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Protective Effects of Dietary Chamomile Tea on Diabetic Complications

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Matricaria chamomilla L., known as "chamomile", has been used as an herbal tea or supplementary food all over the world. We investigated the effects of chamomile hot water extract and its major components on the prevention of hyperglycemia and the protection or improvement of diabetic complications in diabetes mellitus. Hot water extract, esculetin (**3**) and quercetin (**7**) have been found to show moderate inhibition of sucrase with IC_{50} values of 0.9 mg/mL and 72 and 71 μM, respectively. In a sucrose-loading test, the administration of esculetin (50 mg/kg body weight) fully suppressed hyperglycemia after 15 and 30 min, but the extract (500 mg/kg body weight) and quercetin (50 mg/kg body weight) were less effective. On the other hand, a long-term feed test (21 days) using a streptozotocin-induced rat diabetes model revealed that the same doses of extract and quercetin showed significant suppression of blood glucose levels. It was also found that these samples increased the liver glycogen levels. Moreover, chamomile extract showed potent inhibition against aldose reductase (ALR2), with an IC_{50} value of 16.9 μg/mL, and its components, umbelliferone (**1**), esculetin (**3**), luteolin (**6**), and quercetin (**7**), could significantly inhibit the accumulation of sorbitol in human erythrocytes. These results clearly suggested that daily consumption of chamomile tea with meals could contribute to the prevention of the progress of hyperglycemia and diabetic complications.

KEYWORDS: *Matricaria chamomilla*; chamomile tea; α-glucosidase; hyperglycemia; aldose reductase; diabetic complications

INTRODUCTION

While tea is a part of dietary habits in many countries, evidence of medicinal properties has only been elucidated in the last 30 years. One of the most commonly consumed single-ingredient herbal teas is chamomile. Chamomile tea is prepared with dried flowers from *Matricaria chamomilla* L., and this plant has been used as an herbal medicine component in Europe. Especially, chamomile has been used to treat various inflammations, irritations, and pains such as skin diseases, wounds, eczema, ulcers, gout, neuralgia, and rheumatic pains (*1, 2*). Furthermore, a recent study demonstrated that chamomile plant extract suppresses the growth of human cancer cells and causes apoptosis (*2*). Major secondary components from *M. chamomilla* belong to three different chemical classes: sesquiterpenes, coumarins, and flavonoids (*1*). The major components of the essential oil are (−)-α-bisabolol and α-farnesene, and the yield of the essential oil from the flowers is about 0.4%. This plant also has high levels of polyphenolic compounds such as coumarins and flavonoids. The coumarins herniarin, umbelliferone, and esculetin make up approximately 0.1% of the total constituents. The major flavonoid components are apigenin, luteolin, and quercetin, which comprise 16.8, 1.9, and 9.9%, respectively, of total flavonoids. Thus, chamomile is one of the richest sources of dietary antioxidants. These coumarins and flavonoids are soluble in hot water, and the amounts obtained from frequent consumption of tea are not negligible. There is substantial evidence that these compounds have suppressive activity on oxidative damage to skins, membranes, proteins, and DNA by inhibiting free radical scavenging activity and contribute to protection against chronic health disorders such as atherosclerosis and hypertension (*3, 4*).

Quite recently, a consensus has developed that herbal tea and its components may cause various beneficial effects by directly influencing the activities of key enzymes involved in disorders, although the exact mechanisms are not known. Particularly interesting is the possibility of preventing the onset of diabetes using dietary supplements and/or herbal medicines; this has attracted increasing attention (*5*−*7*). It has been realized that inhibition of all or some of the intestinal disaccharidases and pancreatic α-amylase by inhibitors could regulate the absorption of carbohydrate, and these inhibitors could be used therapeuti-

