Ethnopharmacology of Medicinal Plants
“Observation and experiment for gathering material, induction and deduction for elaborating it; these are our only good intellectual tools.”

F. Bacon, 1561–1626
Preface

In 1860, Oliver Wendell Holmes pointedly expressed himself to the Massachusetts Medical Society: “I firmly believe that if the whole *Material Medica*, as now used, could be sunk to the bottom of the sea, it would be all the better for mankind, and all the worst for the fishes.” Should one think the same about the current approach in drug discovery from plants? Probably yes. Despite the spending of billions of US dollars, and three decades of efforts, high-throughput screenings have only allowed the discovery of a couple of drugs. One could have reasonably expected the discovery of an arsenal of drugs from the millions of plant extracts randomly tested, but “hits” can be inactive in vitro or too toxic, some molecules need to be metabolized first to be active, and false-positive and false-negative results are common.

The bitter truth is that the robotic approach in discovering drugs from plants has proven, to date, its inability to excavate the hundreds of molecules that will contribute to the health progress of Man. However, one can reasonably see that the last patches of primary rainforest on earth hold still hundreds of spectacularly active drugs that await discovery. The successful isolation of these drugs will depend on rational and selective collection of plants, heightened powers of observation, creation of original concepts, and formulation of new hypotheses to attain the sudden insight of which will be born new theories to extend the frontier of knowledge. As is often the case, that new theory might first be rejected out-of-hand by the dominant conservative group of established scientific schools of thoughts, the proponent of the new theory often being considered a quack. Gradually, however, if that theory is refined, developed and proven and leads to the discovery of wonder drugs, the real therapeutic usefulness, will be identified as a result of serendipity. Perhaps the future will see this new “Hippocratic” way of direct observation and logical interpretation displacing “robotic theories.”

At this point in time, ethnopharmacologists represent a little heteroclite community of scientists who assess the last traditional systems of medicine: Pacific Rim, Amazon, and Africa. For the research scientist who penetrates the unknown of medicinal plants alone, no guide books are possible because the territory they travel is uncharted. For the first time in the history of medicinal plant research, *Ethnopharmacology of Medicinal Plants: Asia and the Pacific* sheds some lights on the pharmacological potentials of one of the most exciting and enormously rich sources of potential drugs: the medicinal plants of the Pacific Rim, which encompasses more than 6000 species that are virtually unexplored for pharmacology.

*Ethnopharmacology of Medicinal Plants: Asia and the Pacific* is written for all who will participate in the field of drug discovery from plants and offers stimulating, thoughtful, and critical information that should contribute in some way to the scientific progress of ethnopharmacology and to the discovery of drugs.
Asia and the Pacific emphasizes the fundamental importance of the precise observation of the use of each medicinal plant, combined with pharmacological experiments and its botanical classification, and provides the base for a new theory of ethnopharmacology.

Christophe Wiart
Pharm.D.
Preface .............................................................................................................................. vii

1. ANTI-INFLAMMATORY PLANTS ........................................................................ 1
   General Concept ....................................................................................................... 1
   Inhibitors of Phospholipase A$_2$ ........................................................................... 4

      Medicinal Aristolochiaceae ................................................................. 4
         Aristolochia indica L.
         Aristolochia kaempferi Willd.
         Aristolochia recurvilabra Hance
         Thottea grandiflora Rottb.

      Medicinal Myristicaceae ........................................................................ 8
         Horsfieldia amygdalinia (Wall.) Warb.
         Horsfieldia valida (Miq.) Warb.

      Medicinal Caprifoliaceae ........................................................................ 10
         Lonicera japonica Thunb.
         Sambucus javanica Reinw. ex Bl.
         Weigela floribunda (Sieb. & Zucc.) K. Koch.

      Medicinal Asteraceae .............................................................................. 11
         Cirsium japonicum DC
         Crossotephium chinense L.

   Inhibitors of COX .......................................................................................... 15

      Medicinal Apocynaceae ........................................................................ 16
         Trachelospermum asiaticum (Sieb. & Zucc.) Nak.

      Medicinal Clusiaceae .............................................................................. 18
         Garcinia atroviridis Griff.

      Medicinal Asteraceae .............................................................................. 21
         Chrysanthemum sinense Sab.

      Medicinal Polygonaceae .......................................................................... 23
         Polygonum amphibium L.

