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Kochujang, a Korean fermented red pepper plus soybean paste, improves glucose homeostasis in 90% pancreatectomized diabetic rats

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Abstract

Objectives: Red pepper and soybeans have been reported to modulate energy and glucose metabolism. However, the antidiabetic effect of *kochujang*, the fermented product of red pepper plus soybeans, has not been studied. We examined whether *kochujang* affected insulin secretion from β-cells and/or peripheral insulin resistance in 90% pancreatectomized diabetic rats fed high-fat diets.
Methods: Diabetic rats consumed a high-fat diet containing two different kinds of 5% *kochujang* powder or the equivalent amount of nutrients for 8 wk. Two types of *kochujang* were made through the fermentation of two different kinds of *meju* (soybeans), red peppers, glutinous rice, and malts. *Meju* was produced by fermenting soybeans in a traditional method (TMK) or in a more modern method in which soybeans are inoculated with *Bacillus subtilus* and *Aspergillus sojae* (MMK).
Results: TMK and MMK decreased body weight, visceral fat, and serum leptin levels without modulating caloric intake in diabetic rats compared with the control. TMK and MMK also improved glucose tolerance by enhancing insulin sensitivity but did not potentiate glucose-stimulated insulin secretion. The improvement in hepatic insulin sensitivity caused by TMK and MMK was explained by the potentiated phosphorylation of signal transducer and activator of transcription-3 → adenosine monophosphate kinase → acetyl-coenzyme A carboxylase and decreased phosphoenolpyruvate carboxykinase expression. *Kochujang* diets reduced hepatic glucose output and triacylglycerol accumulation and increased glycogen storage.
Conclusion: The combination of red pepper and fermented soybeans in *kochujang* improves glucose homeostasis by reducing insulin resistance, not by enhancing β-cell function, in diabetic rats. The improvement is associated with decreased hepatic fat storage by the activation of adenosine monophosphate kinase. © 2009 Published by Elsevier Inc.

Keywords: Red pepper; Soybeans; Insulin signaling; Insulin sensitivity; Insulin secretion

Introduction

Type 2 diabetes is a heterogeneous metabolic disorder characterized by insulin deficiency and peripheral insulin resistance [1,2]. Insulin resistance affects insulin secretion with biphasic states. When insulin resistance is initially induced by certain conditions such as obesity, stress, inflammation, and aging, insulin secretion from pancreatic β-cells is sufficiently elevated to maintain normoglycemia to compensate for insulin resistance [3]. However, sustained insulin resistance leads eventually to an inability to release sufficient glucose-stimulated insulin secretion to compensate for insulin resistance, which indicates β-cell failure. This results in type 2 diabetes [2]. Therefore, this imbalance of insulin secretion and insulin resistance initiates and aggravates type 2 diabetes.

The prevalence of type 2 diabetes has been continuously increasing throughout Asia to the point where 7–8% of the populations in Asian countries, including Korea, are now

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believed to be afflicted by this disease, with scientists warning that the figure could rise to 10% by 2020 [4]. However, the mechanism by which this disease develops is still not clearly understood. One possible explanation could be that the abrupt failure of β-cells brought on by insulin resistance is induced by the westernization of traditional lifestyles, e.g., high-fat diets and lack of exercise. The traditional Asian diet was high in carbohydrates and mainly contained plant proteins [5]. This diet is known to prevent obesity and to improve insulin sensitivity in obese animals to counteract hyperinsulinemia, which causes the senescence of islets and eventually induces β-cell dysfunction [5–7]. However, Asian diets may reduce the capacity to sufficiently increase insulin secretion to compensate for developing insulin resistance due to obesity and inflammation. In addition, the consumption of red pepper and foods containing soybeans may affect insulin secretion and insulin resistance—the cause behind the onset and development of type 2 diabetes. Red peppers and red pepper paste are reported to have antiobesity, analgesic, and anti-inflammatory effects in animals and humans [8,9]. This indicates that these products may have the potential to reduce insulin resistance. The aforementioned antiobesity, anti-inflammatory, and analgesic effects are related to the capsaicin in red peppers.

