

Review

The pharmacology and clinical properties of *Kalopanax pictus*

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Kalopanax pictus is known as Castor-Aralia or Prickly Castor-oil tree. *K. pictus* extracts have been used for dietary health supplements and are an important area in drug development with numerous pharmacological functions in East Asia; however, their pharmacological functions have not been introduced in Western countries. This paper briefly reviews the most relevant experimental data on the pharmacological actions of *K. pictus* to overcome the lack of information on this plant. *K. pictus* extracts have proved to be effective in the treatment of inflammation and were shown to have a number of pharmaceutically relevant benefits that include anti-rheumatoidal, hepatoprotective, anti-diabetic, anti-cancer effects, etc. There are a few known active pharmacological components such as kalopanaxsaponin A and I. Although the molecular mechanisms of most of the effects are not fully understood, major mechanisms seem to involve the interplay between active components and signaling mediated by phosphorylation events during stress adaptation.

Key words: *Kalopanax pictus*, araliaceae, Kalopanaxsaponins A, anti-inflammatory, anti-rheumatoidal activity, anti-diabetic, hepatoprotective effect.

INTRODUCTION

Kalopanax pictus (synonyms: *Kalopanax septemlobus*), common name Castor-Aralia or Prickly Castor-oil tree, is a deciduous tree of the Araliaceae family that contains around 900 species and 80 genera in the world and is mainly distributed across East Asia (Chung, 1974). This tree grows up to 30 m high (Figure 1A) and the stems have stout spines which are up to 1 cm long (Figure 1D). The alternate leaves, 15 - 35 cm across, have five or seven palmate lobes, with a finely toothed margin (Figure 1B). The *K. pictus* var. *Maximowiczii*, variety of *K. pictus*, are deeply lobed and almost dissected to the center of the leaf (Figure 1C). In late summer, the plants begin to form flowers (Figure 1E) that are umbels across at the

apex of the stem, with 4 - 5 small white petals (Chung, 1974). This plant has been cultivated as an ornamental tree in Europe and North America due to its tropical appearance, while in East Asia it has been used in traditional herbal medicine to treat rheumatic arthritis and neurotic pain.

In ancient oriental medicine, its stem bark was administered to patients to treat neurotic pain (Jiangsu Medical College, 1977) and used in oriental medicine to treat neuralgia, rheumatic arthritis, lumbago, furuncle, carbuncles, wounds, diarrhea and scabies (Moon, 1991; Namba, 1994; Kim, 1996). Since hederagenin glycosides from *K. pictus*, named kalopanaxsaponins A (1) and B (2), were isolated and the structure was determined (Khorlin et al., 1966), a number of chemical constituents such as polyacetylenic compounds, tannin, flavonoid, coumarin glycosides, alkaloid, essential oils and resin have been isolated from this plant (Shao et al., 1989, 1990; Lee and Hahn, 1991; Park and Ha, 1991; Sano et al., 1991). From current pharmaceutical studies, additional pharmaceutical applications of *K. pictus* have been revealed such as anti-inflammatory and anti-rheumatoidal effects. Although these effects have been introduced in some international

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Abbreviations: IL-1, Interleukin-1; TNF, Tumor Necrosis Factor; FCA, Freund's Complete Adjuvant; RA, Rheumatoid Arthritis; MAPK, Mitogen-Activated Protein Kinase; NF-κB, Nuclear Factor-κB; PMA, Phorbol-12-Myristate-13-Acetate.

