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Review

An overview of neuroprotective and cognitive enhancement properties of lignans from *Schisandra chinensis*

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ABSTRACT

Schisandra chinensis fruits have been traditionally used for thousands of years in Korea, China and Japan to treat various ailments. The fruits contain a variety of bioactive metabolites, especially lignan components have been reported to have various biological activities and have potential in the treatment of numerous neurodegenerative diseases. The lignans from *S. chinensis* are mainly grouped under dibenzocyclooctadiene lignans. Previous studies have reported that the crude extracts and the isolated pure lignan components effectively protect the neuronal cell damage and significantly enhance the cognitive performances. The experimental findings support the extracts and lignan components from *S. chinensis* can be used as new therapeutic agents to treat various neurodegenerative diseases. In the current review, we highlight the lignans from *S. chinensis* as promising resources for the development of natural and effective agents for neuroprotective and cognitive enhancement effects. The lignan extracts and individual compounds from *S. chinensis* were summarized in relation to their neuroprotective and cognitive enhancement activities.

1. Introduction

The genus *Schisandra* belongs to the family of Schisandraceae that comprises about 30 species [1]. Among the various species, *Schisandra chinensis* Turcz. (Baill.) is an important medicinal plant and monograph of its fruit is available in various Pharmacopoeias including Chinese, Japanese, Korean, American, Russian, and International Pharmacopoeias [2]. *S. chinensis* is a dioecious perennial plant and mainly distributed in north-eastern regions of Korea, China and Japan and eastern regions of Russia. In the Chinese Pharmacopoeia, *S. chinensis* has been reported as a tonic and sedative agent and widely used in clinical practice since ancient times [3]. In the traditional medicine, the fruits of *S. chinensis* have been used to treat various disorders including kidney infections, mental problems, asthma, diabetes, cough, spermatorrhea, spontaneous sweating, thirst and insomnia [1,4]. The fruits are the potential source of nutrients and also contain various bioactive metabolites such as lignans, polysaccharides, essential oil, organic acids, and vitamins [5,6]. In the field of drug discovery, *S. chinensis* is an attractive plant, mainly due to the presence of bioactive dibenzocyclooctadiene type lignans in fruits [1].

Lignans are the major bioactive components of the fruits and possess various pharmacological properties such as anticancer, anti-hepatocarcinogenesis, antioxidant, platelet activating factor antagonistic, central nervous system protecting, and anti-inflammatory activities [7,8]. So far, more than 40 lignans have been isolated from this plant and these lignans mainly belong to the dibenzocyclooctane type. Among them, schisandrin, deoxyschisandrin, schisandrin B, schisandrin C, gomisin A, schisanthenol, and schisantherin A are the most important bioactive lignans with various pharmacological properties (Fig. 1). The word schisandrin is also denoted as schizandrin by different authors. In addition, these major lignans have been reported to have similar pharmacological activities. Recently, Chun et al. [9] reviewed the molecular mechanisms behind the protective effects of lignans from the fruits of *S. chinensis* extract against cardiovascular diseases.

In general, neuronal cell damage is the most important factor in many neurodegenerative disorders. Previously, a number of studies reported that the lignans of this plant markedly showed neuroprotective effect against glutamate, amyloid-β, 6-hydroxydopamine (6-OHDA) and lipopolysaccharide (LPS)-induced neurotoxicity [10–13]. Further, the lignans showed protective effects against various neuronal cell damage-mediated diseases including stroke, Alzheimer's disease, Parkinson's disease and other neurodegenerative diseases [12,14]. In addition to neuroprotective effects, the lignans significantly enhance the cognitive performances. Due to multi-targeted actions of these dibenzocyclooctane type lignans, they could represent a promising natural product to develop new and safe neuroprotective drugs.

