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RESEARCH ARTICLE

Triterpenoid saponins from the roots of *Rosa rugosa* Thunb. as rat intestinal sucrase inhibitors

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Abstract Medicinal plants constitute an important source of potential therapeutic agents for diabetes. The purpose of present study is to investigate the effect of root extract of *Rosa rugosa* Thunb. on inhibition of sucrase related to diabetes mellitus (DM). Bioassay-guided fractionation of the methanol extract led to the identification of 13 triterpenoid saponins (**1–13**). Their structures were elucidated on the basis of extensive spectroscopic analysis, including 1D, 2D NMR, and MS. The *n*-butanol fraction showed potent rat intestinal sucrase inhibitory activity with value of 87.62 ± 5.84 % inhibition compared to the positive control acarbose (50.96 ± 2.97 % inhibition at 0.02 mM). Subsequently, compounds **11–13** (1.0 mM) exhibited significant sucrase inhibitory activity, with inhibition percentage values of 41.17 ± 3.52, 46.80 ± 4.00, and 39.39 ± 4.19 %, respectively. Whereas, compounds **2–6**, **8**, and **10** showed moderate sucrase inhibitory activity (ranging from 13.26 ± 7.00 to 32.08 ± 6.04 % inhibition) at a same concentration. The data provide a starting point for creating new sucrase inhibitors, which may be useful for the development of effective therapies for the treatment of DM.

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Introduction

Diabetes mellitus is a complex endocrine disorder characterized by abnormalities in insulin secretion and/or insulin action that leading to the progressive deterioration of glucose tolerance and causes hyperglycemia (Pereira et al. 2011). DM is a major and growing public health problem throughout the world, affecting about 171 million people and most of them have type 2 diabetes (Gershell 2005). This increasing trend in type 2 DM has become a serious medical concern worldwide. It accounts for 9 % of deaths; thus, great efforts are being made in the search for new therapeutic agents to stem its progress (Kumar et al. 2011). One therapeutic approach for decreasing postprandial hyperglycemia is to retard the absorption of glucose via the inhibition of carbohydrate-hydrolyzing enzymes, such as α-glucosidases (i.e. sucrase, maltase, isomaltase, glucoamylase, and lactase inhibition) in the intestine (Holman et al. 1999).

In recent years, much effort has been made to identify effective α-glucosidase inhibitors from natural sources in order to develop a physiologic functional food or to identify compounds for use against diabetes. Many α-glucosidase inhibitors have been isolated from plants, including flavonoids, alkaloids, terpenoids, anthocyanins, glycosides, and phenolic compounds (Kumar et al. 2011). On the other hand, medicinal plants were widely used for treatment of diabetes throughout the world as they are effective, non-toxic, and less or no side effects (Clifford and Caroline 1989). More than 1,200 plants have been used to treat

diabetes in folk medicine (Marles and Farnsworth 1995), and 136 plants clearly showed the anti-diabetic effects (Kavishankar et al. 2011). Thus, many researchers are trying to search for more effectively anti-diabetic compounds from medicinal plants.

Rosa rugosa Thunb. ex Murray (Rosaceae) is a deciduous tree that grows in Asia, Europe, North Africa, and North America (Li et al. 2013a; Yu et al. 1985). *R. rugosa* is a 1–2 m tall shrub characterized by vegetative reproduction using root suckers. Its single large red-pink flowers, which are 6–12 cm in diameter, occur in clusters of 3–6 (Sulborska et al. 2012). The plant has been used in traditional medicine to treat stomach-ache, diarrhea, and women's diseases. Recent studies have also shown that *R. rugosa* exhibited anti-HIV, antitumor activity, anti-nociceptive, anti-tobacco, and anti-inflammatory activities (An et al. 2011; Fu et al. 2006). In northern Japan, where this wild rose occurs naturally, the dried petals have been used as antidiarrheal and hemostatic agents. The dried petals of *R. rugosa* have been used in China for preparation of rose tea because of their sweet fragrance; moreover, the tea is believed to provide nourishment (Hshidoko 1996). In Korea, the plant has been used for the treatment of diabetes, chronic inflammatory diseases, pain, and cancer (Lee et al. 2008).