      Medicinal Lamiaceae .............................................................................. 24
         Ocimum basilicum L.
         Glechoma brevituba Kuprian.
CONTENTS

Inhibitors of Lipoxygenases ................................................................. 27

Medicinal Myrsinaceae ................................................................... 27
Ardisia villosa Roxb.

Medicinal Clusiaceae .................................................................... 28
Hypericum erectum Thunb.

Medicinal Asteraceae .................................................................... 30

Medicinal Apiaceae ....................................................................... 31
Bupleurum chinense DC

Inhibitors of Elastase ....................................................................... 32

Medicinal Asteraceae .................................................................... 33
Sigesbeckia orientalis L.
Sigesbeckia glabrescens Mak
Mikania cordata (Burm.f.) B.L. Robinson

Medicinal Droseraceae ................................................................... 37
Drosera rotundifolia L.

Inhibitors of Nitric Oxide Synthetase ............................................... 38

Medicinal Asteraceae .................................................................... 39
Inula chinensis Rupr. ex Maxim.
Carpesium divaricatum Sieb. et Zucc

Medicinal Lauraceae ..................................................................... 42
Neolitsea zeylanica Nees (Merr.)
Litsea cubeba (Lour.) Pers.
Litsea odorifera Val.

Medicinal Solanaceae ................................................................... 45
Physalis alkekengi

Conclusion and Future Prospects ......................................................... 48

References ............................................................................................ 50

2. PLANTS AFFECTING THE CENTRAL NERVOUS SYSTEM .................................... 57

General Concept .................................................................................. 57

Plants Affecting the Serotonergic Neurotransmission ......................... 60
Artabotrys suaveolens Bl.
Fissistigma fulgens (Hk. f. et Th.) Merr.
Friesodielsia latifolia Hk. f. et Th.
CONTENTS

Medicinal Lauraceae ................................................................. 160
P. thunbergii (Sieb. & Zucc.) Kosterm.
Lindera tzumu Hemsl.
Cassycya filiformis L.

Medicinal Hernandiaceae .......................................................... 163
Illigera luzonensis L.

Medicinal Ebenaceae ................................................................. 165
Diospyros sumatrana Miq.
Diospyros topoioides King & Gamble

Medicinal Rubiaceae ................................................................. 167
Prismatomeris alflora Thaw, non King
Knoxia valerianoide Thorel
D. indicus Gaertn.
Neonauclea pallida (Reinw. ex Havil.) Bakh f.
Morinda officinalis How

Medicinal Rutaceae ................................................................. 174
Z. ailanthoides Sieb. & Zucc.
Zanthoxylum bungei Planch.
Zanthoxylum piperitum (L.) DC.
Zanthoxylum schinifolium Zieb. & Zucc.

Medicinal Euphorbiaceae ......................................................... 179
Alchornea villosa (Benth.) Muell.- Arg.
Alchornea rugosa (Lour.) Muell. Arg
Phyllanthus acidus (L.) Skeels
Macaranga triloba (Reinw.) Muell.-Arg.

Medicinal Hamamelidaceae ....................................................... 186
Altingia excelsa Noronha

Medicinal Lamiaceae ................................................................. 187
Salvia plebeia R.Br.
Salvia japonica Thunb.
Salvia miltiorrhiza Bunge

Apoptosis .................................................................................... 194

Medicinal Annonaceae ............................................................... 195
Goniothalamus species.
Pseudouvaria setosa (King) J. Sinclair

Medicinal Asteraceae ................................................................. 202
Elephantopus mollis Kunth.
Blumea riparia (Bl.) DC.
Spilanthes paniculata Wall. ex DC
Lactuca indica L.
CONTENTS

Summary and Future Prospects .......................................................... 208
References .......................................................................................... 210
Index ............................................................................................................. 219
GENERAL CONCEPT

