CHAPTER 2

LITERATURE REVIEWS

2.1 Previous reports of *Ostodes* plants

Ostodes is a member of the Euphobiacaeae family which is composed of more than seven thousands species belonging to three hundreds genera are numbered around the world.[1- 4] Furthermore, in asia, *Ostodes* were found approximately four hundred and twenty five species. Besides, not much study has been reported on their phytochemical and bioactivities studies so far, although they demonstrated a wide variety of biological activities.[8-10] For instance, The first literature of this genus was indicated by Handa and colleagues in 1983.[14] They reported two cytotoxic diterpenoids; 12-*O*-undecadienoylphorbol-13-acetate (**1**) and ostodin (**2**) which has a Δ5,6-7□-hydroperoxide as a core structure (**3**) (Figure 2). These compounds were isolated from chloroform extract of stems and fruits of *O. paniculata.* They found that compound **1** is the most active compound against the P-388 lymphocytic leukemia cell system. Additionally, the ethanol extract of the aerial parts of this plant has been reported to evoke hypotensive activity in dogs and antipasmodic activity on the guinea pig ileum.

Certainly, in 2007, Gunjun *et al.*[15] revealed the biological and the effects of phorbol (**4**) (Figure 3). In according to Handa *et al.* (1983), phorbol esters are defined as polycyclic compound in which two hydroxyl groups on neighboring carbon atoms that esterified to fatty acid. Their structures are dependent on the tetracyclic diterpene carbon skeleton known as tigilane (**5**) (Figure 3). They occur naturally in many plants of the family of Euphobiacaeae and Thymelacaeae and their biological activities are highly structures specific. The active phorbol ester, 12-*O*-undecadienoylphorbol-13-acetate (**1**), was first found in *O. paniculata*.[14]

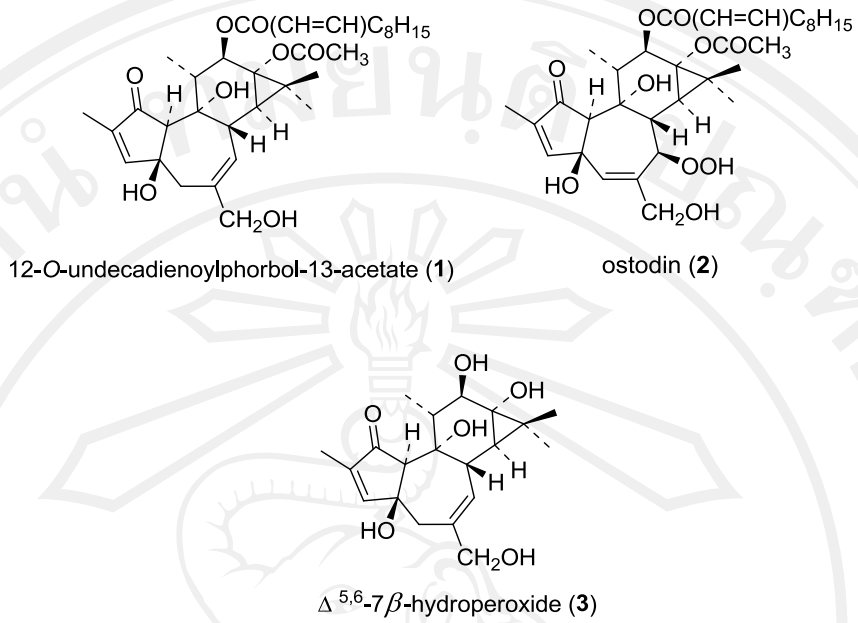


Figure 2 Structure of compounds **1**, **2** and **3**

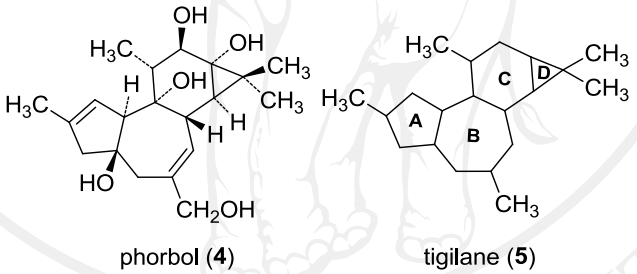


Figure 3 Structure of compounds **4** and **5**

Indeed, according to Hamburger *et al*. (1987) discovered ostopanic acid (**6**) (Figure 4). From the chloroform extract of the stems and fruits of *O. paniculata* which was found significantly inhibit the P-388 lymphocytic leukemia test system.[9]