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cally in the oral treatment of noninsulin-dependent diabetes mellitus (type II diabetes). Furthermore, in type II diabetes, hepatic glucose production is increased (*8*). Thus, a new possible way to suppress hepatic glucose production and lower blood glucose in type II diabetes patients may be through the inhibition of hepatic glycogen phosphorylase (GP) (*9*). It is well-known that prolonged hyperglycemia is a primary factor of several diabetic complications, and careful control of the blood glucose level delays or protects against the development of severe complications. However, some patients develop several complications at an early stage in spite of careful control of their glucose levels, because development of complications is affected by many promoters such as the activation of polyol metabolism, glycation, protein-kinase C, or oxidative stress. The polyol pathway plays an important role in these. Aldose reductase (alditol: $NADP^+$ oxidoreductase, EC 1.1.1.21, ALR2) is the rate-determining enzyme of the polyol pathway and catalyzes the NADH-dependent reduction of glucose to sorbitol, which is then oxidized to fructose by sorbitol dehydrogenase (L-iditol: NAD^+ 5-oxidoreductase, EC 1.1.1.14, SDH) (*10*). ALR2 is cell-based and has a low affinity for glucose; thus, this pathway plays a minor role in glucose metabolism in blood. In a diabetic condition, however, sufficient glucose can enter the tissues, and the pathway operates to produce both sorbitol and fructose. These cells accumulate them because of their poor penetration across the membranes. These abnormal metabolic results have been reported to be factors responsible for diabetic complications such as cataracts (*11*), retinopathy (*12*), neuropathy (*13*), and nephropathy (*14*). Therefore, ALR2 inhibitors have considerable potential for the treatment of these diseases.

The aim of the present study is to elucidate the beneficial effects of chamomile and its major components on the prevention of hyperglycemia and the protection or improvement of diabetic complications in diabetes mellitus. We describe the inhibitory effects of them against intestinal α-glucosidases, pancreatic α-amylase, and hepatic GP in vitro and the effect on blood glucose and hepatic glycogen levels using streptozotocin (STZ)-induced rat diabetes model. We also investigated the inhibitory effects against ALR2 and SDH in vitro and the suppressive effects on the accumulation of sorbitol in human erythrocytes.

MATERIALS AND METHODS

Materials. Flowers of *M. chamomilla* L. were purchased in November 2006 from Tochimoto Tenkaido Co. (Osaka, Japan). A voucher specimen (no. RJN200701) was deposited at the herbarium of the Institute of Grassland and Environmental Research, Aberystwyth. The standard samples **1** and **3** were purchased from Tokyo Kasei Kogyo Co. (Tokyo, Japan). Compound **2** was purchased from Sigma-Aldrich Chemical Co. (St. Louis, MO). Compound **4** was purchased from Funakoshi Co. (Tokyo, Japan), and compounds **5**−**7** were purchased from Nacalai Tesque. Inc. (Kyoto, Japan). Compounds **8** and **9** were purchased from Wako Pure Chemical Industries (Osaka, Japan).

Assay of Enzyme Activity. Brush border membranes prepared from rat small intestine according to the method of Kessler et al. (*15*) were used as the source of rat intestinal glucosidases. The activities of rat intestinal α-glucosidases were determined using the appropriate disaccharides as substrates. The released D-glucose was determined colorimetrically using the Glucose CII test from Wako (Wako Pure Chemical Ind., Osaka, Japan). α-Amylase (from porcine pancreas, assayed at pH 6.8) was purchased from Sigma Chemical Co. The activity of porcine pancreatic α-amylase was determined using starch as the substrate. The remaining starch was determined colorimetrically using the Amylase test from Wako (Wako Pure Chemical Ind., Osaka, Japan). The GP activity was assayed in the direction of glycogen synthesis by the method of Hue et al. (*16*) by liberation of phosphate from glucose 1-phosphate. Amylo-1,6-glucosidase was prepared from rabbit skeletal muscle according to the literature (*17*) and assayed using 6-*O*-α-D-glucosyl-α-cyclodextrin as the substrate (*18, 19*). The released D-glucose was determined colorimetrically using the Glucose CII test from Wako. Recombinant ALR2, which retains the same properties exhibited by human muscle and retina, was purchased from Wako Pure Chemical Industries (Osaka, Japan). The ALR2 activity was spectrophotometrically measured at 37 °C by using 100 mM D,L-glyceraldehyde as the substrate (*20*).

