Original Article

Evaluation of *Rhodiola crenulata* and *Rhodiola rosea* for management of Type II diabetes and hypertension

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In the current study, we investigated 2 species of the genus *Rhodiola* for the inhibition of α-amylase, α-glucosidase and angiotensin converting enzyme (ACE) inhibitory activity. Water extracts of *Rhodiola crenulata* had the highest α-amylase inhibitory activity (IC_{50}, 98.1 μg total phenolic/ml) followed by ethanol extract of *R.crenulata* (IC_{50}, 120.9 μg total phenolic/ml) and ethanol extract of *R.rosea* (IC_{50}, 173.4 μg total phenolic/ml). Ethanol *R.rosea* (IC_{50}, 44.7 μg total phenolic/ml), water extract of *R.rosea* (IC_{50}, 52.3 μg total phenolic/ml), water extract of *R.crenulata* (IC_{50}, 60.3 μg total phenolic/ml) and ethanol extract of *R.crenulata* (IC_{50}, 60.2 μg total phenolic/ml) also showed significant α-glucosidase inhibitory activity. The α-glucosidase inhibitory activity of the extracts was compared to standard tyrosol, which was significantly detected in the extracts using HPLC. Tyrosol had strong α-glucosidase inhibitory activity (IC_{50}, 70.8 μg total phenolic/ml) but did not have any inhibitory effect on the α-amylase activity. Results suggested that α-glucosidase inhibitory activities of both *Rhodiola* extracts correlated to the phenolic content, antioxidant activity and phenolic profile of the extracts. The ability of the above *Rhodiola* extracts to inhibit rabbit lung angiotensin I-converting enzyme (ACE) was investigated. The ethanol extracts of *R.rosea* had the highest ACE inhibitory activity (38.5 %) followed by water extract of *R.rosea* (36.2 %) and *R.crenulata* (15.4 %).

Key Words: *Rhodiola*, tyrosol, salidroside, antioxidants, amylase, glucosidase, angiotensin converting enzyme, enzyme inhibitors, type 2 diabetes, hypertension.

Introduction

Carbohydrates are the major constituents of the human diet and mono-, di- and polysaccharides are major components of carbohydrates that mainly play a role in the energy supply. However, the relatively less frequently used monosaccharides from the diet (glucose and fructose) can be absorbed following hydrolysis and mobilization from polysaccharides and are readily taken up in the small intestine.[1]

Therefore, the components of dietary carbohydrates should be broken down to monosaccharides by the α-glucosidases such as sucrase, maltase, glucoamylase, dextrinase and the pancreatic α-amylase before they can be absorbed. This enzymatic process usually takes place rapidly in the upper part of the small intestine.

It is now believed that inhibition of these enzymes involved in the digestion of carbohydrates can significantly decrease the postprandial increase of blood glucose level after a mixed carbohydrate diet and therefore can be an important strategy in the management of postprandial blood glucose level linked to type II diabetes.[2] Several α-glucosidase inhibitors such as acarbose[3], trestatin[4], amylostatin[5] and valiolamine[6] have been isolated from microorganisms. A main drawback of using drugs such as acarbose is the side effects such as abdominal distention, flatulence, meteorism and possibly diarrhea.[5,6] It has been suggested that such adverse effects might be caused by the excessive inhibition of pancreatic α-amylase resulting in the abnormal bacterial fermentation of undigested carbohydrates in the colon.[2, 7]

Natural inhibitors from plants have shown to have a lower inhibitory effect against α-amylase activity and a stronger inhibition activity against α-glucosidase[2]. Such plant-based extracts can be targeted for effective therapy for postprandial hyperglycemia with minimal side effects.[2] Therefore natural α-amylase and α-glucosidase inhibitors from food-grade plant sources offer an attractive strategy for the control of post-prandial hyperglycemia.

One of the long-term complications of diabetes is hypertension, or high blood pressure. Angiotensin I-Converting Enzyme (ACE) is an important enzyme involved in maintaining vascular tension. Inhibition of Angiotensin I-Converting Enzyme (ACE) is considered a useful therapeutic approach in the treatment of high blood pressure in both diabetic and non-diabetic patients.[8, 9]

Anti-hypertensive drugs have been isolated from a number of plant species.[10] It is now believed that screening plant extracts for inhibition of ACE is potentially an effective method to develop new anti-hypertensive agents.[11]

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Rhodiola species, also known as "golden root" belongs to the plant family Crassulaceae.[12] *Rhodiola* species grows primarily in dry sandy soils at high altitudes in the Arctic and mountain areas of Asia and Europe.[13] Although food-grade *Rhodiola* species have been extensively studied as an adaptogen with various health-promoting effects, its properties remain largely unknown in the west. Traditional folk medicine in the Arctic and Himalayan areas used *Rhodiola* species as salads to increase physical endurance, longevity, resistance to high altitude sickness and to treat fatigue, depression, anemia, impotence, gastrointestinal ailments and infections.[14] Studies in cell cultures, animals and humans have revealed antifatigue[13], anti-stress, antihypoxic protection against the damaging effects of oxygen deprivation, anticancer, antioxidant, and immune enhancing effects.[14] *Rhodiola* species increased essential energy metabolites, adenosine triphosphate (ATP), and creatine phosphate in the muscle and brain mitochondria in mice made to swim to their limit[15]. There are numerous chemical components of the *Rhodiola* extracts that may be responsible for these beneficial health properties, but salidroside and its aglycone form, tyrosol, are considered the more important constituents in *Rhodiola rosea* and *Rhodiola crenulata*.

The major objectives of this investigation are to determine how dietary phytochemicals can be used as chemopreventive or therapeutic agents in the treatment of diabetes and hypertension. In this study Rhodiola extracts were found to inhibit the carbohydrate hydrolyzing enzymes, α-amylase and α-glucosidase and to also inhibit the angiotensin I converting enzyme *in vitro*.