Previous phytochemical researches on the *R. rugosa* have shown that tannins, flavonoids, and terpenoids are the major components of this plant (An et al. 2011; Fu et al. 2006; Hashidoko et al. 1993; Ochir et al. 2010). In the course of our search for biologically active compounds from plant resources, the *n*-butanol-soluble part of a 95 % methanol extract of *R. rugosa* roots was found to inhibit rat intestinal sucrase. We herein focused on the sucrase inhibitory effect of the extracts and 13 triterpenoid saponins (**1–13**) from the roots of this plant (Table 1; Fig. 1).

Table 1 Rat intestinal sucrase inhibitory activity of the extracts and isolated compounds **1–13**

Compounds	Enzyme inhibition (%)
1	NI
2	30.42 ± 4.25*
3	19.45 ± 4.23
4	13.26 ± 7.00
5	27.09 ± 4.02
6	32.08 ± 6.04*
7	NI
8	15.09 ± 6.13
9	NI
10	25.84 ± 7.72
11	41.17 ± 3.52*
12	46.80 ± 4.00*
13	39.39 ± 4.19*
CH_2Cl_2 fraction	84.67 ± 5.37**
n-BuOH fraction	87.62 ± 5.84**
Aqueous fraction	NI
MeOH extract	81.91 ± 2.90**
Acarbose[a]	50.96 ± 2.97**

Data presented is the mean ± SD of samples run in triplicate. * $P < 0.05$, ** $P < 0.01$ different versus control group. Percentage of enzyme inhibition at concentrations of 1.0 mM (compounds) and 0.5 mg/mL (extracts)

NI no inhibition (less than 10 % inhibition)

[a] Acarbose (0.02 mM) was used as a positive control

Materials and methods

Plant material

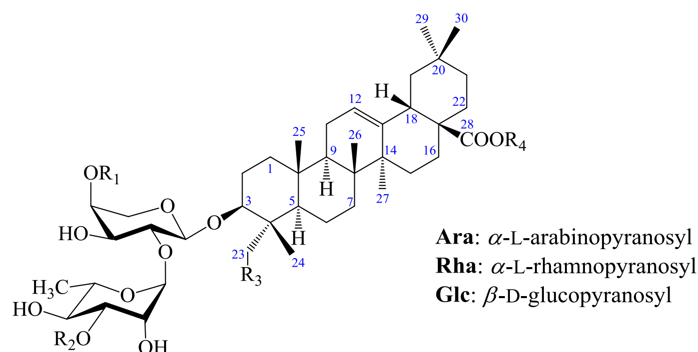
The samples of the roots of *R. rugosa* Thunb. were purchased from an herbal market at Kumsan, Chungnam, Republic of Korea, in August 2011. The plant material was identified by Professor Young Ho Kim, and a voucher specimen (CNU-11104) was deposited at the Herbarium of College of Pharmacy, Chungnam National University.