Determination of Sorbitol in Human Erythrocytes. Human blood was obtained from a healthy female volunteer, who was fully informed of this study and gave written consent. Erythrocytes from heparinized blood were separated from the plasma and buffy coat by centrifugation at 3000*g* for 30 min. The cells were routinely washed three times with isotonic saline at 4 °C. In the final washing, the cells were centrifuged at 2000*g* for 5 min to obtain a consistently packed cell preparation. The packed cells (1 mL) were then incubated in a Krebs−Ringer bicarbonate buffer (pH 7.4) (4 mL) containing 50 mM glucose in the presence or absence of samples at 37 °C in 5% CO_2 for 60 min. The erythrocytes were washed with cold saline by centrifugation at 2000*g* for 5 min, precipitated by adding 6% of cold perchloric acid (3 mL), and centrifuged again at 2000*g* for 10 min. The supernatant was neutralized with 2.5 M K_2CO_3 at 4 °C and used for sorbitol determination (*21, 22*).

Disaccharide Loading Test. The animal experimental protocols in this study were approved by the Animal Experiments Committee of the University of Toyama. Male ddy mice (29−33 g) after an overnight fast were used for acute disaccharide loading tests. Sucrose (2.5 g/kg body weight) as well as the inhibitors, acarbose, were dissolved in 0.9% NaCl solution and administered to mice via a stomach tube. A control group was loaded with saline only. The blood glucose levels were measured by a portable kit, Antsence II (Sankyo Co. Ltd. Tokyo, Japan).

Experimental Design Using STZ-Induced Rat Diabetes Model. Male Wistar rats with body weights of 290−330 g were obtained from Japan SLC, Inc. (Hamamatsu, Japan). The rats were kept in wire-bottomed cages under a conditional lighting regimen with dark light. The room temperature (about 23 °C) and humidity (about 60%) were controlled automatically. Diabetes was induced by intravenous injection of STZ (45 mg/kg body weight) dissolved in saline. STZ-injected animals were given 10% glucose solution for 24 h to prevent initial drug-induced hyperglycemic mortality. After 2 weeks of STZ administration, the rats were divided into five groups (group A−E), and the blood glucose levels were measured by the portable Antsence II kit every 7 days. Every group was fed a basal 18% casein diet. Normal rats (group A) and untreated STZ-diabetic rats (group B) received no further treatment for 21 days. The other three groups received an aqueous extract of chamomile (500 mg/kg bodyweight/day, group C), esculetin (50 mg/kg bodyweight/day, group D), or quercetin (50 mg/kg bodyweight/day, group E).

RESULTS AND DISUSSION

Inhibition Activities against Pancreatic α-Amylase and Intestinal α-Glucosidases. α-Glucosidase inhibitors have the potential for the treatment of diabetes because they reduce diet-induced hyperglycemia by inhibiting intestinal α-glucosidases (*23, 24*). A pseudo tetrasaccharide, acarbose, was introduced on the market in Germany in 1990, and voglibose is also on the market in Japan. More recently, the *N*-hydroxyethyl-1-deoxynojirimycin has been marketed as an antidiabetic drug with a long-lasting effect in vivo (*25, 26*). We compared the ability of chamomile hot water extract and its components **1**−**9** to inhibit a porcine pancreatic α-amylase and rat intestinal maltase and sucrase activities (**Table 1**). Acarbose was used as a positive control. Major components from chamomile belong to three different chemical classes: coumarins including umbelliferone (**1**), herniarin (**2**), esculetin (**3**), isoscopoletin (**4**), flavonoids including apigenin (**5**), luteolin (**6**), and quercetin (**7**), and sesquiterpenes including α-bisabolol (**8**) and α-farnesene (**9**) (**Figure 1**). The

Table 1. Concentration of Chamomile Extract and Components Giving 50% Inhibition of α-Amylase and Intestinal α-Glucosidase Activities

compounds	inhibition (%) at 400 μM		
	α-amylase	maltase	sucrase
chamomile extract	5.2 mg/mL[b]	2.6 mg/mL[b]	0.9 mg/mL[b]
1	2.2%	22.9%	5.4%
2	4.3	27.8	15.5
3	0.5	40.9 (534 μM)[b]	72.5 (72 μM)[b]
4	0.2	32.2	20.9
5	30.7	35.3	18.0
6	46.1	14.9	24.3
7	42.5	63.0 (216 μM)[b]	83.5 (71 μM)[b]
8	0.2	1.8	4.2
9	0.5	1.9	3.3
acarbose	19.3 μM[b]	0.16 μM[b]	2.9 μM[b]

[b] The inhibitory activity was expressed as the mean of 50% inhibitory concentration (IC_{50}).

