Glycative Stress Research

Online edition : ISSN 2188-3610
Print edition : ISSN 2188-3602
Received : October 18, 2021
Accepted : November 17, 2021
Published online : December 31, 2021
doi:10.24659/gsr.8.4_162

*Original article*

# Anti-glycative effect and total phenolic content of rice water of different *Japonica* and *Indica* varieties

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## Abstract

Glycation is a non-enzymatic reaction between reducing sugars and amino group proteins which leads to the formation of advanced glycation end products (AGEs). The buildup of AGEs in the body is a key factor in the onset of aging and lifestyle-related diseases. In this study, the inhibitory effect on the formation of AGEs by rice water was investigated. Rice water is a common ingredient used traditionally as a beautifying agent but lacks proper scientific research. 14 *Japonica* and *Indica* rice varieties were used to prepare rice water samples using three different methods, namely type 1, type 2, and type 3 (n = 42). The human serum albumin (HSA) glycation model was used to evaluate the inhibitory effect on the formation of fluorescent AGEs by rice water. The total phenolic content (TPC) in rice water was determined according to the Folin-Ciocalteau procedure. All 42 rice water samples showed an inhibitory effect on the formation of fluorescent AGEs, and positive correlations were observed between the inhibitory effect and the TPC at $p < 0.05$; type 1 rice water (r = 0.906), type 2 rice water (r = 0.918), and type 3 rice water (r = 0.765). It was also observed that rice water prepared from pigmented rice varieties showed the highest inhibitory values, for example, type 1 sample number 1 (66.4 ± 0.4%), type 2 sample number 1 (66.6 ± 0.7%), and type 3 sample number 12 (69.6 ± 0.8%). Consequently, the results from this study verifies the anti-glycative effect of rice water and suggests the TPC plays a role on the anti-glycative effect of rice water.

**KEY WORDS:** rice water, glycative stress, advanced glycation end products (AGEs), total phenolic content

## Introduction

Rice is one of the most widely consumed staple foods for a large part of the world's population, mainly in Asia and it is also an important beautifying agent. Traditionally, women from Japan, China, and some Southeast Asian countries have used rice water to beautify their face, skin, and hair. *Oryza sativa* is the plant species most commonly referred to as rice. It contains two major subspecies; the sticky, short-grained *Japonica* variety, and the non-sticky, long-grained *Indica rice* variety [1]. Rice also occurs in a variety of colors, including white, brown, black or purple, and red. However, the benefits of rice water are not supported by enough scientific research although cosmetic manufacturers greatly assert the benefits of rice water on skin.

Recently, the search for new, natural, and most importantly organic bioactive compounds to prevent skin aging has greatly increased. Rice water is natural, economical and simple, and could be easily included in skincare products. Different types of rice are readily available as it is a large part of the human diet, and it can easily be obtained from the rice industry as well. Rice bran oil is recognized for containing antioxidant-rich components such as ferulic acid, γ-oryzanol, and phytic acid [2]. These components have been established and used in the cosmetic industry, and in the management of skin diseases [3]. Rice bran bioactive compounds have been found to be efficient in the treatment of alopecia [4] and also have an anti-aging potential [5]. Starch, which is the major component in rice grains, is a biodegradable polymer with safe application in the pharmaceutical industry. Starch is recommended to be added to bath water as it is said to help with the treatment of atopic dermatitis or other skin diseases associated with pruritus [6]. A study done in Portugal presented *in vitro* biological antioxidant activity and elastase inhibitory effects by rice water. Their clinical study done using a topical gel formulation containing 96% rice water was shown to be biocompatible with the human skin and presented suitable cosmetic properties [7]. It has also been shown that the bioactive compounds present in rice have huge potential for

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many health benefits and has anti-tumor, anti-atherosclerosis, anti-diabetic, anti-allergic agents, alleviation of gallstones, anti-cancer activity, anti-inflammatory, and other effects [8].

Rice water, which is used as folklore medicine in Sri Lanka, is classified into three types according to the difference in manufacturing method, and there are various varieties such as those from Southeast Asia and Japan. The main purpose of this study is to verify the presence or absence of anti-glycation effect as a new function of rice water. Glycation is a non-enzymatic chemical reaction between amino acids or proteins and reducing sugars, which was discovered by Louis-Camille Maillard, a French scientist. This reaction is also called the Maillard reaction [9]. These glycated proteins lead to the formation of advanced glycation end products (AGEs) that are accumulated in various tissues and organs. AGEs induce inflammation, pigmentation, and deterioration of physiological function that lead to aging [10]. The phenomenon of the accumulation of these cytotoxic and irreversibly-formed sugar-derived AGEs that contribute to aging, age-related diseases, and other metabolic diseases such as diabetes, cancer, kidney, ocular, and cardiovascular diseases is known as glycative stress [11]. In addition, we will compare the difference in effect depending on the variety and manufacturing method and the total phenol content (TPC), as it has been reported that TPC was responsible for the anti-glycation potential of rice [12]. We would like to know the varieties and manufacturing methods that efficiently exert anti-glycation effects.

## Materials and methods

### Samples and reagents

The 14 rice samples used in this study were purchased randomly at readily available stores across Japan and Sri Lanka (*Table 1*). Human serum albumin (HSA) was purchased from Sigma-Aldrich (Meguro-ku, Tokyo). All other chemicals were analytical grade and purchased from Fujifilm Wako Pure Chemical Corporation (Osaka, Japan) or Nacalai Tesque, Inc. (Kyoto, Japan).

### Rice water preparation by three different methods

Based on the traditional usage in Sri Lanka, the following three types of rice water samples were prepared.