General experimental procedures

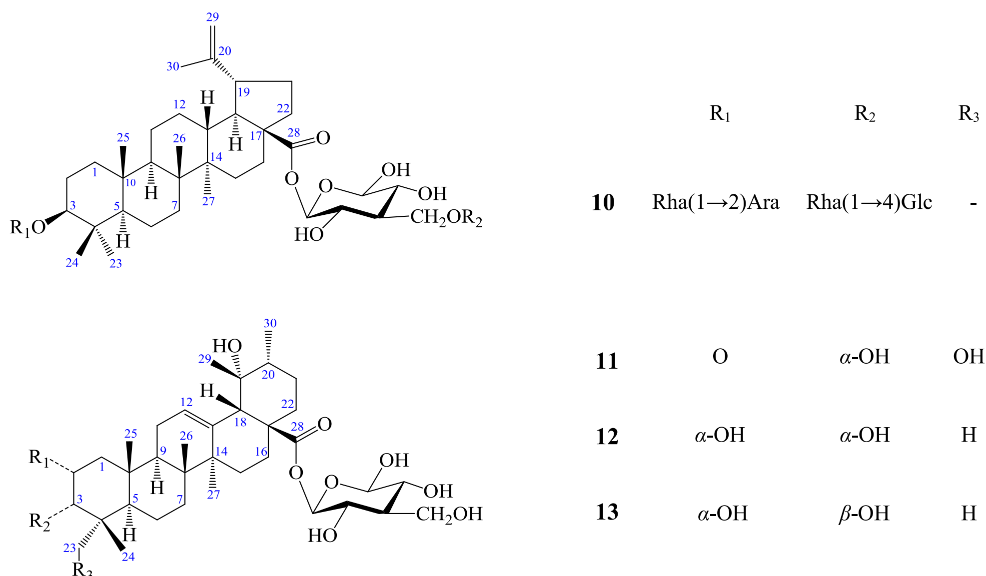
Optical rotations were determined using a Jasco DIP-370 digital polarimeter. The FT-IR spectra were measured using a Jasco Report-100 infrared spectrometer. ESI mass spectra were obtained using an Agilent 1200 LC-MSD Trap spectrometer. The NMR spectra were recorded on a JEOL ECA 600 spectrometer using TMS as an internal standard. TLC was performed on Kieselgel 60 F_{254} (1.05715; Merck, Germany) or RP-18 F_{254s} (Merck) plates. Spots were visualized by spraying with 10 % aqueous in H_2SO_4 solution, followed by heating for 3–5 min. Column chromatography (CC) was performed on silica gel (Kieselgel 60, 70–230 mesh and 230–400 mesh, Merck) and YMC RP-18 resins (1.15685.0001, Merck, Germany). Automated flash chromatography was performed on a Teledyne CombiFlash R_f200 using C-18 RediSep columns.

Extraction and isolation

Dried *R. rugosa* roots (1.45 kg) were extracted with MeOH using ultrasonic maceration (2 × 3 h) at 30 °C. The resulted solutions were filtered, combined, and concentrated under reduced pressure to give a MeOH extract (A, 118 g). This extract was suspended in H_2O and successively partitioned with CH_2Cl_2, EtOAc, and *n*-BuOH to give CH_2Cl_2 (B, 21.3 g), EtOAc (C, 12.4 g), and *n*-BuOH (D, 31.5 g) fractions, respectively. Bioactivity-guided fractionation of the *n*-butanol-soluble fractions was carried out using in vitro rat



	R_1	R_2	R_3	R_4
1	Glc	Glc(1→4)Glc	OH	Rha(1→4)Glc(1→6)Glc
2	Glc	H	OH	Rha(1→4)Glc(1→6)Glc
3	Glc	Glc	H	Rha(1→4)Glc(1→6)Glc
4	H	H	OH	Rha(1→4)Glc(1→6)Glc
5	Glc	H	H	H
6	H	Glc	OH	Rha(1→4)Glc(1→6)Glc
7	H	Glc	H	H
8	Glc	H	H	Glc
9	H	H	H	Rha(1→4)Glc(1→6)Glc



	R_1	R_2	R_3
10	Rha(1→2)Ara	Rha(1→4)Glc	-
11	O	α-OH	OH
12	α-OH	α-OH	H
13	α-OH	β-OH	H

Fig. 1 Structures of triterpene saponins **1**–**13** from *R. rugosa* roots

intestinal sucrase assay. The *n*-butanol fraction showed potent rat intestinal sucrase inhibitory activity with a value of 87.62 ± 5.84 % inhibition.