Inflammation is a dynamic process that is elicited in response to mechanical injuries, burns, microbial infections, and other noxious stimuli that may threaten the well-being of the host. This process involves changes in blood flow, increased vascular permeability, destruction of tissues via the activation and migration of leukocytes with synthesis of reactive oxygen derivatives (oxidative burst), and the synthesis of local inflammatory mediators, such as prostaglandins (PGs), leukotrienes, and platelet-activating factors induced by phospholipase A₂, cyclooxygenases (COXs), and lipoxygenases. Arachidonic acid is a key biological intermediate that is converted into a large number of eicosanoids with potent biological activities. The two major pathways of arachidonic acid metabolism are the COX pathway, which results in the formation of both PGs and thromboxanes, and the 5-lipoxygenase pathway, which is responsible for the formation of leukotrienes and 5S-hydroxy-6E, 8Z, 11Z, 14Z-eicosatetraenoic acid (5-HETE). Classic examples of herbs traditionally used to treat inflammation in Western medicine are Matricaria chamomilla L. and Arnica montana L. (Asteraceae), Salix alba (Salicaceae), and Glycyrrhiza glabra (Fabaceae).

The dried capitula of Matricaria chamomilla L. (Asteraceae), or German chamomile, have been used as anti-inflammatory and antispasmodic remedies since very early times on account of its contents in bisabolol oxides the activity of which has been experimentally substantiated. The plant is listed in several European pharmacopeias, and is used in the form of tinctures, extracts, lotions, ointments, shampoos, and sunscreen products.

Arnica montana L. (Arnica) has been used for treating bruises and swelling in Western medicine on account of its ability to elaborate sesquiterpene lactones, such as helennalin and dihydrohelenalin, which are thought to inhibit the activation of transcription factor nuclear factor (NF)-κB, which is responsible for the transcription of genes involved in encoding mediators for the inflammatory process.

Many topical preparations containing arnica are commercially available. Arnica is most commonly prepared as a tincture that can also be used as the base for creams, ointments, compresses, and poultices. Arnica oil may also be used in topical preparations.
The effect of *Salix alba* L. (white willow) is largely owed to a glycoside, salicin. Salicin is antipyretic and analgesic and has been used in the treatment of rheumatic fever (salicilin tablets; *British Pharmaceutical Codex*, 1949). In 1893, Felix Hofmann, a chemist working for the Bayer chemical company in Germany, first synthesized acetyl-salicylic acid, the acetylated form of salicin. Aspirin is one of the most commonly used pharmaceuticals containing salicin. Today, the main commercial sources of salicin are *Salix fragilis* and *Salix purpurea* (Salicaceae), which are native to Eurasia.

The mechanism by which aspirin elicits its anti-inflammatory activity is based on the fact that it irreversibly inactivates COX by covalent acetylation.

The roots of *Glycyrrhiza glabra* (liquorice) were known to Roman physicians as *Radix dulcis* and to Arab physicians as a remedy for cough, and the plant has been cultivated in Europe since the 18th century for its peculiar taste. *Glycyrrhiza glabra* is listed in the *British Pharmaceutical Codex* (1973 ed.) and contains triterpenes glycyrrhizin (6–13%) and glycyrrhizic acid, which have anti-inflammatory activity.

Glycyrrhizic acid is mainly absorbed after hydrolysis as glycyrrhetic acid, which is a potent inhibitor of 11-β-hydroxysteroid dehydrogenase an enzyme that catalyzes the conversion of cortisol to cortisone, hence mineralocorticoid action. A large amount of commercial teas, ointments, tobaccos, and suppositories are available on the market. In cosmetology, the drug is used for sunscreen and skin-care products. Other well-known plant products with anti-inflammatory activity are the distillate of *Hamamelis virginiana* (witch hazel; Hamamelidaceae), *Echinacea* species including *Echinacea angustifolia* (purple coneflower; Asteraceae), and *Ananas comosus* (pineapple; Bromeliaceae).
Common examples of Asian anti-inflammatory plants are *Curcuma domestica* Val. and *Curcuma longa* L. (turmeric), *Curcuma xanthorrhiza* Roxb. (temoe-lawaq), and *Zingiber officinale* Rosc. (Zingiberaceae). The rhizomes of *C. longa* L. (turmeric) from Java were introduced in Europe probably through Arab traders. Dioskurides mentions it as an Indian plant that looks like ginger but contains a yellow dye and has a bitter taste. The Indians and Chinese have been using *Curcuma longa* L. for centuries as a cosmetic and for the making of curry, and it was found in a list of medicinal plants sold in Frankfurt in 1450.