#### Type 1

Three grams of rice was boiled in 36 mL of distilled water at 100 °C for 30 minutes. Samples were centrifuged at 2,500 rpm for ten minutes at room temperature, and filtered.

#### Type 2

Five grams of rice was oven-dried at 160 °C for 30 minutes. Three grams of oven-dried rice was boiled in 36 mL of distilled water at 100 °C for 30 minutes. Samples were centrifuged at 2,500 rpm for ten minutes at room temperature, and filtered.

***Table 1. Rice samples used in this study.***

| Sample number | Sample name | Subspecies | Color | Country of origin and purchase | Additional details regarding source of material |
|---|---|---|---|---|---|
| 1 | Asamurasaki | *Japonica* | Black | Japan | Purchased from Tomizawa Shoten (TOMIZ), Product No. 00347802 |
| 2 | Black Kodaimai | *Japonica* | Black | Japan | Purchased from Asuka Kanko |
| 3 | Dik Vee | *Indica* | Red | Sri Lanka | Purchased from Siriketha Products, Ethkandura |
| 4 | Hitomebore | *Japonica* | Brown | Japan | Purchased from Rice Friend, Takashimaya Osaka store |
| 5 | Koshihikari | *Japonica* | Brown | Japan | Purchased from Rice Friend, Takashimaya Osaka store |
| 6 | Kuruluthuda | *Indica* | Red | Sri Lanka | Purchased from Siriketha Products, Ethkandura |
| 7 | Ma Vee | *Indica* | White | Sri Lanka | Purchased from a local farmer in the Gampaha district |
| 8 | Madathavalu | *Indica* | White | Sri Lanka | Purchased from a local farmer in the Gampaha district |
| 9 | Martin Samba | *Indica* | White | Sri Lanka | Purchased from a local farmer in the Gampaha district |
| 10 | Mixed Kodaimai | *Japonica* | Mixed (black, green, red) | Japan | Purchased from Asuka Kanko |
| 11 | Pachchaperumal | *Indica* | Red | Sri Lanka | Purchased from a local farmer in the Gampaha district |
| 12 | Red Kodaimai | *Japonica* | Red | Japan | Purchased from Asuka Kanko |
| 13 | Suduru Hel | *Indica* | White | Sri Lanka | Purchased from a local farmer in the Gampaha district |
| 14 | Yuyakemochi | *Japonica* | Red | Japan | Purchased from Tomizawa Shoten (TOMIZ), Product No. 00347901 |

### Type 3

Three grams of rice was soaked in 9 mL of distilled water at room temperature for six hours. Samples were centrifuged at 2,500 rpm for ten minutes at room temperature, and filtered.

A solid concentration (mg/mL) was obtained after 3 mL of rice water was placed on an aluminum tray and the weights were measured before and after dehydration at 120 ºC for 120 minutes. Samples were prepared for the experiments by adjusting the concentration with distilled water to 1 mg/mL of solid concentration.

### *Preparation of glycated proteins*

The HSA glycation model [13] was used to evaluate the effect of type 1, type 2, and type 3 rice water on glycation. 25 μL of the samples were added to 125 μL of 0.1 mol/L phosphate buffer solution (pH 7.4), 25 μL of distilled water, 50 μL of 40 mg/mL HSA, and 25 μL of 2.0 mol/L glucose (solution A). Distilled water was added instead of the glucose of solution A as a blank (solution B). At the same time, distilled water was added instead of the samples of solution A as a blank (solution C). A mixed solution containing purified water instead of the glucose solution of solution C was also prepared (solution D). 1 mg/mL aminoguanidine (AG) [14], a known AGE formation inhibitor, was used as a positive control. The reaction mixtures were incubated at 60 ºC for 40 hours.

### *Measurement of fluorescent AGEs*

The volume of fluorescent AGEs after incubation was measured as reported previously [13]. Concisely, 200 μL of the reaction mixture was used to measure fluorescence by a Varioscan® Flash microplate reader (Thermo Scientific, Waltham, MA) at an excitation wavelength of 370 nm and an emission wavelength of 440 nm. The fluorescence intensity was calculated as a relative value when the fluorescence intensity of 5 μg/mL quinine sulfate was 1,000. The production inhibition rate (%) of fluorescent AGEs was calculated by the following formula.

Inhibition of fluorescent AGE formation (%) =
$[1 - (A - B) / (C - D)] \times 100$

### *Measurement of total phenolic content (TPC)*

TPC was determined according to the Folin–Ciocalteau procedure [15] with some modifications that do not change the final result. Concisely, 50 μL of the reaction mixture (5 μL sample, 20 μL distilled water and 25 μL ethanol) was mixed with 250 μL of 0.4 M sodium carbonate followed by 25 μL of 50 % Folin-Ciocalteau reagent. Distilled water was used instead of Folin-Ciocalteau reagent as a blank. The mixtures were well mixed and incubated at 30 ºC for 30 minutes. The mixtures were then allowed to stand at room temperature for another 30 minutes. Absorbance was measured at 660 nm by a Varioscan® Flash microplate reader (Thermo Scientific, Waltham, MA). TPC was expressed as catechin equivalent (μM catechin eq) determined by a calibration curve, which was graphed following the same procedure using catechin as the standard phenolic compound [15].

### *Statistical analysis*

The measured values are shown as mean ± standard deviation. Comparisons between groups were performed in measurements using the Tukey's test. Correlation analysis between the measured values was performed using the Pearson correlation coefficient. Differences were considered significant at $P$ values less than 0.05.