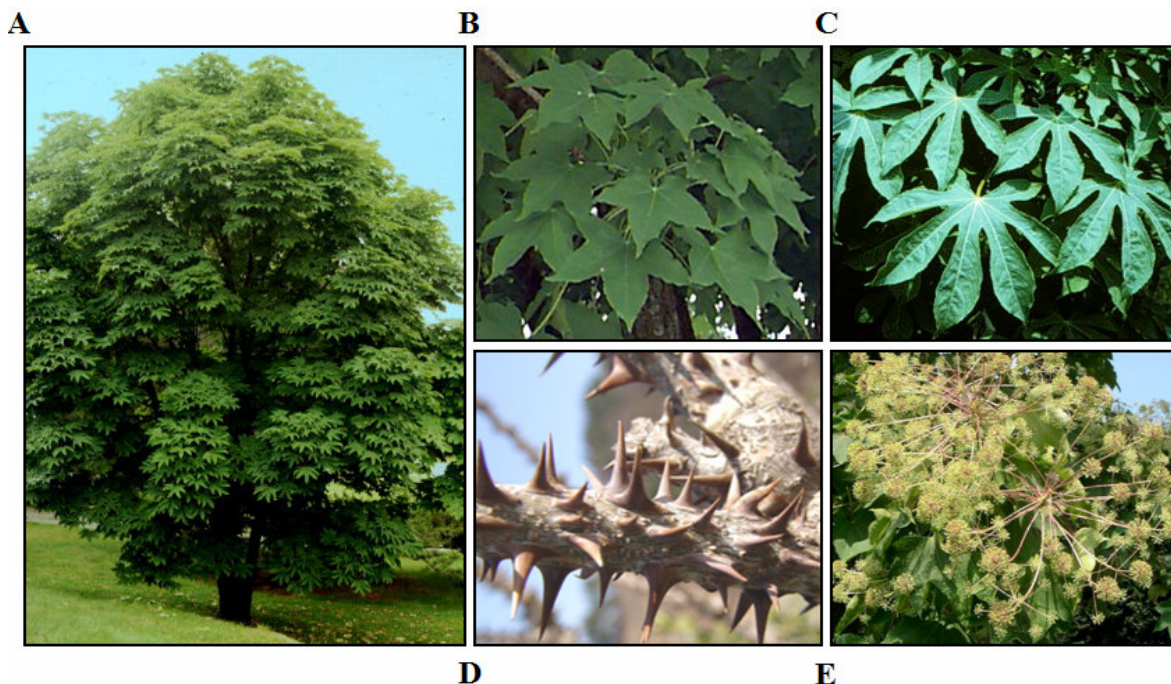


Figure 1. *Kalopanax pictus* (Castor-Aralia or Prickly Castor-oil tree) is characterized by spiny stems and alternate leaves with seven palmate lobes and a finely toothed margin. (A) *Kalopanax pictus*, (B) leaves, (C) leaves of *Kalopanax pictus* var. *Maximowiczii*, (D) stem and (E) flower. Source for A, B and C: <http://www.hort.uconn.edu/Plants/>, D and E: <http://blog.daum.net/wildplay/>.

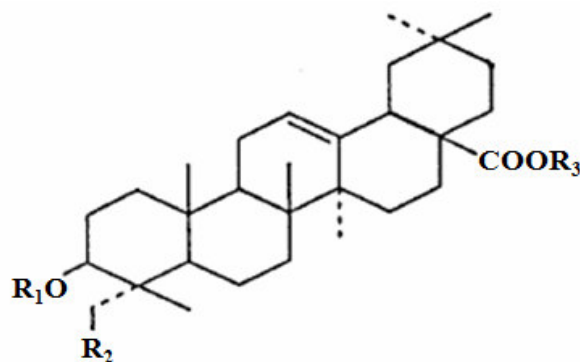
journals, most previous works and different pharmaceutical applications have been filed in non-indexed journals and by several patent holders.

The aim of this present review is to introduce *K. pictus* as a potent medicinal plant by highlighting its traditional applications in East Asia, the recent findings for novel applications and *K. pictus*'s relevant pharmacological mechanisms related to inflammation and rheumatoid arthritis. We have also particularly tried to cover original publications on *K. pictus* that have been published in localized Asian Journals that are not readily available in standard databases.