The yellow principle of *Curcuma longa* L. is a yellow pigment, curcumin. This dye inhibits the enzymatic activity of both COX and nitric oxide synthetase (NOS) and showed clinical potentials for the treatment of inflammation. *Zingiber officinale* L. (ginger) is native to Gingi area near Pontichery, India and the first European to have seen the whole living plant is said to be the Venetian Marco Polo around 1285. It was used to flavor food and beverages by the Greeks and Romans, who imported it via the Red Sea. During the Middle Ages, ginger was an important economical product controlled by the Venetians. Venetians had established houses of business at Constantinople and Sudak on the shore of the Black Sea, had the monopol of ginger, which was brought by caravannes following the Silk Road. The Venetian monopol survived until the late 15th century when Portuguese navigators were able to sail via the cape to Mozambique.
and then direct to India to Calicut. Ginger was brought in South America for cultivation by Francisco Mendoza and was exported to Spain as early as 1547. The plant contains arylalkalones, which inhibit the enzymatic activity of COX with potentials for the treatment of inflammation.

Encompassing approx 6000 medicinal plant species, the medicinal flora of Asia and the Pacific comprise a fantastic source of pharmacologically active products, and the number of plant species principally used for the treatment of inflammation can be estimated to be more that 380. This chapter will focus on the potentials of medicinal plants of Asia as a source of original anti-inflammatory drugs, with particular interest payed to inhibitors of phospholipase $A_2$, COX, lipoxygenases, elastase, and NOS.

**INHIBITORS OF PHOSPHOLIPASE $A_2$**

Phospholipase $A_2$ or phosphatide acylhydrolase 2, is an enzyme that catalyzes the hydrolysis of the acyl group attached to the 2-position of intracellular membrane phosphoglycerides. This hydrolysis release arachidonic acid from membrane phosphoglycerides. Arachidonic acid is the precursor of PGs, thromboxanes, and leukotrienes (Fig. 1). In regard to the possible mechanisms observed so far, the inhibition of phospholipase $A_2$ is mediated via lipocortine or by direct interaction with the enzyme itself. The former mechanism utilizes a protein known as lipocortine, the synthesis of which is commanded by steroidal hormones and steroid-like plants known as triterpenoids. Examples of lipocortine-mediated phospholipase $A_2$ inhibitors that are of therapeutic value and potent anti-inflammatory drugs are cortisone, prednisolone, and betamethasone. The other possible mechanism involves a direct binding with the enzyme itself, a mechanism thus far unused in therapeutics, but with promise. One such compound is also a triterpene: betulinic acid (1). When looking for an inhibitor of phospholipase $A_2$ from medicinal plants, one could look into plant species that are traditionally used as snake-bite antidotes because hemolytic and myolytic phospholipases $A_2$ are often present in snake venom, which results in damage to cell membranes, endothelium, skeletal muscle, nerves, and erythrocytes.

Other medicinal features to consider when searching for plants with potential as phospholipases $A_2$ are abortifacient, analgesic, antipyretic, and hypoglycemic uses. Such features are present in the following plant species.

**Medicinal Aristolochiaceae**

The family Aristolochiaceae is a family of herbaceous plants often used in Asia and the Pacific to counteract snake poisoning, promote urination and menses, mitigate stomachache, and treat dropsy and skin diseases. During the past 20 years, members of this family, especially from the genus Aristolochia have attracted much interest and has been the subject of numerous chemical and pharmacological studies. The anti-inflammatory property of Aristolochia species is probably the result of a direct
Fig. 1. Biosynthetic pathway of arachidonic acid metabolites.
interaction between aristolochic acid and derivatives of phospholipase A\textsubscript{2}. *Aristolochia indica* L., *Aristolochia kaempferi*, and *Aristolochia recurvilabra* Hance are used for the treatment of inflammatory conditions.

**A. indica** L. Indian *Aristolochia*, also known as Indian birthwort, *ishvara* (Sanskrit), or *adagam* (Tamil), is a bitter climber native to India. The medicinal material consists of the rhizome, which is to resolve inflammation (India), counteract insect poison, and as an antipyretic (Philippines and Vietnam). The rhizome contains aristolochic acid, which inhibits in vitro and dose-dependent phospholipid hydrolysis by the human synovial fluid phospholipase A\textsubscript{2}, snake venom phospholipase A\textsubscript{2}, porcine pancreatic phospholipase A\textsubscript{2}, and human platelet phospholipase A\textsubscript{2} (2).