## *Results*

### *Inhibitory effect on formation of AGEs*

The inhibitory effect on the formation of AGEs by type 1, type 2 and type 3 rice water prepared using 14 rice samples (n = 42), and AG are shown in ***Fig 1***. All 42 rice water samples inhibited the formation of fluorescent AGEs. Sample number 1 showed the highest inhibition on the formation of fluorescent AGEs among type 1 rice water samples (66.4 ± 0.4 %, ***Fig. 1-a***). Sample number 1 also showed the highest inhibition on the formation of fluorescent AGEs among type 2 rice water samples (66.6 ± 0.7 %, ***Fig. 1-b***). Sample number 12 showed the highest inhibition on the formation of fluorescent AGEs among type 3 rice water samples, and among all 42 rice water samples (69.6 ± 0.8 %, ***Fig. 1-c***). There was a significant difference ($p < 0.05$) between the different types of rice water samples except in sample number 1, as shown in ***Fig 2***. Comparing within the groups, sample numbers 2 and 3 showed the highest inhibition on the formation of fluorescent AGEs in type 1 rice water, sample number 1 showed the highest inhibition in type 2 rice water, and sample numbers 5, 6, 7, 8, 9, 10, 11, 12, 13, and 14 showed the highest inhibition in type 3 rice water. Among the 14 rice samples studied, all rice water samples (n = 42) showed lower inhibition that that of AG.

### *Total phenolic content (TPC) in rice water*

The TPC in type 1, type 2 and type 3 rice water prepared using 14 rice samples (n = 42) are shown in ***Fig. 3***. All 42 rice water samples contained phenolic compounds. Sample number 1 showed the highest TPC among type 1 rice water samples (94.7 ± 4.9 μM catechin eq), type 2 rice water samples (124.8 ± 7.5 μM catechin eq), and type 3 rice water samples (176.2 ± 3.4 μM catechin eq). Comparing within the groups, sample numbers 3 and 11 had the highest TPC in type 1 rice water, and sample numbers 1, 2, 4, 5, 6, 7, 8, 9, 10, 12, 13, and 14 had the highest TPC in type 3 rice water.

### *Correlation analysis*

***Fig. 4*** shows the correlation results between the TPC and the inhibitory effect on the formation of fluorescent AGEs. ***Fig. 4-a*** shows that there is a strong positive correlation between TPC and inhibition of fluorescent AGEs in type 1 rice water (r = 0.906). Similarly, a strong positive correlation was observed between TPC and inhibition of fluorescent AGEs in type 2 rice water (r = 0.918, ***Fig. 4-b***). A moderately strong positive correlation was seen between TPC and inhibition of fluorescent AGEs in type 3 rice water (r = 0.765, ***Fig. 4-c***).

