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# Corn silk maysin ameliorates obesity *in vitro* and *in vivo via* suppression of lipogenesis, differentiation, and function of adipocytes

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ABSTRACT

Present study was aimed to investigate the potential anti-obesity effects of maysin, a major flavonoid of corn silk, *in vitro* and *in vivo* using 3T3-L1 preadipocyte cells and C57BL/6 mice. Maysin decreased the levels of intracellular lipid droplets and triglycerides (TG), and down-regulated the protein expression levels of C/EBP-β, C/EBP-α, PPAR-γ, and aP2 in 3T3-L1 preadipocyte cells, suggesting that maysin inhibits lipid accumulation and adipocyte differentiation. In addition, maysin was shown to induce the apoptotic cell death in 3T3-L1 preadipocyte cells *via* activation of caspase cascades and mitochondrial dysfunction, which may ultimately lead to reduction of adipose tissue mass. Furthermore, oral administration of maysin (25 mg/kg body weight) decreased weight gain and epididymal fat weight in high-fat diet (HFD)-fed C57BL/6 mice. Administration of maysin also reduced serum levels of TG, total-cholesterol, LDL-cholesterol, and glucose. Taken collectively, these results suggest for the first time that the purified maysin exerts an anti-obesity effect *in vitro* and *in vivo*. These observations may support the applicability of maysin as a potent functional ingredient in health-beneficial foods or as a therapeutic agent to prevent or treat obesity.



## 1. Introduction

Obesity is a risk factor for numerous metabolic disorders such as type 2 diabetes, hypertension, and coronary heart disease and is characterized as a medical condition with increased body weight due to increased adipogenesis [1]. Adipogenesis ultimately result in an increase in both number (hyperplasia) and size (hypertrophy) of adipocytes [1]. Pre-adipocytes can propagate and differentiate into mature adipocytes, a process termed adipogenesis that determines the number of fat cells [2]. The size of a fat cell depends on the lipid accumulation in adipocytes. Therefore, the amount of adipose tissue mass can be regulated by inhibiting adipogenesis, preventing lipid accumulation, and inducing apoptosis in adipose cells [3]. Accordingly, most anti-obesity studies have focused on reducing pre-adipocyte differentiation and proliferation, inhibiting lipogenesis, and enhancing lipolysis.

Corn silk (CS) and its extracts have long been consumed as a traditional folk medicine in many parts of the world to treat various symptoms, such as cystitis, oedema, kidney stones, and diuretic disorders [4]. CS extracts are also currently marketed as a tea in Korea. Recently, many studies have reported various biological activities of CS extracts, including neuroprotective, anti-diabetic, anti-oxidative, and anti-inflammatory activities [4]. CS diets have been reported to have anti-hyperlipidaemic and anti-diabetic properties [5]. However, most of these studies were performed using crude extracts of CS, which are a mixture of various compounds. Thus, information on the biological and pharmacological activities of individual components of CS extracts has been scarce.

The predominant phenolic compounds in CS extracts have been identified as maysin, apimaysin, 3′-methoxymaysin, isoorientin, and luteolin derivatives, among which maysin [rhamnosyl-6-C-(4-ketofucosyl)-5,7,3′,4′ tetrahydroxyflavone], a flavone glycoside containing a rhamnose residue, is the most abundant flavonoid [6,7]. Recently, we have reported that the purified CS maysin exerts anticancer [8], neuroprotective [9], and immunomodulating activities [10]. However, the anti-obesity properties and

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underlying action mechanisms of the purified CS maysin have not yet been extensively explored.

The literature of the purified maysin on anti-obesitic properties is limited. Recently, Park et al. reported that the extract of centipede grass has anti-adipogenic activity [11]. The centipede grass extract used by these authors was composed of mainly 6 different types of flavones, luteolin-6-C-boivinopyranoside, isoorientin 2-*O*-α-L-rhamnoside, orientin, isoorientin, derhamnosylmaysin, luteolin [12], most of which are the precursors of maysin synthesis in this plant. Although Bai et al., reported that they could increase the content of maysin and maysin derivatives in this plant by wounding treatment, the major components of centipede grass extract were still isoorientin and derhamnosylmaysin, not maysin [13]. The maysin content of this extract was only approximately 20% (w/v) at the maximum. Therefore, which individual component of centipede grass extract exerted the observed anti-adipogenic activity of this plant and whether the pure maysin was the key molecule for the anti-obesity activity of this plant was not clear. Furthermore, Kim et al., demonstrated that *Spirodela polyrhiza* extracts which contain orientin and luteolin as major components, which are the maysin derivatives or precursor compounds, not maysin, have anti-obesity activity [14].

In this regard, we assumed that the purified maysin, not those of crude extracts containing low level of maysin, would give clearer evidence for its anti-obesity effects *in vivo* and *in vitro*. Therefore, purified maysin, which was extracted and purified from the corn silk (CS) with over 93% purity according to the methods described by Kim et al., was used to evaluate its anti-obesity effects in this study [10,15]. Specifically, the effects of CS maysin on the apoptosis, differentiation and function of pre-adipocytes during adipogenesis were determined by measuring the lipid accumulation, expression levels of adipogenesis-specific transcription factors and apoptosis signalling proteins in murine 3T3-L1 pre-adipocytes. Herein, we report for the first time that administration of maysin reduced body weight gain, epididymal fat weight and serum levels of triglyceride (TG), total cholesterol (Total-c), low-density lipoprotein cholesterol (LDL-c), and glucose in high fat diet-fed C57BL/6 mice.