Fraction D was chromatographed over silica gel CC eluting with MeOH in CH_2Cl_2 (from 30 to 100 %, stepwise), yielding four subfractions (D-1 to D-4). Subfraction D-1 (5.6 g) was chromatographed over silica gel CC eluting with CH_2Cl_2–MeOH (10:1) to yield three smaller subfractions (D-1.1 to D-1.3). Subfraction D-1.1 (0.82 g) was chromatographed over silica gel CC eluting with EtOAc–MeOH (17:1) and then further purified by YMC RP-18 CC using MeOH–H_2O (1:1) as the eluent to afford **13** (11.2 mg). Next, subfraction D-1.2 (1.1 g) was chromatographed over silica gel CC and eluted with CH_2Cl_2–MeOH (10:1) to obtain **11** (32.8 mg) and **12** (18.5 mg). Fraction D-2 (3.5 g) was chromatographed on a column of highly porous polymer (Diaion® HP-20), using stepwise eluent of MeOH–H_2O (0/10, 2.5/10, v/v) to give three

smaller fractions (D-2.1 to C-2.3) after removal of fraction eluted with H_2O 100 %. Subfraction D-2.1 (0.73 g) was separated by YMC RP-18 CC using MeOH–H_2O (1:2) as the eluent to afford **5** (12.2 mg) and **7** (14.5 mg). Similarly, subfraction D-2.3 (0.84 g) was separated by YMC RP-18 CC, using MeOH–H_2O (1:3) as eluent, and further purified by silica gel CC, with CH_2Cl_2–MeOH–H_2O (5:1:0.1), to obtain **8** (17.3 mg). Fraction D-3 (10.1 g) was separated by normal-phase medium-pressure liquid chromatography (MPLC) using CH_2Cl_2–MeOH (8:1) as the eluent to afford **4** (14.8 mg), **9** (15.4 mg), and a crude mixture of triterpenoid saponins. The latter was further separated by Sephadex LH-20 CC using H_2O–MeOH (1:1) as the mobile phase, followed by YMC RP-18 CC using acetone–H_2O (1.5:2.5) to afford **2** (13.5 mg) and **6** (18.7 mg). Next, fraction D-4 (12.2 g) was separated by YMC RP-18 CC eluting with acetone–H_2O (1.2:3) to provide three smaller fractions (D-4.1 to D-4.3). Subfraction D-4.2 (0.8 g) was separated by YMC RP-18 chromatography using MeOH–H_2O (1:2) as the eluent and further purified by silica gel CC, with CH_2Cl_2–MeOH–H_2O (2:1:0.2), to obtain **3** (14.4 mg) and **10** (11.3 mg). And finally, subfraction D-4.3 (0.51 g) was subjected to silica gel CC with CH_2Cl_2–MeOH–H_2O (1.5:10.2) and further separated by YMC RP-18 CC using acetone–H_2O (1.2:1.5) as the eluent to afford **1** (20.1 mg).

Compounds

Thirteen compounds **1–13** were isolated and structurally elucidated from the roots of *R. rugosa*. Their purity (96–98 %) was determined by NMR and HPLC analyses. Stock solutions of tested compounds in DMSO were prepared, kept at −20 °C, and diluted to the desired final concentration in fresh medium before each experiment. To avoid influencing cell growth, the final DMSO concentration did not exceed 0.5 % in all experiments.

In vitro sucrase inhibition assay

Rat intestinal acetone powders were purchased from Sigma Chemical Co. (St. Louis, MO, USA). A slightly modified version of rat intestinal sucrase assay method developed by Kwon et al. was used (Kwon et al. 2006). A total of 1.0 g of the rat intestinal acetone powder was suspended in 3.0 mL of 0.9 % saline, and the suspension was sonicated 12 times for 30 s at 4 °C. After centrifugation (10,000×*g*, 30 min, 4 °C), the resulting supernatant was used for the assay. The sample solution (50.0 µL) and 0.1 M phosphate buffer (pH 6.9, 100 µL) containing sucrase solution (1.0 U/mL) was incubated at 25 °C for 10 min. After preincubation, 5.0 mM *p*-nitrophenyl-α-D-glucopyranoside solution (50.0 µL) 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 min. Before and after incubation, the absorbance was read at 405 nm by a microplate reader Sunrise (Tecan, Salzburg, Austria) and compared to a control which had 50.0 µL of buffer solution in place of the extract or compound. Sucrase inhibitory activity was expressed as % inhibition and was calculated as follows:

$$\%\ \text{inhibition} = \left(\left[\frac{\Delta A_{405}^{Control} - \Delta A_{405}^{Extract}}{\left[\Delta A_{405}^{Control}\right]}\right]\right) \times 100$$

