

Inhibitory Effect of Several *Mangifera indica* Cultivar Leaf Extracts on the Formation of Advanced Glycation End Products (AGEs)

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Abstract

As a part of our ongoing research to find novel functions in mango leaves, we have reported that the methanolic extract of pruned old dark green mango leaf (*Mangifera indica* 'Irwin') exhibited inhibitory effects on the formation of advanced glycation end products (AGEs) in nonenzymatic glycation of albumin. The purpose of this study was to find other mango cultivars with more potent activity in this regard. We examined the inhibitory effect of seventeen mango (*Mangifera indica*) cultivar leaf extracts on AGEs formation. We also investigated the relationship between the inhibitory activity of the extracts and the contents of their active components, 3-C- β -D-glucosyl-2,4,4',6-tetrahydroxybenzophenone (**1**), mangiferin (**2**) and chlorophyll (**3**). On the basis of the evaluation of the inhibitory activity of mango cultivar leaf extracts, the HPLC determination of the contents of **1** and **2**, and the spectrophotometric determination of **3**, it was found that almost all extract showed a significant activity, and the content of **2** and **3** detected in each was similar. In contrast, AGEs formation inhibition tended to be higher as the content of **1** in the leaf extracts increased. This is the first report of phytochemical analysis of compounds **1**, **2** and **3** in various cultivars of mango leaf. From the phytochemical point of view, these results suggest that the pruned leaves of any cultivar of *Mangifera indica* except 'Chiin Hwang No. 1' and 'Kyo Savoy' may be useful for the preparation of natural ingredients with inhibitory activity of AGEs formation.

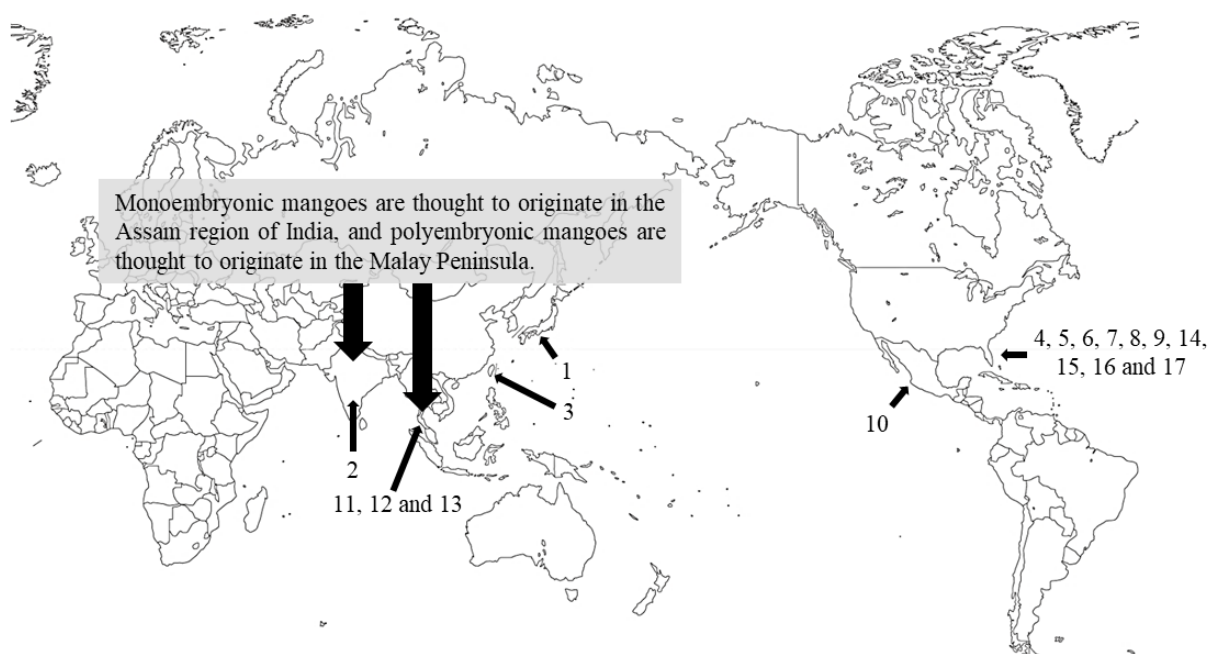
Keywords: advanced glycation end products (AGEs) formation inhibition, 3-C- β -D-glucosyl-2,4,4',6-tetrahydroxybenzophenone, glycation, *Mangifera indica*, mango cultivar

