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A Short Review on the Chemistry, Pharmacological Properties and Patents of Obovatol and Obovatal (Neolignans) from *Magnolia obovata*

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Abstract – This short review on the chemistry, pharmacological properties and patents of obovatol and obovatal from *Magnolia obovata* is the first publication. Pharmacological properties are focused on anti-cancer, anti-inflammatory, anti-platelet and neuroprotective activities. Obovatol and obovatal were first isolated from the leaves of *M. obovata.* Also reported in the bark and fruits of *M. obovata*, obovatol and obovatal are neolignans i.e., biphenolic compounds bearing a C–O coupling. Other classes of compounds isolated and identified from *M. obovata* include sesquiterpene-neolignans, dineolignans, trineolignan, lignans, dilignans, phenylpropanoids, phenylethanoid glycosides, flavonoids, phenolic acids, alkaloids, sesquiterpenes, ketone and sterols. The anti-cancer properties of obovatol and obovatal involve apoptosis, inhibition of the growth, migration and invasion of cancer cell lines. However, obovatol displays cytotoxicity against cancer cells but not obovatal. Similarly, anti-inflammatory, anti-platelet, neuroprotective, anxiolytic and other pharmacological activities were only observed in obovatol. The disparity in pharmacological properties of obovatol and obovatal may be attributed to the –CHO group present in obovatal but absent in obovatol. From 2007 to 2013, eight patents were published on obovatol with one mentioning obovatal. They were all published at the U.S. Patent and Trademark Office by scientists of the Korea Research Institute of Bioscience and Biotechnology (KRIBB) as inventors and assignee, respectively. Some future research and prospects are suggested.
Keywords – *Magnolia obovata*, Obovatol, Obovatal, Neolignans, Patents

Introduction

Neolignans are plant secondary metabolites derived from the oxidative coupling of phenylpropanoids.[1] They are dimeric structures linking two units. Neolignans are phenolic compounds having a C–C linkage or a C–O linkage. The latter group is sometimes referred to as oxyneolignans.[2] Among *Magnolia* species, bioactive neolignans that are well-studied include those of magnolol, honokiol, 4-*O*-methylhonokiol and obovatol.[3] Biological activities of neolignans include anticancer, estrogenic, antiviral, antimicrobial, neuroprotective, anti-hypersensitive and antioxidant properties. Other classes of compounds isolated from *Magnolia* bark include alkaloids, coumarins, flavonoids, lignans, phenylpropanoids and terpenoids.[3]

The chemistry and pharmacological properties of magnolol and honokiol from *Magnolia officinalis* are well reviewed.[4-7] Their pharmacological activities include anti-oxidant, anti-inflammatory, anti-tumor, anti-diabetic, anti-microbial, anti-depressant, pain control, hormone regulation, gastrointestinal and uterus modulation, neuroprotective, cardiovascular protective, and liver protective properties.[8] Magnolol and honokiol from *Magnolia* species also possess anxiolytic, anti-cancer, anti-arrhythmic, anti-asthmatic, anti-atherosclerotic, anti-stroke, anti-platelet, anti-neurodegenerative, anticonvulsant, antinociceptive and hepato-protective activities.[3,9]

In this article, the chemistry and pharmacological properties of obovatol and obovatal from *Magnolia obovata* are reviewed for the first time. Focus is on their anti-cancer, anti-inflammatory, anti-platelet, neuroprotective and anxiolytic properties. Patents on obovatol published at the U.S. Patent and Trademark Office are presented. Sources of information procured for this short review were from Google Scholar, PubMed, PubMed Central, Science Direct, J-Stage, PubChem, Directory of Open

