

CUDRANIA TRICUSPIDATA LEAVES EXTRACT AND ITS INHIBITORY ACTIVITY AGAINST HFD-INDUCED OBESITY IN ZEBRAFISH (*DANIO RERIO*)

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ABSTRACT

The research on screening active ingredients from natural resources that effectively for the treatment of metabolic disorders such as obesity and diabetes has received much attention recently. In this study, the compounds extracted from *Cudrania tricuspidata* (CT) leaves were analyzed through FT-IR, HPLC and GC-MS methods. The results showed that 50% ethanol extract (EtOH50) from CT leaves contains several bio-active substances such as catechins, quercetin, gallic acid, etc. In addition, to evaluate the obesity-preventing activity of the extract, an obesity model in adult zebrafish by high-fat diet was carried out. As the results, EtOH50 extract of CT leaves has good efficacy in preventing weight gain, regulating BMI and hyperglycemia in zebrafish. At the same time, based on qRT-PCR results have confirmed that the anti-obesity effect of CT leaves extract via the modulation of several biomarkers related to lipid metabolism, energy expenditure, cytokines genes. Taken together, these data suggest that *Cudrania tricuspidata* (CT) leaves can be developed as a treatment for obesity.

Keywords: *Anti-obesity, Cudrania tricuspidata, HFD-induced obesity, phytochemicals, zebrafish.*

1. INTRODUCTION

Among metabolic disorder syndrome, obesity and diabetes are considered as one of the health problems worldwide. Obesity remains a major risk factor for the development of chronic diseases such as insulin resistance, type 2 diabetes mellitus, and cardiovascular disease (Sato and Mukai, 2020). Obesity is characterized by expansion of adipose tissue resulting in an increase in size and number of adipocytes. To develop therapy for controlling obesity, the regulation of adipogenesis, a complex process of differentiation of pre-adipocytes to adipocytes, is crucial. Adipogenesis is controlled by expression of several adipogenetic transcription factors and genes (Huang *et al.*, 2014; Hirata *et al.*, 2011). During adipogenesis, both transcription factors enhance each other's expression, and activate the expression of lipid metabolism related proteins, such as fatty acid synthetase (*FAS*), and *Leptin*. Moreover, adenosine 5'-monophosphate-activated protein kinase (*AMPK*), a metabolic master switch between anabolism and catabolism, regulates the activities including cholesterol formation, lipogenesis, and lipolysis (Hardie, 2011; Dong *et al.*, 2014; Ahn *et al.*, 2008; Blagih *et al.*, 2015). Although several methods have become an important treatment for metabolic diseases, there has been no current medication that can efficiently prevent obesity.

The zebrafish model (*Danio rerio*), a fascinating subject for biomedical research in recent years,

has been widely used to effectively assess safety and bio-ability. In the recently results have suggested that zebrafish can serve as a suitable animal model in research into obesity induced by a HFD (Meguro, Hasumura and Hase, 2015a; Tran *et al.*, 2019; Oka *et al.*, 2010; Meguro, Hasumura and Hase, 2015b; Landgraf *et al.*, 2017). One of the important advantages is that they share a significant amount of genetic characteristics with humans and some zebrafish organ systems are similar to those in humans (Oka *et al.*, 2010). Up to 2013, the zebrafish genome was fully sequenced, which is an important basis for understanding and clarifying biological mechanisms (Howe *et al.*, 2013).

Recent reports have indicated that the numerous biological activities of phenolic compounds from natural plants. Currently, the search for natural active ingredients with antioxidant, anti-inflammatory or obesity and diabetes treatment support has received much attention. *Cudrania tricuspidata* (CT) Bureau (*Moraceae*) is cudrang, mandarin melon berry and silkworm thron, which has been used as a traditional Chinese medicine (Jeong, Lee and Kim, 2009). Several functions of bioactive compounds from CT plant have been studied. Phytochemicals isolated from the root barks of *Cudrania tricuspidata*, which exhibited a significant hepatoprotective effect (Tian *et al.*, 2005). Glycoprotein isolated from *Cudrania*

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