1. Introduction

Tropical and subtropical fruits are highly valued owing to their nutritional benefits as well as for the presence of health-promoting ingredients. The fruit of *Mangifera indica* L. (mango) is considered as "the king of fruits" because it is the most popular fruit in the tropical regions (Lauricella, Emanuele, Calvaruso, Giuliano, & D'Anneo, 2017). It is the national fruit of India and the Philippines, and *M. indica* is the national tree of Bangladesh (Usman, Fatima, & Jaskani, 2001). The mango belongs to the genus *Mangifera*, which includes numerous species of tropical plants in the family of Anacardiaceae (Scartezzini & Speroni, 2000). The mango is native to India and Southeast Asia where it has been cultivated for at least 4000 years and over 1000 cultivars are recognized (Mukherjee, 1953). Almost all of them derive from wild open-pollinated seedlings. However, Ravishankar *et al.* (2011) demonstrated via random amplification-of-polymorphic DNA-analysis, the mono- and polyembryonic types of the Indian mango cultivars have a different genetic origin. Monoembryonic mangoes are thought to originate in the Assam region of India, while polyembryonic mangoes are thought to originate in the Malay Peninsula as shown in Figure 1. Thanks to the Chinese Hwen T'sang, who lived in the 7th century, the mango also attained renown outside of India. In the first half of the 18th century, the mango was exported to other tropical countries by the Portuguese (Calabrese, 1993). The cultivation of mango thus gradually spread to tropical and subtropical countries throughout the world, where selections to adapt the plants to specific growth conditions were made. Thus, human selection has played the most significant role in the development of new

mango cultivars. In Buddhism, the mango is considered a sacred tree (Litz, 2009) and in Hinduism, the mango is believed to be "Prajapati" meaning "the God that rules everything" (Litz, 2009). The spread of Buddhism and Hinduism contributed to the distribution of mangoes in South-east Asia (Litz, 2009).

To date, we have collected seventeen popular mango cultivars, which are currently still cultivated in the plastic greenhouse of Kindai University. A notable cultivar 'Aiko' grown in our experimental farm is the result of the interbreeding between the mainstay domestic cultivar 'Irwin' (cultivar 9) and the Taiwanese cultivar 'Chiin Hwang No. 1' (cultivar 3; Ueda, Sasaki, Utsunomiya, & Shimabayashi, 2001). Breeding and cultivation test for 'Aiko' started in 1999 in our experimental farm and it was registered in 2008 as the first new mango cultivar in Japan (Sasaki, Nakajima, Shimizu, Kanzaki, & Utsunomiya, 2008). Florida, the southernmost state in the contiguous U.S.A, has a mild climate, suitable for growing fruits such as citrus and mango. In Florida, many families plant mangoes in their gardens as garden trees; in the late 19th and early 20th centuries, this state became the secondary center for mango cultivation, contributing to generation of more new varieties than in Southeast Asia (Litz, 2009). In Southeast Asian countries, such as India, Thailand and Taiwan, cultivars such as Alfonso (cultivar 2), Chiin Hwang No. 1 (cultivar 3), Khom (cultivar 11), Kyo Savoy (cultivar 12) and Nam Doc Mai (cultivar 13) are listed as native varieties.



