Journal of Traditional and Complementary Medicine Vo1. 3, No. 1, pp. 7-15

Journal of Traditional and Complementary Medicine
Journal homepage http://www.jtcm.org

Mulberry (桑葚子 Sang Shèn Zǐ) and its Bioactive Compounds, the Chemoprevention Effects and Molecular Mechanisms *In Vitro* and *In Vivo*

Hui-Pei Huang[1,2,3], Ting-Tsz Ou[1], Chau-Jong Wang[2,3]

[1]Department of Biochemistry, School of Medicine, Chung Shan Medical University, Taichung 40242, Taiwan.
[2]Institute of Biochemistry and Biotechnology, Medical College, Chung Shan Medical University, Taichung 40242, Taiwan.
[3]Clinical laboratory, Chung Shan Medical University Hospital, Taichung 40242, Taiwan.

ABSTRACT

Mulberry (桑葚子 sāng shèn zǐ), a traditional Chinese medicine (TCM) in Taiwan, has many bioactive substances, including polyphenol and anthocyanins compounds. Over the past decade, many scientific and medical studies have examined mulberry fruit for its antioxidation and antiinflammation effects both *in vitro* and *in vivo*. This review thus focuses on the recent advances of mulberry extracts (MEs) and their applications in the prevention and treatment of human cancer, liver disease, obesity, diabetes, and cardiovascular disease. The ME modulates several apoptotic pathways and matrix metalloproteinases (MMPs) to block cancer progression. Mulberry can increase detoxicated and antioxidant enzyme activities and regulate the lipid metabolism to treat hepatic disease resulting from alcohol consumption, high fat diet, lipopolysaccharides (LPS) and CCl_4 exposure. Of the various compounds in ME, cyanidin 3-glucoside (C3G) is the most abundant, and the active compound studied in mulberry research. Herein, the antioxidant and antiinflammatory actions of C3G to improve diabetes and cardiovascular disease are also discussed. These studies provide strong evidence ME may possess the bioactivity to affect the pathogenesis of several chronic diseases.

Key words: Chemoprevention effects, Cyanidin-3-glucoside, Mulberry extracts (ME), Traditional Chinese medicine (TCM)

INTRODUCTION

Mulberry (桑葚子 Sang Shèn Zǐ) belongs to the genus *Morus* of the family Moraceae [Figure 1]. It is widely distributed in Asia, Europe, North America, South America, and Africa. For more than 5000 years, mulberry has been planted for sericulture and has been a valuable resource. The fruit is commonly eaten, often dried, or made into wine, fruit juice, jam, and canned food. Mulberry can grow in a wide range of climatic, topographical, and soil conditions, which can affect the chemical composition and nutritional status of plants. Studies have been reported on the chemical composition and nutritional potentials of some mulberry species worldwide.[1-6]

The deep colored mulberry fruits are rich in phenolic compounds, including flavonoids, anthocyanins, and carotenoids.[7-9] They represent one of the most widely distributed classes of flavonoids in plants. Such natural substances extracted from plants have been shown to have greater antioxidant and antiinflammatory effects and have been used for health maintenance and disease management since the beginning of recorded history.[10] Mulberry is traditionally used in Chinese medicines

Correspondence to:
Dr. Chau-Jong Wang, Institute of Biochemistry and Biotechnology, Chung Shan Medical University, No. 110, Sec. 1, JianguoN. Road, South District, Taichung 402, Taiwan. Tel: +886 424730022, ext. 11670; Fax: +886423248167. E-mail: wcj@csmu.edu.tw

as a pharmaceutical for antifever diuretics, liver protection, eyesight improvement, blood pressure reduction, and cardiovascular disease prevention. Dietary mulberry has been reported to have not only antioxidative, antiinflammatory, antitumor, and antidiabeticeffects, but also cardiovascular, hepato-, and neuro-protectiveproperties[11-16] [Figure 2]. This review will highlight the current understanding of the mulberry and discuss the mechanism of its chemopreventive effects.