Chemical composition

The commonly known phytochemical compounds from *K. pictus* are saponins and phenol compounds. Since two hederagenin saponins, kalopanaxsaponin A (1) and B (2), were isolated from this plant in 1966 (Khorlin et al., 1966), a number of other hederagenin saponins (Figure 2), named kalopanaxsaponin C (3), D (4), E (5), F (6), G (7), H (8), I (9), J (10) and K (11), sapindoside C (12) and septemloside III (13), have been isolated and analyzed from the leaves, roots and bark of *K. pictus* (Shao et al., 1989, 1990; Lee and Hahn, 1991; Park and Ha, 1991; Sano et al., 1991; Choi et al., 2002b, Kim et al., 1998b, 2002a, 2002c; Yin et al., 2005). These saponins are contained in *K. pictus* extracts as monodesmosidic or

bidesmosidic forms of hederagenin. Among the hederagenin monodesmosides, the pharmacological functions of kalopanaxsaponin A (1) and I (9) have been ascribed anti-inflammatory and anti-rheumatoidal effects (Choi et al., 2001b; Kim et al., 2002c). However, there is no experimental evidence regarding the pharmacological effects of hederagenin bidesmosides. In addition, lignans, isoquinoline alkaloid (erythrakine (14)) and a number of phenolic compounds have also been isolated from this plant (Jiangsu Medical College, 1977). In 1991, several phenolic compounds from *K. pictus* bark (Figure 3) were isolated and reported (Sano et al., 1991). Among these, two substances (called liri dendrin (15) and syringin (17)) are lignans and have shown hepatoprotective effects in mice during response to carbon tetrachloride (CCl_4) (Lee et al., 1995). Phenolic glycosides and phenylpropanoid glycosides such as ferulyaldehyde (16), 6'-O-(4-O- α -L-rhamnopyranosyl)-syringate (coniferin), 4-O-[6-O-(4-O- α -L-rhamnopyranosyl)-syringyl]- β -D-glucopyranoside (2-methoxyhydroquinone), coniferyl alcohol (18), methyl syringate (21), protocatechuic acid (19), glucosyringic acid and chlorogenic acid (20) were isolated from the phenolic fraction of the methanol extracted from the *K. pictus* bark (Sano et al., 1991). Some of these compounds like protocatechuic acid (19) and chlorogenic acid (20) have been reported to protect cells against oxidative stress, acting as antioxidant agents (Babich et al., 2002; Johnston et al., 2003). In addition, protocatechuic acid 19



	R ₁	R ₂	R ₃	Trivial name	Ref.
1	α -L-Rha-(1→2)- α -L-Ara	OH	H	Kalopanaxsaponin A	Khorlin et al., 1966
2	α -L-Rha-(1→2)- α -L-Ara	OH	α -L-Rha-(1→4)- β -D-Glc-(1→6)- β -D-Glc	Kalopanaxsaponin B	Khorlin et al., 1966
3	α -L-Rha-(1→2)-[β -Glc-(1→2)]- α -Ara	OH	α -L-Rha-(1→4)- β -D-Glc-(1→6)- β -D-Glc	Kalopanaxsaponin C	Shao et al., 1989
4	α -L-Rha-(1→2)-[β -Glc-(1→2)]- α -Ara	H	α -L-Rha-(1→4)- β -D-Glc-(1→6)- β -D-Glc	Kalopanaxsaponin D	Shao et al., 1989
5	β -Glc-(1→3)- β -GlcUA	H	H	Kalopanaxsaponin E	Shao et al., 1989
6	α -Ara-(1→2)-[β -Glc-(1→3)]- β -GlcUA	H	β -Glc	Kalopanaxsaponin F	Shao et al., 1989
7	H	OH	α -L-Rha-(1→4)- β -D-Glc-(1→6)- β -D-Glc	Kalopanaxsaponin G	Shao et al., 1991
8	β -D-Xyl-(1→3)- α -L-Rha-(1→2)- α -L-Ara	OH	α -L-Rha-(1→4)- β -D-Glc-(1→6)- β -D-Glc	Kalopanaxsaponin H	Choi et al., 2002b
9	β -D-Xyl-(1→3)- α -L-Rha-(1→2)- α -L-Ara	OH	H	Kalopanaxsaponin I	Kim et al., 1998b
10	β -D-Glc-(1→4)- β -D-Xyl-(1→3)- α -L-Rha-(1→2)- α -L-Ara	OH	H	Kalopanaxsaponin J	Kim et al., 2002a
11	β -D-Glc-(1→4)- β -D-Xyl-(1→3)- α -L-Rha-(1→2)- α -L-Ara	OH	α -L-Rha-(1→4)- β -D-Glc-(1→6)- β -D-Glc	Kalopanaxsaponin K	Kim et al., 2002a
12	β -D-Glc-(1→4)- β -D-Xyl-(1→3)- α -L-Rha-(1→2)- α -L-Ara	OH	H	Sapindoside C	Kim et al., 2002c
13	β -D-Xyl-(1→4)- β -D-Xyl-(1→3)- α -L-Rha-(1→2)- α -L-Ara	OH	β -D-Xyl-(1→3)- β -D-Xyl-(1→2)-[α -L-Rha-(1→4)- β -D-Glc-(1→6)]- β -D-Glc	Septemloside III	Yin et al., 2005