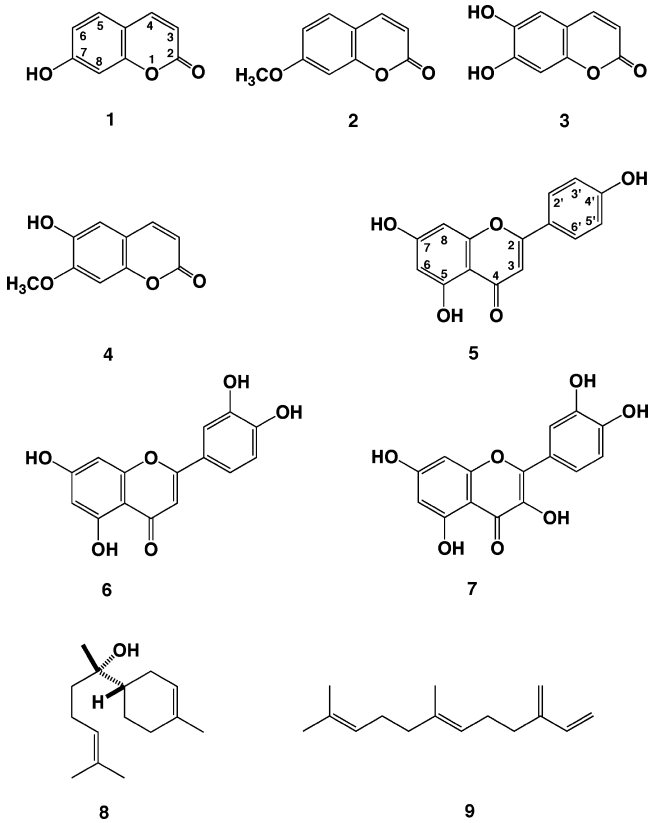

Figure 1. Structure of major components from *M. chamomilla* L. Umbelliferone (**1**), herniarin (**2**), esculetin (**3**), isoscopoletin (**4**), apigenin (**5**), luteolin (**6**), quercetin (**7**), α-bisabolol (**8**), and α-farnesene (**9**).

hot water extract of chamomile showed weak inhibitory activity against rat intestinal maltase and sucrase, with IC_{50} values of 2.6 and 0.9 mg/mL, respectively. All compounds were much weaker inhibitors than acarbose (IC_{50} = 0.16 and 2.9 μM against maltase and sucrase, respectively), but compounds **3** and **7** showed moderate inhibitory activity toward sucrase (IC_{50} = 72 and 71 μM, respectively) and maltase (IC_{50} = 534 and 216 μM, respectively). Although no compound showed significant inhibition toward pancreatic α-amylase, flavonoids (**5**−**7**) were much better inhibitors than coumarins and sesquiterpenes. In addition, essential oils **8** and **9** showed no significant inhibition toward any glycosidase tested.

Carbohydrate Loading Test. To confirm that chamomile hot water extract, esculetin (**3**), and quercetin (**7**) had significant effects on blood glucose levels in vivo, we attempted a sucrose

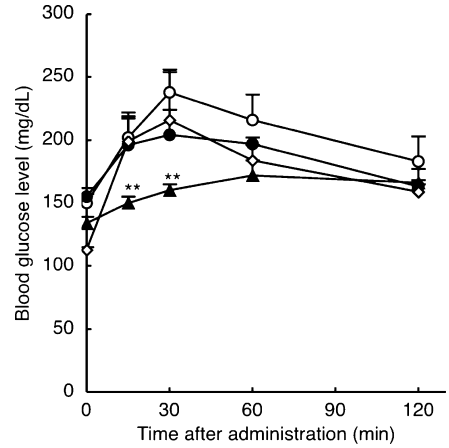

Figure 2. Effects of chamomile hot water extract, esculetin (**3**), and quercetin (**7**) on blood glucose levels. Blood glucose concentrations of male ddy mouse after an oral load with sucrose, 2.5 g/kg body weight, with 500 mg/kg body weight chamomile hot water extract (◇), 50 mg/kg body weight esculetin (▲), and quercetin (●). A control group was loaded with saline (○). Each value represents the mean ± SEM (n = 3−5). **Significant difference (p < 0.01) as compared with the control.