The mango cultivar of 1, Aiko (Japan); 2, Alphonso (India); 3, Chiin Hwang No. 1 (Taiwan); 4, Dot (U.S.A.); 5, Edward (U.S.A.); 6, Florigen (U.S.A.); 7, Glenn (U.S.A.); 8, Golden Lippens (U.S.A.); 9, Irwin (U.S.A.); 10, Kent (Mexico); 11, Khom (Thailand); 12, Kyo Savoy (Thailand); 13, Nam Doc Mai (Thailand); 14, Sensation (U.S.A.); 15, Spirit of 76 (U.S.A.); 16, Tommy Atkins (U.S.A.); 17, Valencia Pride (U.S.A.).

Figure 1. The origin of mango cultivars prepared in the experiment

During the cultivation of mango fruits, pruning is an essential process. Hitherto, the pruned leaves have been considered to be unworthy and have discarded. Thus, in the course of our ongoing research on mango leaf for finding novel functions, we first focused on the pruned leaves of the 'Irwin' mango cultivar. We have previously reported that the methanolic extract of pruned old dark green mango (*Mangifera indica* 'Irwin') (OML-ext) exhibited inhibitory activity of AGEs formation in nonenzymatic glycation of albumin (Itoh *et al.*, 2017). Glycation is a non-enzymatic browning reaction caused by amino-carbonyl reactions between reducing sugars and amino groups of proteins and lipids (Tsuji-Naito, Saeki, & Hamano, 2009). By glycation of these compounds, AGEs are irreversibly synthesized in the body (Huebschmann, Regensteiner, Vlassara, & Reusch,

2006), and the accumulation in organs is induced by hyperglycemia and is one of the causes of diabetic complications (Sourris, Harcourt, & Forbes, 2009). And, AGEs accumulate in the skin and correlated with skin aging (Dyer et al, 1993). Thus in recent years, the inhibition of AGEs formation can be one of the effective strategies for direct alleviation of the development of novel antiaging cosmeceutical ingredients. An AGEs formation inhibitor aminoguanidine (Dyer et al 1993) was under development in U.S.A. as a drug for the treatment of diabetic complications such as diabetic nephropathy. We also reported that the inhibitory activity of OML-ext was partially attributable to 3-C- β -D-glucosyl-2,4,4',6-tetrahydroxybenzophenone (**1**), mangiferin (**2**) and chlorophyll (**3**) (Itoh et al., 2017) on the basis of activity-guided fractionation followed by chromatographic isolation. Among them, the compound **2** showed the most potent inhibitory activity (IC₅₀, 18 μ M). And the IC₅₀ values of **1** and **3** were 85 μ M and 41 μ g/mL, respectively. Thus, the pruned leaves of Irwin mango cultivar may be reasonable natural sources for the preparation of ingredients with inhibitory activity of AGEs formation. The purpose of this study was to find other mango cultivar with having more potent inhibitory activity of AGEs formation, therefore we examined the inhibitory effects of pruned leaf extracts of seventeen mango cultivars on AGEs formation. And we also investigated the relationship between the inhibitory activity of the extracts and the content of active compounds **1**, **2** and **3**.

2. Materials and Methods

2.1 Plant Materials

The pruned old dark green mango leaves of seventeen cultivars of *M. indica* (cultivars in alphabetical order, 'Aiko', 'Alphonso', 'Chiin Hwang No. 1', 'Dot', 'Edward', 'Florigon', 'Glenn', 'Golden Lippens', 'Irwin', 'Kent', 'Khom', 'Kyo Savoy', 'Nam Doc Mai', 'Sensation', 'Spirit of 76', 'Tommy Atkins' and 'Valencia Pride') were collected in the Experimental Farm of Kindai University (34° 2' N, 135° 11' E, 17 m ASL), located in Wakayama Prefecture, Japan. Leaves of 'Irwin' were prepared as described in the preceding paper (Itoh et al., 2017). The trees of the other sixteen cultivars grown using commercial methods in a plastic greenhouse under the controlled conditions {temperature: winter, min. 2 °C (room) and 10 °C (soil); summer, max. 35 °C (room) and 31 °C (soil)}. Each leaf was collected from 3 each mango trees which were propagated by grafting (the height of trees; 2.5 m, the age of trees; 12-15 years old, the life span of trees; 40-50 years). Leaves of 'Irwin' were collected in August 2015 and August 2016, while those for the other 16 cultivars were all collected in August 2016. The experimental farm personnel identified and collected the leaves. The samples were air-dried at 50 °C for 72 h in an automatic air-drying apparatus (Vianove Inc., Tokyo, Japan), and powdered. Voucher specimens of leaves were deposited in the Experimental Farm, Kindai University. The average water content in each dried leaf was less 0.5% by assessment of moisture meter.