Figure 2. Structures of hederagenin saponins from *Kalopanax pictus*. Ara: arabinopyranosyl, Rha: rhamnopyranosyl, Glc: glucopyranosyl, GlcUA: glucuronopyranosyl and Xyl: xylopyranosyl.

induced the apoptosis of human leukemia cells and inhibited the apoptosis of neural stem cells (Babich et al., 2002; Guan et al., 2009).

POTENTIAL OF *K. pictus* IN PHYTOTHERAPIES

K. pictus is used in traditional Korean and Chinese medicine to treat rheumatoid arthritis and neurotic pain. Although the anti-inflammatory and anti-rheumatoid effects of *K. pictus* bark extract have been well documented and are a potential non-steroidal anti-inflammatory herbal drug in East Asia, so far the therapeutic potential has not been exploited by Western countries. In recent years, accumulating evidence indicates that not only is *K. pictus* important in treating inflammation and rheumatoid arthritis, but that it also contains anti-

diabetic, anti-fungal, anti-cancer and anti-malarial effects.

Anti-inflammatory effect

Although a number of steroidal or non-steroidal anti-inflammatory drugs have been developed, researchers are changing their focus to natural products to develop new anti-inflammatory agents because of the side-effects of chemical drugs.

The stem bark of *K. pictus* has been functionally used as a traditional crude drug for the treatment of various inflammations and there are several reports describing the influence of *K. pictus* extracts on inflammation (Byun and Shin, 1986; Lee et al., 2001; Kim et al., 2002c, 2004; Li et al., 2002, 2003; Lee and Li, 2003; Jang et al., 2005; Park et al., 2005). In animal models, the methanol extracted from *K. pictus* bark has shown similar anti-inflammatory effects to aspirin, a well-known non-steroid