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Magnolia obovata

Magnolia obovata Thunb. (syn. *Houpoëa obovata* and *Magnolia hypoleuca*) belongs to the family Magnoliaceae. Known as bigleaf magnolia or silver magnolia, the species is native to the deciduous broad-leaved temperate forests of Hokkaido, Japan,[10] is cultivated in China[11] and has naturalized in Korea.[12] In Japan, *M. obovata* occurs as a beautiful tree that is highly valued for its light and soft timber.[13] A deciduous tree that grows up to 20 m in height, the bark is brown, thick and not fissured. Leaf shoots are purplish and leaves are clustered at the end of twigs, leathery, obovate and large. Leaf blades are green and glaucous above, and blue-white and slightly downy beneath. Flowers are large, strongly scented and cup-shaped, producing creamy white tepals and purplish red stamens with yellow anthers in the center of the flower (Fig. 1). Each flower lasts for 34 days and the flowering period of each tree exceeds 40 days (late May to early July) in Japan.[10] Fruits are brilliant red, cone-shaped and have a tapering tip. *M. officinalis*, on the other hand, is native to the mountains of China at altitudes of 300–1500 m.[11] Young shoots are yellowish-grey, flowers are white and the elongated fruits have a rounded tip.[13]

In traditional medicine, the bark and flowers of *Magnolia* species notably those of *M. obovata* and *M. officinalis* are used for the treatment of gastrointestinal disorders, anxiety and allergic diseases including bronchial asthma in Korea, Japan and China.[14] In Japan, prescriptions containing *Magnolia* bark are still being used in clinical practice.[3]

Phytoconstituents

From the bark, fruits and leaves of *M. obovata*, neolignans (17), sesquiterpene-neolignans (9), dineolignans (7), trineolignan (1), lignans (6), dilignans (2), phenylpropanoids (4), phenylethanoid glycosides (5), flavonoids (3), phenolic acids (6), alkaloids (10), sesquiterpenes (3), sterols (2) and ketone (1) have isolated and identified (Table 1).

Fig. 1. Flowers (left) and fruit (right) of *Magnolia obovata*.

Table 1. Compounds isolated and identified from *Magnolia obovata*

No.	Compound type	Compound name	Plant part	Reference
1	Neolignans	4,4'-Diallyl-2,3'-dihydroxybiphenyl ether	Bark	15
2		Fargesone C	Bark	16
3		Honokiol	Fruit	17,18
			Bark	14–16,18–23
4		2-Hydroxyobovaaldehyde	Fruit	17,23
5		Isomagnolol	Fruit	17,23
6		Isoobovatol	Fruit	23
7		Magnaldehyde B	Bark	16,20
8		Magnaldehyde E	Bark	16

Table 1. continued

No.	Compound type	Compound name	Plant part	Reference
9		Magnolol	Fruit	17,18
			Bark	14–16,18–22
10		Magnobovatol	Fruit	17,23
11		4-Methoxyhonokiol	Bark	16
12		9-Methoxyobovatol	Fruit	17,23
13		4-*O*-Methylhonokiol	Bark	14,20,22
14		6′-*O*-Methylhonokiol	Bark	14
15		Obovaaldehyde	Fruit	17,23
16		Obovatal	Leaf	24
			Fruit	17,23
17		Obovatol	Leaf	24
			Fruit	17,27
			Bark	14,16,18,20–22
18	Sesquiterpene-neolignans	Caryolanemagnolol	Bark	14,25
19		Clovanemagnolol	Bark	14,21,25
20		Eudeshonokiols A and B	Bark	14,20,21,25
21		Eudesmagnolol	Bark	14,25
22		Eudesobovatols A and B	Bark	14,21,25
23		Obovatalignans A and B	Fruit	26
24	Dineolignans	Obovatalignans C–I	Fruit	27
25	Trineolignan	Magnolianin	Bark	14,25
26	Lignans	Coumanolignan	Bark	16
27		Liriodendrin	Bark	14
28		Magnolignan C	Bark	16
29		4-Methoxymagnaldehyde B	Bark	16
30		(±)-Syringaresinol	Leaf	28
31		(+)-Syringaresinol 4′-*O*-β-D-glucopyranoside	Bark	14
32	Dilignans	Obovatolins A and B	Bark	29
33	Phenylpropanoids	Coumaric acid	Bark	20
34		*p*-Coumaric acid	Bark	20,30
35		*trans*-*p*-Coumaryl aldehyde	Bark	30
36		Syringin	Fruit	18
			Bark	14,16
37	Phenylethanoid glycosides	Magnolosides A, D, and F–H	Fruit	31
38	Flavonoids	Quercetin 3-*O*-rhamnoside	Leaf	28
39		Quercetin 3-(2′-rhamnosyl rutinoside)	Leaf	28
40		Rutin	Leaf	28
41	Phenolic acids	4-Hydroxybenzaldehyde	Leaf	28
42		4-Hydroxybenzoic acid	Leaf	28
43		4-Hydroxycinnamic acid	Leaf	28
44		Isoferulic acid	Leaf	32
45		Methyl caffeate	Fruit	28
46		Vanillic acid	Leaf	28
47	Alkaloids	Anonaine	Leaf	32

