# CHAPTER II
# HISTORICAL

## 2.1 Introduction to the *Artemisia* family

*Artemisia* is a fairly large genus within the family Asteraceae (Compositae), with 200 individual species known, which are usually found in dry areas such as Europe and Asia (Pappas and Sheppard-Hanger, 2000). In Thailand, *Artemisia* has been found 8 species, namely (Smitinand, 2001)

*Artemisia annua* L.
*Artemisia dubia* Wall. ex Bess.
*Artemisia indica* Willd. var. *indica*
*Artemisia indica* Willd. var. *heyneana* Pampan.
*Artemisia lactiflora* Wall. ex Bess. var. *genuine* Pampan.
*Artemisia pallens* Wall. ex Bess.
*Artemisia roxburghiana* Bess.
*Artemisia scoparia* Waldst. & Kit.

They are invariably found as small fragrant shrubs or herbs and most yield essential oils. Some of these oils have found uses in perfumery and medicine (as, for example, vermifuges, stimulants, etc.) whereas the leaves of some species are used as culinary herbs. The plant themselves as are popular among gardeners as cultivated ornamentals (Pappas and Sheppard-Hanger, 2000).

## 2.2 Example of the *Artemisia* species that produce essential oils

The genus *Artemisia* is a rich source of terpenoids which are used in perfumery and pharmaceutical industries (Benjamin *et al.*, 1990). Several of the *Artemisia* species that produce essential oils are presented in table 9 (Pappas and Sheppard-Hanger, 2000).

Table 9 Selected examples of the *Artemisia* species that produce essential oils (Pappas and Sheppard-Hanger, 2000)

| Plant | Common name | Habitat | Essential oil use | Safety information |
|---|---|---|---|---|
| *A.afra afra* von Jacquin | Lanyana, layana, African absinthe, wildeals, South African wormwood | | Exhibits antifungal activity | No formal safety testing of EO; appears possible irritant, moderately toxic; potentially very toxic |
| *A. absinthium* L. | Absinthe, absinthium, wormwood, green ginger, armoise | Europe | Antihelmintic, insect repellant, digestive stimulant, mild tonic, febrifuge, One of the best sources of azulene | Test at low doses non toxic; non irritant and non sensitizing; banned for use bases on absinthe poisoning |
| *A. annua* L. | Annual wormwood, sweet Annie | Europe, naturalized in North America | Antihelmintic, antispasmodic, carminative, mucolytic | No formal safety testing of - EO; presumed moderately toxic |
| *A. arborescens* | Artemisia, great mugwort, arborescent mugwort | Morocco, Pacific, North West USA | Anti-inflammatory, antihistamine, anticatarrh, choleretic, mucolytic | No formal safety testing; appears safe at lo doses |

Table 9 Selected examples of the *Artemisia* species that produce essential oils (Pappas and Sheppard-Hanger, 2000) (cont.)

| Plant | Common name | Habitat | Essential oil use | Safety information |
|---|---|---|---|---|
| *A dracunculus* L. | tarragon | Eurasia | Antihelmintic, antibacterial, anti-inflammatory antispasmodic, carminative | Tested at low dose: not toxic, non irritant, non sensitizing Mutagenic data |
| *A. herba alba* Asso | White mugwort | Mediterranean | Anti-infectious, antibacterial, emmenagogue, lipolytic, mucolytic, cholagogue, parasiticide, viricide (the genuine "Armoise oil" of perfumery) | Non-irritant, non-sensitizing, and non-phototoxic Assumed very toxic |
| *A. pallens* Wall. | Davana | | Used in flavor (cakes, pastries, tobacco and costly beverages); anticatarrh, bactericidal, cicatrizant, mucolytic, nervine (arti-anxiety, low dose) | Non-irritant, non-sensitizing and non-phototoxic Low toxicity |
| *A. vulgaris* L. | Common mugwort, armoise, Indian wormwood | Eurasia | Antihelmintic, antispasmodic, stimulant, tonic, vermifuge | Oral toxin, low dose on skin: non-irritant, non-sensitizing |

## 2.3 Production of essential oil from *Artemisia* spp. cell and tissue cultures

Production of essential oil from *Artemisia* spp. cell and tissue cultures has been studied since 1990. The selected examples of *Artemisia* spp. have been studied in essential oil production from cell and tissue cultures are presented in table 10

Table 10 Selected examples of *Artemisia* spp. which have been studied in essential oil production from cell and tissue cultures

| Plant species | Reference |
|---|---|
| *Artemisia absinthium* L. | Kennedy *et al.*, 1993, Nin *et al.*, 1996, Nin, *et al.*, 1997 |
| *Artemisia annua* L. | Brown *et al.*, 1994, Fulzele *et al.*, 1995 |
| *Artemisia balchanorum* L. | Bavrina *et al.*, 1994 |
| *Artemisia dracunculus* L. | Cotton *et al.*, 1991 |
| *Artemisia pallens* Wall. ex Bess. | Benjamin *et al.*, 1990 |

## 2.4 *Artemisia dubia* Wall. ex Bess.

*Artemisia dubia* Wall. ex Bess. (Fig. 3) is belonging to the plant family Asteraceae (Compositae), subfamily Anthemideae. It has synonym namely *A. vulgaris* L. var. *indica* Maxim. This plant is commonly known as Akajedaw, Fleabane, Indian wormwood, Mugwort, Mug-wort and Titepati. It is native to Europe and continental Asia. The used of this plant are in the various ways such as; anthelmintic, asthma, scabies, skin rashes, headache, stomachache, homeostatic for nose bleed and bleeding wound, antiseptic and antipyretic (NAPRALERT database).