**Aristolochia kaempferi** Willd. (*Aristolochia chrysops* [Stapf] E.H. Wilson ex Rehder, *Aristolochia dabieshanensis* C.Y. Cheng and W. Yu, *Aristolochia heterophylla* Hemsl., *Aristolochia kaempferi* f. *heterophylla* S. M. Hwang, *Aristolochia kaempferi* f. *mirabilis* S. M. Hwang, *Aristolochia neolongifolia* J.L. Wu and Z.L. Yang, *Aristolochia mollis* Dunn, *Aristolochia shimadae* Hayata, *Isotrema chrysops* Stapf, *Isotrema heterophyllum* [Hemsl.] Stapf, and *Isotrema iasiops* Stapf), or yellow mouth Dutchman’s pipe, *ma tou ling*, *yi ye ma dou ling* (Chinese), is a perennial climber that grows to a height of 1 m in forests, thickets, and the mountain slopes of China, Taiwan, and Japan. The plant is herbaceous and develops small yellow flowers in the summer. The fruits are cylindrical or ovoid, 3–7 × 1.5–2-cm, dehiscing capsules. The drug consists of the fruit, which is shaped like human lungs, and is therefore recommended in China for all forms of pulmonary infections. Other diseases for which they are prescribed are hemorrhoids, ascite, and heartburn. The plant is known to contain phenanthrene alkaloid derivatives
including aristoliukine-C, aristofolin A and E, aristolochic acid-Ia methyl ester, and
aristolochic acid, as well as kaempferol-3-O-rutinoside and quercetin kaempferol-3-O-rutinoside (3,4).
The plant is known elaborate a series of quite unusual phenanthrene alkaloid derivatives,
of which aristoliukine-C, aristofolin A and E, aristolochic acid-Ia methyl ester, and
aristolochic acid. Other chemical constituents found in this plant are flavonoid glycosides such as kaempferol-3-O-rutinoside and quercetin kaempferol-3-O-rutinoside (3,4).
Exposure to Aristolochiaceae family is associated with the development of cancer in
humans. A significant advance is the toxicological effects of aristolochic acid has been
provided by the work of Pezzuto et al. They showed that aristolochic acid is a mutagen (5).

*Aristolochia recurvilabra* Hance (*Aristolochia debilis* Sieb. et Zucc, *Aristolochia sinarum*
Lindl., *Aristolochia longa* L.), or *ch’ing-mu-hsiang, pai-shu, ma dou ling, sam pai liang yin yao* (Chinese), is a climber that grows to a height of 1.5 m in thickets, mountain slopes,
and moist valleys to 1500 m altitude in China, Taiwan, and Japan by roadsides, in
thickets, and in meadows. The flowers are tubular and dark purple at the throat (Fig. 2).
The drug consists of the rhizome. It is highly esteemed and was, at one time, worth 300
silver taels. The rhizome can be easily mistaken for ginger. It is used to treat digestive
disorders, fluxes, diarrhea, dysentry, and snake bites. Levi et al. reported cases of hepa-
titis following ingestion of teas containing aristolochic acid (6).
Hong et al. showed that a methanol extract of *Aristolochia debilis* is a potent inhibitor of COX-2 activity (7).

*Thottea grandiflora* Rottb. is a shrub that grows in the primary rainforests of Malaysia, Thailand, and Singapore. The stems are terete and hairy. The leaves are simple, alternate, thick, glossy, and glaucous underneath and grow up to 25 cm long. The flowers are axillary, 15 cm long, purple, membranaceous, and three-lobed. The fruits are linear follicles (Fig. 3). The roots are used to invigorate, break fevers, treat agues, and as a postpartum remedy. The pharmacological potential of this plant is unexplored.