Materials and Methods

Rhodiola rosea and *Rhodiola crenulata* were supplied by Barington Nutritionals (Harrison, NY). *α*-amylase (EC 3.2.1.1), *α*-glucosidase (EC 3.2.1.20), angiotensin converting enzyme (EC 3.4.15.1) and Tyrosol standard were purchased from Sigma Chemical Co. (St. Louis, MO). Unless noted, all chemicals also were purchased from Sigma Chemical Co. (St. Louis, MO).

Sample extraction

Water extracts:

A total of 1g of dried *Rhodiola* powders were added to 10 ml of distilled water and stirred for half an hour. The extract was then filtered through a Whatman # 2 filter and centrifuged at 10,000 x g for 10 min.

Ethanol extracts [12%]:

A total of 1g of dried *Rhodiola* powder were stirred in 10 ml of 12% concentration of ethanol at 40 °C for 2 hrs and cooled. The extract was then filtered through a Whatman # 2 filter and centrifuged at 10,000 x g for 10 min.

Total phenolics assay

The total phenolics was determined by an assay modified from Shetty *et al*., (1995)[16] Briefly, one millilitre of extract was transferred into a test tube and mixed with 1ml of 95% ethanol and 5 ml of distilled water. To each sample 0.5 ml of 50% (v/v) Folin-Ciocalteu reagent was added and mixed. After 5 min, 1 ml of 5% Na_2CO_3 was added to the reaction mixture and allowed to stand for 60 min. The absorbance was read at 725 nm. The absorbance values were converted to total phenolics and were expressed in milligram equivalents of gallic acid per grams dry weight (DW) of the sample. Standard curves were established using various concentrations of gallic acid in 95% ethanol.

Antioxidant activity by 1, 1-diphenyl-2-picrylhydrazyl radical (DPPH) inhibition assay

To 3 ml of 60 μM DPPH in ethanol, 250 μl of each extract was added, the decrease in absorbance was monitored at 517 nm until a constant reading was obtained. The readings were compared with the controls, which contained 250 μl of 95% ethanol instead of the extract. The % inhibition was calculated by:

$$\%\ \text{inhibition} = \left(\left[\frac{A_{517}^{Control} - A_{517}^{Extract}}{\left[A_{517}^{Control} \right]} \right] \right) x100$$

α-Amylase inhibition assay

Porcine pancreatic *α*-amylase (EC 3.2.1.1) was purchased from Sigma Chemical Co. A total of 500μl of extract and 500 μl of 0.02 M sodium phosphate buffer (pH 6.9 with 0.006 μM sodium chloride) containing α-amylase solution (0.5 mg/ml) were incubated at 25°C for 10 minutes. After pre-incubation, 500 μl of a 1% starch solution in 0.02 M sodium phosphate buffer (pH 6.9 with 0.006 M sodium chloride) was added to each tube at timed intervals. The reaction mixtures were then incubated at 25°C for 10 minutes. The reaction was stopped with 1.0 ml of dinitrosalicylic acid colour reagent. The test tubes were then incubated in a boiling water bath for 5 minutes and cooled to room temperature. The reaction mixture was then diluted after adding 10ml distilled water and absorbance was measured at 540 nm.

$$\%\ \text{inhibition} = \left(\left[\frac{A_{540}^{Control} - A_{540}^{Extract}}{\left[A_{540}^{Control} \right]} \right] \right) x100$$

The IC_{50} of α-amylase inhibitory activity was defined as the amount of soluble phenolics that inhibits absorbance at 540 nm to 50 % of the maximum.

α-Glucosidase inhibition assay

α-Glucosidase (EC 3.2.1.20) was purchased from Sigma Chemical Co. 50 μl of sample solution and 100 μl of 0.1 M phosphate buffer (pH 6.9) containing α-glucosidase solution (1.0 U/ml) were incubated in 96 well plates at 25°C for 10 minutes. After pre-incubation, 50 μl of 5 mM p-nitrophenyl-α-D-glucopyranoside solution in 0.1 M phosphate buffer (pH 6.9) was added to each well at timed intervals. The reaction mixtures were incubated at 25°C for 5 minutes. Before and after incubation, absorbance readings were recorded in a micro-array reader (Thermomax, Molecular device Co., Virginia, USA) at 405 nm and compared to a control which had 50 μl of buffer solution in place of the extract. The α-glucosidase inhibitory activity was expressed as % inhibition and was calculated as follows:

$$\%\ \text{inhibition} = \left(\left[\frac{\Delta A_{405}^{Control} - \Delta A_{405}^{Extract}}{\left[\Delta A_{405}^{Control} \right]} \right] \right) x100$$

IC_{50} of α-glucosidase inhibitory activity was defined as the amount of soluble phenolics that inhibits absorbance at 405nm to 50% of the maximum.

Angiotensin Converting Enzyme Inhibition Assay

ACE inhibition was assayed by a method modified by Kwon *et al*., (2006).[17] The substrate, hippuryl-histidyl-leucine (HHL) and angiotensin I-converting enzyme (ACE) from rabbit lung (EC 3.4.15.1) were purchased from Sigma Chemical Co.. Fifty microliters of extracts were incubated with 100 µl of 1.0 M NaCl-borate buffer (pH 8.3) containing 2.0 mU ACE-I solution at 37 ^{o}C for 10 minutes. After pre-incubation, 100 µl of a 5.0 mM substrate (HHL) solution was added to the reaction mixture. Test solutions were incubated at 37 ^{o}C for 1 hour. The reaction was stopped with 150 µl of 0.5 N HCl. The hippuric acid formed was detected and quantified by the HPLC method. 5 µl of sample was injected using Agilent ALS 1100 autosampler into an Agilent 1100 series HPLC (Agilent Technologies, Palo Alto, CA) equipped with DAD 1100 diode array detector. The solvents used for gradient were (A) 10 mM phosphoric acid (pH 2.5) and (B) 100% methanol. The methanol concentration was increased to 60% for the first 8 min and to 100% for the 5 min, then decreased to 0% for next 5 min (total run time, 18 min). The analytical column used was Nucleosil 100-5C18, 250x4.6 mm i.d., with packing material of 5 µm particle size at a flow rate 1ml/ min at ambient temperature. During each run the chromatogram was recorded at 228nm and integrated using Agilent Chemstation enhanced integrator for detection of liberated hippuric acid. Pure hippuric acid (purchased from Sigma Chemical Co., St. Louis, MO) was used to calibrate the standard curve and retention time.

