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Homoisoflavanones from *Polygonatum odoratum* Rhizomes Inhibit Advanced Glycation End Product Formation

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Protein glycation inhibitors from *Polygonatum odoratum* rhizomes were investigated using a bioassay-guided procedure to characterize active compounds for preventing and treating diabetic complications. The EtOH extract and soluble fractions were evaluated using an *in vivo* model of renal advanced glycation end-product (AGE) accumulation in streptozotocin-induced diabetic rats and an *in vitro* bovine serum albumin-glucose assay. Three homoisoflavanones 3-(4'-hydroxybenzyl)-5,7-dihydroxy-6-methyl-8-methoxychroman-4-one (**1**), 3-(4'-hydroxybenzyl)-5,7-dihydroxy-6,8-dimethylchroman-4-one (**2**), and 3-(4'-methoxybenzyl)-5,7-dihydroxy-6-methyl-8-methoxychroman-4-one (**3**), isolated from the active $CHCl_3$-soluble fraction of the EtOH extract, were subjected to *in vitro* bioassays to evaluate their inhibitory activities against AGE formation. All the isolates inhibited AGE formation more effectively than the positive control, aminoguanidine. These results indicate that pending further study these compounds could be used as novel natural product drug for mitigating diabetic complications.

Key words: *Polygonatum odoratum*, Homoisoflavanones, Advanced glycation end-products (AGEs), Diabetic complications

INTRODUCTION

Hyperglycemia, the primary clinical manifestation of diabetes, is associated with the development of diabetic complications. Several studies have suggested that hyperglycemia may play important roles in the pathogenesis of diabetic complications via several mechanisms, including increased aldose reductase-related polyol pathway flux, increased formation of advanced glycation end-products (AGEs), activation of protein kinase C isoforms, increased hexosamine pathway flux, and overproduction of superoxide (Brownlee, 2001). AGEs are a group of complex and heterogeneous compounds, including brown and fluorescent cross-linking substances (e.g., pentosidine), non-fluorescent cross-linking products (e.g., methylglyoxal-lysine dimmers), or non-fluorescent, non-crosslinking adducts (e.g., carboxymethyllysine) (Dyer et al., 1991; Ikeda et al., 1996). Increasing evidence identifies AGE formation as the critical pathogenic link between hyperglycemia and long-term complications of diabetes: nephropathy, neuropathy, and retinopathy (Ahmed, 2005; Wada and Yagihashi, 2005). Therefore, another mode of diabetes treatment independent of blood glucose levels, inhibition of AGE formation, could be useful in the prevention or reduction of certain diabetic complications.

Recently, many potent and active synthetic AGE formation inhibitors have been presented to the drug market. One such inhibitor that might be effective, aminoguanidine, has shown some promise in limiting the progression of diabetes-related complications (Sell et al., 2001). However, adverse side effects of this compound were observed in Phase III clinical trials (Bolton et al., 2004). Many pharmaceutical companies and researchers are searching for AGE formation inhibitors through the study of naturally occurring botanical compounds that lack toxicity and/or side-effects (Lee et al., 2008; Jang et al., 2008).

Polygonatum odoratum (Liliaceae) is a perennial

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plant that grows in the wild and is cultivated in the central and southwest areas of China. The dried rhizome of *P. odoratum*, Rhizoma Polygonati Odorati, is an important herbal medicine that is used in folk medicine for the treatment of diabetes. *P. odoratum* reportedly harbors steroidal glycosides (Lin et al., 1994; Qin et al., 2003), dipeptides (Qin et al., 2004), and homoisoflavanones (Rafi and Vastano, 2007; Wang et al., 2009), which are responsible for its various biological and pharmacological properties. In our previous study, the EtOH extract was shown to have protective effects on renal lesion development in diabetic rats, which might be related to inhibition of AGE formation (Shi et al., 2007). However, the active components in Rhizoma Polygonati Odorati that exhibit inhibitory effects on AGE formation have not been identified. In the present study, bioassay-guided fractionation of the EtOH extract of *P. odoratum* rhizomes used an *in vivo* model of renal AGE accumulation in streptozotocin-induced diabetic rats and an *in vitro* bovine serum albumin-glucose assay. These models led to the identification of three homoisoflavanones (**1**-**3**) as the active constituents. Here, the isolation and biological evaluation of **1**-**3** are described. To the best of our knowledge, this is the first report describing the inhibitory activity of homoisoflavanones on AGE formation.