Capsaicin, a major component or ingredient in red peppers, desensitizes vanilloid subfamily member-1 (TRPV1), which is believed to function as a molecular integrator of noxious stimuli, including heat, acids, pollutants with negative electric charges, and endogenous proinflammatory substances [10,11]. TRPV1 is manifest in pancreatic β-cells and the desensitization of TRPV1 potentiates glucose-stimulated insulin secretion. Systemic capsaicin administration (100 mg/kg of body weight) into the scruff of the neck improves glucose intolerance in type 1 and type 2 diabetes and prevents obesity [10,11]. However, it has not been investigated whether the consumption of red peppers or foods containing red peppers improves glucose-stimulated insulin secretion and insulin sensitivity by desensitizing TRPV1. Previous studies have demonstrated that the consumption of foods containing red pepper decreases body fat storage and enhances glucose tolerance [8,12]. However, it remains controversial whether foods containing red peppers can improve glucose-stimulated insulin secretion.

In addition to red pepper, *kochujang* (red pepper paste) contains fermented soybeans and is believed to improve insulin sensitivity. We previously showed that *chungkookjang*, soybeans that have been fermented for a short time, enhances antidiabetic actions in diabetic rats [13]. *Kochujang* contains *meju*, fermented soybeans, and these contain isoflavonoids and small peptides. These entities are involved in the modulation of insulin sensitivity and insulin secretion [14,15]. Thus, we resolved to investigate whether red pepper paste, fermented red peppers, soybean, and glutinous rice enhance glucose-stimulated insulin secretion and insulin sensitivity in 90% pancreatectomized (Px) diabetic rats, a mild and non-obese type 2 diabetic animal model. In the present study we used two different kinds of *kochujang* that contained two different kinds of *meju*. *Meju*, the major component of *kochujang*, takes 2 mo to make if traditional techniques are employed; however, in modern times *meju* can be made in 6 d by inoculating specific bacteria. If the modern form of *meju* has similar qualities and produces the beneficial effects of traditional *meju*, then it would be better to use the former because the fermentation period to make *kochujang* is greatly shortened and the production process is much improved. Therefore, we compared the traditional variety of *kochujang* with the modern variety to see what differences, if any, the two varieties produced with regard to insulin action and insulin secretion.

Materials and methods

Kochujang preparation

Traditional *kochujang* (TMK) was made by a traditional processing method at Moonokrae Foods (Soonchang, Korea), and the modern *kochujang* (MMK) was made through a modified processing method. The two types of *kochujang* were distinguished by the method in which the *meju* was processed. *Meju*, when made in a traditional manner, was prepared by fermenting boiled and then cooled soybeans in the open air for 60 d. This was the process used for making the TMK variety. The other variety of *meju* was made by inoculating *Bacillus subtilus* and *Aspergillus sojae* (a spore suspension diluted to 7 log spore/mL with sterile water) into boiled and cooled soybeans that were fermented for 6 d in a fermentation chamber. This *meju* was used for making MMK, a modern variety *kochujang*. The processes that produced these two kinds of *kochujang* were the same except in the manner of the production of *meju*. In the process to make *kochujang*, the dried red peppers after removing the seeds were ground. Water was boiled, cooled, and mixed with powdered malts for 12 h and their remnants were removed with a sieve. The supernatant and glutinous rice powder were mixed and boiled. After cooling, ground *meju* and red pepper powder were mixed in the water with the glutinous rice. The product, *kochujang*, was fermented for 6 mo outside and the final product was freeze-dried to make *kochujang* powder. *Kochujang* powders made by both methods contained 32.1% glutinous rice, 10.7% *meju* (fermented soybeans), 7.1% powdered malts, 31.4% red pepper powder without seeds, and 18.7% salts.

Animals and diets

Male Sprague-Dawley rats, weighing 211 ± 15 g, were housed individually in stainless-steel cages in a temperature- and humidity-controlled environment (23°C and 60%) on a normal 12-h light/dark cycle. All surgical and experimental procedures were performed in accordance with the recommendations found in the Guide for the Care and Use