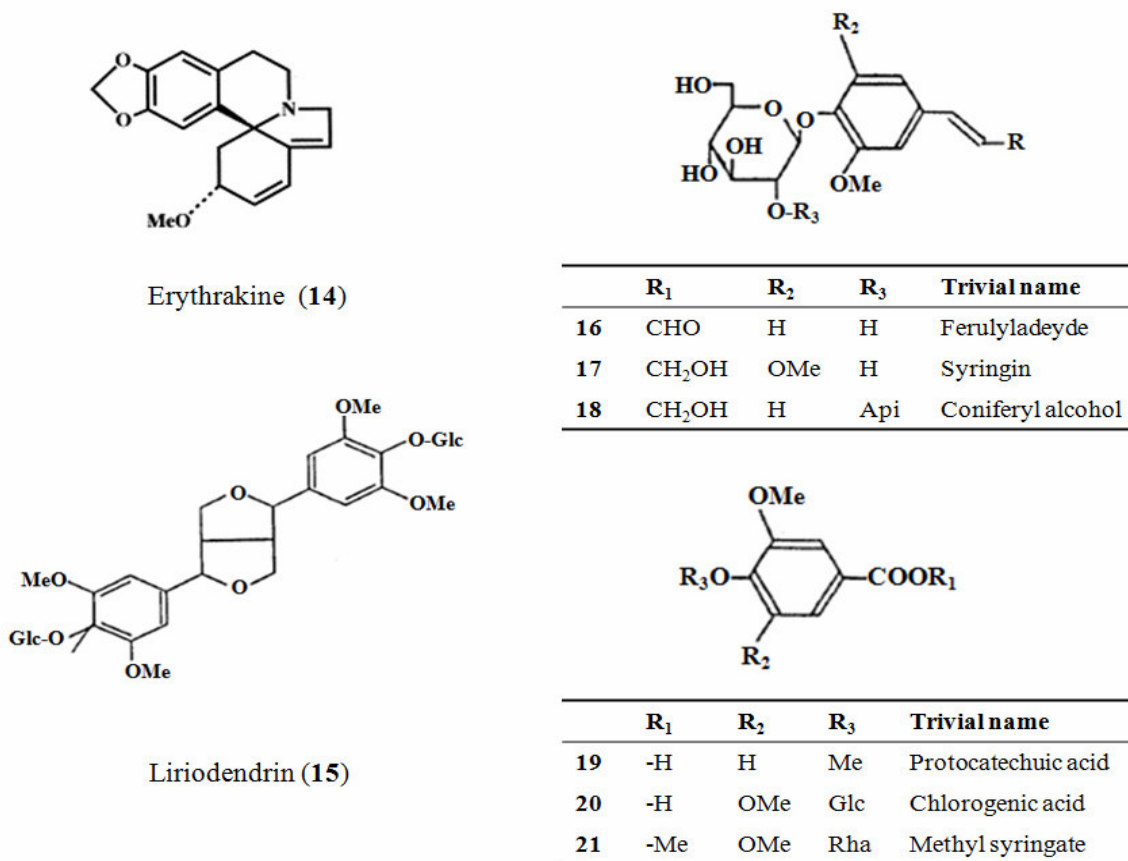


Figure 3. Structures of phytochemical compounds from *Kalopanax pictus* (data from Jiangsu Medical College, 1977; Sano et al., 1991). Rha: rhamnopyranosyl, Api: apifuranosyl.

anti-inflammatory drug (NSAID), via the inhibition of acetic acid-induced vascular permeability in mice and leucocyte emigration in the CMC-pouch of rats (Lee et al., 2001). The alkaline hydrolysate of the butanol-soluble fraction of the methanol extracted from *K. pictus* stem bark caused the inhibition of carrageenan-induced edema and vascular permeability induced by acetic acid, whereas the butanol-soluble fraction of the methanol extract did not have any effect (Li et al., 2003). The differential effect of the butanol-soluble fraction and the modified butanol-soluble fraction observed with alkaline hydrolysate indicates that the active compounds might be the hederagenin monodesmosides rather than the hederagenin bisdesmosides. This can be assumed because bisdesmosidic saponins usually enrich the butanol-soluble fraction of the methanol extracted from *K. pictus* stem bark (Choi et al., 2000b) and can be transformed into monodesmosidic saponines through ester bond cleavage (Ohtani et al., 1984). In fact, numerous studies on the isolation of anti-inflammation compounds from *K. pictus* bark extracts suggest that kalopanaxsaponin A (1) and I (9) and hederagenin monodesmosides, have anti-inflammatory effects on RAW 264.7 murine macrophage cells stimulated with

bacterial endotoxic lipopolysaccharide (LPS) (Kim et al., 2002c) and in rats during a response to Freund's complete adjuvant (FCA) (Choi et al., 2002b; Li et al., 2002, 2003).

During inflammation, the activated interleukin-1 (IL-1) and tumor necrosis factor (TNF) up-regulate the proinflammatory, type II phospholipase (PL) A₂, cyclooxygenase (COX)-2 and induce nitric oxide (NO) synthesis, resulting in increased prostaglandins (PGs: synthesized by COX) and NO synthesis. More relevant to pain and inflammation is the increase in PG-E₂ mediated by IL-1 or/and TNF (Charles and Dinarello, 2000). Therefore, the inhibition of COX has been targeted by anti-inflammatory drugs to reduce pain and inflammation. In fact, aspirin exhibits this anti-inflammatory property by inhibiting COX activity (Vane and Botting, 2003). In the macrophage cell line RAW 264.7, kalopanaxsaponin A (1) and I (9) inhibited the production of TNF- α and resulted in down-regulation of iNOS and COX-2 expression during LPS stimulation. In addition, kalopanaxsaponin A (1) inhibited the DNA binding activity of nuclear factor- κ B (NF- κ B: TNF- α transcription factor) by blocking I κ B- α (inhibitor of NF- κ B) degradation induced by LPS in a dose-dependent manner (Kim et al., 2002c). Taken together, these findings