Table 1. continued

No.	Compound type	Compound name	Plant part	Reference
			Bark	15
48		*N*-Acetylanonaine	Leaf	33
49		*N*-Acetylxylopine	Leaf	33
50		Asimilobine	Bark	15
51		*N*-Formylanonaine	Leaf	34
52		Izolaureline *N*-oxide	Leaf	32
53		Lanuginosine	Leaf	32,33
54		Liriodenine	Leaf	32,33
			Bark	15
55		Remerine	Leaf	32
56		Remerine *N*-oxide	Leaf	32
57	Sesquiterpenes	Caryophyllene oxide	Bark	14
58		Cryptomeridiol	Bark	30
59		Eudesmol	Bark	14,30
60	Sterols	Daucosterol	Bark	16
61		β-Sitosterol	Bark	16
62	Ketone	4*R*-4,8-Dihydroxy-β-tetralone	Bark	30

Neolignans are the dominant compound type, and honokiol, magnolol and obovatol are the most commonly isolated neolignans especially from the bark of *M. obovata*. From the leaves, obovatol and obovatal are the only neolignans reported. Flavonoids and phenolic acids are only reported in the leaves of *M. obovata*. It is interesting to note that quercetin glycosides including rutin are the only flavonoids reported.

Neolignans in *M. obovata* can take the form of sesquiterpene-neolignans, dineolignans and trineolignans. Sesquiterpene-neolignans are neolignans attached to sesquiterpenoids.[14] Dineolignans (obovatalignans C–I) have a benzodioxane moiety without or up to two methoxy groups in the molecule.[27] Trineolignan (magnolianin) is characterized by a 1,4-benzodioxane ring and three phenolic hydroxyl groups.[34] The chemical structures of honokiol, magnolol, 4-*O*-methylhonokiol, obovaaldehyde, obovatal and obovatol (neolignans); obovatalignan A and obovatalignan B (sesquiterpene-neolignans); and obovatalignan D and obovatalignan I (dineolignans) are illustrated in Fig. 2. These compounds of *M. obovata* have also been reported in the bark of *Magnolia officinalis*.[35]

Besides neolignans, other compounds such as flavonoids, phenolic acids and alkaloids are also found in *M. obovata* (Table 1). Flavonoids are ubiquitous phenolic compounds having a C6–C3–C6 skeleton in which two benzene rings are linked by a C3 ring while phenolic acids are derivatives of benzoic acid (C6–C1) and cinnamic acid (C6–C3).[36] Alkaloids of great diversity are characterized by having nitrogen atoms as their distinguishing feature.[37]