loading test. The blood glucose levels were measured by the portable Antsence II kit. A control group was loaded with saline only. Administration of sucrose (2.5 g/kg body weight p.o.) to fasted mice resulted in a rapid increase in blood glucose concentrations from 150 ± 12 to a maximum of 238 ± 18 mg/dL after 30 min (**Figure 2**). Thereafter, blood glucose levels recovered to the pretreatment level at 120 min. A significant suppressive effect of the blood glucose level was achieved with 50 mg/kg body weight esculetin (**3**) after 15 and 30 min. Chamomile hot water extract and quercetin (**7**) also decreased the blood glucose concentrations at 30 and 60 min after sucrose loading. Interestingly, esculetin and quercetin showed almost the same moderate inhibitory activity toward sucrase, with IC_{50} values of 72 and 71 μM, respectively (**Table 1**), but the suppressive effects on the blood glucose levels were obviously greater in the esculetin-treated group. Ramesh et al. (*27*) have reported that umbelliferone significantly elevated the plasma insulin level as compared with nontreated diabetic rat, and it caused a reduction in the blood glucose level. In the present study, we were not able to find any significant inhibitory activity of umbelliferone (**1**) against α-amylase, maltase, and sucrase (**Table 1**). These results suggest that the suppressive effect of esculetin (**3**) might be independent of intestinal α-glucosidase inhibition.

Inhibition Activities against Glycogen-Degrading Enzmyes. The liver is an important source of blood glucose. Cytosolic glycogen in mammals is cleaved by GP and the debranching enzyme amylo-1,6-glucosidase. It is generally recognized that the hepatic glucose output in type II diabetes is elevated and thus significantly contributes to hyperglycemia (*28*−*30*). A possible way to suppress hepatic glucose production and lower blood glucose in type II diabetes may be through inhibition of GP (*9*). The inhibitory activity of chamomile and its components **1**−**9** against GP and amylo-1,6-glucosidase were compared with that of 1,4-dideoxy-1,4-imino-D-arabinitol (D-AB1). As shown in **Table 2**, chamomile hot water extract showed inhibitory activity against rabbit muscle GP, with an IC_{50} value of 197 μg/mL. Moreover, luteolin (**6**) and quercetin (**7**) showed good inhibitory activities toward rabbit muscle GP with IC_{50} values of 31.7 and 34.8 μM, respectively, whereas no other compounds showed obvious inhibition toward the enzyme. D-AB1 was a potent inhibitor of GP, with an IC_{50} value of 11.9 μM but also

Table 2. Concentration of Chamomile Extract and Components Giving 50% Inhibition of GP and Amylo-1,6-Glucosidase Activities

compounds	IC_{50} (μM)[a] GP	inhibition (%)[b] amylo-1,6-glucosidase
chamomile extract	197 μg/mL[a]	>5 mg/mL[a]
1	>100	7.0[b]
2	>100	7.2
3	>100	33.4
4	>100	6.3
5	>100	3.1
6	31.7[a]	22.6
7	34.8[a]	39.8
8	>100	5.6
9	>100	1.2
D-AB1	11.9[a]	8.4 μM[a]

[a] The inhibitory activity was expressed as the mean of 50% inhibitory concentration (IC_{50}). [b] Inhibition % at 400 μM.

Table 3. Effects of Chamomile Extract, Esculetin (**3**), and Quercetin (**7**) on Blood Glucose Levels and Liver Glycogen Levels of STZ-Diabetic Rats[a]

animal group	blood glucose (mg/dL) day 1	blood glucose (mg/dL) day 21	glycogen (mg/100 mg tissue)
normal rats	121 ± 3	123 ± 4	13.4 ± 1.7
diabetic rats			
untreated rats	500 ± 30	572 ± 42	11.2 ± 4.1
+chamomile extract (500 mg/kg body weight/day)	494 ± 25	423 ± 48*	39.8 ± 8.3*
+esculetin (50 mg/kg body weight/day)	499 ± 20	432 ± 25*	14.8 ± 2.4
+quercetin (50 mg/kg body weight/day)	503 ± 18	486 ± 22*	59.3 ± 7.7**

