

# Neuroprotective effects of vitexin by inhibition of NMDA receptors in primary cultures of mouse cerebral cortical neurons

Le Yang · Zhi-ming Yang · Nan Zhang ·  
Zhen Tian · Shui-bing Liu · Ming-gao Zhao

Received: 30 July 2013 / Accepted: 9 October 2013  
© Springer Science+Business Media New York 2013

**Abstract** The accumulation of glutamate can excessively activate the *N*-methyl-D-aspartate (NMDA) receptors and cause excitotoxicity. Vitexin (5, 7, 4-trihydroxyflavone-8-glucoside, Vit) is a c-glycosylated flavone which was found in the several herbs, exhibiting potent hypotensive, anti-inflammatory, and neuroprotective properties. However, little is known about the neuroprotective effects of Vit on glutamate-induced excitotoxicity. In present study, primary cultured cortical neurons were treated with NMDA to induce the excitotoxicity. Pretreatment with Vit significantly prevented NMDA-induced neuronal cell loss and reduced the number of apoptotic neurons. Vit significantly inhibited the neuronal apoptosis induced by NMDA exposure by regulating balance of Bcl-2 and Bax expression and the cleavages of poly (ADP-ribose) polymerase and pro-caspase 3. Furthermore, pretreatment of Vit reversed the up-regulation of NR2B-containing NMDA receptors and the intracellular Ca<sup>2+</sup> overload induced by NMDA exposure. The neuroprotective effects of Vit are

related to inhibiting the activities of NR2B-containing NMDA receptors and reducing the calcium influx in cultured cortical neurons.

**Keywords** Vitexin · Excitotoxicity · Neuron · Apoptosis · Calcium

## Abbreviation

Caspase	CysteinyI aspartate-specific protease
MTT	(3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide
NMDA	<i>N</i> -methyl-D-aspartate
NMDAR	NMDA receptor
Vit	Vitexin

## Introduction

Vitexin (5, 7, 4-trihydroxyflavone-8-glucoside, Vit) is a c-glycosylated flavone (Fig. 1a), which was found in the *Passion flower* [1], *Phyllostachys nigra* bamboo leaves [2], *Vitex agnus-castus* (chaste tree or chasteberry) [3], *Pearl millet* (*Pennisetum millet*) [4], and *Hawthorn* [5]. Vit has received much attention because of its wide spectrum of pharmacological effects, such as anticancer effect [6, 7], antioxidant activity [8], antidepressant-like effect [9], antinociceptive activity [10], and anti-inflammatory activity [11]. In addition, Vit has neuroprotective effects on pentylenetetrazole-induced seizure in rats. Vit reduces minimal clonic seizures and generalized tonic-clonic seizures by increasing the seizure onset time, which possibly through interaction at the benzodiazepine site of the  $\gamma$ -aminobutyric acid type A receptor complex [12]. However, the effect of Vit on neural excitotoxicity induced by glutamate is not well known.

Le Yang and Zhi-ming Yang have contributed equally to this work.

L. Yang · N. Zhang · Z. Tian · S. Liu (✉) · M. Zhao (✉)  
Department of Pharmacology, School of Pharmacy, Fourth  
Military Medical University, Xi'an 710032, China  
e-mail: liushb1974@yahoo.com.cn

M. Zhao  
e-mail: minggao@fmmu.edu.cn

Z. Yang  
Department of Emergency,  
Urumqi Friendship Hospital, Ürümqi 830049, China

M. Zhao  
Center for Neuron and Disease, Frontier Institute of Science  
and Technology, Xi'an Jiaotong University,  
Xi'an 710032, China