Obovatol and obovatal

Obovatol (5,4′-diallyl-2,3-dihydroxybiphenyl ether) and obovatal [2,3-dihydroxy-5-(*p*-allylphenoxy) cinnamic aldehyde] are neolignans that were first isolated and identified from the leaves of *M. obovata*.[24] The IUPAC name of obovatol is 5-prop-2-enyl-3-(4-prop-2-enyl-phenoxy) benzene-1,2-diol. Its appearance is pale green, its molecular formula is $C_{18}H_{18}O_3$ and its molecular weight is 282 g/mol. The IUPAC name of obovatal is (*E*)-3-[3,4-dihydroxy-5-(4-prop-2-enylphenoxy)phenyl]prop-2-enal. Its appearance is pale yellow, its molecular formula is $C_{18}H_{16}O_4$ and its molecular weight is 296 g/mol. Both obovatol and obovatal are biphenolic compounds bearing a C–O coupling.[24] Fig. 3 shows the C–O linkage at C1 and C1′. At C9, obovatol has a methylene (–CH_2) group while obovatal has an aldehyde (–CHO) group instead. Previous neolignans isolated and identified from *M. officinalis* such as magnolol and honokiol have a C–C phenol coupling.

Obovatol and obovatal have been reported in the leaves and fruits of *M. obovata*.[17,23,24,41] In the dried bark of *M. obovata*, the content of obovatol has been reported to be 0.26%.[13] Obovatol has also been isolated from the stem bark of *M. obovata*.[21,22] A study on the content of obovatol in the leaves of *Magnolia* species was 0.76% in *M. obovata* compared to 0.57% in *M. officinalis* and