**Medicinal Myristicaceae**

The Myristicaceae family has attracted a great deal of interest on account of its ability to produce series of unusual phenylacylphenols—of possible symbiotic origin—that might have some potential for the treatment of inflammation. One such compound is YM-26567-1 from *Horsfieldia amygdalinia* (Wall.) Warb. isolated by Mikaye et al. (8) *Horsfieldia amygdalinia* (Wall.) Warb (*Myristica amygdalina* Wall, *Horsfieldia tonkinensis* H. Lecomte, *Horsfieldia thorelii* H. Lecomte, *Horsfieldia tonkinensis* var. *multiracemosa* H. Lecomte, *Myristica glabra* auct. non Blume, *Horsfieldia glabra* auct. non (Blume)
Warb, Horsfieldia prunoides C.Y. Wu), or feng chui nan (Chinese), is a timber tree that grows to a height of 25 m in hilly, sparse forests or dense forests of mountain slopes and groves in China, India, Laos, Burma, Pakistan, Thailand, Vietnam, Malaysia, and Indonesia. The bark is grayish-white and exudes sticky blood-like latex. The mature fruits are ovoid to elliptical drupes that are orange and to 2.5 cm long. The seeds are oily and completely enclosed in a crimson tunic (Fig. 4). The leaves and bark are used to make a tea to treat intestinal discomfort, and the bark is used to heal sores and pimples. The anti-inflammatory property of Horsfieldia amygdalinia (Wall.) Warb is confirmed in vitro. Mikaye et al. reported that YM-26567-1 from the fruit of this plant competitively inhibits the enzymatic activity of phospholipase A₂. In the course of further screening for YM-26567-1 derivatives, YM-26734 was selected, and inhibited phospholipase A₂ from rabbit platelets with an inhibition concentration 50% (IC₅₀) value of 0.085 mM (8).

Horsfieldia valida (Miq.) Warb. (Myristica valida Miq., Endocoria macrocoma [Miq.] de Wilde subsp. prainii [King] de Wilde; Horsfieldia merrillii Warb.; Horsfieldia oblongata Merr., Horsfieldia prainii [King] Warb., Myristica prainii King.), or yunnan feng chui nan (Chinese), is a buttressed tree that grows to a height of 25 m and a girth of 50 cm in the

primary rainforests of Indonesia, Malaysia, and the Philippines. The bark is red-brown and minutely scaly. Red sap is present. The stems are terete, pubescent to puberulous, lenticelled, and longitudinally fissured. The leaves are simple, spiral, and exstipulate. The petiole is 2.3 cm × 3 mm, woody, and cracked. The blade is obovate-oblong, 19 cm long by 6 cm large, 24 cm long by 8 cm large, 24 cm long by 6 cm large, and shows 18–25 pairs of secondary nerves prominent on both surfaces. Male flowers are yellowish or subglobose, three- to five-lobed, and minute. The female flowers are ovoid-globose and 2.5–2.8 mm long. The fruits are red, ovoid, edible, and resinous in flavor, and 6 × 3.5 cm on a 5-mm-long pedicel. The seeds are 2–4 cm long and enclosed in a waxy, orange aril (Fig. 4). In Indonesia, the bark is used to treat sprue. Pharmacological properties are unexplored.

Medicinal Caprifoliaceae

The family Caprifoliaceae comprises approx 400 species, of which *Lonicera japonica* Thunb., *Lonicera affinis* Hook and Arn, *Lonicera confusa* DC, *Sambucus javanica* Reinw. ex. Bl, *Sambucus sieboldiana* (Miq.) Graebn, and *Weigela floribunda* (Sieb. and Zucc.) K. Koch. are used to treat inflammatory conditions in Asia and the Pacific. There is an expanding body of evidence to suggest that biflavonoids from this family might hold some potential as phospholipase A₂ inhibitors. One such compound is ochnaflavone from *Lonicera japonica* Thunb.

*Lonicera japonica* Thunb. (*Lonicera chinensis* Wats, *Lonicera brachypoda* DC. var. *repens* Sieb.), or Chinese honeysuckle, *kim ngam*, *day nhan dong* (Vietnamese), *jen-tung* (Chinese), is a climbing shrub. The flowers are tubular, up to 4 cm long, and white when fresh but yellow when dry. In China, the flowers, stems, and leaves are used in medicine as febrifuge, correctives, and astringents and are used to treat infections and poisoning. The dried flowers are a common sight in the Chinese pharmacies of Malaysia, where they are prescribed as an antipyretic. In Vietnam, a decoction of stems or flowers is drunk to treat syphilis and rheumatism. The anti-inflammatory and antipyretic properties of *Lonicera japonica* Thunb. are confirmed and involve a biflavonoid, ochnaflavone, strongly inhibited the enzymatic activity of rat platelet phospholipase A₂ (IC₅₀ approx 3 μM). This activity was strong and dependent of the
pH, noncompetitive, and irreversible. In addition, the inhibitory activity of ochnaflavone is rather specific against group II phospholipase A₂ than group I phospholipase A₂ (IC₅₀ approx 20 μM). These results indicate that the inhibition of phospholipase A₂ by ochnaflavone may result from direct interaction with the enzyme (9).