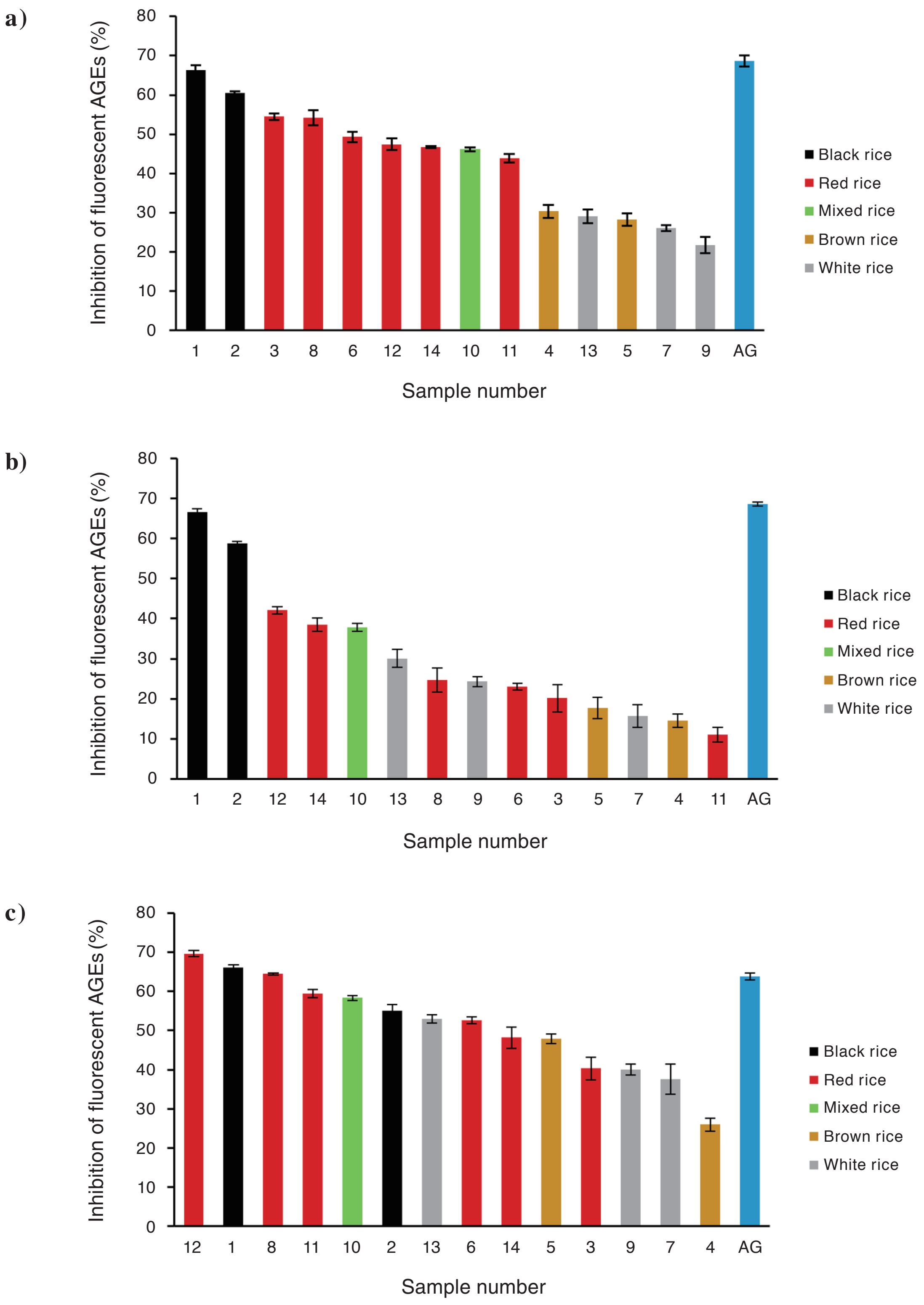


***Fig. 1.*** **Inhibition of fluorescent AGE formation by (a) type 1 rice water and AG, (b) type 2 rice water and AG, (c) type 3 rice water and AG.**

Rice water samples were introduced into glycation models containing 8 mg/mL HSA and 0.2 mol/L glucose. After 40 hours incubation at 60 °C, fluorescent AGEs were measured at 370/440 nm. The final concentration of samples was 1 mg/mL and that of AG was 0.1 mg/mL. Results are expressed as mean ± standard deviation, n = 3. Sample number; 1, Asamurasaki, 2, Black Kodaimai, 3, Dik Vee, 4, Hitomebore, 5, Koshihikari, 6, Kuruluthuda, 7, Ma Vee, 8, Madathavalu, 9, Martin Samba, 10, Mixed Kodaimai, 11, Pachchaperumal, 12, Red Kodaimai, 13, Suduru Hel, 14, Yuyakemochi. AGEs, advanced glycation end products; AG, aminoguanidine; HSA, human serum albumin.

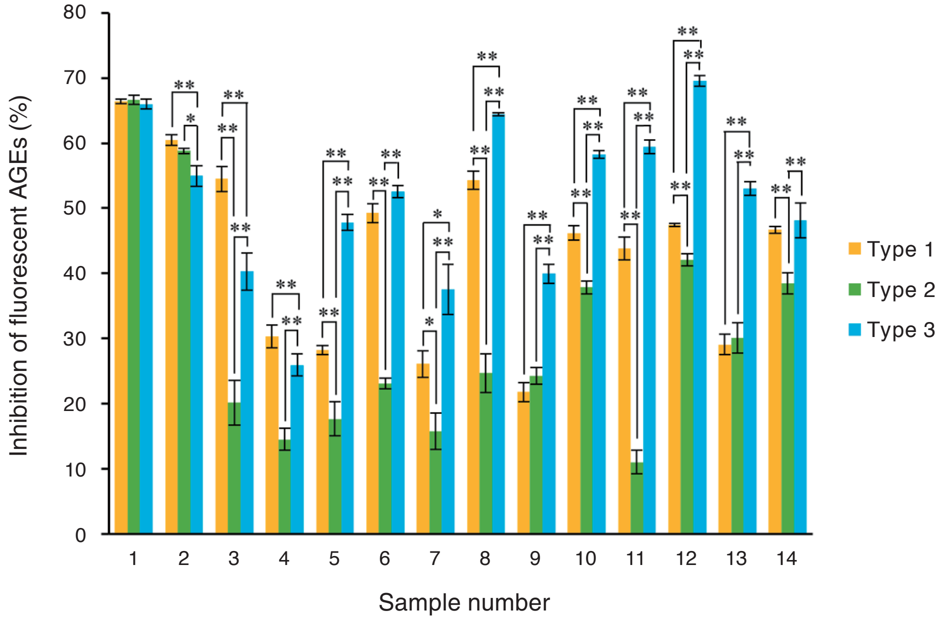


***Fig. 2.*** **Comparison of the inhibition of fluorescent AGEs formation by the 3 types of rice water.**

The final concentration of samples was 1 mg/mL. Results are expressed as mean ± standard deviation, n = 3, *$p < 0.05$, **$p < 0.01$ by Tukey's test. Sample number; 1, Asamurasaki, 2, Black Kodaimai, 3, Dik Vee, 4, Hitomebore, 5, Koshihikari, 6, Kuruluthuda, 7, Ma Vee, 8, Madathavalu, 9, Martin Samba, 10, Mixed Kodaimai, 11, Pachchaperumal, 12, Red Kodaimai, 13, Suduru Hel, 14, Yuyakemochi. AGEs, advanced glycation end products.