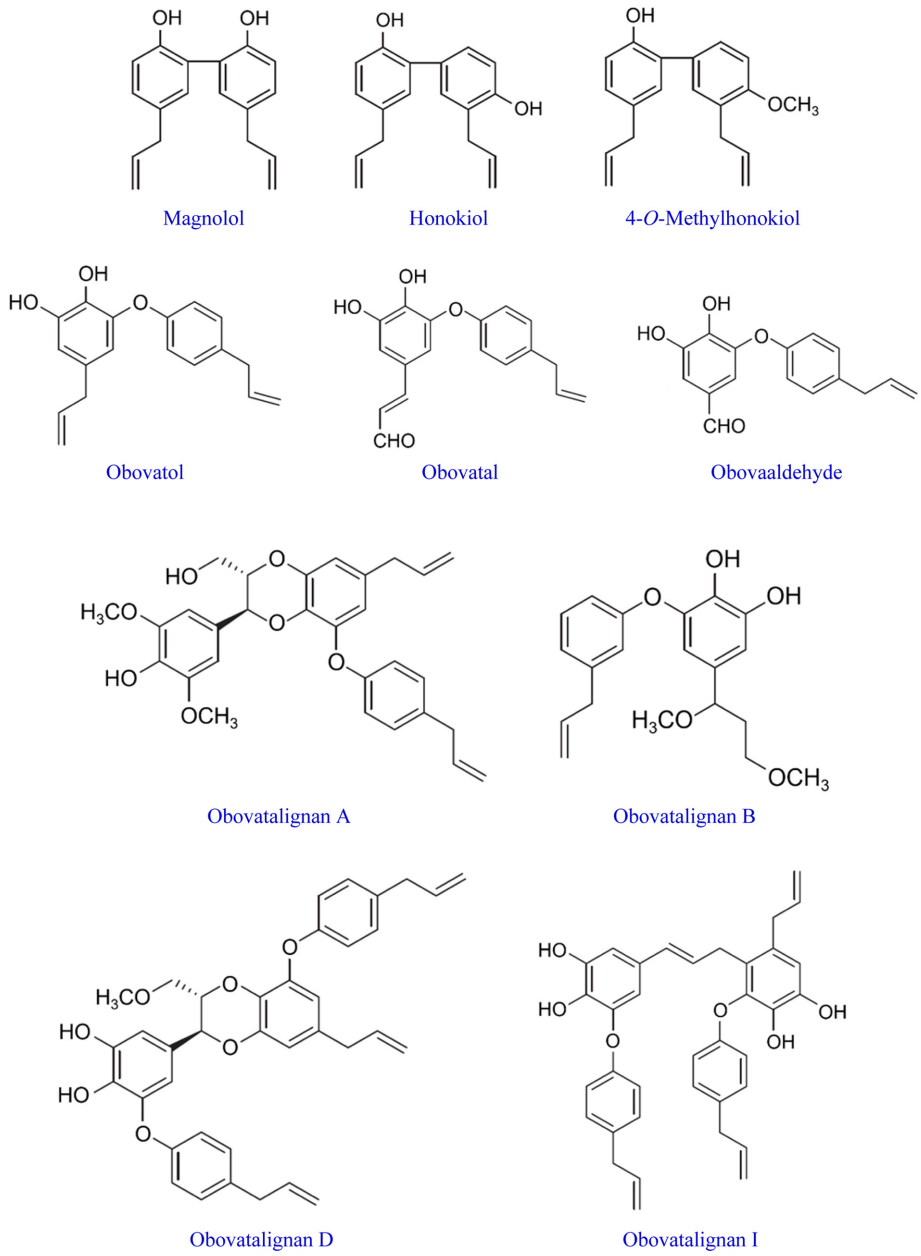

Fig. 2. Chemical structures of some neolignans, sesquiterpene-neolignans and dineolignans of *Magnolia obovata*.

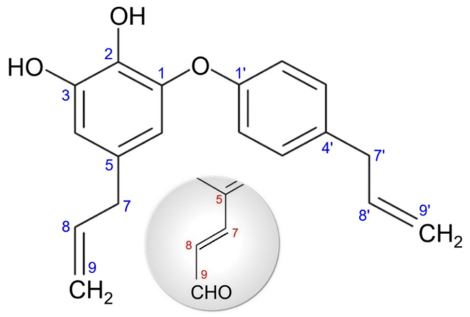

Fig. 3. Chemical structure of obovatol with that of obovatal shown as inset.

1.54% in *M. biloba*.[38] Upon extraction with 2.0 kg of *M. obovata* leaves with methanol, 120 g of the extract was obtained from which 25 g of obovatol and 1.5 g of obovatal were yielded.[39] From 5.3 kg of *M. obovata* dried leaves, a yield of 12 mg of obovatal was obtained.[40]

Magnolol and honokiol are the other neolignans reported in the bark of *M. obovata*.[19] Major components of essential oils of *M. obovata* are β-eudesmol (23.6%) and cadalene (17.2%) in the bark,[41] and (*E*)-β-caryophyllene (23.7%), α-humulene (11.6%) and geraniol (9.10%) in the leaves.[42]

Pharmacological properties

Anti-cancer – Studies have shown that the anti-cancer properties of obovatol are stronger than obovatal but weaker than those of magnolol and honokiol. The cytotoxicity of obovatol and obovatal from fruits of *M. obovata* was tested against a panel of seven cancer cell lines.[27] Results showed that obovatol inhibited SK-BR-3 breast, MCF-7 breast, SK-MEL-5 melanoma, SKOV-3 ovarian, HCT-116 colon and HeLa cervical cancer cells with IC_{50} values of 43–74 μM.[23] HepG2 liver cancer cells were the only exception where obovatol was non-cytotoxic. On the contrary, obovatal showed no cytotoxic activities against all the seven cancer cell lines, with IC_{50} values > 100 μM. From *M. obovata* stem bark, obovatol showed weak cytotoxic activity against the HeLa cervical, A549 lung and HCT-116 colon cancer cells with IC_{50} values ranging from 12.4, 14.1 and 14.4 μg/mL.[21] IC_{50} values of obovatol were 1.2–1.8 time weaker than magnolol, and 1.1–1.3 time weaker than honokiol.

Obovatal isolated from *M. obovata* leaves inhibited HT1080 colon cancer cells.[40] At 20 μM concentration, obovatal inhibited cancer cell growth, migration and invasion *via* the inhibition of matrix metalloproteinase (MMP)-2. It was observed that obovatal reduced the invasion of HT1080 cancer cells by 70% without cytotoxicity.[40] MMPs are zinc-dependent enzymes implicated in tumor growth, invasion and metastasis, and are overexpressed in malignant tumors.[43] MMP inhibitors are known to have the ability to delay primary tumor growth and to block metastasis.