Statistical analysis

All experiments were performed in triplicate. Data is presented as the mean ± standard deviation (SD) the results were statistically analyzed by ANOVA and Duncan's multiple range tests (GraphPad Prism version 6.02). Statistical significance was accepted at a level of $*P < 0.05$ and $**P < 0.01$ using the SPSS software package (SPSS Inc. Chicago, IL, USA version 10.0).

Results and discussion

Natural resources provide a huge and highly diversified chemical bank from which we can search for potential therapeutic agents using bioactivity-targeted screening. Given the development of the herbal industry and continued interest in herbal medicine (i.e. phytopharmaca), opportunities for the exploration of medicinal plants are widely available (Lam et al. 2008). As an economically important plant, *R. rugosa* has been widely cultivated in several areas of Korea for use as an ornamental flowers, food, and incense materials (Gao et al. 2013). In addition the legumes of this plant are used to treat various diseases (Guo et al. 2011; Horváth et al. 2012).

To our knowledge, there have been only a few reports on α-glucosidase inhibitory effects of *R. rugosa* (Feng et al. 2013; Li et al. 2014), but rat intestinal sucrase inhibition of the extracts and/or pure compounds from this plant have not been reported. A methanol extract prepared from the roots of *R. rugosa* was screened and found to exhibit potent rat intestinal sucrase inhibitory activity, with value of 81.91 ± 2.90 % inhibition. Subsequently, this extract was successively partitioned with dichloromethane and *n*-butanol. Bioassay-guided screening indicated that the *n*-butanol-soluble fraction (0.5 mg/mL) of the *R. rugosa* roots showed strong rat intestinal sucrase inhibitory activity, with inhibition percentage value of 87.62 ± 5.84 % (Table 1), relative to the positive control acarbose (0.02 mM), with value of 50.96 ± 2.97 % inhibition. Previously, acarbose isolated from *Actinoplanes* sp. is now

used in the management of type 2 diabetes. A main drawback of using drugs such as acarbose is their side effects including abdominal distention, flatulence, meteorism, and possibly diarrhea (Kimura et al. 2004).

Therefore, the *n*-butanol-soluble fraction was selected for further separation using various chromatographic methods, which resulted in the isolation of 13 secondary metabolites **1–13** (see "Materials and methods" section). These compounds were identified as pulsatilloside F (**1**) (Li et al. 2013b), hederacolchiside F (**2**) (Kang 1989), cernuoside B (**3**) (Zhang et al. 2000), kalopanaxsaponin B (**4**) (Sano et al. 1991), 3-*O*-{[β-D-glucopyranosyl(1→4)]-[α-L-rhamnopyranosyl-(1→2)]-α-L-arabinopyranosyl} oleanolic acid (**5**) (Ekabo and Farnsworth 1996), patrinia saponin H3 (**6**) (Kang and Kim 1997), 3-*O*-β-D-glucopyranosyl(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranosyl oleanolic acid (**7**) (Saito et al. 1990), 3-*O*-[β-D-glucopyranosyl(1→3)-α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranosyl(1→4)]-α-L-arabinopyranosyl oleanolic acid (**8**) (Schenkel et al. 1991), hederasaponin B (**9**) (Sano et al. 1991), cussosaponin C (**10**) (Mimaki et al. 2001), 3β,19α,23α-trihydroxy-2-oxo-12-ursen-28-oic acid β-D-glucopyranosyl ester (**11**) (Jia et al. 1993), kaji-ichigoside F1 (**12**) (Liang and Cao 1992), and rosamultin (**13**) (Liang and Cao 1992) by comparison of their spectroscopic data with the literature values. This is the first integrated chemical investigation of triterpenoid saponins from *R. rugosa* roots.