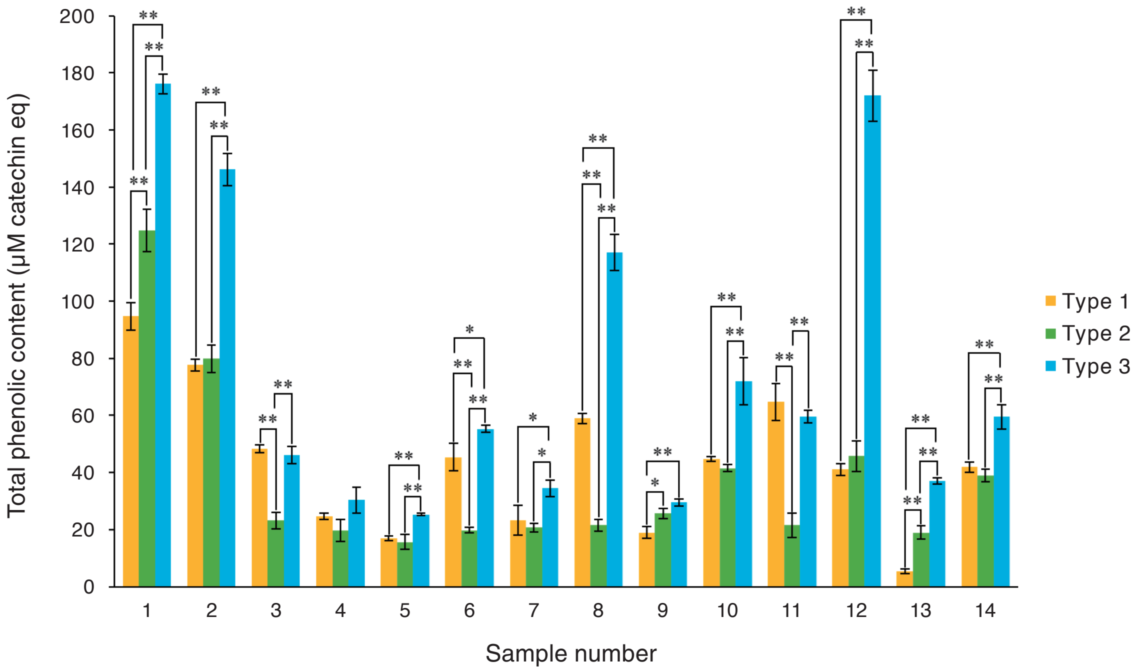


***Fig. 3.*** **Comparison of the TPC in the 3 types of rice water.**

The final concentration of samples was 1 mg/mL. Results are expressed as mean ± standard deviation, n = 3. *$p < 0.05$, **$p < 0.01$ by Tukey's test. Sample number; 1, Asamurasaki, 2, Black Kodaimai, 3, Dik Vee, 4, Hitomebore, 5, Koshihikari, 6, Kuruluthuda, 7, Ma Vee, 8, Madathavalu, 9, Martin Samba, 10, Mixed Kodaimai, 11, Pachchaperumal, 12, Red Kodaimai, 13, Suduru Hel, 14, Yuyakemochi. TPC, total phenolic content.

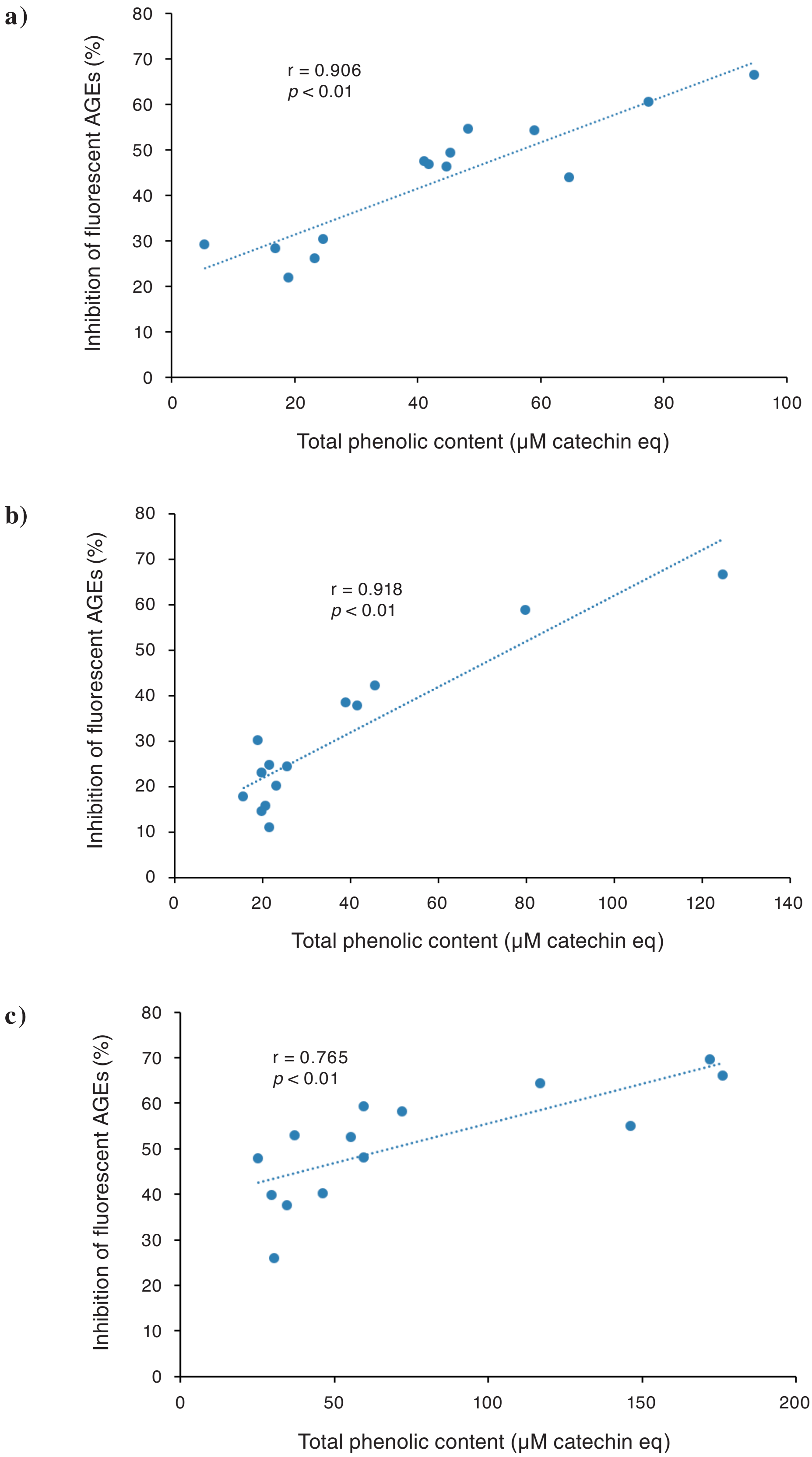


***Fig. 4.*** **Correlation of inhibition of fluorescent AGEs formation to TPC of (a) type 1 rice water, (b) type 2 rice water, (c) type 3 rice water.**

