Bioorganic & Medicinal Chemistry Letters 26 (2016) 2680–2684

Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry Letters

journal homepage: www.elsevier.com/locate/bmcl

Increase of rutin antioxidant activity by generating Maillard reaction products with lysine

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ARTICLE INFO

Article history:
Received 22 January 2016
Revised 22 March 2016
Accepted 5 April 2016
Available online 5 April 2016

Keywords:
Rutin
Lysine
Maillard reaction
Antioxidant
Reactive oxygen species

ABSTRACT

Rutin exists in medicinal herbs, fruits, vegetables, and a number of plant-derived sources. Dietary sources containing rutin are considered beneficial because of their potential protective roles in multiple diseases related to oxidative stresses. In the present study, the change and antioxidation activity of rutin in Maillard reaction with lysine through a heating process were investigated. There is release of glucose and rhamnose that interact with lysine to give Maillard reaction products (MRPs), while rutin is converted to less-polar quercetin and a small quantity of isoquercitrin. Because of their high cell-membrane permeability, the rutin–lysine MRPs increase the free radical-scavenging activity in HepG2 cells, showing cellular antioxidant activity against Cu^{2+}-induced oxidative stress higher than that of rutin. Furthermore, the MRPs significantly increased the Cu/Zn SOD (superoxide dismutase) activity and Cu/Zn SOD gene expression of HepG2 cells, consequently enhancing antioxidation activity.

High levels of reactive oxygen species (ROS) are produced in organisms by various stimuli through endogenous metabolic processes. ROS include a large number of reactive molecules such as hydrogen peroxide, superoxide, and hydroxyl radical. The ROS of higher levels in the form of free radicals can lead to a variety of damages and pathophysiological processes in human cells.[1,2] It is well proven that natural dietary antioxidants can exert health-promoting and disease-preventing by scavenging free radicals in humans and animals.

Flavonoid is a group of plant secondary metabolites that shows high level of antioxidation activity by scavenging or preventing ROS formation with the involvement of chelating transition-metal ions such as those of iron and copper.[3] Rutin is a glycoside that belongs to the flavonoid group, and widely exists in medicinal herbs, vegetables, fruits, beverages, and plant-derived dietary sources. It was reported that rutin and its derivatives exhibit various kinds of free radical-scavenging activities.[4]

Maillard reaction products (MRPs) are formed when the nucleophilic amino groups of amino acids, peptides, or proteins react with reducing sugars under thermal treatment. They are well-recognized as a pivot source of compounds related to enhanced antioxidation activity during heating processes of various crude drugs or foods.[5]

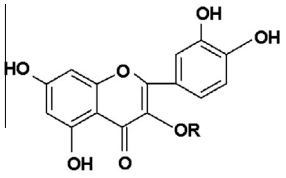

Figure 1. The structure of rutin, isoquercitrin and quercetin. Glc: D-glucopyranosyl, Rha: L-rhamnopyranosyl.

Rutin has a flavonol (quercetin) structure with two reducing hydrophilic sugar moieties (α-L-rhamnose and β-D-glucopyranose) at carbon-3 (Fig. 1). In Maillard reaction (MR) with special amino acid, the reducing sugars in glycosides can easily be separated.[6,7] In this kind of investigations, lysine was a frequently used amino acid.[8,9] The aim of the present study is to investigate the course of rutin change in MR as well as the antioxidant action of rutin MRPs, focusing on the free radical scavenging activity of DPPH (2,2-diphenyl-1-picrylhydrazyl), total phenolic contents, Cu^{2+} chelating activity, and superoxide dismutase (SOD) expression in HepG2 cells.

To investigate the antioxidation activity of the MRPs, equal molar amounts of rutin and lysine were heated together at 120 °C for 4 h to prepare the MRPs.[10] The MRPs of glucose–lysine and rhamnose–lysine mixture were also prepared for comparison

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http://dx.doi.org/10.1016/j.bmcl.2016.04.008
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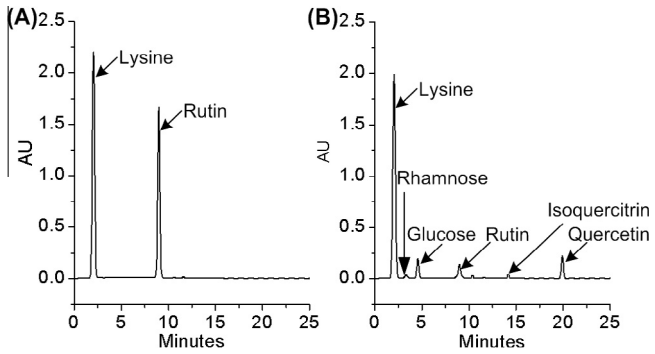

Figure 2. HPLC chromatogram of (A) non-heated and (B) heated rutin–lysine mixture.