Against LNCaP prostate, PC-3 prostate, HCT116 colon and SW620 colon cancer cells, the treatment of obovatol displayed cytotoxicity with IC_{50} values of 18, 23, 23 and 23 μM, respectively.[44] With tumor necrosis factor-α (TNF-α) and tetradecanoyl phorbolacetate (TPA) added, obovatol treatment yielded stronger cytotoxicity with IC_{50} values of 14 and 18 μM in LNCaP cells, 18 and 18 μM in PC-3 cells, 18 and 18 μM in HCT116 cells, and 19 and 15 μM in SW620 cells, respectively.

Other studies on the growth inhibition of obovatol were focused on prostate (LNCaP and PC-3) and colon (HCT116 and SW620) cancer cells.[44-46] Processes and mechanisms involved induction of apoptosis and inhibition of the NF-κB pathway.[44,45] The inhibitory effects of the combination of obovatol and docetaxel against both prostate and colon cancer cell growth were synergistic and involved greater inactivation of NF-κB.[46] The inhibitory effect of the combination against prostate cancer cell growth is more potent than against colon cancer cells.

The anti-cancer mechanisms of obovatol towards other cancer cells have also been reported. Obovatol inhibited proliferation and induced apoptosis of MM6 acute myeloid leukemia cells through activation of the mitogen-activated protein kinase (MAPK) pathway and the intrinsic apoptotic pathway.[47] Inhibition of A549 and H460 non-small cell lung cancer cells by obovatol involved C/EBP homologous protein (CHOP) activation.[48] Against SCC9 tongue carcinoma cells, inhibition was *via* suppression of the epidermal growth factor (EGF)-mediated Janus kinase (JAK)-signal transducer and activator of transcription-3 (STAT-3) signaling pathways.[49] STAT-3 is a transcription factor that is associated with inflammation, and proliferation, invasion, angiogenesis and metastasis of cancer cells.[50] STAT-3 inhibitors are therefore potential chemopreventive agents. Inhibition of uterine fibroid (leiomyoma) cancer cells by obovatol was accompanied by reduction of various pro-inflammatory cytokines, elevation of caspase-3 and -9, and regulation of apoptosis regulatory proteins such as Bcl2 and Bax.[51]

Anti-inflammatory – From the leaves of *M. obovata*, obovatol inhibited nitric oxide (NO) production in lipopolysaccharide (LPS)-induced RAW264.7 cells with an IC_{50} value of 0.9 μM, possibly *via* the inhibition of nuclear factor (NF)-κB/mitogen activated protein kinase (MAPK) activity.[52] Similarly, obovatol from the fruits of *M. obovata* inhibited NO production in LPS-induced RAW264.7 cells with an IC_{50} value of 6.2 μM.[17] This anti-inflammatory activity was not observed in obovatal.

Obovatol has the ability to attenuates microglia-mediated neuro-inflammation by modulating redox regulation and hence may be a promising drug candidate against neuro-inflammatory diseases.[53] Obovatol inhibits nucleotide-binding oligomerization domain, leucine-rich repeat and pyrin domain containing 3 (NLRP3), absent in melanoma 2 (AIM2), and non-canonical inflammasomes, suggesting that it can be used for the treatment of atherosclerosis.[54] The attenuation of inflammasome by obovatol involved the inhibition of ASC pyroptosome formation and mitochondrial reactive oxygen species (ROS) production. ROS are key signaling molecules that are important in the progression of inflammatory disorders.[55] Their disproportional increase can induce cancer cell cycle arrest, senescence and apoptosis.[56]