$p < 0.01$, r = Pearson correlation coefficient. TPC, total phenolic content; AGEs, advanced glycation end products.

# Discussion

## *Research background*

In this study, the anti-glycative effect and the TPC of three different rice water preparations using 14 rice samples was studied. The 14 rice samples included two black rice varieties, five red rice varieties, two brown rice varieties, four white rice varieties, and one mixed rice variety. Different pigmented rice varieties were chosen as previous studies have shown various health benefits of pigmented rice compared to white rice. Although white rice makes a major contribution to the calorific intake of most Asian populations and other populations around the world, its nutritional quality is low compared to that of pigmented rice varieties [16]. Pigmented rice have been reported as a potent source of phytonutrients including antioxidant compounds, and that they have marked health benefits in preventing diabetic complications as well [17, 18]. Pigmented rice contains a range of bioactive compounds including phenolic acids and flavonoids [19]. Several epidemiological studies have suggested that a high dietary consumption of polyphenols is associated with a decreased risk of various diseases including cardiovascular disease [20, 21] and neurodegenerative diseases [22]. It has been shown that the concentration of phenolic compounds are positively associated with the antioxidant activity and could aid in the prevention of cancer [23-25].

## *Anti-glycation effect as a new functionality*

In this study, rice water, which is a natural, economical and simple product was used as the primary test sample. Rice water is prepared by different methods with different purposes globally, however, it always involves rice grains in contact with water. In order to examine which rice water preparing method would result in rice water with a higher anti-glycative effect, three traditional methods from Sri Lanka were replicated in the lab and used in this study to prepare the rice water. Type 1 was made by boiling, type 2 by oven-drying and boiling, and type 3 by soaking in water. A study conducted in Japan has shown hair care benefits by rinsing with water obtained from the washing of rice [26], which is quite similar to the type 3 rice water of this study.

The anti-glycative effect of rice water was verified by measuring the inhibitory effect on the formation of fluorescent AGEs using the HSA glycation model [13]. Rice water was incubated with HSA and glucose at 60ºC for 40 hours to evaluate its anti-glycative effect. This glycation reaction is a non-enzymatic one controlled by reaction temperature and time. Previous studies show that the formation of fluorescent AGEs at 60 ºC for 40 hours was equivalent to that obtained from a reaction time of about 60 days at 37 ºC [27]. The positive control used when measuring the inhibitory effects of AGEs, aminoguanidine (AG), is an inhibitory agent of the glycation reaction. AG is an AGE formation inhibitor developed with the aim of curing diabetic complications [28]. AG blocks the carbonyl group in molecules of the intermediate products of glycative reactions. However, AG is not approved as a medical product in the domestic market, because a side effect was recognized in Japan. All 42 rice water samples showed an inhibitory effect on the formation of fluorescent AGEs. This could be due to the transference to the water of several phenolic compounds identified in rice, such as tocopherols, tocotrienols and $\gamma$-oryzanol [29].

## *Relationship with total phenolic content (TPC)*

Rice water application has been a popular folk remedy for skin lightening, increasing elasticity of skin, and soothing sun damage. This study verifies the anti-glycative effects of rice water from a viewpoint of skin aging prevention. However, there is a significant difference of inhibition values between the different types of rice water preparations, and between the different varieties of pigmented rice. Type 3 rice water showed higher inhibition values in average compared to type 1 and type 2 rice water. Black and red rice varieties showed higher inhibition values in average compared to brown, mixed, and white rice varieties. This suggests that the pigment, which is located in the aleurone layer of rice contains higher amount of phenolic compounds such as anthocyanins [17]. A previous study has shown that the TPC was positively correlated to the anti-AGE formation capacity of different pigmented Thai rice varieties [12]. These results also agree with previous studies that have reported pigmented rice having higher phenolic compounds [17, 30].

Also in this study, strong positive correlation results can be seen between the TPC and inhibitory effect on the formation of fluorescent AGEs by all three types of rice water. Similar results have been observed in another study that shows a positive correlation of the TPC, antioxidant activities, and anti-AGEs formation capacity of rice bean in China [31]. Additionally, similar relationships have been observed in garcinol from *Garcinia indica* fruit rind [32], and in *Camellia sinensis* [33]. These results indicate that the inhibition of AGEs formation depend on the TPC. Type 3 rice water showing higher inhibition of fluorescent AGEs could be due to the fact that boiling in water led to the loss of soluble phenolic compounds in type 1 and type 2 rice water. In most rice samples, the type 2 rice water preparation method led to lower inhibition rates. This could be due to the extreme heat applied to the rice over a longer period of time (160 ºC for 30 minutes and 100 ºC for another 30 minutes) when compared to the other two rice water preparing methods. The extreme heat over a longer period of time might have led to a higher loss or degradation of phenolic compounds, thus decreasing the inhibition potential of type 2 rice water. A previous study has shown that cooking of rice led to a significant decrease in inhibitory capacity of angiotensin I-converting enzyme (ACE) accompanied by a relative reduction in the soluble phenolic content [34]. These results also agree with another study that shows the TPC was lower in rice water prepared by the boiling process [7]. It has also been shown that heat significantly affected the amount of phenolic compounds in other foods [35-37]. This could also be the reason for type 3 rice water to show a moderately strong positive correlation with its TPC. It could also be that another factor in addition to the TPC is playing a role in the inhibition of AGEs in type 3 rice water. However, this remains unknown therefore future research efforts should be focused on identifying other factors except TPC that are responsible for the anti-glycation effect of type 3 rice water.