Subsequently, all isolated compounds were tested for their sucrase inhibitory activity. Among them, compounds **11–13** (1.0 mM) showed significant sucrase inhibitory activity, with values of 41.17 ± 3.52, 46.80 ± 4.00, and 39.39 ± 4.19 % inhibition, respectively. This is in agreement with recent reports suggesting that the sucrase inhibitory activity increased significantly as compared to the other compounds when a sugar unit attached at C-28 position of the aglycone (Benalla et al. 2010; Jabeen et al. 2013; Kang et al. 2011; Lai et al. 2012; Wei et al. 2012). Moreover, compounds **2–6**, **8**, and **10** (with additional the sugar units attached at C-3 position) showed mild sucrase inhibitory activity, with percentage inhibition values ranging from 13.26 ± 7.00 to 32.08 ± 6.04 % at a same concentration. The other compounds did not exert significant inhibitory effects on the enzyme (less than 10 % inhibition, Table 1).

Consideration of the structure–activity relationship (SAR) of these triterpenoid saponins suggested that the presence of the sugar units at C-3 and/or C-28 of the aglycone might play an important role in the sucrase inhibitory activity of these compounds. Interestingly, rat intestinal sucrase inhibitory activity of the methanol extract and *n*-butanol fraction was stronger than that of the isolated triterpenoid saponins. This evidence suggested that rat intestinal sucrase inhibitory activity of methanol extract and *n*-butanol fraction might arise from the synergy of many compounds but not of each individual.

In conclusion, the enzyme inhibition of the extract/fractions and isolated constituents was less than that of the reference inhibitor acarbose. However, keeping in mind with the multiple health benefits of herbal medicines, this report provides a basis for further evaluation and/or utilization of *R. rugosa* roots alone or in combination with other agents for the treatment or management of diabetic complications. The research on the *R. rugosa* Thunb. provides support for the ethnomedicinal use of the plant in the treatment of diabetes and also partly defines the mechanism underlying the anti-diabetic properties.

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References

An, H.J., I.T. Kim, H.J. Park, H.M. Kim, J.H. Choi, and K.T. Lee. 2011. Tormentic acid, a triterpenoid saponin, isolated from *Rosa rugosa*, inhibited LPS-induced iNOS, COX-2, and TNF-α expression through inactivation of the nuclear factor-κB pathway in RAW 264.7 macrophages. *International Immunopharmacology* 11: 504–510.

Benalla, W., S. Bellahcen, and M. Bnouham. 2010. Antidiabetic medicinal plants as a source of alpha glucosidase inhibitors. *Current Diabetes Reviews* 6: 247–254.

Clifford, B., and D. Caroline. 1989. Traditional plant medicines as treatments for diabetes. *Diabetes Care* 12: 553–564.

Ekabo, O.A., and N.R. Farnsworth. 1996. Antifungal and molluscicidal saponins from *Serjania salzmanniana*. *Journal of Natural Products* 59: 431–435.

Feng, S., L. Song, Y. Liu, F. Lai, G. Zuo, G. He, M. Chen, and D. Huang. 2013. Hypoglycemic activities of commonly-used traditional Chinese herbs. *The American Journal Chinese Medicine* 41: 849–864.

Fu, M., T.B. Ng, Y. Jiang, Z.F. Pi, Z.K. Liu, L. Li, and F. Liu. 2006. Compounds from rose (*Rosa rugosa*) flowers with human immunodeficiency virus type 1 reverse transcriptase inhibitory activity. *Journal of Pharmacy and Pharmacology* 58: 1275–1280.

Gao, X.M., L.D. Shu, L.Y. Yang, Y.Q. Shen, Y.J. Zhang, and Q.F. Hu. 2013. Phenylethanoids from the flowers of *Rosa rugosa* and their biological activities. *The Bulletin of the Korean Chemical Society* 34: 246–248.

Gershell, L. 2005. Type 2 diabetes market. *Nature Reviews Drug Discovery* 4: 367–368.

