行政院國家科學委員會補助專題研究計畫成果報告

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※ 六種本土植物及三種中藥活性成分之研究 ※
※ (Chemical and Biological Studies of the Six ※
※ Native Plants and Three Chinese Herbs) ※
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計畫類別：■個別型計畫 □整合型計畫
計畫編號：NSC －96－2113－M－039－001
執行期間：96 年 8 月 1 日至 97 年 7 月 31 日

計畫主持人：郭悅雄
共同主持人：
計畫參與人員：邱錫臨

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□國際合作研究計畫國外研究報告書一份

執行單位：中國醫藥大學中國藥物研究所

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行政院國家科學委員會專題研究計畫成果報告

六種本土植物及三種中藥活性成分之研究

Chemical and Biological Studies of the Six Native Plants and Three Chinese Herbs

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一、中文摘要

台灣扁柏是最好的建材，由其材部分離出二種新骨架化合物，其一且有抗癌活性。水丁香是民間用藥，用於腎臟炎、水腫及高血壓，由其全草分出二種新的三萜化合物。由治療風濕症之黃心柿莖中找出二種新的萘醌化合物。福杉被用為治療哮喘、解熱及關節炎，由其心材有二種新的木酚素化合物被發現。山藥含女性賀爾蒙之代用品，其中發現二種新化合物及三種已知化合物，被確認可活化女性荷爾蒙之 α 及 β 型。由可治療腹瀉及抗瘧疾之羅氏鹽膚木之根找出六種新化合物，其中三種化合物可以抗煙草之馬賽克病毒。台灣杉可以抗腐蝕徽為有價值建材，由其根分七種倍半萜化合物，其中六種為新化合物，另外亦有找出九種木酚素，其中有六種被確認為新化合物。

關鍵詞：台灣扁柏；水丁香；黃心柿；福杉;山藥；羅氏鹽膚木；台灣杉；細胞毒；病毒；植物女性荷爾蒙。

Abstract

Chamaecyparis obtusa var. *formosana* is an important building material, two novel skeleton compounds were isolated from its heartwood. One of two components exhibited strong cytotoxic activity. *Ludwigia octovalvis* was used for the treatment of oedema, nephritis, and hypertension. And two new oleanane type derivatives were isolated and elucidated from the its whole plant. Two new naphthoquines were elucidated from the stem of *Diospyros maritima*, which has been used in a folk medicine as traditional treatments for rheumatic disease. *Cunninghamia lanceolata*, a large evergreen tree, is culitivated at low altitude. It has long been used for treatment of asthma, as an analgesic, and of arthritis. Two new lignans were purified from its heartwood. Yams (*Dioscorea alata*) have been implicated in the promotion of the health of postmenopausal women. The active components were isolated and purified by HPLC. Five compounds exhibited to activate ERα and β. The root of *Rhus javanica* var. *roxburghiana* were traditionally used in Taiwan as a fold herbal remedy for diarrhea, spermatorrhea, and malaria. In preliminary test, its methanolic extraction showed anti-tobaco mosaic virus. Under the activity-guide, we have discovered three new lignans glycosides possessing this activity, and also purified eight new compounds. *Taiwania cryptomerioides* , an important building material with high value in Taiwan. Its heartwood contains more than 6% of essential oil, and many interesting and different skeleton compounds have been reported. In order to survey the secondary metabolism compounds, we have found six new cadinane derivalives together with five new lignans.

Keywords: *Chamaecyparis obtusa* var. *formosana*; *Ludwigia octovalvis*; *Diospyros maritima*; *Cunninghamia lanceolata*; *Dioscorea alata*; *Rhus javanica* var. *roxburghiana ; Taiwania cryptomerioides*; Cytoxicity; Anti-Tobaco-Mosaic Virus; Phytoestrogen

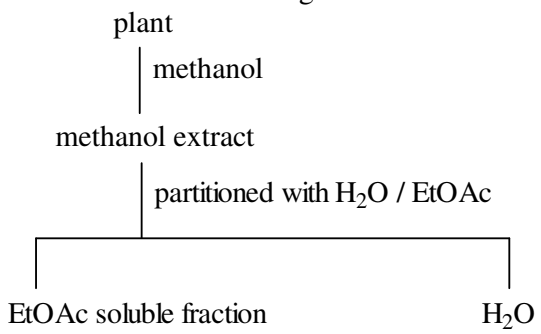
二、Purpose of Project

In this study, we try to find the biological components and search different compounds in order to understand the plants biosynthesis. The trunk of *Chamaecyparis obtusa* var. *formosana* is an important building material in Taiwan due to its decay-resistant characteristic. We have previously investigated many components of heartwood of this plant, and various monoterpenes, sesquiterpenenes, diterpenes,

