AMP-activated protein kinase mediates insulin-like and lipo-mobilising effects of β-glucan-rich polysaccharides isolated from Pleurotus sajor-caju (Fr.), Singer mushroom, in 3T3-L1 cells

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ABSTRACT
Mushrooms have been used to treat various diseases for thousands of years. In the present study, the effects of Pleurotus sajor-caju mushroom on lipogenesis, lipolysis, and lipo-mobilisation in 3T3-L1 cells were investigated. The β-glucan-rich polysaccharides (Gt) from P. sajor-caju stimulated lipogenesis and lipolytic activities in 3T3-L1 cells. This extract caused an increase in the expression of 8-AMP-activated protein kinase subunitγ-2 (PRAG2) and 8-AMP-activated protein kinase subunitγ-3 (PRAG3) compared to control (untreated) cells. Moreover, Gt induced the expression of hormone-sensitive lipase, adiponectin, triglyceride lipase (adipe), leptin, adiponectin, and glucose transporter-4 in 3T3-L1 cells which may have contributed to the lipolytic and insulin-like activities observed in this study. These findings suggest that Gt is a novel AMPK activator that may be valuable in the formulation of nutraceuticals and functional foods for the prevention and treatment of diabetes mellitus.

1. Introduction
The increasing worldwide incidence of diabetes mellitus (DM) in adults constitutes a global public health burden. The prevalence of DM was estimated to be 2.8% of the general population in the year 2000. It is predicted to be double by the year 2030 to about 360 million (Kanagasabapathy et al., 2012) and India, China and the United States will have the largest numbers of people with diabetes (Prode & Medeiros, 2008). Hence, there is a clear need for effective pharmaceutical intervention for treating DM (Umar, Ahmad, Muhammad, Dogarai, & Maz Soad, 2010). The most effective hypoglycemic drugs are insulin, sulphonylurea derivatives, biguanides, thiazolidinediones and alpha glucosidase inhibitors. However, these agents have undesirable side effects such as obesity, high blood pressure and heart disease (Slovorek, Pastil, & Slavacic, 2008).

Adipose tissue (composed of adipocytes) plays a critical role in lipid metabolism, glucose homeostasis and energy balance. The primary role of adipose tissue is to store energy in the form of triglycerides when energy intake exceeds energy expenditure and to release it in the form of free fatty acids in starvation. Lipolysis and lipogenesis, known as lipogenesis, is the anabolic process of fat cell development (Lee et al., 2010) while lipolysis is the catabolic process that causes the breakdown of triglycerides stored in fat cells to fatty acids and glycerol (Jain et al., 2004). Insulin favours lipid storage through the activation of lipogenesis, lipoprotein lipase synthesis and export to the vascular endothelium and triglyceride accumulation through the production of glycerol-phosphate from glucose. By contrast, adrenocorticosteroids (glucagon and epinephrine) activate lipolysis through binding to a β-adrenergic receptor and production of cAMP in adipose tissue, lipolysis (fasting and exercise) activates AMP-activated protein kinase (AMPK). AMPK acts as a fuel sensor and regulates glucose and lipid homeostasis in adipocytes (Kong, Xin, & Klein, 2006). Once activated, AMPK phosphorylates a number of proteins and mediates the transcription of genes implicated in the regulation of energy metabolism to switch on catabolic pathways that produce ATP and switch off anabolic pathways that consume ATP (David, Fontelle, & Ferre, 2006).

Polysaccharides have been studied extensively because they are known to possess many medicinal properties, such as antiinflammatory, immune-modulating, antioxidant, anti-hypercholesterolemic (Oyetayo, 2008), antiviral, antibacterial, anti-inflammatory and anti-diabetic activities (Nishizawa, Chisti, Fujikura, Sekonyama, & Patane, 2003). In Malaysia, the widely