In the current review, we emphasize the lignan components as

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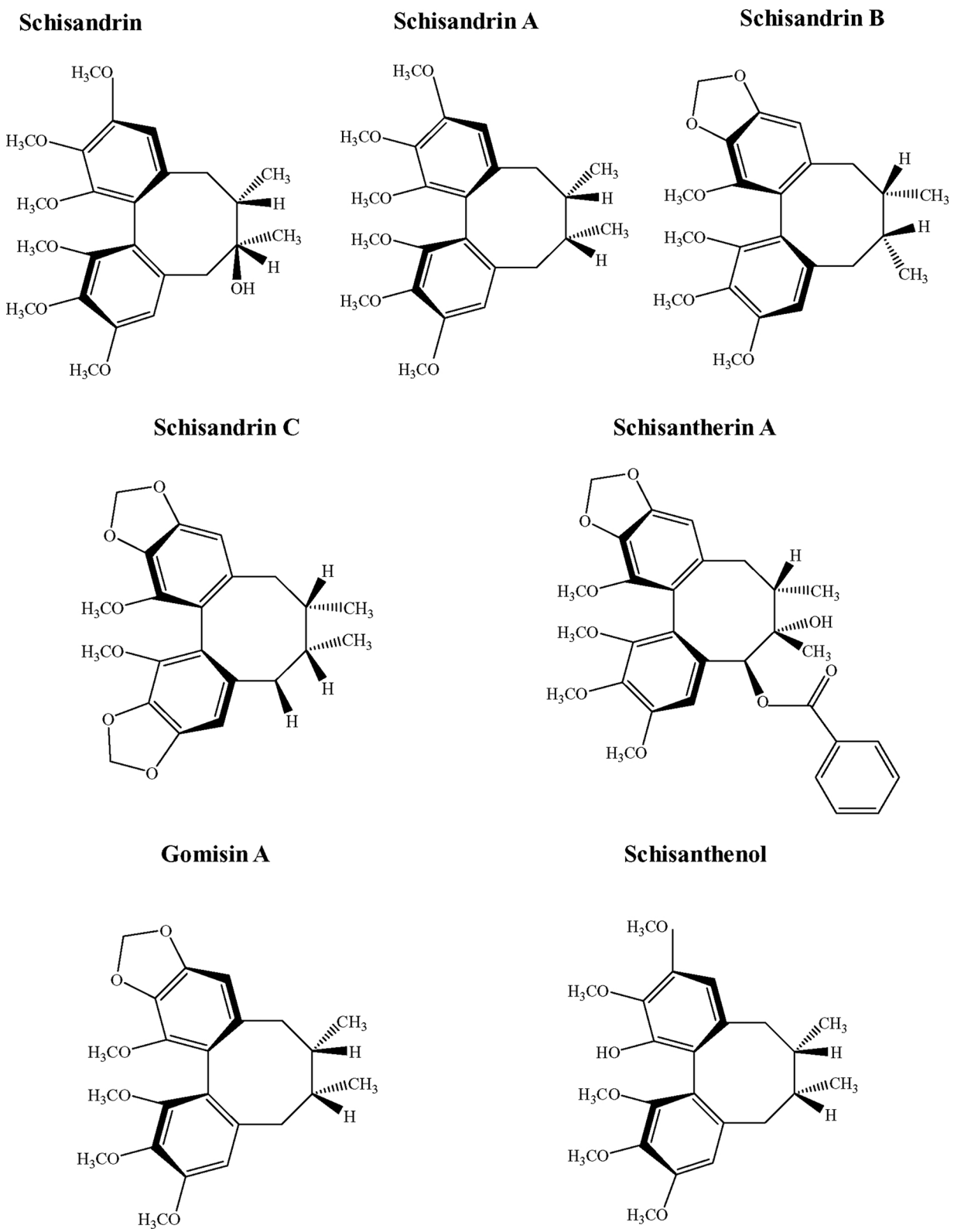

Fig. 1. Chemical structure of some important lignans from *Schisandra chinensis*. These *Schisandra* lignan components are mainly grouped under dibenzocyclooctadiene lignans. In the lignans, the two C6–C3 units are linked by a bond between positions 8 and 8′.

promising resources for the development of natural neuroprotective and cognitive enhancing agents. We summarize the current knowledge about the effects of *Schisandra* lignans on neuroprotective and cognitive enhancement activities under *in vitro* and *in vivo* animal models (Table 1; Figs. 2 and 3). Further, this review provides a sufficient knowledge regarding the neuroprotective properties of lignans from *S. chinensis* and their molecular mechanisms against the neurotoxicity mediated diseases.