\[
\text{Ochnaflavone}
\]

**Sambucus javanica** Reiw. ex Bl. (*Sambucus hookeri* Rehd, *Sambucus thunbergiana* Bl.), or so tiao, chieh ku ts’aois (Chinese), or kambiang beriak (Indonesian), is a deciduous shrub of open spaces of land in town or countryside that are abandoned and where plants can grow freely, village outskirts, and wasteland. The flowers are white, starry, and small, and the fruits are red berries (Fig. 5). In Indonesia, the leaves and bark are used to cure itching. The plant is also used to treat rheumatism, assuage pain, reduce fever, and resolve swellings. The pharmacological potentials of this plant are unknown.

**Weigela floribunda** (Sieb. & Zucc.) K. Koch. (*Diervilla versicolor* Sieb. & Zucc.), crimson weigela, or Japanese wisteria, is a deciduous shrub that grows up to 2.5 m in Asia and was introduced as an ornamental shrub in the United States. The flower appears from May to June, and is large and purplish (Fig. 6). The plant is medicinal in China and Indonesia, where it is used to wash sores. The pharmacological potentials of the plant are unknown.

**Medicinal Asteraceae**

Classical examples of anti-inflammatory Asteraceae are *Arnica montana* and *Calendula officinalis*, both used in European medicine to treat bruises and contusions. There is an expanding body of evidences to suggest that Asteraceae could be a useful source of anti-inflammatories, such as sesquiterpene lactones and/or triterpene alcohols, the latter being known to inhibit 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation in mice as efficiently as commercial indomethacin by possible inhibition of phospholipase A₂ (10).
Fig. 5. *Sambucus javanica* Reinw. ex Bl. From Plants of Indonesia. Bali Timur, Karangasem. On skirt of Gunung Agung, 1–3 km of Besakih. Altitude: 1100 m, 8° 21’ S – 115° 26’ E. in secondary forest.

Fig. 6. *Weigela floribunda* (Sieb. & Zucc.) K. Koch.
One of the most exiting findings in this area is perhaps the isolation of Bt-CD, a neoclerodane diterpenoid from *Baccharis trimera* (Less) DC or *carqueja* (Brazil) used to treat rheumatism and diabetes that shows anti-phospholipase A₂ activity (11). Note also the anti-phospholipase A₂ and anti-inflammatory activity of *Santolina chamaecyparissus* (12). *Cirsium japonicum* DC, *Crossotephium chinense* L. Makino, *Inula chinensis* Rupr. ex Maxim., and *Sigesbeckia orientalis* L. are used in Asia for the treatment of inflammatory conditions.

**Cirsium japonicum** DC (*Cnicus japonicum* Maxim, *Cnicus spicatus*), or Japanese thistle, *azami* (Japanese), *ta chi, hu chi, ma chi, tz'u chi, shan nin p'ang, chi hsiang ts'ao, yeh hung hua, and ch'ien chen ts'ao* (Chinese), is an herb that grows to 2 m in height. The plant is spiny and produces conspicuous purple capitula (Fig. 7). The drug consists of the root and is used to treat menstrual difficulties, irritable uterus, wounds, and snake bites. A decoction of the aerial part is used to stop bleeding from the nose. In Taiwan, the plant is used to heal burns. In Cambodia and Laos, the root is applied to ulcers and abscesses. The pharmacological properties of this herb are unknown.
Crossotephium chinense L. Makino (Crossostephium artemisoides Less, Artemisia judaica sensu Lour, Artemisia loureiro Kostel.) is a sub-shrub growing in crevices in the rocks in Japan and is cultivated in other Asian countries as pot ornamental. The plant is glaucous with dissected fleshy leaves (Fig. 8). In China, the leaves are used to calm itching. In Taiwan, the leaves are applied to contusions and wounds. In Vietnam, Cambodia, and Laos, an infusion of the plant is drunk to treat congestion. The plant is known to elaborate taraxerol, taraxeryl acetate, and taraxerol, which might participate in the medicinal uses (13). It would be interesting to know whether further studies on this herb discloses inhibitors of phospholipase A₂.