The % inhibition was calculated by:

$$\%\ \text{inhibition} = \left(\left[\frac{E^{Control} - E^{Sample}}{\left[E^{Control} - E^{Blank} \right]} \right] \right) x100$$

HPLC Analysis

Tyrosol

Quantitative determination of tyrosol was assayed by modifying a method developed by Pham *et al*.(2000).[18] Two ml of dried *Rhodiola* extracts were filtered through a 0.2 µm filter. 5 µl of sample was injected using Agilent ALS 1100 autosampler into Agilent 1100 series HPLC (Agilent Technologies, Palo Alto, CA̧ equipped with DAD 1100 diode array detector. The solvent used for elution was 6.5 % methanol. The analytical column used was Nucleosil C18, 250x4.6 mm i.d., with packing material of 5µm particle size at a flow rate of 1 ml/min at ambient temperature. During each run the chromatogram was recorded at 225 nm and integrated using Agilent Chemstation enhanced integrator. Pure standard of tyrosol (purchased from Sigma Chemical Co., St. Louis, MO) in 70% ethanol was used to calibrate the standard curve and retention times.

Phenolic phytochemicals:

Two ml of extracts were filtered through a 0.2 µm filter. 5 µl of sample was injected using Agilent ALS 1100 autosampler into Agilent 1100 series HPLC (Agilent Technologies, Palo Alto, CA̧ equipped with DAD 1100 diode array detector. The solvents used for gradient elution were (A) 10 mM phosphoric acid (pH 2.5) and (B) 100% methanol. The methanol concentration was increased to 60% for the first 8 min and to 100% over the next 7 min, then decreased to 0% for the next 3 min and was maintained for the next 7 min (total run time, 25 min). The analytical column used was Agilent Zorbax SB-C18, 250x4.6 mm i.d., with packing material of 5µm particle

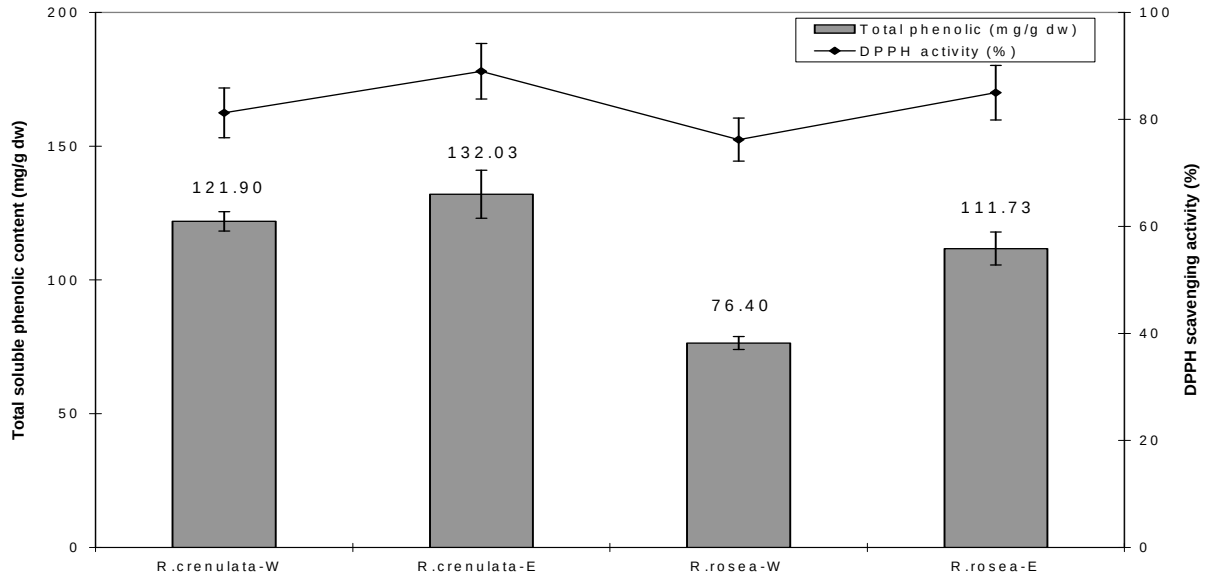

Figure 1. Total soluble phenolics (mg/g dw) and DPPH (%) scavenging activity of water and 12% ethanol extracts of *Rhodiola* species (*R.crenulata*-W; water extract of *Rhodiola crenulata*, *R.crenulata*-E; 12 % ethanol extract of *Rhodiola crenulata*, *R.rosea*-W; water extract of *Rhodiola rosea*, *R.rosea*-E; 12 % ethanol extract of *Rhodiola rosea*).

size at a flow rate of 1 ml/min at ambient temperature. During each run the chromatogram was recorded at 306 nm and 333 nm and integrated using Agilent Chemstation enhanced integrator. Pure standards of gallic acid and Coumaric acid (purchased from Sigma Chemical Co., St. Louis, MO) in 100% methanol were used to calibrate the standard curve and retention times.

Statistical analysis

All experiments were performed at least in duplicates. Analysis at every time point from each experiment was carried out in duplicates or triplicates. Means, standard errors and standard deviations were calculated from replicates within the experiments and analyses using Microsoft Excel XP.

