γ : peroxisome proliferator-activated receptor γ

SGLT1: sodium-dependent glucose transporter 1

TII DM: Type 2 diabetes

Declarations

Ethics approval and consent to participate

Animal experiments were approved by the Xiamen Medical College Animal Ethics Committee (SYXK,2018-0010) and the "Guide for the Care and Use of Laboratory Animals" of Xiamen Medical College was

followed.

Consent for publication

All authors reviewed and approved the final version of the manuscript as well as agree to publish this study.

Availability of data and materials

Not applicable

Declaration of Conflict of Interest

The authors declare no conflict of interest.

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Authors' Contributions

Lebin, TH, and Liyue participated in the experiments and data analysis; Dong and YS did prepare the manuscript draft. YS and CF critically discussed and reviewed the manuscript.

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Figures

(a)

(b)

Figure 1

The alterations of blood glucose after extract of cinnamon, purple onion, and tea treatment via oral starch tolerance test. (a) normal mice and (b) diabetic mice. Diabetic mice were induced by high fat plus high fructose. After starvation overnight, the fasting blood glucose level of each mouse was measured. Then, mice were grouped into the Control (non-treatment), Acarbose (50 mg/kg), Vildagliptin (5 mg/kg Bwt) plus Metformin (85 mg/kg Bwt), Cinnamon (15 mg/kg Bwt), Da Hong Pao tea (15 mg/kg Bwt), Purple

onion (15 mg/kg Bwt), and mixed extracts (each 5 mg/kg Bwt,1:1;1). Normal mice were grouped into the control (A) and mixed solution (B). Mice were oral gavaged with drug and herbal supplements prior to starch solution (3 g/kg) and blood glucose of mouse was measured by an Accu-Chek for every 30 min until 180 min. ** P<0.01, *** P<0.005, **** P<0.001 as compared with the starch alone.

Figure 2

The alterations of blood glucose after extract of cinnamon, purple onion, and tea treatment via oral glucose tolerance test. (a) normal mice and (b) diabetic mice. Diabetic mice were induced by high fat plus high fructose. After starvation overnight, the fasting blood glucose level of mouse was measured. And mice were grouped into the Control (non-treatment), Metformin (14 mg/kg Bwt), Cinnamon (15 mg/kg Bwt), Da Hong Pao tea (15 mg/kg Bwt), Purple onion (15 mg/kg Bwt), and mixed extracts (each 5 mg/kg Bwt, 1:1:1). Normal mice were grouped into the control (A) and mixed solution (B). Mice were oral gavage with drug and herbal supplements prior to glucose solution (4 g/kg) and blood glucose of mouse was measured by an Accu-Chek for every 30 min for 120 min. ** P<0.01, *** P<0.005, **** P<0.001 as compared with the glucose alone.

Figure 3

The binding interactions of specific chemicals from tea and purple onion with various key enzymatic proteins.

Figure 4

Summary of nutraceutical combination of Cinnamon, Purple Onion, and Tea linked with key enzymes on treatment of type 2 diabetes.