indicate that the anti-inflammatory activity of kalopanaxsaponin A (1) and I (9) might interact with the inflammation cascade triggered by IL-1 and TNF. Although the impact of hederagenin monodesmosides from *K. pictus* on human metabolism in the context of anti-inflammation is still a matter of further investigation, these findings support the possibility of utilizing phytotherapy in the treatment of inflammation. It would be interesting to investigate the interaction between hederagenin monodesmosides and mitogen-activated protein kinase (MAPK) cascades. Although the production of TNF is regulated by the NF- κ B activated by MAPKs (Lee et al., 1994; Han et al., 1995; Meldrum et al., 2001), it has been shown that the activation of MAPKs by TNF- α was involved in the induction of inflammation in lung epithelial cells (Ekstrand-Hammarstroem et al., 2006). Further understanding of the relationship between MAPK activation and hederagenin monodesmosides will give a clear view of hederagenin monodesmosides during the anti-inflammatory process.

Anti-rheumatoid activity

Rheumatoid arthritis (RA) may be defined as an autoimmune disease characterized by chronic inflammation and subsequent tissue damage (Billingham, 1983; Cassim et al., 2002) and intimately associated with an imbalance in the cytokine network (Calixto et al., 2004). Even though significant attention has been paid to plant based drugs, the development of herbal medicines to treat autoimmune diseases is still in the preliminary stages.

The extended studies of the pharmacological function of *K. pictus* in animal models with induced chronic inflammation strongly support not only the anti-inflammatory activity, but also the anti-rheumatoid potential of *K. pictus* (Choi et al., 2000a, 2001b, 2002a, b; Kim et al., 2002a; Lee and Li, 2003; Li et al., 2003; Kim and Lee, 2007). The EtOA-soluble fraction of methanol extracted from *K. pictus* stem bark (500 mg/kg) inhibited the activity of lactate dehydrogenase (LDH) in blood from RA induced in rats through injections of FCA. In addition, the significantly inhibited activity of LDH (72.8% reduced activity in comparison to the control group) was seen when 20 mg/kg of kalopanaxsaponin A (1) was intraperitoneally injected into RA induced rats (Choi et al., 2001b). LDH activity is known to increase in rheumatoid synovial fluid and is derived from the disruption of leucocytes (Lindy et al., 1971). The inhibition of LDH activity by treatment with kalopanaxsaponin A (1) indicates that kalopanaxsaponin A (1) might be directly, or indirectly, regulating self-immunological reactions such as cell destruction. A more careful analysis using kalopanaxsaponin A (1) showed that the intraperitoneal administration of 20 mg/kg kalopanaxsaponin A (1) caused a significantly decreased level of C-reactive protein and RA-factor and inhibited the activity of the trypsin inhibitor and serine protease in serum from RA induced rats. This

suggests that the anti-rheumatoid effect of kalopanaxsaponin A (1) is mediated by inhibiting kinin formation which regulates the accelerating capillary enlargement and leucocyte migrations (Choi et al., 2002b).

Acupuncture, electroconvulsive therapy, biofeedback and diet cures have been used as complementary therapies for RA, even though these may just help ease and manage pain. Interestingly, there are some reports on the effect of herbal-acupuncture on collagen-induced arthritis (Kim and Lee, 2007). When 1% of acupuncture solution (in D-PBS) manufactured from the ethyl alcohol-soluble fraction of water extracted from *K. pictus* stem bark was injected into the Joksamni (ST36, a space between the tuberosity of the tibia and the head of the fibula, medial to the tibialis anterior muscle) of mice with collagen-induced arthritis (CIA), the incidence of arthritis and arthritis index significantly decreased compared with those of the treated control groups. The group injected with the acupuncture solution exhibited significantly decreasing levels of cytokines, IL-6, IL-1b, interferon (IFN)- γ and TNF- α in serum of CIA mice (Kim and Lee, 2007) and displayed a reduction in cartilage destruction and synovial cell proliferation in histological analysis of the section from CIA mice joints. Although the active compound from the acupuncture solution and the reaction mechanism are still unclear, these findings are important evidence for the practical application of *K. pictus* in the treatment of RA.