Guo, D., L. Xu, X. Cao, Y. Guo, Y. Ye, C.O. Chan, D.K.W. Mok, Z. Yu, and S. Chen. 2011. Anti-inflammatory activities and mechanisms of action of the petroleum ether fraction of *Rosa multiflora* Thunb. hips. *Journal of Ethnopharmacology* 138: 717–722.

Hashidoko, Y., S. Tahara, and J. Mizutani. 1993. Sesquiterpenoids from *Rosa rugosa* leaves. *Phytochemistry* 32: 387–390.

Holman, R.E., C.A. Culli, and R.C. Turner. 1999. A randomized double-blind trial of acarbose in type 2 diabetes shows improved glycemic control over 3 years. *Diabetes Care* 22: 960–964.

Horváth, G., P. Molnár, E.R. Turcsi, J. Deli, M. Kawase, K. Satoh, T. Tanaka, S. Tani, H. Sakagami, N. Gyémánt, and J. Molnár. 2012.

Carotenoid composition and in vitro pharmacological activity of rose hips. *Acta Biochimica Polonica* 59: 129–132.

Hshidoko, Y. 1996. The phytochemistry of *Rosa rugosa*. *Phytochemistry* 43: 535–549.

Jabeen, B., N. Riaz, M. Saleem, M.A. Naveed, M. Ashraf, U. Alam, H.M. Rafiq, R.B. Tareen, and A. Jabbar. 2013. Isolation of natural compounds from *Phlomis stewartii* showing α-glucosidase inhibitory activity. *Phytochemistry* 96: 443–448.

Jia, Z.J., X.Q. Liu, and Z.M. Liu. 1993. Triterpenoids from *Sanguisoraba alpine*. *Phytochemistry* 32: 155–159.

Kang, S.S. 1989. Saponins from the roots of *Pulsatilla koreana*. *Archives of Pharmacal Research* 12: 42–47.

Kang, S.S., and J.S. Kim. 1997. A triterpenoid saponin from *Patrinia scabiosaefolia*. *Journal of Natural Products* 60: 1052–1060.

Kang, W.Y., Y.L. Song, and L. Zhang. 2011. α-Glucosidase inhibitory and antioxidant properties and antidiabetic activity of *Hypericum ascyron* L. *Medicinal Chemistry Research* 20: 809–816.

Kavishankar, G.B., N. Lakshmidevi, S.M. Murthy, H.S. Prakash, and S.R. Niranjana. 2011. Diabetes and medicinal plants: A review. *International Journal of Pharmacy and Biomedical Sciences* 2: 65–80.

Kimura, A., J.H. Lee, I.S. Lee, H.S. Lee, K.H. Park, S. Chiba, and D. Kim. 2004. Two potent competitive inhibitors discriminating α-glucosidase family I from family II. *Carbohydrate Research* 339: 1035–1040.

Kumar, S., S. Narwal, V. Kumar, and O. Prakash. 2011. α-Glucosidase inhibitors from plants: A natural approach to treat diabetes. *Pharmacognosy Reviews* 5: 19–29.

Kwon, Y.I., D.A. Vattem, and K. Shetty. 2006. Evaluation of clonal herbs of *Lamiaceae* species for management of diabetes and hypertension. *Asia Pacific Journal of Clinical Nutrition* 15: 107–118.

Lai, Y.C., C.K. Chen, S.F. Tsai, and S.S. Lee. 2012. Triterpenes as α-glucosidase inhibitors from *Fagus hayatae*. *Phytochemistry* 74: 206–211.

Lam, S.H., J.M. Chen, C.J. Kang, C.H. Chen, and S.S. Lee. 2008. α-Glucosidase inhibitors from the seeds of *Syagrus romanzoffiana*. *Phytochemistry* 69: 1173–1178.

Lee, Y.H., M.G. Jung, H.B. Kang, K.C. Choi, S. Haam, W. June, Y.J. Kim, H.Y. Cho, and H.G. Yoon. 2008. Effect of anti-histone acetyltransferase activity from *Rosa rugosa* Thunb. (Rosaceae) extracts on androgen receptor-mediated transcriptional regulation. *Journal of Ethnopharmacology* 118: 412–417.