Herein, we report for the first time that administration of purified maysin reduced body weight gain, epididymal fat weight and serum levels of triglyceride (TG), total cholesterol (Total-c), low-density lipoprotein cholesterol (LDL-c), and glucose in high fat diet-fed C57BL/6 mice.

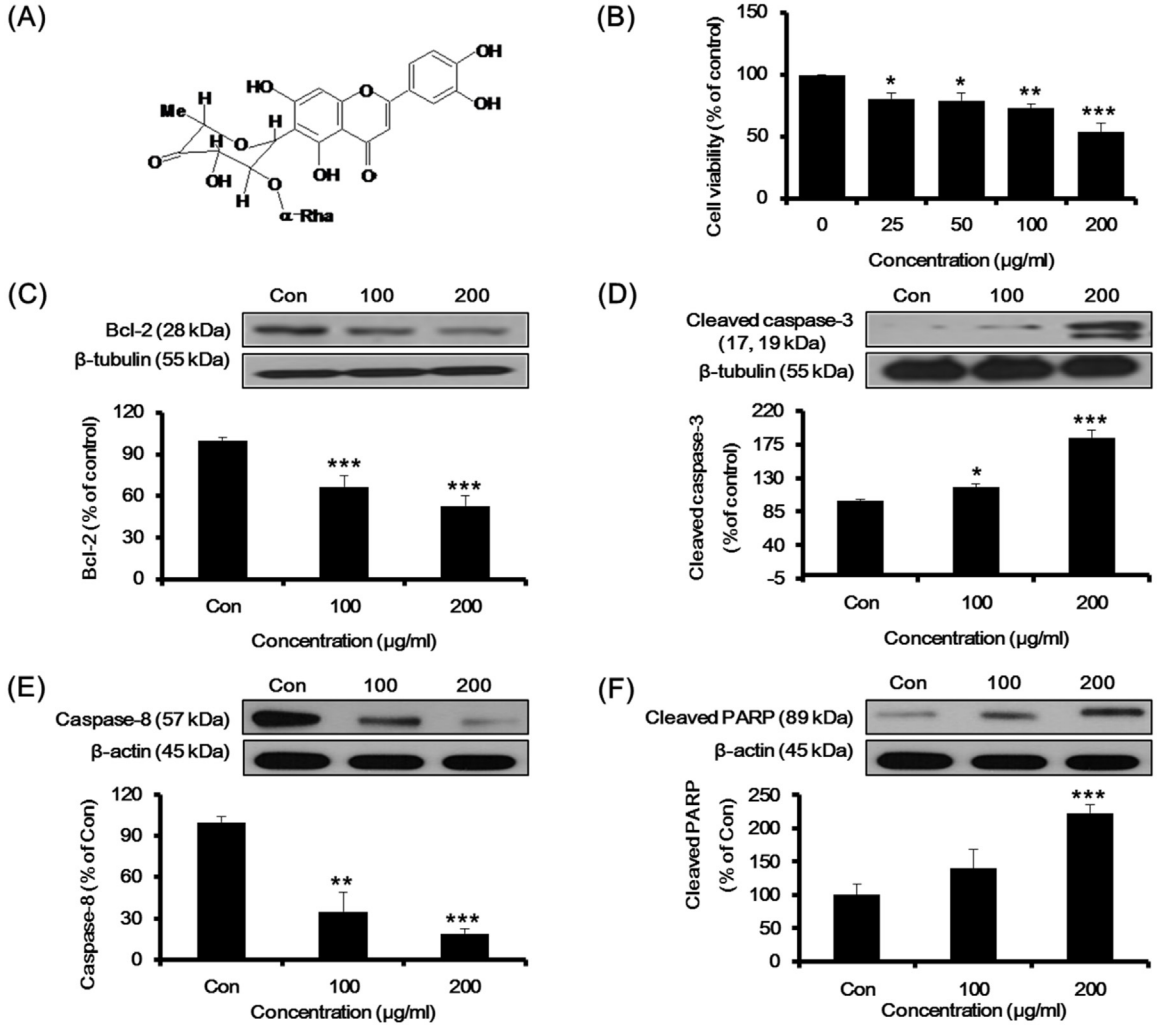


**Fig. 1.** Effects of maysin on the viability and the expression of apoptosis-related signalling molecules of 3T3-L1 pre-adipocyte cells. (A) Structure of maysin. (B) Cells were cultured in DMEM containing maysin (0–200 μg/ml) for 24 h, and cell viability was assessed with a MTT assay. To measure apoptosis, cells were collected 24 h after maysin treatment and processed for western blotting analysis for (C) Bcl-2, (D) cleaved caspase-3, (E) pro caspase-8, and (F) cleaved PARP. β-Tubulin and β-actin were used as a loading control. The data are expressed as percentages normalized to the un-treated control (Con, 0 μg/ml). Data are the means ± SD, $n = 3$. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$, Student's *t*-test compared to Con.