Anti-diabetic effect

Diabetes mellitus is a metabolic disorder and results in high blood sugar levels due to defective insulin production (the typical diabetes cases in children, type I insulin-dependent diabetes mellitus/ IDDM) or the combination of resistance to insulin action and an inadequate compensatory insulin-secretory response (the most common type of diabetes cases, type II noninsulin-dependent diabetes mellitus/ NIDDM) (American Diabetes Association, 2005). A wide array of plant derived active principles have been suggested for the possible treatment of NIDDM by improving insulin sensitivity and/or reducing glucose production by inhibition of α -glucosidases (Grover et al., 2002; Yeh et al., 2003; Abesundara et al., 2004).

K. pictus extracts have also been investigated for their effect on diabetes treatment (Kim et al., 1998a; Park et al., 1998; Ko et al., 2002). In mouse-derived 3T3-L1 adipocyte, a significantly increased level of glucose uptake has been observed when 3 μ g/ml insulin with 0.3 μ g/ml 10 or 30% methanol-soluble fraction of water extracted from *K. pictus* stem bark was used in treatment.

The increased level of glucose uptake via the combination of 3 μ g/ml insulin and the *K. pictus* extract was similar to the treatment with 50 μ g/ml insulin in 3T3-L1 adipocyte, but the extract itself did not regulate the glucose uptake (Ko et al., 2002). In the blood of

streptozotocin-induced diabetic rats, the group administered intraperitoneally with 25 mg/ml kalopanaxsaponin A (1) displayed a significantly reduced level of glucose, cholesterol, total lipids and triglycerides (Kim et al., 1998a).

Metformin from *Galega officinalis*, an insulin-sensitizing agent, primarily acts on hepatic glucose production via the activation of AMP-activated protein kinase (AMPK) and has additional effects on insulin sensitivity by improving insulin binding to receptors (Bailey and Turner, 1996; Kirpichnikov et al., 2002; Towler and Hardie, 2007). Based on the anti-diabetic actions of Metformin, it can be proposed that *K. pictus* extracts, including kalopanaxsaponin A (1), may play an important role in glucose metabolism and/or lead to sensitivity in insulin receptors. Clearly, more information is needed before the efficacy of *K. pictus* on diabetes treatment can be properly assessed. Further functional analysis of *K. pictus* extracts and active compounds, their targets and their interplay in insulin signalling triggered by insulin receptors will further contribute to our understanding of anti-diabetic mechanisms.

Hepatoprotective effect

There are a variety of plant substances being used as protective herbal liver drugs such as phenols, coumarins, lignans, essential oils, monoterpenes, carotenoids, glycosides, flavanoids, organic acids, lipids, alkaloids and xanthenes (Sharma et al., 2002).

Advanced studies using *K. pictus* extracts suggested that liriiodendrin (15) and syringin (17) are possible hepatoprotective agents (Lee et al., 1995; Park et al., 1999; Choi et al., 2002a). In the case of carbon tetrachloride (CCl₄) induced liver injury, the groups pre-treated with liriiodendrin (15) before induction of liver injury displayed lower levels of glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT) and lactate dehydrogenase (LDH) compared with those of the controls (Lee et al., 1995). Similarly, syringin (17) regulated the microsomal oxidative enzyme activities, resulting in the inhibition of lipid preoxidation in the liver during responses to D-galactosamine/lipopolysaccharid (D-GalN/LPS)-induced liver injury (Park et al., 1999). The liver injury induced by CCl₄ or D-GalN/LPS is mediated by the production of toxic free radicals (Cederbaum, 1989; Neihorster et al., 1992; Kondo et al., 1994), suggesting that the reduction of ROS may be one of the possible mechanisms of the compounds in hepatoprotection, although the interaction between liriiodendrin (15) and reactive oxygen species (ROS) have not been clearly studied.