[a] Each value represents the mean ± SEM ($n = 4$). Significant difference ($p < 0.05$) as compared with the untreated diabetic rats. Significant difference ($p < 0.01$) as compared with the untreated diabetic rats. The glycogen content was determined by using the acid hydrolysis method, and the released D-glucose was determined colorimetrically using the Glucose CII test.

another glycogen-degrading enzyme, amylo-1,6-glucosidase, with an IC_{50} value of 8.4 μM. In contrast, luteolin (**6**) and quercetin (**7**) showed only weak inhibition against amylo-1,6-glucosidase (22.6 and 39.8% at 400 μM, respectively).

Effects on Blood Glucose and Hepatic Glycogen Levels of STZ-Induced Diabetes Rats. Chamomile hot water extract, esculetin (**3**), and quercetin (**7**) were compared for their abilities to inhibit glycogen degradation using an STZ-induced rat diabetes model (**Table 3**). STZ treatment resulted in significant elevation of blood glucose level as compared to normal rats (121 ± 3 vs 500 ± 30 mg/dL) at day 1. Thereafter, blood glucose levels continued to rise gradually and reached 572 ± 42 mg/dL at day 21. It is noteworthy that treatments of hot water extract (500 mg/kg body weight p.o.) and quercetin (50 mg/kg body weight p.o.) for 21 days significantly inhibited the liver glycogen degradation as compared to untreated STZ-diabetic rats (39.8 ± 8.3 and 59.3 ± 7.7 vs 11.2 ± 4.1 mg/100 mg tissue, respectively). Furthermore, these two groups showed significant decrease of blood glucose level as compared with the untreated STZ-diabetic rats group. Esculetin (50 mg/kg body weight p.o.) also affected the blood glucose level, but it had no effect on the liver glycogen level. These results suggested that one of the possible mechanisms by which chamomile extract and quercetin (**7**) bring about their antihyperglycemic action is due to inhibition of hepatic glycogen degradation. Moreover, esculetin (**3**) and quercetin (**7**) have obviously different ways to suppress the blood glucose level.

Table 4. Concentration of Chamomile Extract and Components Giving 50% Inhibition of ALR2 and SDH Activities

compounds	IC_{50} (μM)[a] ALR2	IC_{50} (μM)[a] SDH
chamomile extract	16.9 μg/mL	554 μg/mL
1	85.7	120
2	131	124
3	36.5	NI
4	101	NI
5	11.8	182
6	5.1	181
7	12.6	101
8	NI	NI
9	NI	NI
epalrestat	0.7	NI[b]

[a] The inhibitory activity was expressed as the mean of 50% inhibitory concentration (IC_{50}). [b] NI, less than 50% inhibition at 250 μM.

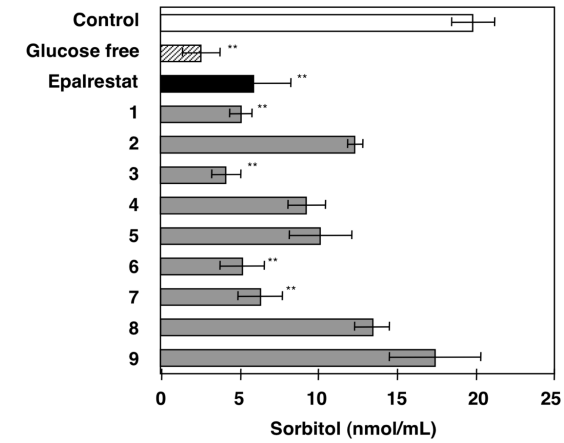

Figure 3. Effects of chamomile components (**1**−**9**) on sorbitol accumulation in human erythrocytes. Erythrocytes were incubated for 60 min in a Krebs−Ringer biscarbonate buffer containing 50 mM glucose and in the presence or absence of 200 μM compounds. Epalrestat (25 μM) was used as a positive control. Each value represents the mean ± SEM ($n = 3$). **Significant difference ($p < 0.01$) as compared with the control.