Total phenolics and HPLC analysis of extract

The total phenolic content in water extracts and the ethanol extracts was analyzed by the Folin-Ciocalteu method. Ethanol extracts of *R.crenulata* had 132.0 mg/g dw of phenolics which was highest among all the extracts tested (Fig. 1). Water extract of *R.crenulata* had 121.9 mg/g dw of soluble phenolics (Fig. 1). Ethanol and water extracts of *R.rosea* had 111.7 mg/g dw and 76.4 mg/g dw of soluble phenolics, respectively (Fig. 1).

Table 1. Individual phenolic compounds analyzed by HPLC in water and 12 % ethanol extracts of *Rhodiola* species

Phenolics (mg/g dw)	*Rhodiola crenulata*		*Rhodiola rosea*	
	Water ext.	12% Ethanol ext.	Water ext.	12% Ethanol ext.
Tyrosol	1.47±0.06	2.07±0.08	2.19±0.04	2.78±0.09
Coumaric	0.59±0.02	0.33±0.01	0.14±0.01	0.10±0.01
Gallic aid	10.72±0.10	6.17±0.31	2.64±0.03	1.66±0.07
Total	12.78	8.57	4.97	4.54

Three major phenolics were identified in the extracts using HPLC and these were; gallic acid, coumaric acid and tyrosol (Table 1). In general, ethanol extracts had a slightly higher content of these phenolics than the water extracts. In both the water and ethanol extracts of *R.crenulata*, gallic acid was found to be a major phenolic. Ethanol extract of *R.rosea* had higher content of tyrosol than water extract. Water extracts of *R.crenulata* had high concentrations of gallic acid (10.72 mg/g dw), coumaric acid (0.59 mg/g dw) and tyrosol (1.47 mg/g dw) (Table 1). Water extracts of *R.rosea* had a lower gallic acid content (2.64 mg/g dw) compared to *R.crenulata* but a higher one than its ethanol extracts (1.66 mg/g dw). The phenolic phytochemical found at the next highest concentration was tyrosol. Figure 2 shows the chromatograms of standard of tyrosol and sample with the mobile phase 6.5% methanol in water. The peak of tyrosol from the standard mixture and extracts were identified by retention time and spectrum. In *R.rosea* extracts, tyrosol was found at levels of 2.19 mg/g dw in water extracts and 2.78 mg/g dw in ethanol extracts. Ethanol extracts of *R.crenulata* also had a high tyrosol content (2.07 mg/g dw) compared to 1.47 mg/g dw in water extracts. Other phenolics such as coumaric acid was generally found in lower concentrations in the water extracts than the ethanol extracts (Table 1).

Antioxidant activity by DPPH

The antioxidant activity of the extracts was monitored using the DPPH radical inhibition (DRI) assay. The ability of phenolics to inhibit the DPPH radical formation was measured both in water and ethanol extracts. The ethanol extracts of *R.crenulata* had the highest DPPH radical inhibition activity (90.7%) followed by ethanol extract of *R.rosea* (84.6%), water extract of *R.crenulata*

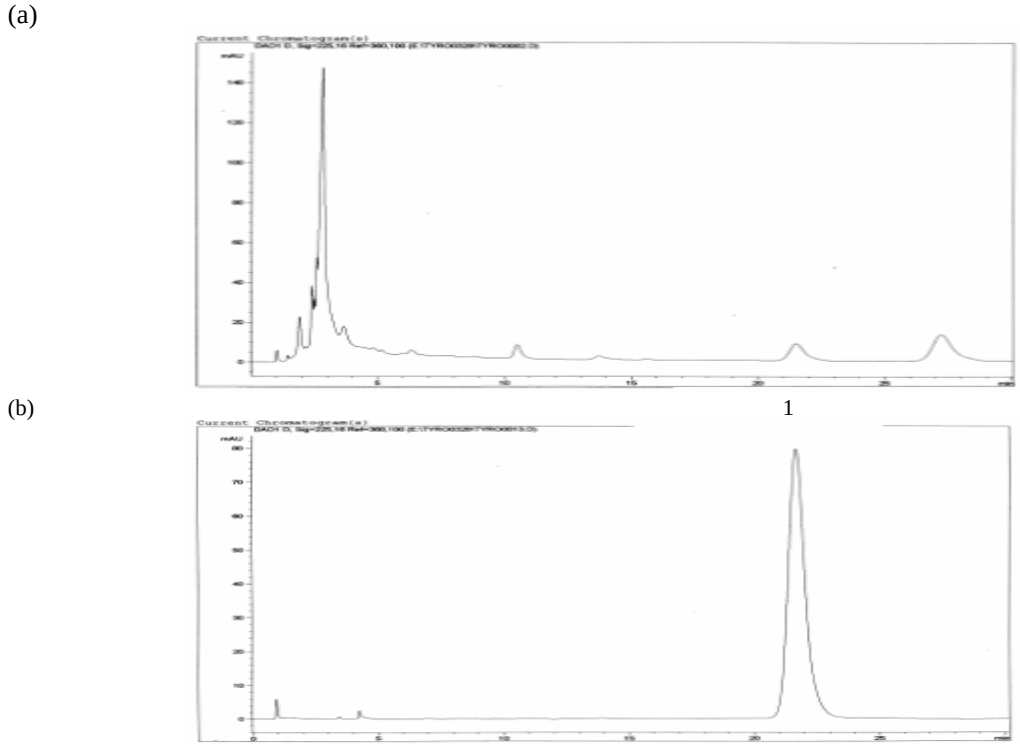

Figure 2. Chromatograms of *Rhodiola* extract (a) and a tyrosol standard (b). Stationary phase; Nucleosil C18 (25cmX4.6mm), mobile phase; 6.5 % methanol in water, flow rate; 1.0 ml/min, detection; UV 225nm. Peak: 1. Tyrosol.