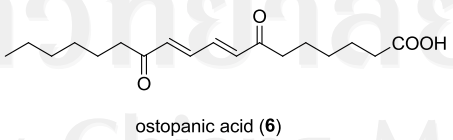
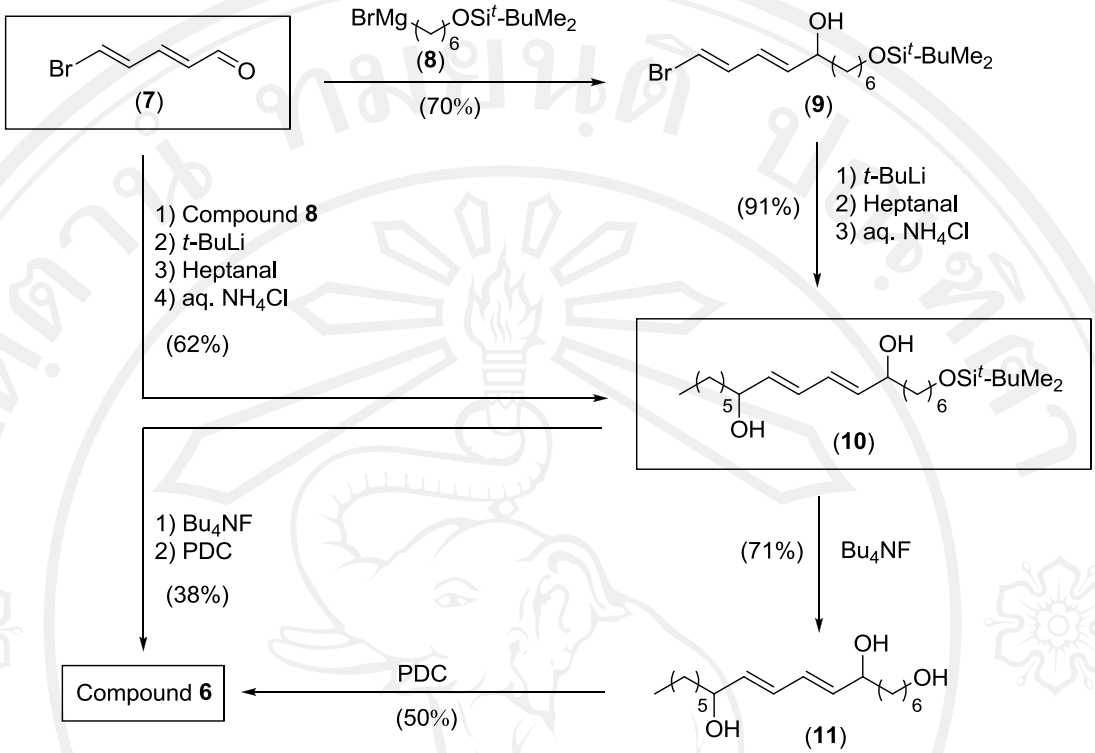


Figure 4 Structure of compound **6**

Bhakani and colleagues reported the biological activity tests of the alcoholic crude extracts from male plant excluding root in 1990. The compound **16** separated from the *O. paniculata* exhibited various bioactivities such as antibacterial, antifungal, antihelminthic, antifertility and anti inflammatory including, effect on the nervous and respiration systems.[15]

The conjugated polyene has been shown that double bond geometry is crucial for their biological activity. One of fatty acids with conjugated polyene structure found in *O. paniculata* was ostopanic acid (**6**). According to, Lucette and colleagues showed total syntheses of ostopanic acid (**6**) which was a plant anticancer agent. Ostopanic acid (**6**) was isolated from the stems and fruits of *O. paniculata* and inhibited the growth of P-388 lymphocytic leukemia system.[17]