MATERIALS AND METHODS

General experimental procedures

The ESI-MS and HR ESI-MS spectra were obtained using a Mariner Mass 5304 instrument. NMR spectra were acquired on a Bruck AV-500 FT-NMR, and the chemical shifts were referenced to the residual solvent signals. Column chromatography was performed with RP-18 reversed-phase silica gel (PEGASIL PREP ODS-5015-12A, Senshu). Preparative HPLC was performed using a Shimadzu LC-6AD pump connected to a Shimadzu SPD-20A UV-VIS detector (at 254 nm) with a Shim Pak ODS column (250 mm × 21.2 mm, i.d., 5 um, Shimadzu). TLC was conducted on pre-coated TLC plates with silica gel RP-18 60 F_{254} (0.25 mm, Merck). Detection was achieved by spraying the sample with 10% H_2SO_4 in MeOH followed by heating. HPLC-grade was purchased from Merck. HPLC-grade water was purified using a Milli-Q system (Millipore). All solvents used for the chromatographic separations were distilled before use.

Plant material

The *P. odoratum* rhizomes were purchased in September 2005 from a Chinese crude-drug market in Anguo, China, and authenticated by Prof. Wen Ting Li, Changchun University of Chinese Medicine. A voucher specimen (YZ20050901) was deposited at the Institute of Phytochemistry, Jilin Academy of Chinese Medicine Sciences.

Animals

All experimental procedures were conducted in accordance with Jilin Academy of Chinese Medicine Sciences Guidelines for the Care and Use of Laboratory Animals. Wistar rats (190-210 g) were obtained from Changchun Gaoxin Medical Animal Experimental Research Center, kept in cages, and exposed to a 12-h light/dark cycle. The room temperature and humidity were maintained automatically at approximately 25°C and 60%, respectively. The rats were allowed free access to food (normal rat chow) and water.

Extraction and isolation

The dried and ground plant material (5.90 kg) was reflux extracted twice with 95% EtOH (59 L) for 2 h. After the solvent was removed under reduced pressure, a brown residue was obtained (PO-E, 1.04 kg). The 95% EtOH extract (1000 g) was suspended in H_2O (4 L) and successively partitioned with $CHCl_3$ (5 × 3 L) and *n*-BuOH (5 × 3 L) to yield $CHCl_3$- (PO-E-C, 32 g) and *n*-BuOH-soluble fractions (PO-E-B, 76 g).

The $CHCl_3$-soluble fraction (27 g) was chromatographed over RP-18 reversed-phase silica gel eluting with a gradient of increasing MeOH (70-100%) in water and separated into eight fractions (I-VIII) on the basis of TLC analyses. Fraction III (400 mg) was isolated by reverse-phase preparative HPLC, using MeOH-H_2O (60:40) as the mobile phase, to yield 3-(4'-hydroxybenzyl)-5,7-dihydroxy-6-methyl-8-methoxychroman-4-one (**1**, 160.4 mg). Fraction IV (340 mg) was isolated by reverse-phase preparative HPLC, using MeOH-H_2O (65:35) as the mobile phase, to yield 3-(4'-hydroxybenzyl)-5,7-dihydroxy-6,8-dimethylchroman-4-one (**2**, 112.2 mg). Fraction V (420 mg) was isolated by reverse-phase preparative HPLC, using MeOH-H_2O (70:30) as the mobile phase, to yield 3-(4'-methoxybenzyl)-5,7-dihydroxy-6-methyl-8-methoxychroman-4-one (**3**, 167.2 mg).