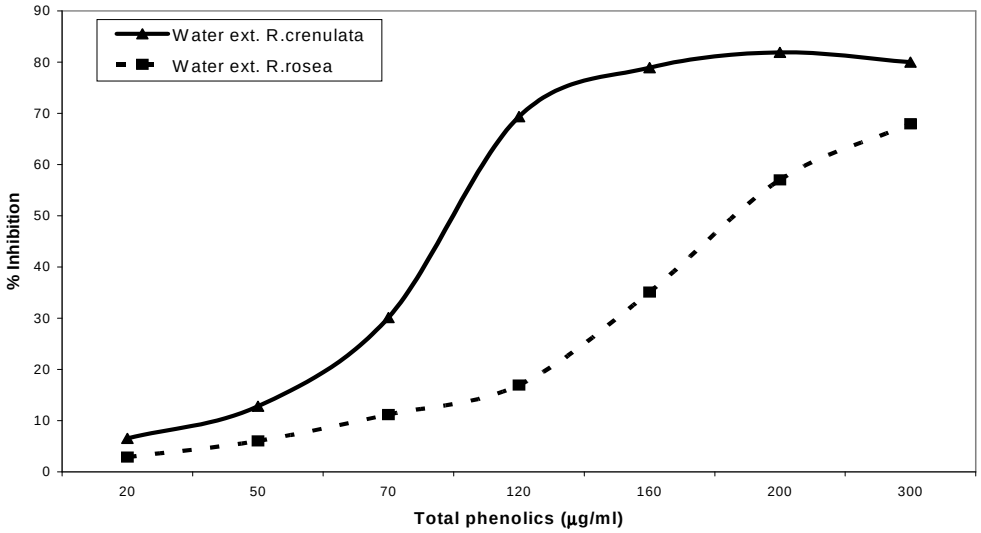

Figure 3. Dose dependent changes in α-Amylase inhibitory activities of water extracts of *Rhodiola crenulata* and *Rhodiola rosea* (µg/ml total phenolics).

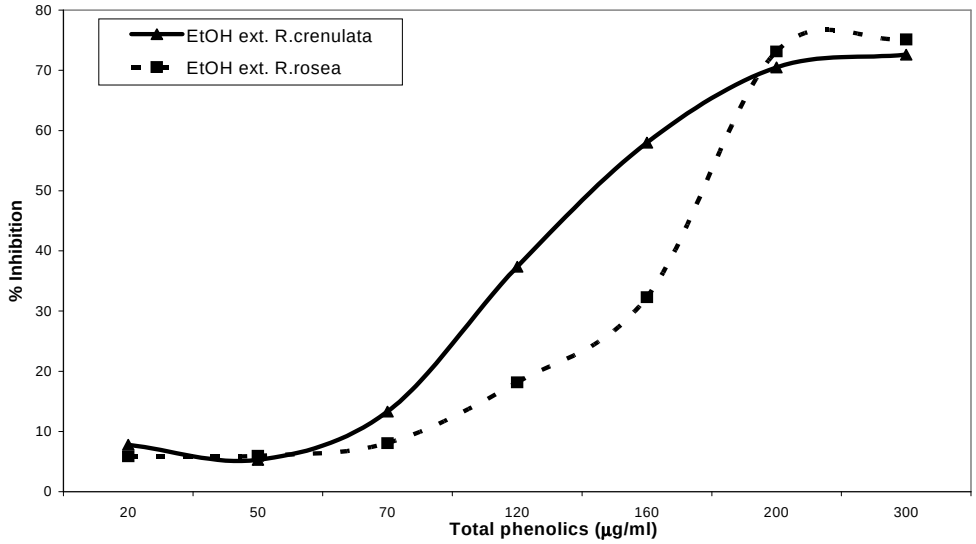

Figure 4. Dose dependent changes iṇ α-Amylase inhibitory activities of 12 % ethanol extracts of *Rhodiola crenulata* and *Rhodiola rosea* (µg/ml total phenolics).

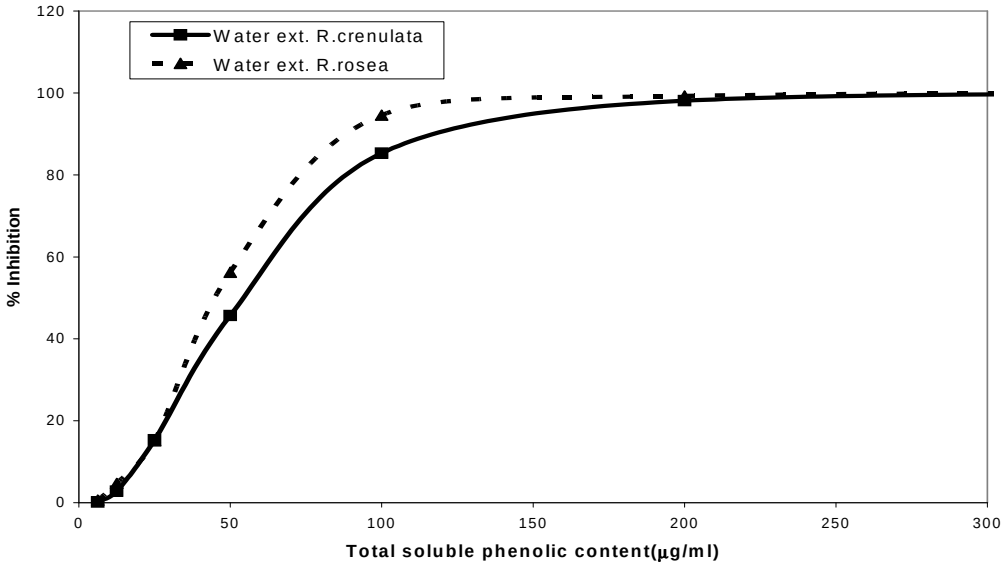

Figure 5. Dose dependent changes iṇ α-glucosidase inhibitory activities of water extracts of *Rhodiola crenulata* and *Rhodiola rosea* (µg/ml total phenolics).