The description of this plant is as below (Harada *et al.*, 1987):

Perennial herb. Stem erect, ascending, branched, furrowed, densely whitish hairy. Leaves alternate, short-stalked to sessile, pinnatipartile to bipinnate, densely white-lanate-arachnoid beneath, and thinly hairy above. Inflorescences terminal and axillary panicles, heads sessile, corolla light green.

Common weed in open localities, fallow fields, waste places, roadsides, rare in regularly cultivated fields. Propagated mainly by underground stolons. Blooming period: November-April.

Figure 3 *Artemisia dubia* Wall. ex Bess. (*A. vulgaris* L. var. *indica* Maxim.)

## 2.5 Davanone

(+)-Davanone, a sesquiterpene ketone isolated from the flowering herb *Artemisia pallens*, was first characterized in 1968 by Sipma and van der Wal (Bartlett *et al.*, 1983). During the past decade there have been several syntheses of davanone and related compounds by several groups (Bartlett *et al.*, 1983), and in recently, the total synthesis of (±)-davanone has been described in 1999 (Molander and Haas, 1999).

Davanone is also found in other plants, for example *Tanacetum vulgare* (Hethelyi *et al.*, 1981), *Artemisia pallen* (Benjamin *et al.*, 1990), *Artemisia thuscula* (Perfumi *et al.*, 1995), and *Artemisia persica* (Bicchi *et al.*, 1985).

Davanone has been reported the spasmolytic activity by Perfumi *et al.* in 1995. It demonstrated a strong dose-dependent antispasmodic action, with an $IC_{50}$ of 0.0495 μg/ml (Perfumi *et al.*, 1995).

## 2.6 Biosynthesis of davanone

A novel biosynthesis of davanone has been described by Akhila *et al.* as shown in Fig. 4. Isopenthenylpyrophosphate (IPP) condenses with dimethylvinylcarbinylpyrophosphate (DMVCPP) to give geranyl-pyrophosphate, which further condenses with another molecule of IPP to produce farnesylpyrophosphate (FPP), the traditional precursor of sesquiterpenes. It is well established now that FPP isomerises to nerolidylpyrophosphate to metabolise many acyclic and cyclic sesquiterpenoids. In this case, -OPP from C-5 of FPP would shift to C-3 to give nerolidylpyrophosphate (analogy to geraniol-linalool interconversion). Nerolidylpyrophosphate is expected to undergo cyclization and oxidation at C-2 to metabolise davanone (Akhila *et al.*, 1986).

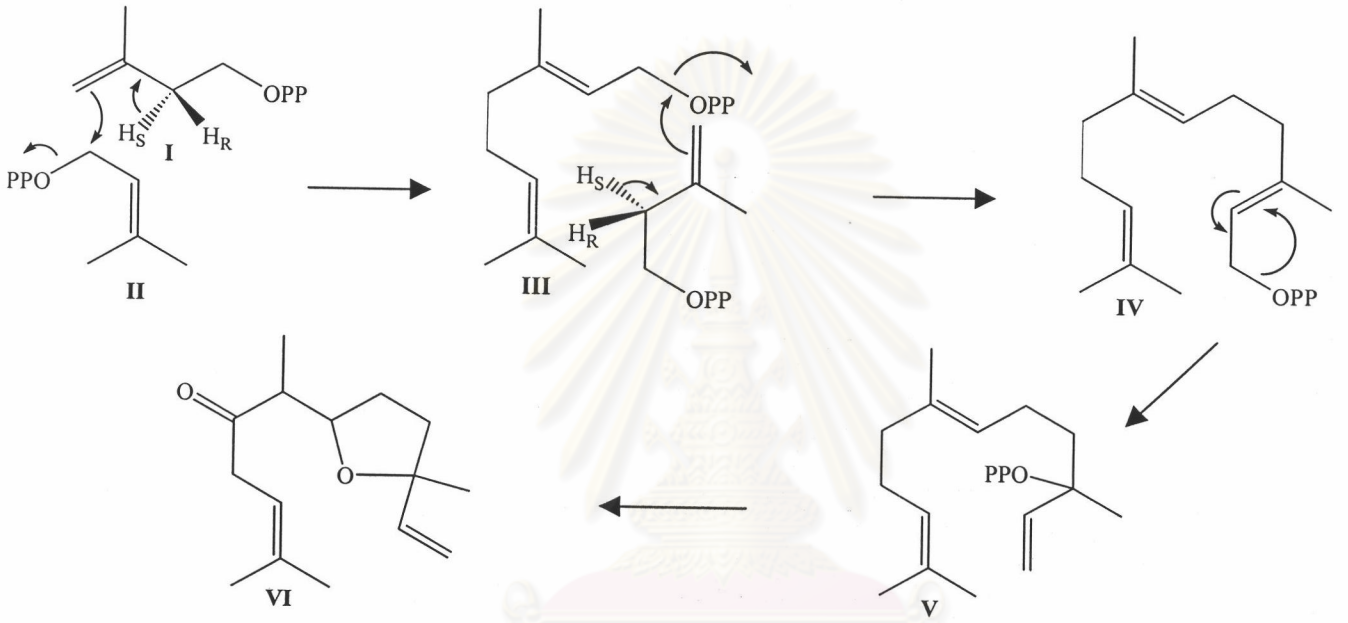


Figure 4 Possible biosynthetic pathway of davanone (I = Isopenthenylpyrophosphate (IPP), II = dimethylvinylcarbinylpyrophosphate (DMVCPP), III = geranylpyrophosphate, IV = farnesylpyrophosphate (FPP), V = nerolidylpyrophosphate and VI = davanone) (Akhila *et al.*, 1986)