HPLC analysis

The HPLC analyses were performed using a Shimadzu 2010A HT series liquid chromatographic system equipped with a quaternary solvent delivery system, an on-line degasser, an auto-sampler, a column temperature controller, and an SPD-M10A photodiode-array detector coupled with an analytical workstation.

The chromatographic separation was carried out on a ZORBAX Eclipse XDB (5 μm, 250 mm × 4.6 mm, Agilent Technologies). The mobile phase consisted of methanol (A) and water (B). A gradient program was used: 0-5 min, isocratic elution with A-B (60:40, v/v); 5-20 min, linear change from A-B (60:40, v/v) to A-B (80:20, v/v); and 20-30 min, isocratic elution with A-B (80:20, v/v). The flow rate was 1.0 mL/min, and the column temperature was maintained at 30°C. The product was detected by monitoring UV absorption at 297 nm. The samples were filtered through a 0.45 μm Nylon membrane filter, and 20 μL were injected for HPLC analysis.

Induction of STZ-induced diabetes and determination of AGE levels in the kidney

After several days of adaptation, the food was withdrawn 12-h before the experiment, but the rats were allowed free access to water. The rats were injected intraperitoneally with streptozotocin (STZ, Wako, 60 mg/kg body weight) in 10 mM citrate buffer (pH 4.5). Five days after the injection the body weight was measured, blood samples were collected from the tail vein, and the induction of diabetes was confirmed by the determination of blood glucose level using commercial reagents (Beijing Dingguochangsheng Biotechnology Co. Ltd.). Rats with plasma glucose levels greater than 300 mg/dl were considered diabetic rats. The rats were randomly divided into seven experimental groups: group 1, diabetic rats that received water (diabetic control, $n = 8$); groups 2 and 3, diabetic rats that received 2000 and 1000 mg/kg body weight/d of EtOH extract orally via gavage once a day (diabetic + PO-E2000 and 1000, $n = 9$, respectively); groups 4 and 5, diabetic rats that received 64 and 32 mg/kg body weight/d of $CHCl_3$-soluble fraction orally via gavage once a day (diabetic + PO-E-C64 and 32, $n = 9$, respectively); groups 6 and 7, diabetic rats that received 152 and 76 mg/kg body weight/d of *n*-BuOH-soluble fraction orally via gavage once a day (diabetic + PO-E-B152 and 76, $n = 9$, respectively). The rats that underwent a sham injection of citrate buffer without STZ were used as controls ($n = 8$). After an 80 day administration period, the kidneys were removed from each rat and frozen at -80°C until analysis.

The renal AGE levels were determined using the fluorescence assay method as described by Soulis-liparota et al. (Soulis-liparota et al., 1991). The tissue was minced and homogenated in phosphate buffered saline (PBS). The homogenate was centrifuged, and the pellet was washed in PBS. After two repetitions, the pellet was delipidated with chloroform and methanol (2:1, v/v) overnight at 4°C. After being spun again, the tissue was homogenized in methanol and water (4:1, v/v), followed by centrifugation at 4°C. The precipitate was extracted in 1% pepsin in 0.5 M acetic acid for 18-h at 4°C. The pepsin extraction was performed three times. After the sample was spun, the remaining precipitate was incubated in a solution containing 0.1% proteinase K and 0.1% collagenase IV for 60-h with low speed shaking at 37°C. The sample was centrifuged, and the supernatant was used for analysis. The final supernatant was diluted with water for fluorescence measurement using a spectrofluorometric detector (Luminescence Spectrometer LS50B, Perkin-Elmer Ltd.) at an excitation wavelength of 370 nm and an emission wavelength of 440 nm. The remaining final supernatant was used for hydroxyproline measurement, and collagen-linked fluorescence was calculated as arbitrary fluorescence units per milligram of collagen. The degree of advanced glycation of renal collagen was determined by the expression of collagen-specific fluorescence per milligram of hydroxyproline.