## Conclusion

This study is the first report on a correlation between the inhibition of AGE formation and the TPC in rice water of various pigmented and non-pigmented *Japonica* and *Indica* varieties. This study shows that rice water has an anti-glycation effect (AGE production inhibitory effect) as a novel function. This study also shows that rice water produced using pigmented rice varieties have a higher inhibitory effect against fluorescent AGE formation, and that there is a strong positive correlation between the inhibitory effect and the TPC of rice water. Among the traditional manufacturing methods, type 3 rice water, produced by soaking rice in water, has the strongest action, and among the varieties, sample number 1 (Asamurasaki, black *Japonica* variety) and sample number 12 (Red Kodaimai, red *Japonica* variety) have strong actions. A correlation was found between the strength of the anti-glycation effect and the TPC content, suggesting TPC (*i.e.*, phenolic compounds in rice such as ferulic acid [38]) as a component involved. From the above, it was suggested that rice water may contribute to beauty and health maintenance through its anti-glycation function when topically used on skin.

## Acknowledgements

A part of this study was presented at the 18th meeting of the Society for Glycative Stress Research in October 2018, Tokyo, Japan. This study was presented at the 23rd Glycation Stress Study Group Lecture in August 2021, Kumamoto, Japan. This study was also presented at IMARS-14 in September 2021, Doha, Qatar. This study was carried out at the Graduate School of Life and Medical Sciences, Doshisha University. We thank Mr. M.C. Wickramasinghe and Mrs. T.M.L.K. Thilakaratna for providing the *Indica* rice samples. The publication of this study was supported by the Isyoku-Dogen Research Foundation (IDF#22002).

## Conflict of interest declaration

This study was supported by the Japanese Council for Science, Technology and Innovation, SIP (Project ID: 14533567), “Technologies for creating next-generation agriculture, forestry and fisheries” (funding agency: Bio-oriented Technology Research Advancement Institution, NARO), and the Research Foundation of Crude Drug gained from the same source of Medicine & Food (funding number: IDF#21002). Funding acquisition by Y.Y. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

## References

1) Garris AJ, Tai TH, Coburn J, et al. Genetic structure and diversity in *Oryza sativa* L. *Genetics*. 2005; 169: 1631-1638.
2) Pal YP, Pratap AP. Rice bran oil: A versatile source for edible and industrial applications. *J Oleo Sci*. 2017; 66: 551-556.
3) Lerma-García MJ, Herrero-Martínez JM, Simó-Alfonso EF, et al. Composition, industrial processing and applications of rice bran γ-oryzanol. *Food Chemistry*. 2009; 115: 389-404.
4) Choi J-S, Park JB, Moon W-S, et al. Safety and efficacy of rice bran supercritical $CO_2$ extract for hair growth in androgenic alopecia: A 16-week double-blind randomized controlled trial. *Biol Pharm Bull*. 2015; 38: 1856-1863.
5) Kanlayavattanakul M, Lourith N, Chaikul P. Jasmine rice panicle: A safe and efficient natural ingredient for skin aging treatments. *J Ethnopharmacol*. 2016; 193: 607-616.
6) De Paepe K, Hachem JP, Vanpee E, et al. Effect of rice starch as a bath additive on the barrier function of healthy but SLS-damaged skin and skin of atopic patients. *Acta Derm Venereol*. 2002; 82: 184-186.
7) Marto J, Neves Â, Gonçalves L, et al. Rice water: A traditional Ingredient with anti-aging efficacy. *Cosmetics*. 2018; 5(2): 26.
8) Samyor D, Das AB, Deka SC. Pigmented rice a potential source of bioactive compounds: A review. *International Journal of Food Science & Technology*. 2017; 52: 1073-1081.
9) Zhang Q, Ames JM, Smith RD, et al. A perspective on the Maillard reaction and the analysis of protein glycation by mass spectrometry: Probing the pathogenesis of chronic disease. *J Proteome Res*. 2009; 8: 754-769.
10) Nagai R, Mori T, Yamamoto Y, Kaji Y, et al. Significance of advanced glycation end products in aging-related disease. *Anti-Aging Med*. 2010; 7: 112-119.
11) Rowan S, Bejarano E, Taylor A. Mechanistic targeting of advanced glycation end-products in age-related diseases. *Biochim Biophys Acta Mol Basis Dis*. 2018; 1864: 3631-3643.
12) Daiponmak W, Senakun C, Siriamornpun S. Antiglycation capacity and antioxidant activities of different pigmented Thai rice. *International Journal of Food Science & Technology*. 2014; 49: 1805-1810.
13) Ishioka Y, Yagi M, Ogura M, et al. Antiglycation effect of various vegetables: Inhibition of advanced glycation end product formation in glucose and human serum albumin reaction system. *Glycative Stress Res*. 2015; 2: 22-34.
14) Hammes HP, Martin S, Federlin K, et al. Aminoguanidine treatment inhibits the development of experimental diabetic retinopathy. *Proc Natl Acad Sci U S A*. 1991; 88: 11555-11558.
15) Stevanato R, Fabris S, Momo F. New enzymatic method for the determination of total phenolic content in tea and wine. *J Agric Food Chem*. 2004; 52: 6287-6293.
16) Mbanjo EGN, Kretzschmar T, Jones H, et al. The genetic basis and nutritional benefits of pigmented rice grain. *Front Genet*. 2020; 11: 229.