2.2 Extraction

Methanolic (MeOH) extracts of old dark green 'Irwin' leaves (OML-ext) were obtained in a yield of 23% as previously described (Itoh et al., 2017). The yields of MeOH extract obtained from old dark green leaves of cultivars, 'Aiko', 'Alphonso', 'Chiin Hwang No. 1', 'Dot', 'Edward', 'Florigon', 'Glenn', 'Golden Lippens', 'Kent', 'Khom', 'Kyo Savoy', 'Nam Doc Mai', 'Sensation', 'Spirit of 76', 'Tommy Atkins' and 'Valencia Pride' were 21%, 16%, 15%, 20%, 22%, 20%, 16%, 14%, 16%, 17%, 17%, 19%, 18%, 21%, 20%, and 21%, respectively.

2.3 Reagents

The reagents used in this study were the same as those used by Itoh et al. (2017).

2.4 In vitro Evaluation of AGEs Formation Inhibitory Activity

The AGEs formation inhibitory activity of each sample was evaluated according to the method of Shimoda et al. (2011) with minor modification as described in the preceding paper (Itoh et al., 2017).

Each assay was performed in triplicate (P value < 0.01). IC₅₀ value represents the concentration required to inhibit 50% of AGEs formation by incubation of glucose and albumin.

2.5 Determination of **1**, **2** and **3** Content in Each Mango Cultivar Leaf Extract

In this paper, determination of each compound in leaf extracts was performed in triplicate, and values represent the mean \pm standard deviation. The HPLC determination method for the contents (mg/g extract) of **1** and **2** in each mango leaf extract was described in our previous paper (Itoh et al., 2016). Spectrophotometric determination of the content of **3** (mg/g extract) was carried out with 80% aqueous acetone solution containing 2.5 mM sodium phosphate buffer (pH 7.8) according to the method of Porra et al. (Porra, Thompson, & Kriedemann, 1989).

2.6 Statistical Analysis

The experimental data were evaluated for statistical significance using Bonferroni/Dunn's multiple-range test with GraphPad Prism for Windows, Ver. 5 (GraphPad Software Inc., 2007; Armonk, NY, USA).

3. Results and Discussion

To find the most suitable mango cultivar for preparation of natural ingredients with inhibitory activity of AGEs formation, we compared the inhibitory effect of seventeen mango (*Mangifera indica*) cultivar leaf extracts listed in Table 1 on AGEs formation. The results are shown in Table 1. As described in the section of 2.2. *Extraction*, the yields of MeOH extract of 17 mango cultivars did not differ significantly. Thus, the following discussion was done without consideration of the yield of MeOH extract of each cultivar. As depicted in Table 1, all cultivars exhibited significant inhibitory activity except for 'Chiin Hwang No. 1' (cultivar 3, IC₅₀, 105 µg/ml) and Kyo Savoy (cultivar 12, IC₅₀, 98 µg/ml). IC₅₀ value of 'Irwin' (cultivar 9) was 43 µg/ml, confirming the data presented in our preceding paper (Itoh et al., 2017). Of the cultivars evaluated in this experiment, 'Alfonso' (cultivar 2, IC₅₀, 11 µg/ml) showed the highest activity, followed by 'Dot' (cultivar 4, IC₅₀, 12 µg/ml), 'Florigon' (cultivar 6, IC₅₀, 15 µg/ml), and 'Glenn' (cultivar 7, IC₅₀, 19 µg/ml). In contrast, the cultivar 'Chiin Hwang No. 1' (cultivar 3, IC₅₀, 105 µg/ml) showed the weakest inhibitory effect.