Determination of AGE formation

The AGE formation was assessed by a typical, previously-reported fluorescence method with slight modifications (Rahbar et al., 1999). Briefly, 10 mg/mL of bovine serum albumin (BSA, Sigma) in 200 mM phosphate buffer (pH 7.4), with 0.02% sodium azide to prevent bacterial growth, were added to 200 mM D-glucose (Sigma). The reaction mixture was mixed with various concentrations of the EtOH extract, soluble fractions, isolated compounds, and aminoguanidine (Sigma). After incubating at 37°C for seven days, the fluorescence intensity of the reaction products was determined using a spectrofluorometric detector (Luminescence Spectrometer LS50B, Perkin-Elmer Ltd.) at an excitation wavelength of 370 nm and an emission wavelength of 440 nm. The reaction mixture without D-glucose was used as a blank solution. Measurements were performed in triplicate, and the concentrations of each test compound showing 50% inhibition of AGE formation (IC_{50}) were estimated from the least-squares regression line of four plots of the logarithmic concentrations *versus* the remaining activity.

RESULTS AND DISCUSSION

AGEs are irreversible end-products of the protein glycation reaction that occurs in the body, leading to accumulation of AGEs in plasma and tissues associated with conditions (e.g., diabetes), which have a metabolic overload of reducing sugars and rapidly accelerate AGE formation. AGEs cause numerous types of

protein modification, resulting in structural and functional impairments, such as intra- and intermediate cross-linking, absorption and fluorescence at specific wavelengths, and alteration of enzyme activity. Thus, the discovery and investigation of AGE formation inhibitors would offer a potential therapeutic approach for preventing diabetic complications.

To identify the active compounds from *P. odoratum*, the EtOH extract was subjected to subsequent solvent extractions with increasing polarity. The EtOH extract and soluble fractions were administered to streptozotocin-induced diabetic rats in doses dependent upon their ratio in original EtOH extract to evaluate their effects on renal AGE accumulation. The present study confirmed the renal AGE formation increase in streptozotocin-induced diabetic rats by Maillard-type fluorescent measurement. The EtOH extract reduced the AGE formation of diabetic rats, but the $CHCl_3$-soluble fraction possessed significant inhibitory activity (Table I). The EtOH extract and soluble fractions were tested for inhibitory effects on AGE formation *in vitro*. In this study, protein glycation was demonstrated in the reaction mixture of BSA with glucose *in vitro*. Glucose is used as the glycation agent, which is commonly adopted in Maillard reaction studies, and BSA might serve as a target for the glycation agent. The $CHCl_3$-soluble fraction showed significantly higher inhibition in a concentration dependent. The present findings from systematic fractions supported the proposal that the $CHCl_3$-soluble fraction contains the bioactive components that inhibit AGE formation; thus, special attention was focused on isolating the active component from this soluble fraction. HPLC analyzes of the $CHCl_3$-soluble fraction demonstrated that peaks 1-3 were the primary components (Fig. 1).

Table I. Effects of EtOH extract and soluble fractions on renal AGE levels in streptozotocin-induced diabetic rats *in vivo*[a]

Group	AGE (AFU)
Control (n = 8)	15.88 ± 4.52 *
Diabetic control (n = 8)	24.15 ± 4.89
Diabetic + PO-E2000 (n = 9)	17.46 ± 3.55 *
Diabetic + PO-E1000 (n = 9)	14.65 ± 3.78 *
Diabetic + PO-E-C64 (n = 9)	12.76 ± 2.55 *
Diabetic + PO-E-C32 (n = 9)	16.73 ± 0.95 *
Diabetic + PO-E-B152 (n = 9)	22.15 ± 6.64
Diabetic + PO-E-B76 (n = 9)	21.33 ± 3.71

[a] Value was expressed as mean ± S.D. (n = 8 or 9). Statistical differences were calculated by Student's t-test, $^*p < 0.01$ *vs.* diabetic control.

