Pharmacology & Therapeutics 130 (2011) 157–176

Contents lists available at ScienceDirect

Pharmacology & Therapeutics

journal homepage: www.elsevier.com/locate/pharmthera

Associate Editor: I. Kimura

Therapeutic applications of compounds in the *Magnolia* family

Young-Jung Lee [a], Yoot Mo Lee [a,b], Chong-Kil Lee [a], Jae Kyung Jung [a], Sang Bae Han [a], Jin Tae Hong [a,*]

[a] College of Pharmacy and Medical Research Center, Chungbuk National University, 12 Gaesin-dong, Heungduk-gu, Cheongju, Chungbuk 361-763, Republic of Korea
[b] Reviewer & Scientific officer, Bioequivalence Evaluation Division, Drug Evaluation Department Pharmaceutical Safety Breau, Korea Food & Drug Administration, Republic of Korea

ARTICLE INFO

Keywords:
Magnolia
Magnolol
Obovatol
Honokiol
4-*O*-methylhonokiol
Cancer
Nerve
Alzheimer disease
Cardiovascular disease
Inflammatory disease

ABSTRACT

The bark and/or seed cones of the *Magnolia* tree have been used in traditional herbal medicines in Korea, China and Japan. Bioactive ingredients such as magnolol, honokiol, 4-*O*-methylhonokiol and obovatol have received great attention, judging by the large number of investigators who have studied their pharmacological effects for the treatment of various diseases. Recently, many investigators reported the anti-cancer, anti-stress, anti-anxiety, anti-depressant, anti-oxidant, anti-inflammatory and hepatoprotective effects as well as toxicities and pharmacokinetics data, however, the mechanisms underlying these pharmacological activities are not clear. The aim of this study was to review a variety of experimental and clinical reports and, describe the effectiveness, toxicities and pharmacokinetics, and possible mechanisms of *Magnolia* and/or its constituents.

Contents

1. Introduction

The *Magnolia* bark is an herbal material obtained from *Magnolia officinalis* and from other species of the Family Magnoliaceae. The attractive features of a Magnolia tree generally include fragrant and dazzling flowers and petiolate leaves with large stipules, which at first surround the stem, but fall off later and leave a characteristic scar around the node. Among *Magnolia* species, *M. obovata* and *M. officinalis* are very

Abbreviations: ACH, acetylcholine; ACHE, acetylcholinesterase; AIF, apoptosis inducing factor; ATP, adenosine triphosphate; Bax, Bcl2-associated protein; Bcl2, B-cell lymphoma protein-2; B-CLL, B-cell chronic lymphocytic leukemia; CDK, cyclin-dependent kinase; CFA, complete Freud's adjuvant; Cg, carrageenan; COX, cyclooxygenases; ERK, extracellular signaling-regulated kinase; GABA, gamma-aminobutyric acid; IL, interleukin; IAP, inhibitor of apoptosis protein; iNOS, inducible NO synthase; i.v., intravenous; LDH, lactate dehydrogenase; LDL, low-density lipoprotein; LMP1, latent membrane protein1; LPS, lipopolysaccharides; MAPK, mitogen activated protein kinases; Mcl-1, myeloid-cell leukemia sequence 1; mGluR5, metabotropic glutamate 5 receptors; NGF, nerve growth factor; NO, nitric oxide; NMDA, N-methyl-D-aspartic acid; PARP, poly (adenosine diphosphate-ribose) polymerase; PG, prostaglandins; PGE2, prostaglandin E2; PTEN, phosphatase and tensin homolog; ROS, reactive oxygen species; SAMP8, senescence-accelerated-prone 8; SSRI, selective serotonin reuptake inhibitors; TNF, tumor necrosis factor; TPA, tissue plasminogen activator; VSMC, vascular smooth muscle cell; TXA, thromboxanes; XIAP, X-linked inhibitor of apoptosis protein.

* Corresponding author. Tel.: +82 43 261 2813; fax: +82 43 268 273.
E-mail address: jinthong@chungbuk.ac.kr (J.T. Hong).

0163-7258/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.pharmthera.2011.01.010

Table 1
Main components of Magnoliaceous plants and their major characteristics.

Components	MW	Contents on methanol or ethanol extract					Major characteristics
		M. obovata (Matsuda et al., 2001)	*M. obovata* (Min, 2008)	*M. obovata* (Choi et al., 2009)	*M. officinalis* (Yahara et al., 1991)	*M. officinalis* (Lee et al., 2009e)	
Magnolol 5,5′-diallyl-2,2′-dihydroxybiphenyl	266.3 ($C_{18}H_{18}O_2$)	7.65%	2%	0.78%	1%	1.25%	Anti-cancer and anti-inflammatory effects. Anxiolytic and anti-depressant effects, anticonvulsant and anti-nociceptive effects. Anti-stroke. Neurite outgrowth effects. Anti-platelet effects. Relaxation of smooth muscle. Anti-asthmatic effects. Anti-oxidant activity.
Honokiol [2-(4-hydroxy-3-prop-2-enylphenyl)-4-prop-2-enylphenol]	266.3 ($C_{18}H_{18}O_2$)	0.55%	1.25%	1.25%	0.17%	1.81%	Anti-cancer and anti-inflammatory effects. Anxiolytic and anti-depressant effects, anticonvulsant and antinociceptive effects. Anti-stroke. Neurite outgrowth effects. Anti-platelet effects. Relaxation of smooth muscle. Anti-asthmatic effects. Anti-oxidant activity.
4-*O*-methylhonokiol 2-[4-Methoxy-3-(2-propenyl)phenyl]-4-(2-propenyl)phenol	280.4 ($C_{19}H_{20}O_2$)	0.012%	0.21%	0.13%	0.0003%	1.24%	Anti-stroke, neurite outgrowth effects, anti-inflammatory effects, anti-oxidative, anti-Alzheimer effects.
Obovatol [5-prop-2-enyl-3-(4-prop-2-enylphenoxy) benzene-1,2-diol]	282.3 ($C_{18}H_{18}O_3$)	0.33%	0.125%	0.078%	–	–	Anti-cancer effects, anxiolytic effects, anti-inflammatory effects, and anti-oxidant activity.
Eudesmagnolol		0.12%					
Clovanemagnolol		0.0075%					
Caryolanemagnolol		0.0055%					
Eudeshonokiols A		0.0023%					
Eudeshonokiols B		0.0022%	0.0025%				
Eudesobovatols A		0.054%					
Eudesobovatols B		0.031%	0.00125%				
Magnolianin		2.2%					
Syringin		0.36%	0.0125%				
Liriodendrin		0.14%					
(+)-syringaresinol 4'-O-β-D-glucopyranoside		0.027%			0.0016%		
Caryophyllene oxide		0.018%					
α-eudesmol		0.12%					
β-eudesmol		0.22%					
γ-eudesmol		0.11%					
Coumaric acid			0.00075%				
Magaldehyde B			0.0075%		0.02%		
Sinapic aldehyde					0.0078%		
Syringaresinol					0.081%		