ADDITIONAL BENEFITS OF *K. pictus*

Free radicals are highly reactive species that have been implicated in the development of over 100 diseases and

lead to various further complications (Aniya et al., 2005). It has been shown that two hederagenin monodesmosides, kalopanaxsaponin A (1) and sapindoside C (12), exhibited a significant anti-lipid peroxidation effect in bromobenzene-treated rats (Choi et al., 2001a). In addition, FCA treatment in rats causes the reduction of superoxide dismutase, catalase and glutathione peroxidase enzyme activities; however, administration of kalopanaxsaponin A (1) resulted in elevated activities of superoxide dismutase, catalase and glutathione peroxidase during response to FCA (Choi et al., 2002a).

Since *K. pictus* extracts have shown anti-inflammatory and anti-rheumatoidal properties, they have been analyzed for other pharmaceutical functions. Kim et al. (1998b) reported that kalopanaxsaponin A (1) and I (9) exhibit anti-fungal activity (MIC = 25 µg/ml) against *Candida albicans* KCTC 940 and *Cryptococcus neoformans* KCIC 7224. Park et al. (2003) reported that *K. pictus* water extracts showed anti-malarial activity (EC₅₀ = 4.6 µg/ml) and higher selective toxicity than other traditional Korean medicinal plants. The hexane or ethyl acetate soluble fraction of the methanol extracted from *K. pictus* stem bark inhibited the growth of human breast, lung and liver cancer cells (Kim et al., 2002b; Park et al., 2009). When kalopanaxsaponin A (1) was used to treat MDA-MB-231 and MCF-7 human breast cancer cells, it down-regulated the extracellular signaling pathways mediated by extracellular signal-regulated kinase (ERK) 1/2 and phosphoinositide-3-kinase/protein kinase B (PI3K/Akt) and resulted in the inhibition of phorbol-12-myristate-13-acetate (PMA, selective activator of protein kinase C)-induced invasion (Hwang et al., 2008; Park et al., 2009).

The pharmacological actions of kalopanaxsaponin A (1) might result from the interaction with signal transduction pathways mediated by protein kinase activations such as MAPKs, IκB kinase (Ikk) and Akt. The inhibited activity of those kinases caused the reduction of AP-1 and NF-κB DNA-binding activities and resulted in down-regulation of IL-1, TNF-α, IFN-γ and MMP-9. It might be possible to develop specific mediators for anti-NF-κB therapy using kalopanaxsaponin A (1). However, it will be necessary to determine the specificity of kalopanaxsaponin A (1) as a mediator and to determine the regulation between kalopanaxsaponin A (1) and the human metabolic mechanism during its pharmacological actions. We are of the view that kalopanaxsaponin A (1) may not alter humans' metabolic state by virtue of its protective and synergetic effects.

Conclusion

In spite of tremendous strides in modern medicine, numerous natural products from traditional medicinal plants have been introduced in the development of theoretical drugs. In addition, many products containing herbal extracts are sold in the Asian market as substitutes

or supplements of modern medicine. The objective of this review has been to show the recent advances in the exploration of *K. pictus* as phytotherapy and to illustrate its potential as a therapeutic agent. With the current information, it is evident that *K. pictus* has pharmacological functions including anti-inflammatory, anti-rheumatoid, hepatoprotective, anti-diabetic, anti-cancer effects, etc. As the current information shows, it is also possible that hederagenin monodesmosides might be useful in the development of new drugs to treat inflammation and RA. In fact, *K. pictus* is the highlight of dietary health supplements and functional foods due to its pharmacological functions in East Asia (Park, 2000; Jang et al., 2005; Kim and Cheun, 2006; Kim, 2007). However, it must be kept in mind that clinicians should remain cautious until more definitive studies demonstrate the safety, quality and efficacy of *K. pictus*. For these reasons, extensive pharmacological and chemical experiments, together with human metabolism will be a focus for future studies. Last but not the least, this review emphasizes the potential of *K. pictus* to be employed in new therapeutic drugs and provide the basis for future research on the application of transitional medicinal plants.

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