Mulberry composition and effectiveness

The proximate composition of mulberry fruits was reported by Imran *et al*.[17] [Table 1]. The moisture contents were in the range of 78.03–82.4 g/100 g fresh weight (FW). The ash contents ranged between 0.46 and 0.87 g/100 g dry weight (DW). The total lipid contents were in the range of 0.48–0.71 g/100 g DW. The total protein contents of the fruit samples were small, varying between 0.96 and 1.73 g/100 g DW. The crude fiber contents of the fruit samples varied widely between 0.57 and 11.75 g/100 g DW. The total carbohydrate contents showed slight variations among the studied fruits samples. The carbohydrate concentration was found to be in the range of 13.83–17.96 g/100 g DW. Interestingly, the main sugars identified in the analyzed mulberry were glucose and fructose, with sucrose not being detected. The calorific value, calculated on a dry weight basis, ranged between 64.11 and 84.22 kcal/100 g. The overall results showed the fruit samples could be a potential source of lipids, proteins, fibers, carbohydrates, and hence energy.

Phenolic acids constitute about one-third of the dietary phenols and are present in plants in free and bound forms.[18] For the different species of mulberry the yield of extract (%), total phenolics and total flavonoids of 6.9–54.0%, 201–2287 mg/100 g DW and 110–1021 mg/100 g DW, respectively, varied significantly as fruit maturity progressed[19] [Table 1]. Among the flavonols, the content of myricetin was found to be high in *Morus alba* (88 mg/100 g DW). The amount of quercetin was as high in *Morus laevigata* (145 mg/100 g DW) at the fully ripened stage. *M. laevigata* and *M. nigra* contained *p*-coumaric acid and vanillic acid while *M. macroura* and *M. alba* contained *p*-hydroxy-benzoic acid and chlorogenic acid as the major phenolic acids. Overall, a trend to an increase in the percentage of extraction yield, total phenolics and total flavonoids, flavonols and phenolic acids was observed as maturity progressed from unripened to fully ripened stages. The nutrient compositions of ME were analyzed in our laboratory as shown in [Table 2].[20] Analysis of ME revealed the presence of gallic acid (0.31%), protocatechuic acid (2.92%), catechin (0.54%), epigallocatechingallate (2.68%), caffeic acid (1.10%), epicatechin (1.21%), *p*-coumaric acid (0.35%), rutin (3.22%), ferulic acid (0.27%), gossypin (0.26%), hesperetin (0.34%), resveratrol (0.35%), quercetin (0.50%), naringenin (0.52%), and hydroxyflavin (0.58%) [Table 3]. Further, HPLC/ESI/MS/MS (High performace liquid chromatography/ electrospray ionization/ Tandem mass spectrometry) analysis of mulberry fruits revealed the presence of four anthocyanins recognized

Figure 1. The fruits of mulberry

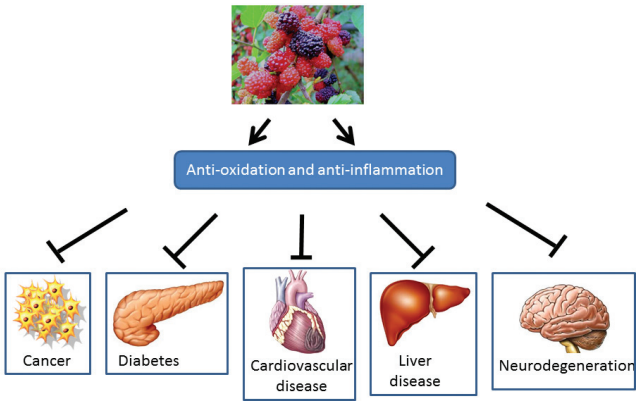

Figure 2. Summary of biological activity of ME on various diseases

Table 1. The proximate composition of mulberry fruits

Composition	Content range
Moisture (g/100 g FW)	78.03- 82.4
Ash (g/100 g DW)	0.46- 0.87
Lipid (g/100 g DW)	0.48- 0.71
Protein (g/ 100 g DW)	0.96- 1.73
Crude fiber (g/ 100 g DW)	0.57- 11.75
Carbohydrate (g/ 100 g DW)	13.83- 17.96
Calorific value (Kcal/ 100 g DW)	64.11- 84.22
Phenolics (mg/ 100 g DW)	201- 2287
Flavonoids (mg/ 100 g DW)	110- 1021

FW: fresh weight; DW: dry weight

Table 2. Composition of Mulberry water extracts

The components of mulberry extracts (%)	
Components	**MWEs**
Phenolic acids	5.12% ± 1.55
Flavonoids	8.23% ± 1.94
Anthocyanins	5.61% ± 1.59
Protein	1.67% ± 0.08
Fat	4.30% ± 0.47
Polysaccharide	24.73% ± 0.24