Table 1. Inhibitory activities of MeOH extracts obtained from seventeen mango cultivars leaves on AGEs formation and the content of **1**, **2** and **3** in each extract

No.	Cultivar name	IC ₅₀ values ^{a)} (µg/ml or mM)	Content of 1 in each extract (mg/g extract)	Content of 2 in each extract (mg/g extract)	Content of 3 in each extract	
					Chlorophyll a (mg/g extract)	Chlorophyll b (mg/g extract)
1	Aiko	31 µg/ml	228.4±40.6	77.2±1.6	4.60±0.07	0.60±0.01
2	Alphonso	11 µg/ml	304.3±10.8	85.1±0.7	5.71±0.06	0.45±0.02
3	Chiin Hwang No. 1	105 µg/ml	49.2±3.5	75.2±0.4	5.50±0.03	0.74±0.01
4	Dot	12 µg/ml	314.0±7.9	80.2±0.5	3.01±0.03	0.31±0.01
5	Edward	33 µg/ml	172.1±13.7	80.8±0.5	4.61±0.08	0.52±0.01
6	Florigon	15 µg/ml	266.4±9.2	77.7±0.5	6.32±0.06	0.97±0
7	Glenn	19 µg/ml	243.3±5.2	91.7±0.3	4.59±0.11	0.83±0.01
8	Golden Lippens	52 µg/ml	99.9±2.1	72.5±0.1	7.84±0.28	0.88±0.02
9	Irwin	43 µg/ml ^{c)}	205.9±7.6	85.1±0.5	4.79±0.07	0.66±0.01
10	Kent	30 µg/ml	257.1±13.7	75.3±0.1	4.86±0.12	0.66±0.02
11	Khom	60 µg/ml	93.8±0.6	73.2±0.1	4.31±0.05	0.67±0.01
12	Kyo Savoy	98 µg/ml	51.0±3.2	72.4±0.1	4.46±0.04	0.72±0.01
13	Nam Doc Mai	75 µg/ml	38.3±0.4	70.5±0	5.78±0.06	1.24±0
14	Sensation	71 µg/ml	124.3±4.5	77.7±0.6	5.47±0.06	1.00±0.01
15	Spirit of 76	30 µg/ml	246.6±9.6	84.0±0.5	3.90±0.04	0.55±0.01
16	Tommy Atkins	60 µg/ml	146.7±16.3	76.2±0.3	3.94±0.06	0.50±0.01
17	Valencia Pride	51 µg/ml	174.7±4.6	72.3±0.3	2.46±0.04	1.17±0.03
	Aminoguanidine ^{b)}	0.9 mM				

a) IC₅₀ value represents the concentration required to inhibit 50% of AGEs formation. b) Aminoguanidine represents aminoguanidine hydrochloride which was used as the reference compound. c) IC₅₀ value of a methanolic extract of old dark green Irwin mango leaf extract (OML-ext) on AGEs formation inhibition has reported in our preceding paper (Itoh et al., 2017). Compound **1**, 3-C-β-D-glucosyl-2,4,4',6-tetrahydroxy benzophenone; compound **2**, mangiferin; compound **3**, chlorophyll.

The IC₅₀ value of aminoguanidine hydrochloride used as a reference compound was 0.9 mM (= 99 µg/ml) in accordance with the previously reported IC₅₀ value (138 µg/ml) (Shimoda et al., 2011).