Inhibition Activities against ALR2 and SDH. The inhibitory activity of chamomile and its components **1**−**9** against ALR2 and SDH was compared with that of epalrestat. As shown in **Table 4**, umbelliferone (**1**) was a moderate inhibitor of ALR2 ($IC_{50} = 85.7$ μM), while it showed no significant inhibitory activity toward SDH. Introduction of the OH group to C7 in **1** to give esculetin (**3**) enhanced its inhibitory potential toward ALR2, with an IC_{50} value of 36.5 μM. Furthermore, the replacement of the C7 OH group in **1** and **3** by the OCH_3 group to give herniarin (**2**) and isoscopoletin (**4**) lowered their inhibition toward these enzymes. These results mean that the presence of the C7 OH group is one of the essential features for recognition of ALR2. Apigenin (**5**), luteolin (**6**), and quercetin (**7**) were much better inhibitors of ALR2 than coumarins (**1**−**3**), with IC_{50} values of 11.8, 5.1, and 12.6 μM, respectively. Sesquiterpenes (**8** and **9**) showed no significant inhibition toward these enzymes.

Inhibition of Sorbitol Accumulation on Erythrocytes. It has already been reported that the activity of erythrocytes ALR2 increases in diabetic patients (*31*) and erythrocytes sorbitol levels in rats are positively correlated with the levels in the lens, sciatic nerve, and retina (*32, 33*). We compared the ability of compounds **1**−**9** on sorbitol accumulation in human erythrocytes (**Figure 3**). Sorbitol accumulation was 8-fold greater when the cells were incubated in high glucose medium, as compared to

that in a glucose-free incubation. Epalrestat (25 μM) was used as a positive control. Umbelliferone (**1**), esculetin (**3**), luteolin (**6**), and quercetin (**7**) inhibited sorbitol accumulation by almost 74.9, 79.2, 74.0, and 68.4% at 200 μM, respectively. On the other hand, α-bisabolol (**8**) and α-farnesene (**9**), with no inhibitory activity against ALR2, gave no effect on sorbitol accumulation in the cells.

The possibility of preventing the onset of diabetes using dietary supplements and/or herbal medicines has attracted increasing attention. The leaves of Mulberry trees (*Morus alba* L.), which are naturally distributed in forests of China, Korea, and Japan, have been used as a supplementary food in Japan to prevent obesity and diabetes. 1-Deoxynojirimycin (DNJ) has been identified as a α-glucosidase-inhibiting component from the water-soluble fraction of *M. alba* (*34*). The IC_{50} values of DNJ toward rat intestinal maltase, sucrase, and isomaltase are 0.36, 0.21, and 0.30 μM, respectively. The inhibitory activities toward maltase and sucrase are nearly equal to those of acarbose and that toward isomaltase is much more potent than that of acarbose. However, DNJ did not show inhibition of hepatic GP and ALR2. In this study, we attempted to elucidate the beneficial effects of chamomile and its major components on the prevention of hyperglycemia. Our results clearly suggested that chamomile hot water extract also has the potential for the treatment of diabetes because it showed a significantly suppressive effect on the blood glucose levels in an STZ-induced rat diabetes model in a long-term feed test (**Table 3**). The mechanism of suppression looks different from that of *M. alba* because a sucrose-loading test revealed that the suppressive effect of the chamomile extract was obviously weaker than it (**Figure 2**). It is noteworthy that administration of extract (500 mg/kg body weight, p.o.) and one of the major components, esculetin (50 mg/kg body weight, p.o), showed increasing liver glycogen levels in an STZ-induced rat diabetes model comparing day 1 with day 21 (**Table 3**). Moreover, these results meet our expectation based on an in vitro study (**Table 2**). These results suggested that a suppressive effect of chamomile on blood glucose level was independent of the inhibition of intestinal α-glycosidases but depended on the inhibition of hepatic GP. Furthermore, chamomile extract has good inhibitory potency against ALR2, which plays key roles in the polyol pathway and its activation promotes the progress of diabetic complications. Chamomile components, umbelliferone (**1**), esculetin (**3**), luteolin (**6**), and quercetin (**7**), could inhibit sorbitol accumulation in human erythrocytes (**Figure 3**). In conclusion, the present study demonstrated that daily consumption of chamomile tea with meals could be potentially useful in the prevention and self-medication of hyperglycemia and diabetic complications.

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