(81.7%) and *R.rosea* (77.2%) (Fig. 1). The results indicated that the DPPH scavenging activity of all extracts was proportional to the total soluble phenolic content in them (Fig. 1). This result is different compared to clonal lemon balm which showed high DPPH scavenging activity with low total phenolic content.[17] This could be due to the type and quality of phenolics that varied among species.[17]

Amylase/Glucosidase Inhibition

Previous research with water and ethanol extracts of clonal herbs of Lamiaceae family reported an association between antioxidant activity and α-amylase and α-glucosidase inhibition activity.[17] Therefore, the α-glucosidase and α-amylase inhibitory activies with *R.crenulata* and *R.rosea* were compared (Fig. 3-6). The IC_{50} of the *Rhodiola* extracts on the α-glucosidase and α-amylase inhibitory activity was measured for dose dependency using different amount of phenolics (μg/ml). Water extracts of *Rhodiola crenulata* had the highest α-amylase inhibitory activity (IC_{50}, 98.1 μg total phenolic/ml) followed by ethanol extract of *R crenulata* (IC_{50},173.4 μg 120.9 μg total phenolic/ml) and ethanol extract of *R.rosea* total phenolic/ml). The α-glucosidase inhibitory activity of water and ethanol extracts was directly proportional to the concentration of the tyrosol (Table 1). Ethanol extract of *R.rosea* (IC_{50}, 44.7 μg total phenolic/ ml), water extract of *R.rosea* (IC_{50}, 52.3 μg total phenolic/ ml), water extract of *R.crenulata* (IC_{50}, 60.3 μg total phenolic/ml) and ethanol extract of *R.crenulata* (IC_{50}, 60.2 μg total phenolic/ ml) also showed significant α-glucosidase inhibitory activity. The α-glucosidase inhibitory activity of the extracts was compared to standard tyrosol detected in the extracts using HPLC.

Tyrosol had strong α-glucosidase inhibitory activity (IC_{50}, 70.8μg total phenolic/ml). This suggested that the content of tyrosol was critical for high α-glucosidase inhibitory activity and was likely enhanced during the re-adjustment of phenolic content (μg total phenolic/ml) for dose dependency studies. The α-glucosidase inhibitory activity of the ethanol extracts also correlated with tyrosol content (Fig.5,6). These results suggest that phenolic compounds of *Rhodiola* extracts and in particular tyrosol play a role in the inhibition of α-glucosidase activity.

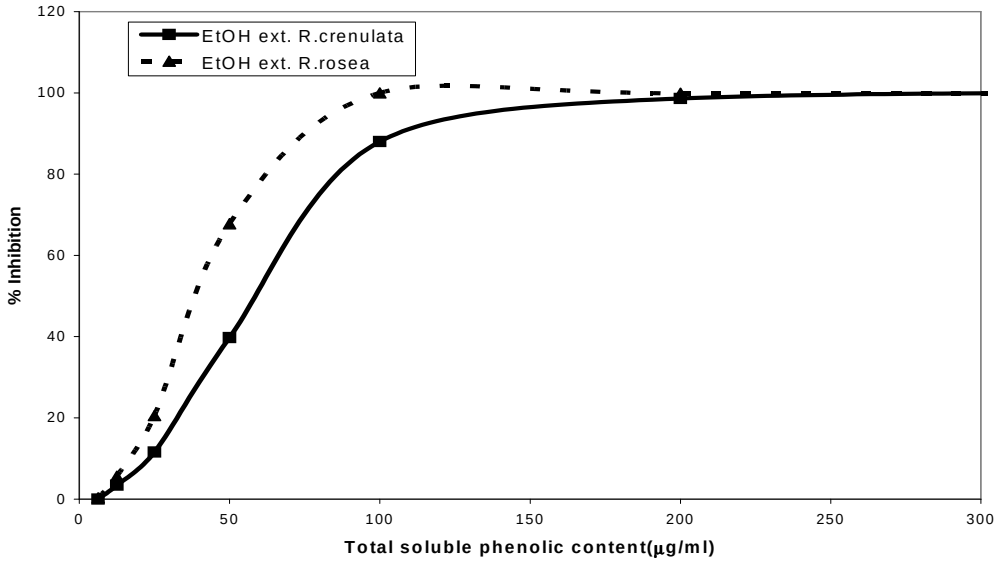

Figure 6. Dose dependent changes in α-Glucosidase inhibitory activities of 12 % ethanol extracts of *Rhodiola crenulata* and *Rhodiola rosea* (μg/ml total phenolics).

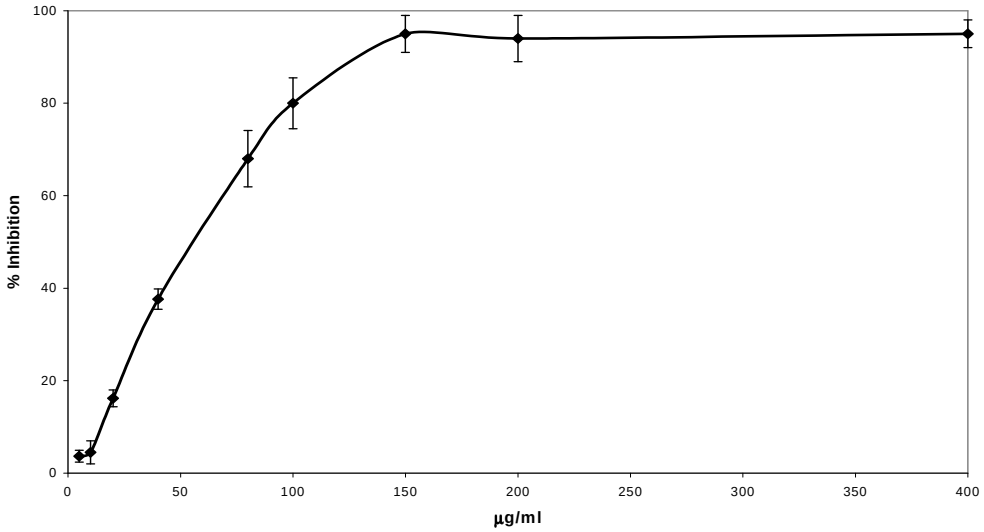

Figure 7. Dose dependent changes in α-Glucosidase inhibitory activities of tyrosol standard.