Since we have been identified **1** (IC₅₀, 85 µM), **2** (IC₅₀, 18 µM) and **3** (IC₅₀, 41 µg/ml) as active components of 'Irwin' (cultivar 9) of AGEs formation inhibition, their contents in each cultivar extract were measured. It was found that the content of **2** (70.5 mg/g extract to 91.7 mg/g extract) and **3** (3.32 mg/g extract to 8.72 mg/g extract) did not differ significantly among all mango cultivar extracts as shown in Table 1. The content of **2** in 'Irwin' (cultivar 9) was higher than other cultivars except 'Glenn' (cultivar 7). 'Glenn' (cultivar 7) showed the highest content of **2**. These two cultivars exhibited potent inhibitory activity, and at the same time, considering with the contents of **1**, **2** and **3** in each cultivar leaf extract, the inhibitory activity of other mango cultivars can be

attributable to these compounds as well as 'Irwin' (cultivar 9). However, we couldn't find the excellent cultivar which may contain a large amount of **1**, **2** or **3**, and may exhibit very potent inhibitory activity in particular. These results are reasonable from the view point of phytochemistry in which the plant species might be classified depending on its chemical components. In conclusion, the pruned leaves obtained from most *Mangifera indica* cultivar except 'Chiin Hwang No. 1' (cultivar 3), and 'Kyo Savoy' (cultivar 12) may be useful resource for the preparation of natural ingredients with inhibitory activity of AGEs formation.

Although **1** had less inhibitory activity (IC_{50} , 85 μ M) than **2** (IC_{50} , 18 μ M), it was interestingly assumed that the higher the content of **1**, the lower the IC_{50} values, moreover the value of correlation coefficient between the contents of **1** and the IC_{50} values was -0.93. This evidence may imply that **1** plays an unknown rule in the inhibition process during AGEs formation. However, more investigations are required to explain this phenomenon.

4. Conclusion

The leaf extracts of cultivars 1, 2, 4, 5, 6, 7, 10 and 15 exhibited more potent inhibitory activity than that of cultivar 9. Leaf extracts of cultivar 8, 11, 13, 14, 16, and 17 showed similar activity to that of cultivar 9. On the other hand, the cultivars of 'Chiin Hwang No. 1' (cultivar 3) and cultivar 12 showed less weak activity than that of cultivar 9. To the best of our knowledge, this is the first comparative phytochemical analysis of **1**, **2** and **3** in the leaf extracts of multiple mango cultivars, and this is the first report on relationship between the inhibitory activity of AGEs formation of the extracts of multiple cultivars of mango leaf and the contents of their active components, 3-C- β -D-glucosyl-2,4,4',6-tetrahydroxybenzophenone (**1**), mangiferin (**2**) and chlorophyll (**3**). On the basis of these investigations, the one cultivar which may be excellent in particular couldn't be found. It was suggested that the pruned leaf of most *Mangifera indica* cultivar including 'Irwin' (cultivar 9) except 'Chiin Hwang No. 1' (cultivar 3), and 'Kyo Savoy' (cultivar 12) may be useful resource for the preparation of natural ingredients with inhibitory activity of AGEs formation.

Hitherto, pruned mango leaves were unworthy and discarded. Thus, from the view point of utility of mango leaves, the pruned leaf of most *Mangifera indica* cultivar may be useful resource for the preparation of natural ingredients with inhibitory activity of AGEs formation. However, further investigations are required to examine the safety of administration and the mechanisms involved and also to reveal other active constituents.