Anti-platelet – Isolated from the bark and fruits of *M. obovata*, obovatol inhibited platelet aggregation induced by epinephrine and sodium arachidonate with IC_{50} values of 59 and 54 μM, respectively.[18] Acetylsalicylic acid used as the positive control had IC_{50} values of 53 and 66 μM, respectively. In rabbits, obovatol was reported to inhibit

arachidonic acid-induced platelet aggregation.[57] In addition, some derivatives of obovatol synthesized also possessed anti-platelet properties by inhibiting arachidonic acid-induced platelet aggregation,[58] and by suppressing cyclooxygenase (COX)-1 and lipoxygenase (LOX) activity.[59]

Neuroprotective – Obovatol attenuated LPS-induced memory impairment in mice[60] and in experimental Alzheimer's disease (AD) mice.[61] The improvement in memory impairment was attributed to inhibition of the NF-κB signaling pathway, which can retard or diminish the neurodegenerative process in AD. Concurrently, obovatol was reported to alleviate scopolamine-induced increase in beta-amyloid peptide (Aβ) generation, and β-secretase and acetylcholinesterase (AChE) activities in the brain of mice.[62] Obovatol attenuated neuronal damage not only by reduction in glial-mediated neuroinflammation but also by decreased glial conditioned medium-induced oxidative stress in SH-SY5Y cells.[63] Both studies suggested that obovatol can be a useful agent for preventing the development or progression of degenerative neurological diseases such as AD and Parkinson disease (PD).

Anxiolytic – Obovatol exerts anxiolytic effects on mice that may be mediated by GABA-benzodiazepine-chloride channel receptors.[64] Obovatol (0.2, 0.5 and 1.0 mg/kg) also produced anxiolytic-like effects, comparable to those of diazepam (1.0 mg/kg), an anxiolytic drug. The anxiolytic effects of obovatol were reversed by flumazenil, a benzodiazepine receptor antagonist, suggesting that the anxiolytic effects of obovatol involved the GABA-benzodiazepine receptors complex. Other findings of obovatol included muscle relaxant, inhibition of spontaneous locomotor activity and selectively increased the $GABA_A$ receptors in the amygdala of the mouse brain.[64] Obovatol also bind to benzodiazepine receptors in the cerebral cortex of the mouse brain and increased chloride influx in primary cultured neuronal cells and IMR-32 human neuroblastoma cells. At 0.05, 0.1 and 0.2 mg/kg, obovatol prolonged the sleeping time of mice induced by pentobarbital (42 mg/kg).[65] In addition, obovatol significantly increased chloride influx in the primary cultured cerebellar granule cells and increased the expression of $GABA_A$ receptor subunits. Results showed that obovatol potentiates pentobarbital-induced sleeping time of mice through the $GABA_A$ receptors/chloride channel activation. $GABA_A$ receptors are fast inhibitory neurotransmitter receptors in the mammalian brain, and targets for many drugs that are widely used in the treatment of anxiety disorders and insomnia.[66]

Other properties – Other pharmacological properties of obovatol included antibacterial,[60]antifungal[67-69] and inhibition of cytochrome P450 enzyme[70] activities. Obovatol also protects against restenosis and atherosclerosis,[71] and