The $CHCl_3$-soluble fraction was subjected to RP-18 reversed-phase silica gel chromatographic separation to yield eight subfractions, and further purification of III, IV, and V yielded three compounds (**1-3**) by reverse-phase preparative HPLC. The structures of **1-3** were identified as 3-(4'-hydroxybenzyl)-5,7-dihydroxy-6-

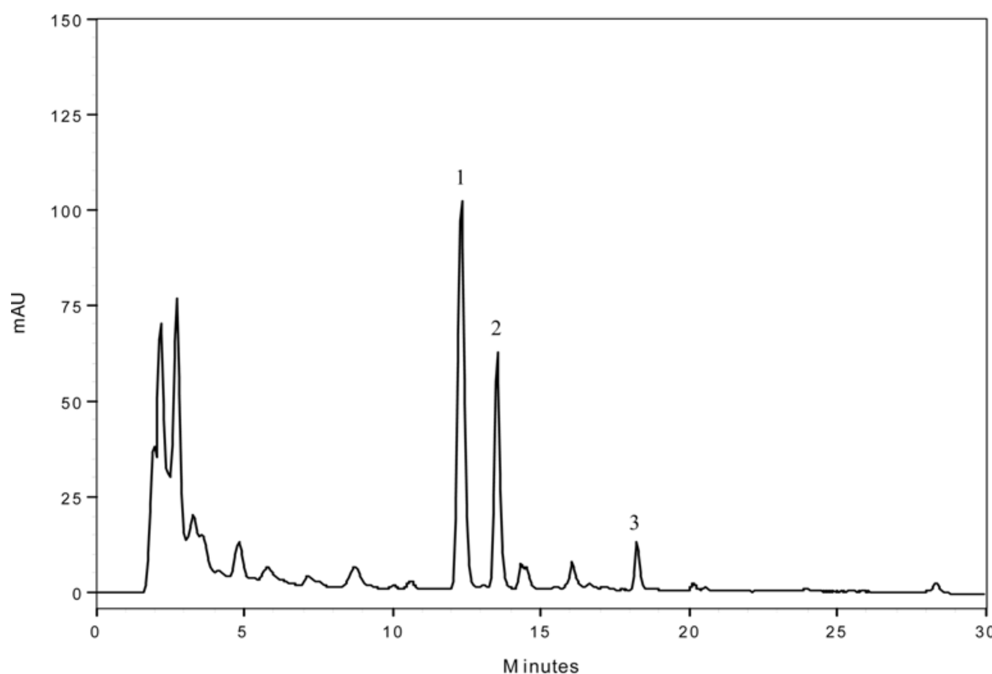

Fig. 1. HPLC chromatogram of the $CHCl_3$-soluble fraction of EtOH extract from the *Polygonatum odoratum* rhizomes. 3-(4'-hydroxybenzyl)-5,7-dihydroxy-6-methyl-8-methoxychroman-4-one (**1**), 3-(4'-hydroxybenzyl)-5,7-dihydroxy-6,8-dimethylchroman-4-one (**2**), and 3-(4'-methoxybenzyl)-5,7-dihydroxy-6-methyl-8-methoxychroman-4-one (**3**) were detected at 297 nm.

methyl-8-methoxychroman-4-one (**1**) (Rafi and Vastano, 2007), 3-(4'-hydroxybenzyl)-5,7-dihydroxy-6,8-dimethylchroman-4-one (**2**) (Huang et al., 1997), and 3-(4'-methoxybenzyl)-5,7-dihydroxy-6-methyl-8-methoxychroman-4-one (**3**) (Wang et al., 2009) by spectroscopic data (MS, ^{1}H-, ^{13}C-, and 2D-NMR) measurement and by comparison with published values. Their structures are shown in Fig. 2.