The *E,E*-diethyl diketone structure of ostopanic acid (**6**), as well as its biological activity, prompted to improve of the specific retrosynthetic by using (2*E*,4*E*)-5-bromopentadienal (**7**). The first step is condensation of the organo mangnesium compound **8** to give bromohydroxydiene (**9**). Bromine lithium exchange reaction, followed by condensation led to triol **10** and then deprotonation of compound **8** following by oxidation reaction of the resulting trienol **11** afforded to ostopanic acid (**6**) (Scheme 1).[17]

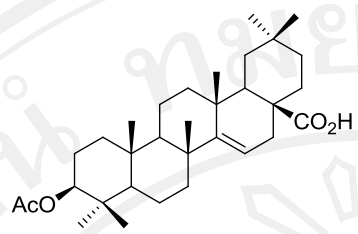


Scheme 1 The strategy for synthesis of ostopanic acid (**6**)

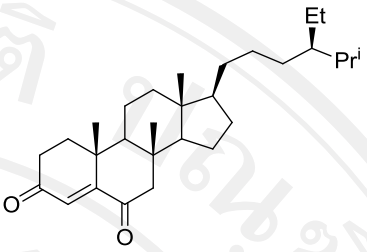
Shuhua and colleagues reported the isolation and structural elucidation of 10 compounds, acetylaleuritolic acid (**12**), stigmast-4-en-3,6-dione (**13**), *β*-sitosterol (**14**), daucosterol (**14**), 5,6-dihydroxy-3,3′,4′,7,8-pentamethoxyflavone (**16**), methyl gallate (**17**), vanilin (**18**), scopoletin (**19**), steric acid (**20**) and octacosanol (**21**) from chloroform extract of the twigs of *O. paniculata* in 2004 is revealed in Figure 5.[10]

Certainly, Carrasco and colleagues (2008s) reported that ostodin (**2**) from the chloroform extract of the stems and fruits of *O. paniculata* can against P-388 lymphocytic leukemia and nasopharynx cell (KB) *in vitro* cell lines at $ED_{50} \leq 4$ mg/ml.[17]

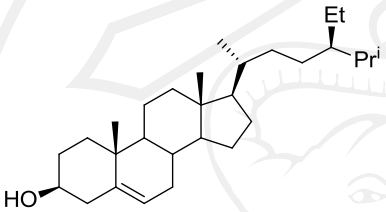
Whereas, *Ostodes* genus not remained to be studied on their phytochemical considerations and no research has been published on this variety too much. Although the tremendous uses in medicinal applications, they evaluated a widely of biological activities. As a result, there has no still thoroughly investigated the chemical constituents so that we aim to investigate the phytochemical study.



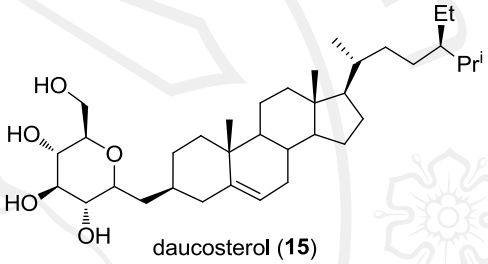
acetylaleuritolic acid (**12**)



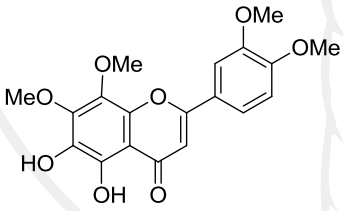
stigmast-4-en-3,6-dione (**13**)



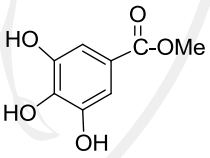
β-sitosterol (**14**)



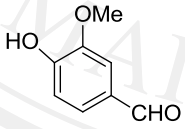
daucosterol (**15**)



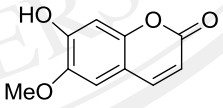
5,6-Dihydroxy-3,3',4',7,8-pentamethoxyflavone (**16**)



methyl gallate (**17**)



vanilin (**18**)



scopoletin (**19**)

$CH_3(CH_2)_{16}CO_2H$

steric acid (**20**)

$CH_3(CH_2)_{26}CH_2OH$

octacosanol (**21**)

Figure 5 Structure of compounds **12-21**