Table 2. Highlights of Korean patents on obovatol

No.	Patent no. (date)	Highlight of Korean patent	Reference
1	8,367,736 B2 (Feb 2013)	Composition of *M. obovata* comprising obovatol or obovatal inhibits the growth of cancer cells by suppressing the expression of MMPs and can thus be useful for the treatment of cancer as well as for the inhibition of cancer metastasis.	39
2	0125103 A1 (May 2010)	A composition containing obovatol and its derivatives effectively increased the activity of AMPK and thus plays an important role in the prevention and treatment of diabetes and metabolic syndrome.	80
3	0185215 A1 (Aug 2007)	Obovatol isolated from *M. obovata* can be used as an active ingredient for a pharmaceutical composition or a neuroprotective agent for preventing and treating neurodegenerative diseases such as AD, PD and multiple sclerosis.	81
4	0139668 A1 (Jun 2008)	The use of a composition of *M. obovata* comprising obovatol as an active ingredient for the prevention and treatment of restenosis after a blood vessel injury was illustrated.	82
5	0311354 A1 (Dec 2009)	Alcohol extracts and fractions of *M. obovata* fruits and flower buds, containing obovatol, honokiol and magnolol, inhibit LPS and NO, and have anti-inflammatory activity and low cytotoxicity, can be used for the prevention and treatment of inflammatory diseases.	83
6	0263521 A1 (Oct 2009)	Alcohol extracts and fractions of *M. obovata* fruits and flower buds inhibit cancer metastasis and induce apoptosis by inhibiting PRL-3 over-expressing cells.	84
7	8,268,292 B2 (Sep 2012)	Obovatol from *M. obovata* has potent anti-anxiety activities, verified by animal studies, can be used as the therapeutics or health care food for treating and preventing anxiety disorders involved in CNS.	85
8	8,183,405 (May 2012)	Obovatol derivatives have the ability to inhibit the growth of cancer cells by inducing apoptosis and suppressing metastasis, and are therefore useful for the prevention and treatment of cancer.	86

Abbreviations: AD = Alzheimer's disease, AMPK = AMP-activated protein kinase, CNS = central nervous system, LPS = lipopolysaccharide, MMPs = matrix metalloproteinases, NO = nitric oxide, PD = Parkinson's disease and PRL-3 = phosphatase of regenerating liver 3.

prevents bone loss by inhibiting osteoclastic bone resorption.[72] Extracts of leaves and bark of *M. obovata* possess pharmacological properties such as depressant effects on the central nervous system (CNS),[73,74] and antifungal,[75] anti-diarrhea,[76] skin whitening,[77] synergistic antimicrobial[78] and anxiolytic[79] activities.

Patents

Eight patents on obovatol from *M. obovata* were published from 2007 to 2013 with one mentioning obovatal. The patents were pharmaceutical composition comprising obovatol or obovatal for the treatment of cancer,[39] composition of obovatol and its derivatives for the treatment of diabetes and metabolic syndrome,[80] composition containing obovatol for the prevention and treatment of neurodegenerative diseases,[81] composition containing obovatol for the prevention and treatment of restenosis,[82] composition containing extracts and fractions of *M. obovata* for the prevention and treatment of inflammation diseases,[83] composition containing extracts and fractions of *M. obovata* for the treatment of cancers and inhibition of metastasis,[84] obovatol from *M. obovata* exhibits anti-anxiety activity,[85] and obovatol derivatives or acceptable salts: their preparation and composition for the prevention and treatment of cancer.[86] Highlights of Korea patents on obovatol from 2007 to 2013 are tabulated in Table 2.

All the patents were published at the U.S. Patent and Trademark Office by scientists of the Korea Research Institute of Bioscience and Biotechnology (KRIBB) as inventors and assignee, respectively. Inventors of seven patents were headed by B. M. Kwon, and one patent by T. L. Huh, both from KRIBB. In the patents, obovatol has been implicated in the prevention and treatment of cancer, diabetes, restenosis and anxiety, including neurodegenerative and inflammatory diseases.

Conclusion

Obovatol and obovatal are neolignans isolated and identified in the bark, leaves and fruits of *M. obovata.* Studies on the pharmacological properties of obovatol and obovatal warrant further studies. Obovatol displayed cytotoxicity against cancer cell lines but not obovatal. The disparity in anti-cancer properties may be attributed to the $–CH_2$ group of obovatol and the –CHO group of obovatal. In addition, anti-inflammatory anti-platelet, neuroprotective and other pharmacological activities were only observed in obovatol. Research on obovatol is on-going with publications as recent as 2020 and 2021. The isolation and identification of two new dilignans (obovatolins A & B) from the bark of *M. obovata* in 2021 indicates that opportunities for scientific discovery still prevail. The prospects for commercialization of research findings on obovatol are bright as eight patents have been published by Korean scientists at the U.S. Patent and Trademark Office.

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