Based on the results above, *Rhodiola* species which have a high content of tyrosol could be used for the management of glycemic response in patients with Type II diabetes. This strategy would likely have lower abdominal side effects arising from excessive inhibition of pancreatic α-amylase, which would result in the abnormal bacterial fermentation of undigested carbohydrates in the colon.

ACE Inhibition

Hypertension which is a risk factor for many cardiovascular diseases is also associated with long term diabetes. Control of hypertension via modulation of angiotensin I-converting enzyme (ACE) by dietary anti-hypertensive agents is potentially an important strategy to manage this risk factor. In this study the ability of the *Rhodiola* extracts to inhibit the activity of rabbit lung ACE was investigated.

Among the sample extracts, ethanol extract of *R.rosea* had the highest ACE inhibitory activity (38.5%), followed by water extract of *R.rosea* (36.2 %), water extract of *R.crenulata* (15.4%) and ethanol extract of *R.crenulata* (11.2%) (Fig. 8). ACE inhibitory activity of the extracts did not correlate well with the total soluble phenolic content, antioxidant activity or the concentration of individual phenolics in the extracts such as tyrosol (Fig. 8).

This was especially true for *R.rosea* extracts which had high ACE-inhibitory activity but did not correlate with antioxidant activity and total soluble phenolic content. Within the same *Rhodiola* species, different extracts had different activities. The lack of correlation of the ACE inhibitory activity of the samples with phenolic content in this assay may suggest these differences could potentially be due to phenolics that were not detected by HPLC or by non phenolic compounds such as small soluble peptides which may be an important factor in contributing to the total ACE inhibitory activity.

Conclusion

The major phenolic components of the *Rhodiola* species: tyrosol, had strong α-glucosidase (EC 3.2.1.20) inhibitory activity. In general *Rhodiola* species has good inhibitory profile on carbohydrate degrading enzyme such as α-glucosidase related to carbohydrate digestion. Water and ethanol extracts from *Rhodiola* species had less inhibitory effect against α-amylase than α-glucosidase. Strong inhibition of α-glucosidase could be potentially used as effective therapy for postprandial hyperglycemia linked to Type II diabetes. This approach has potentially less side-effects such as abdominal distention, flatulence, meteorism and possibly diarrhea caused by the excessive inhibition of pancreatic α-amylase, which results in the abnormal bacterial fermentation of undigested carbohydrates in the colon. Among all the extracts, ethanol and water extracts from *R.rosea* showed strong ACE-inhibitory activity. Control of hypertension via modulation of angiotensin I-converting enzyme (ACE) (EC 3.4.15.1) by dietary anti-hypertensive agents could be an important strategy to manage hypertension which is a risk factor for CVD and often results from long-term diabetes mellitus. Based on these results ethanol and water extracts of *R.rosea* have the potential for the development of an effective dietary or supplement strategy for post-prandial hyperglycemia and hypertension linked to diabetes mellitus and associated cardiovascular diseases.

References

1. Bischoff H. Pharmacology of glucosidase inhibitor. Eur J Clin Invest 1994; 24: 3- 10
2. Horii S, Fukasse K, Matsuo T, Kameda K, Asano N, Masui Y. Synthesis and α -D- glucosidase inhibitory activity of N-substituted valiolamine derivatives as potent oral anti-diabetic agents. J Med Chem 1987; 29: 1038-1046.
3. Schmidt D, Former H, Junge B, Muller M, Wingender W, Trusheit E. α-Glucosidase Inhibitor: New complex Oligosaccharides of Microbial Origin. Naturwissenschaften 1977; 64: 535-536.

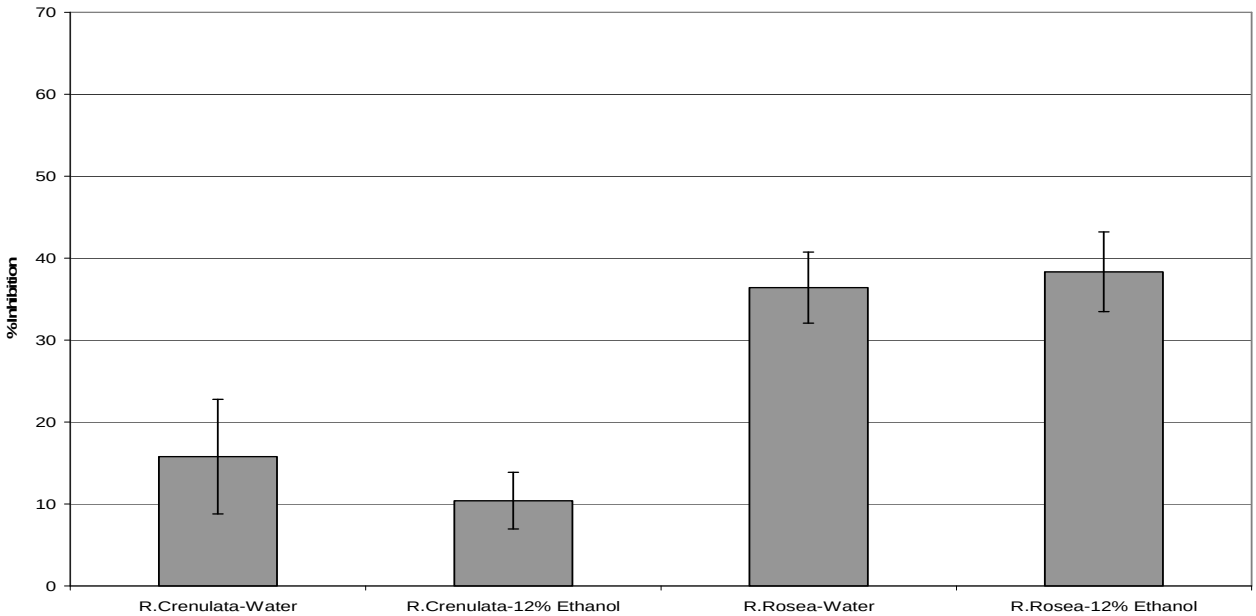

Figure 8. ACE-I inhibitory activity of water and 12% ethanol extracts of *Rhodiola* species (*R.crenulata*-W; water extract of *Rhodiola crenulata*, *R.crenulata*-E; 12 % ethanol extract of *Rhodiola crenulata*, *R.rosea*-W; water extract of *Rhodiola rosea*, *R.rosea*-E; 12 % ethanol extract of *Rhodiola rosea*).