Li, D.Q., J. Zhao, J. Xie, and S.P. Li. 2014. A novel sample preparation and on-line HPLC–DAD–MS/MS–BCD analysis for rapid screening and characterization of specific enzyme inhibitors in herbal extracts: Case study of α-glucosidase. *Journal of Pharmaceutical and Biomedical Analysis* 88: 130–135.

Li, J.R., J. Liu, D.H. He, H.X. Xu, L.S. Ding, W.K. Bao, Z.Q. Zhou, and Y. Zhou. 2013a. Three new phenolic compounds from the leaves of *Rosa sericea*. *Fitoterapia* 84: 332–337.

Li, W., Y. Ding, Y.N. Sun, X.T. Yan, S.Y. Yang, C.W. Choi, J.Y. Cha, Y.M. Lee, and Y.H. Kim. 2013b. Triterpenoid saponins of *Pulsatilla koreana* root have inhibition effects of tumor necrosis factor-α secretion in lipopolysaccharide-induced RAW264.7 cells. *Chemical and Pharmaceutical Bulletin* 61: 471–476.

Liang, D., and X.P. Cao. 1992. Pomolic acid derivatives from the root of *Sanguisorba officinalis*. *Phytochemistry* 31: 1317–1320.

Marles, R.J., and N.R. Farnsworth. 1995. Antidiabetic plants and their active constituents. *Phytomedicine* 2: 137–189.

Mimaki, Y., A. Yokosuka, M. Kuroda, M. Hamanaka, C. Sakuma, and Y. Sashida. 2001. New bisdesmosidic triterpene saponins from the roots of *Pulsatilla chinensis*. *Journal of Natural Products* 64: 1226–1229.

Ochir, S., B. Park, M. Nishizawa, T. Kanazawa, M. Funaki, and T. Yamagishi. 2010. Simultaneous determination of hydrolysable tannins in the petals of *Rosa rugosa* and allied plants. *Journal of Natural Medicines* 64: 383–387.

Pereira, D.F., L.H. Cazarolli, C. Lavado, V. Mengatto, M.S.R.B. Figueiredo, A. Guedes, M.G. Pizzolatti, and F.R.M.B. Silva. 2011. Effects of flavonoids on α-glucosidase activity: Potential targets for glucose homeostasis. *Nutrition* 27: 1161–1167.

Saito, S., S. Sumita, N. Tamura, Y. Nagamura, K. Nishida, M. Ito, and I. Ishiguro. 1990. Saponin from the leaves of *Aralia elata* Seem. *Chemical and Pharmaceutical Bulletin* 38: 411–414.

Sano, K., S. Sanada, T. Ida, and J. Shoji. 1991. Studies on the constituents of the bark of *Kalopanax pictus* Nakai. *Chemical and Pharmaceutical Bulletin* 39: 856–870.

Schenkel, P., W. Werner, and K.E. Schulte. 1991. Saponine from *Thinouia coriacea*. *Planta Medica* 57: 463–467.

Sulborska, A., E.W. Chmielewska, and M. Chwil. 2012. Micromorphology of *Rosa rugosa* Thunb. Petal epidermis secreting fragrant substances. *Acta Agobotanica* 65: 21–28.

Wei, J.F., Y.B. Zhang, and W.Y. Kang. 2012. Antioxidant and α-glucosidase inhibitory compounds in *Lysimachia clethroides*. *African Journal of Pharmacy and Pharmacology* 6: 3230–3234.

Yu, D.J., L.T. Lu, K.J. Guan, and C.L. Li. 1985. *Flora reipublicae popularis sinicae*, Vol. 37, 385–388. Weberling: Science Press.

Zhang, Q., W. Ye, X. Yan, G. Zhu, C.T. Che, and S. Zhao. 2000. Cernuosides A and B, two sucrase inhibitors from *Pulsatilla cernua*. *Journal of Natural Products* 63: 276–278.