The potential of compounds **1**-**3** to inhibit AGE formation is summarized in Table II. A number of flavonoids, including flavones, flavonols, flavanones, isoflavones, flavan-3-ols, and anthocyanins, have been found to exhibit significant *in vitro* inhibitory activity against AGE formation (Matsuda et al., 2003). In the present study, three homoisoflavanones, 3-(4'-hydroxybenzyl)-5,7-dihydroxy-6-methyl-8-methoxychroman-4-one (**1**), 3-(4'-hydroxybenzyl)-5,7-dihydroxy-6,8-dimethylchroman-4-one (**2**), and 3-(4'-methoxybenzyl)-5,7-dihydroxy-6-methyl-8-methoxychroman-4-one (**3**), exhibited much stronger inhibition of AGE formation (IC$_{50}$ value of 56.30, 46.05, 107.10 μM, respectively) than aminoguanidine (IC$_{50}$ value of 123.48 μM), a well-known glycation inhibitor. Although there are some reports addressing the biological activity of homoisoflavanones (Sup et al., 2004; Rafi and Vastano, 2007), this is the first report describing homoisoflavanone inhibition of AGE formation. This suggests the potential development of these compounds into natural drugs for treating diabetic complications.

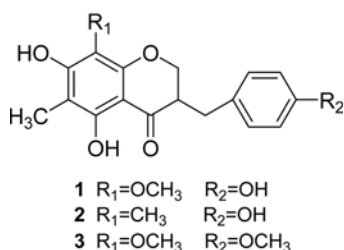

Fig. 2. Structures of compounds **1**-**3** isolated from the rhizomes of *Polygonatum odoratum.*

Table II. Inhibitory activity of compounds from *Polygonatum odoratum* rhizomes on AGE formation *in vitro*[a]

Compound	Conc. (mM)	Inhibition (%)	IC$_{50}$ value (μM)
1	0.0312	36.28 ± 3.05	56.30
	0.0625	49.23 ± 3.01	
	0.125	72.67 ± 3.54	
	0.25	89.75 ± 1.06	
2	0.0312	39.34 ± 0.82	46.05
	0.0625	57.01 ± 0.20	
	0.125	79.47 ± 0.89	
	0.250	92.70 ± 2.13	
3	0.0312	17.79 ± 1.08	107.10
	0.0625	32.16 ± 1.97	
	0.125	55.83 ± 1.62	
	0.250	77.86 ± 1.59	
Aminoguanidine (positive control)	0.0312	22.38 ± 3.21	123.48
	0.0625	32.04 ± 2.60	
	0.125	46.41 ± 4.27	
	0.250	69.26 ± 1.06	

[a] Inhibitory effect was expressed as mean ± S. D. of triplicate experiments. IC$_{50}$ values were calculated from the dose inhibition curve.

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REFERENCES

Ahmed, N., Advanced glycation endproducts-role in pathology of diabetic complications. *Diabetes Res. Clin. Pract.*, 67, 3-21 (2005).

Bolton, W. K., Cattran, D. C., Williams, M. E., Adler, S. G., Appel, G. B., Cartwright, K., Foiles, P. G., Freedman, B. I., Raskin, P., Rather, R. E., Spinowitz, B. S., Whittier, F. C., and Wuerth, J. P., Randomized trial of an inhibitor of formation of advanced glycation end products in diabetic nephropathy. *Am. J. Nephrol.*, 24, 32-40 (2004).

Brownlee, M., Biochemistry and molecular cell biology of diabetic complications. *Nature*, 414, 813-820 (2001)

Dyer, D. G., Blackledge, J. A., Thorpe, S. R., and Baynes, J. W., Formation of pentosidine during nonenzymatic browning of proteins by glucose. *J. Biol. Chem.*, 266, 11654-11660 (1991).

Huang, P. L., Gan, K. H., Wu, R. R., and Lin, C. N., Benzoquinones, a homoisoflavanone and other constituents from *Polygonatum alte-lobatum*. *Phytochemistry*, 44, 1369-1373 (1997).