4. Watanabe K, Furumai TT, Sudoh M, Tokose M, Maruyama HB. New alpha-amylase inhibitor, trestatins. IV. Taxonomy of the producing strains and fermentation of trestatin A J Antibiotics 1984; 37: 479-486
5. Murao S, Ohyyama K, Ogura S. Isolation of amylase inhibitor-produng microorganism. Agric Biol Chem 1977; 41: 919-924
6. Puls W, Keup U. Recent advances in obesity research volume 1. Haward, 1975; 391
7. Bischoff H, Puls W, Krause HP, Schutt H, Thomas G. Pharmacological properties of the novel glucosidase inhibitors BAY m 1099 (miglitol) and BAY o 1248. Diabetes Res Clin Pract 1985; 1: 53
8. Erdos EG, Skidgel RA. The angiotensin I-converting enzyme. Lab Invest 1987; 56: 345-348.
9. Johnston JI., Franz Volhard lecture. Renin-angiotensin system: a dual tissue and hormonal system for cardiovascular control. J Hypertens 1992; 10: 13-26.
10. ActisGoretta L, Ottaviani JI, Keen CL, Fraga CG. Inhibition of angiotensin converting enzyme (ACE) activity by flavan-3-ols and procyanidins. FEBS lett 2003; 555: 597-600.
11. Wagner H, Elbl G, Lotter H, Guinea M. Evaluation of natural products as inhibitors of angiotensin I-converting enzyme(ACE). Pharm Pharmacol Letters 1 1991; 15-18.
12. Engler A. Syllabus der pflanzenfamilien. 1964; 2: 199-200.
13. Saratikov AS, Krasnov EA, Chnikina LA, Duvidson LM, Sotova MI, Marina TF, Nechoda MF, Axenova RA, Tscherdinzeff SG. Rhodioloside, a new glycoside from *Rhodiola rosea* and its pharmacological properties. Pharmazie 1968; 23: 392-395.
14. Richard P, Brown MD, Patricia L, Gerbarg MD, Zakir R. *Rhodiola rosea*: A phytomedicinal overview. Herbal Gram 2002; 56: 40-52
15. Panossian A, Wikman G, Wagner H. Plant adaptogens. III. Earlier and more recent aspects and concepts on their mode of action. Phytomedicine 1999; 6: 287-300
16. Shetty K, Curtis OF, Levin RE, Witkowsky R, Ang W. Prevention of vitrification associated with in vitro shoot culture of oregano (*Origanum vulgare*) by Pseudomonas spp. J Plant Physiol 1995; 147: 447-451
17. Kwon Y-I, Vattem DA, Shetty K. Evaluation of clonal herbs of *Lamiaceae* species for management of diabetes and hypertension. Asia Pac J of Clin Nutr 2006; 15: 107-118.
18. Pham TL, Kim YH, Hong SP, Jian JJ, Kang JS. Quantitative determination of salidroside and tyrosol from the under-ground part of *Rhodiola rosea* by HPLC. Arch Pharm Res 2000; 23: 347-352.

Original Article

Evaluation of *Rhodiola crenulata* and *Rhodiola rosea* for management of Type II diabetes and hypertension

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大花红景天和玫瑰红景天对Ⅱ型糖尿病和高血压的疗效评估

在这项研究中，我们考察了红景天属的两个种对 α-淀粉酶、α-葡萄糖苷酶和血管紧张素转换酶(ACE)的抑制活性。大花红景天的水提取物对 α-淀粉酶的抑制活性最高（IC_{50},981.3μg 总酚/ml），其次为大花红景天的乙醇提取物(IC_{50},1209.1μg 总酚/ml)和玫瑰红景天的乙醇提取物(IC_{50},1734.1μg 总酚/ml)。玫瑰红景天的乙醇提取物(IC_{50},44.7μg 总酚/ml)和水提取物(IC_{50},52.3μg 总酚/ml)，大花红景天的水提取物(IC_{50},60.3μg 总酚/ml)和乙醇提取物(IC_{50}, 60.2μg 总酚/ml)也显示出显著的 α-葡萄糖苷酶抑制活性。运用 HPLC 在提取物中检测到显著水平的红景天苷元，将这些提取物的 α-葡萄糖苷酶抑制活性与红景天苷元的标准品进行了比较。红景天苷元具有强的 α-葡萄糖苷酶抑制活性(IC_{50},70.8μg 总酚/ml)，但对 α-淀粉酶没有任何抑制活性。结果表明，这两种红景天的提取物的 α-葡萄糖苷酶抑制活性和酚含量、抗氧化活性以及提取物的酚组成相关。同时研究了上述红景天提取物对兔肺血管紧张素 I 转换酶的抑制活性。玫瑰红景天的乙醇提取物的 ACE 抑制活性最高（38.5%），其次为玫瑰红景天的水提取物(36.2 %) 和大花红景天的水提取物(15.4 %)。

关键词：红景天、红景天苷元、红景天苷、抗氧化剂、淀粉酶、葡萄糖苷酶、血管紧张素转换酶、酶抑制剂、2 型糖尿病、高血压。