studies. HPLC[11] results of the non-heated and heated rutin–lysine mixture are shown in Figure 2. It is observed that lysine and rutin are detected at 2.01 and 8.94 min, respectively, for the non-heated mixture (Fig. 2A). For the mixture treated at 120 °C, there is dramatical decrease of rutin as well as the detection of quercetin and small amount of isoquercitrin (Fig. 2B). During the thermal process, reducing sugars such as glucose and rhamnose are released from the rutin molecules (Fig. 2B). The results similar to that of ginsenoside Re–lysine MR in which glucose is released from ginsenoside Re at carbon-20 and transforms to ginsenoside Rg2, Rg6 and F4.[8] In the rutin–lysine MR, most of the glucose and rhamnose take part in the reaction with lysine to produce MRPs with structures that are extremely complex and largely unknown.[12]

A change of color is a common feature of MR in which hundreds of brown intermediates possessing strong antioxidation activity are generated.[13] The browning level of rutin alone and that of rutin–lysine mixture were assayed at 420 nm before and after heating at 120 °C.[6] As indicated in Figure 3A, there is no obvious change of absorbance over the former while that over the latter shows an increase from 0.11 to 0.42 (p <0.01). Over the samples of glucose–lysine and rhamnose–lysine mixture, the change of absorbance as a result of heat treatment at 120 °C is more obvious: about 14.4 (p <0.01) and 13.3 (p <0.05) times that before heating, respectively, much higher than that of rutin–lysine (3.8 times). According to the results of the HPLC analysis, most of the glucose and rhamnose released from rutin are transformed into brown intermediates upon interaction with lysine during the heat process. With the browning levels of the samples tested, we turned our attention to the study of DPPH radical-scavenging activity, total phenolic contents, and Cu^{2+} chelating activity of the MRPs.

DPPH is a stable nitrogen-centered free radical that is purple in ethanol/methanol solution; and upon accepting an electron or a hydrogen radical, it becomes colorless or yellow, respectively.[14] Hence the antioxidation ability of an antioxidant can be easily assessed by monitoring the decrease of absorbance intensity of

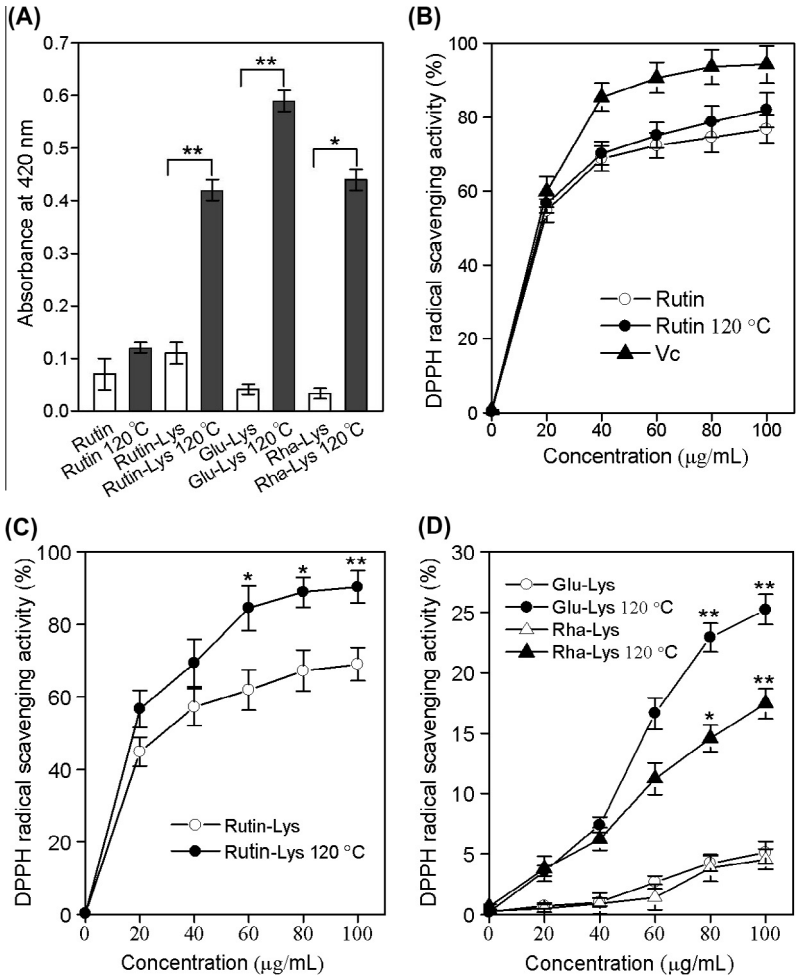

Figure 3. (A) The browning levels of samples after MR at 120 °C for 4 h; DPPH radical-scavenging activities of (B) rutin, (C) rutin–lysine, (D) rhamnose–lysine and glucose–lysine after MR at 120 °C for 4 h. The data represent the means of three independent experiments. The differences between the heated and non-heated (control) experiments are statistically significant ($^{*}p$ <0.05, $^{**}p$ <0.01).