17) Yawadio R, Tanimori S, Morita N. Identification of phenolic compounds isolated from pigmented rices and their aldose reductase inhibitory activities. *Food Chemistry*. 2007; 101: 1616-1625.
18) Morimitsu Y, Kubota K, Tashiro T, et al. Inhibitory effect of anthocyanins and colored rice on diabetic cataract formation in the rat lenses. *International Congress Series*. 2002; 1245: 503-508.
19) Wongsa P. Phenolic compounds and potential health benefits of pigmented rice. *Recent Advances in Rice Research*. 2020. DOI: 10.5772/intechopen.93876.
20) Lo LMP, Kang MY, Yi SJ, et al. Dietary supplementation of germinated pigmented rice (*Oryza sativa* L.) lowers dyslipidemia risk in ovariectomized Sprague–Dawley rats. *Food Nutr Res*. 2016; 60: 30092.
21) Ling WH, Cheng QX, Ma J, et al. Red and black rice decrease atherosclerotic plaque formation and increase antioxidant status in rabbits. *J Nutr*. 2001; 131: 1421-1426.
22) Vargas CG, Da Silva Junior JD, Rabelo TK, et al. Bioactive compounds and protective effect of red and black rice brans extracts in human neuron-like cells (SH-SY5Y). *Food Res Int*. 2018; 113: 57-64.
23) Hu C, Zawistowski J, Ling W, et al. Black rice (*Oryza sativa* L. indica) pigmented fraction suppresses both reactive oxygen species and nitric oxide in chemical and biological model systems. *J Agric Food Chem*. 2003; 51: 5271-5277.
24) Hyun JW, Chung HS. Cyanidin and malvidin from *Oryza sativacv*. Heugjinjubyeo mediate mytotoxicity against human monocytic leukemia cells by arrest of G2/M phase and induction of apoptosis. *J Agric Food Chem*. 2004; 52: 2213-2217.
25) Chen P-N, Kuo W-H, Chiang C-L, et al. Black rice anthocyanins inhibit cancer cells invasion via repressions of MMPs and u-PA expression. *Chem Biol Interact*. 2006; 163: 218-229.
26) Inamasu S, Ikuyama R, Fujisaki Y, et al. The effect of rinse water obtained from the washing of rice (YU-SU-RU) as a hair treatment. *International Journal of Cosmetic Science*. 2010; 44: 29-33.
27) Yagi M, Yonei Y. Glycative stress and anti-aging: 4. The evaluation of glycative Stress: Evaluation for anti-glycative effect. *Glycative Stress Res*. 2017; 4: 87-92.
28) Bolton WK, Cattran DC, Williams ME, et al. Randomized trial of an inhibitor of formation of advanced glycation end products in diabetic nephropathy. *Am J Nephrol*. 2004; 24: 32-40.
29) Walter M, Marchesan E. Phenolic compounds and antioxidant activity of rice. *Brazilian Archives of Biology and Technology*. 2011; 54: 371-377.
30) Itani T, Tatemoto H, Okamoto M, et al. A comparative study on antioxidative activity and polyphenol content of colored Kernel rice. *Nippon Shokuhin Kagaku Kogaku Kaishi*. 2002; 49: 540-543.
31) Yao Y, Cheng X-Z, Wang L-X, et al. Major phenolic compounds, antioxidant capacity and antidiabetic potential of rice bean (*Vigna umbellata* L.) in China. *Int J Mol Sci*. 2012; 13: 2707-2716.
32) Yamaguchi F, Ariga T, Yoshimura Y, et al. Antioxidative and anti-Glycation Activity of garcinol from *Garcinia indica* fruit rind. *J Agric Food Chem*. 2000; 48: 180-185.
33) Ho S-C, Wu S-P, Lin S-M, et al. Comparison of anti-glycation capacities of several herbal infusions with that of green tea. *Food Chemistry*. 2010; 122: 768-774.
34) Massaretto IL, Madureira Alves MF, Mussi De Mira NV, et al. Phenolic compounds in raw and cooked rice (*Oryza sativa* L.) and their inhibitory effect on the activity of angiotensin I-converting enzyme. *Journal of Cereal Science*. 2011; 54: 236-240.
35) Ghafoor K, Ahmed IAM, Doğu S, et al. The effect of heating temperature on total phenolic content, antioxidant activity, and phenolic compounds of plum and mahaleb fruits. *International Journal of Food Engineering*. 2019; 15(11-12).
36) Xu G, Ye X, Chen J, et al. Effect of heat treatment on the phenolic compounds and antioxidant capacity of citrus peel extract. *J Agric Food Chem*. 2007; 55: 330-335.
37) Maghsoudlou Y, Asghari Ghajari M, Tavasoli S. Effects of heat treatment on the phenolic compounds and antioxidant capacity of quince fruit and its tisane's sensory properties. *J Food Sci Technol*. 2019; 56: 2365-2372.
38) Tian S, Nakamura K, Kayahara H. Analysis of phenolic compounds in white rice, brown rice, and germinated brown rice. *J Agric Food Chem*. 2004; 52: 4808-4813.