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References

- Calabrese, F. (1993). Frutticoltura tropicale e sub tropicale. *Edagricole Bologna*, 1, 169-215.
- Dyer, D. G., Dunn, J. A., Thorpe, S. R., Bailie, K. E., Lyons, T. J., McCance, D. R., & Baynes, J. W. (1993). Accumulation of Maillard reaction products in skin collagen in diabetes and aging. *Journal of Clinical Investigation*, 91, 2463-2469. <https://doi.org/10.1172/JCI116481>
- Huebschmann, A. G., Regensteiner, J. G., Vlassara, H., & Reusch, J. E. B. (2006). Diabetes and advanced glycoxidation end products. *Diabetes Care*, 29(6), 1420-1432. <https://doi.org/10.2337/dc05-2096>
- Itoh, K., Murata, K., Sakaguchi, N., Akai, K., Yamaji, T., Shimizu, K., ... Matsuda, H. (2017). Inhibition of advanced glycation end products formation by *Mangifera indica* leaf extract. *Journal of Plant Studies*, 6(2), 102-107. <http://dx.doi.org/10.5539/jps.v6n2p102>
- Lauricella, M., Emanuele, S., Calvaruso, G., Giuliano, M., & D'Anneo, A. (2017). Multifaceted health benefits of *Mangifera indica* L. (Mango): the inestimable value of orchards recently planted in Sicilian rural areas. *Nutrients*, 9(5), 1090-1098. <https://doi.org/10.3390/nu9050525>
- Litz, R. E. (2009). *Breeding and genetics: The mango: botany, production and uses* (2ND edition). Oxfordshire UK: CABI head office. <https://doi.org/10.1079/9781845934897.0000>
- Mukherjee, S. K. (1953). The mango-its botany, cultivation, uses and future improvements, especially as observed in India. *Economic Botany*, 7, 130-162. <https://doi.org/10.1007/BF02863059>
- Porra, R. J., Thompson, W. A., & Kriedemann, P. E. (1989). Determination of accurate extinction coefficients and simultaneous equations for assaying chlorophylls a and b extracted with four different solvents: verification of the concentration of chlorophyll standards by atomic absorption spectroscopy. *Biochimica et*

- Biophysica Acta*, 975, 384-394. [https://doi.org/10.1016/S0005-2728\(89\)80347-0](https://doi.org/10.1016/S0005-2728(89)80347-0)
- Ravishankar, K. V., Mani, B. H., Anand, L., & Dinesh, M. R. (2011). Development of new microsatellite markers from Mango (*Mangifera indica*) and cross-species amplification. *American Journal of Botany*, 98(4), 96-99. <http://dx.doi.org/10.3732/ajb.1000263>
- Sasaki, K., Nakajima, A., Shimizu, K., Kanzaki, S., & Utsunomiya, N. (2008). Registration number, 16162; registration date, 2008/03/05. Registration kind database of Intellectual Property Division, Food Industry Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries, Japan. Retrieved from http://www.hinshu2.maff.go.jp/vips/cmm/apCMM112.aspx?TOUROKU_NO=16162&LANGUAGE=Japanese
- Scartezzini, P., & Speroni, E. (2000). Review on some plants of Indian traditional medicine with antioxidant activity. *Journal of Ethnopharmacology*, 71, 23-43. [http://dx.doi.org/10.1016/s0378-8741\(00\)00213-0](http://dx.doi.org/10.1016/s0378-8741(00)00213-0)
- Shimoda, H., Nakamura, S., Morioka, M., Tanaka, J., Matsuda, H., & Yoshikawa, M. (2011). Effect of cinnamoyl and flavonol glucosides derived from cherry blossom flowers on the production of advanced glycation end products (AGEs) and AGE-induced fibroblast apoptosis. *Phytotherapy Research*, 25, 1328-1335. <http://dx.doi.org/10.1002/ptr.3423>
- Sourris, K. C., Harcourt, B. E., & Forbes, J. M. (2009). A new perspective on therapeutic inhibition of advanced glycation in diabetic microvascular complications: common downstream endpoints achieved through disparate therapeutic approaches?. *American Journal of Nephrology*, 30, 323-335. <https://doi.org/10.1159/000226586>
- Tsuji-Naito, K., Saeki, H., & Hamano, M. (2009). Inhibitory effects of *Chrysanthemum* species extracts on formation of advanced glycation end products. *Food Chemistry*, 116, 854-859. <https://doi.org/10.1016/j.foodchem.2009.03.042>
- Ueda, M., Sasaki, K., Utsunomiya, N., & Shimabayashi, Y. (2001). Changes in properties during maturation and ripening of 'Chiin Hwang No. 1' Mango fruit cultivated in a plastic greenhouse. *Food Science and Technology Research*, 7(3), 207-213. <https://doi.org/10.3136/fstr.7.207>
- Usman, M., Fatima, B., & Jaskani, M. J. (2001). Breeding in Mango. *International Journal of Agriculture and Biology*, 3(4), 522-526.

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