Ikeda, K., Higashi, T., Sano, H., Jinnouchi, Y., Yoshida, M., Araki, T., Ueda, S., and Horiuchi, S., N-epsilon-(carboxymethyl)lysine protein adduct is a major immunological epitope in proteins modified with advanced glycation end products of the Maillard reaction. *Biochemistry*, 35, 8075-8083 (1996).

Jang, D. S., Yoo, N. H., Lee, Y. M., Yoo, J. L., Kim, Y. S., and Kim, J. S., Constituents of the flowers of *Erigeron annuus* with inhibitory activity on formation of advanced glycation end products (AGEs) and aldose reductase. *Arch. Pharm. Res.*, 31, 900-904 (2008).

Lee, E. H., Song, D. -G., Lee, J. Y., Pan, C. -H., Um, B. H., and Jung, S. H., Inhibitory effect of the compounds isolated from *Rhus verniciflua* on aldose reductase and advanced glycation endproducts. *Biol. Pharm. Bull.*, 31, 1626-1630 (2008).

Lin, H. W., Han, G. Y., and Liao, S. X., Studies on the active constituents of the chinese traditional medicine *Polygona-*

tum odoratum (Mill.) Druce. *Acta Pharmacol. Sin.*, 29, 215-222 (1994).

Matsuda, H., Wang, T., Managi, H., and Yoshikawa, M., Structural requirements of flavonoids for inhibition of protein glycation and radical scavenging activities. *Bioorg. Med. Chem.*, 11, 5317-5323 (2003).

Qin, H. L., Li, Z. H., and Wang, P., A new furostanol glycoside from *Polygonatum odoratum*. *Chin. Chem. Lett.*, 14, 1259-1260 (2003).

Qin, H. L., Li, Z. H., Wang, P., and Si, L. X., The new secondary metabolite from *Polygonatum odoratum*. *China J. Chin. Mater. Med.*, 29, 42-44 (2004).

Rafi, M. M. and Vastano, B. C., Identification of a structure specific Bcl-2 phosphorylating homoisoflavone molecule from Vietnamese coriander (*Polygonatum odoratum*) that induces apoptosis and G2/M cell cycle arrest in breast cancer cell lines. *Food Chem.*, 104, 332-340 (2007).

Rahbar, S., Yernini, K. K., Scott, S., Gonzales, N., and Lalezari, I., Novel inhibitors of advanced glycation endproducts. *Biochem. Biophys. Res. Commun.*, 262, 651-656 (1999).

Sell, D. R., Nelson, J. F., and Monnie, V. M., Effect of chronic aminoguanidine treatment on age-related glycation, glycoxidation, and collagen cross-linking in the Fischer 344 rat. *J. Gerontol. A Biol. Sci. Med. Sci.*, 56, B405-B411 (2001).

Shi, H. B., Miao, Y. B., Wang, L. P., and Wang, W., Prection of ethanol extract and fractions from *Polygonatum odoratum* on renal lesion in diabetic rats. *Chin. Tradit. Herb. Drugs*, 37, 1846-1849 (2007).

Shim, J. S., Kim, J. H., Lee, J., Kim, S. N., and Kwon, H. J., Anti-angiogenic activity of a homoisoflavanone from *Cremastra appendiculata. Planta Med.*, 70, 171-173 (2004).

Soulis-liparota, T., Cooper, M., Papazoglou, D., Clarke, B., and Jerums, G., Retardation by aminoguanidine of development of albuminuria, mesangial expansion, and tissue fluorescence in streptozotocin-induced diabetic rat. *Diabetes*, 40, 1328-1334 (1991).

Wada, R. and Yagihashi, S., Role of advanced glycation end products and their receptors in development of diabetic neuropathy. *Ann. N. Y. Acad. Sci.*, 1043, 598-604 (2005).

Wang, D., Li, D., Zhu, W., and Peng, P., A new C-methylated homoisoflavanone and triterpenoid from the rhizomes of *Polygonatum odoratum*. *Nat. Prod. Res.*, 6, 580-589 (2009).