and lignans. We also discovery many noble skeleton compounds. The purpose of this study continued the compound's separation, and try to discover the noble skeletonal compounds. The crude extract of *Ludwigia octovalvis* has been reported possessing antidiabetic and immunosuppressive activity. In our previous reports that showed three new triterpene derivatives inhibiting significant cytotoxicity against KB and HT29 with IC_{50} in the rang of 1.2-3.6μM. The genus *Diospyros maritima* exhibited cytotoxic, ichthyotoxic, germination inhibitory and antimicrobial activities. We try to find the biological active components and continued this chemical study. *Cunninghamia lanceolata* has long been used as a falk medicine. In order to study the biological isolate, the chemical study was studied in this time. Yams(*Dioscorea alata*) have been implicated in the promotion of the health of postmenopausal women. The crude extract of *Dioscorea alata* exhibited to activate ERα and β. The root of *Rhus javanica* var. *roxburghiana* are used in Taiwan as a folk herbal remedy for diarrhea, spermatorrhea, and malaria. The preliminary test, its methanolic extraction showed anti-tobaco mosaic virus. Under the activity guide, we have discovered the biological active compounds. Many components were isolated from the *Taiwania cryptomerioides* possessing many biological activities such as anti-wood decay fungi, cytotoxity, and anti-white ant. Therefore, the chemical investigation was continued.

三、Content of Project

The separative procedure of every plant was achieved as following



Two novel skeleton compounds, **1** and **2** were isolated from the heartwood of *C. obtusa* var. *formosana.* The structure **1** was elucidated as a dimeric of monoterpene and norlignan , and structure **2** was elucidated as a norlignan. Compound **1** exhibits potent cytotoxic active against several human cancer cells with IC_{50} values ranging from 0.19 to 0.52μM. Two new oleanane-type triterpenes, **3** and **4**, together with two know compounds, β-amyrin acetate and β-amyrin palmitate, have been isolated from the whole plant of *L. octovalvis.* We have purified from the stems of *D. maritima* and discovered two new napnthoquinones, **5** and **6**, together with two knowns, 6-hydroxy-5-methoxy-2-methyl -1,4-napnthoquinon and bisisodiospyrin.

From the root of *T. cryptomerioides*, six new lignans, **7**, **8**, **9**, **10**, **11** and **12** were isolated and elucidated. The roots of *Rhus javanica* var. *roxburghiana* do folk herb for treating diarrhea, spermatorrhea and malaria. The methanalic extract of the roots of this plant was divided into three fractions, EtOAc soluble, *n*-BuOH soluble and water soluble fractions. Three new triterpene together with thirty-seven know were reported in the previous reports. In this time, the continuous studies on the *n*-BuOH fraction was achieved. Three new cyclolignans, **13**, **14** and **15**, four new lariciresinol-base lignan glycosides, **16**, **17**, **18** and **19**. Four new diepoxylignan glycoside, **20**, **21**, **22** and **23**, together with eight known compounds were purified from *n*-BuOH soluble fraction. Meanwhile compounds **21**-**23** showed moderate inhibition of multiplication of the tobacco mosaic virus. The continuous studies on the roots of *Taiwania cryptomerioides*, six new cadinane-type sesquiterpenes, **24**, **25**, **26**, **27**, **28** and **29** were isolated. The structure of the new constituents were essentially elucidated by spectral evidence. Two new compounds, hydro-Q_9 chromene (**30**), and γ-tocopherol-9 (**31**), together with three know compounds were identified and shown to activate human ERα and β. These result provide basic evidence for the beneficial effect of yam for menopausal women. Two new lignans, lanceoline (**32**) and 5-methoxytrachelogenin (**33**), together with 5-methoxywikstromal were isolated from the low polar layer of

extract of *C. lanceolata*.

四、**Published papers**

1. Chien, S. C., J. Y. Chang, C. C. Kuo, C. C. Hsieh, N. S. Yang, and Y. H. Kuo,* 2007. Cytotoxic and novel skeleton compounds from the heartwood of *Chamaecyparis obtusa* var. *formosana* , *Tetrahedron Lett*., **48**, 1567-1569.
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4. Chyu, C. F. and Y. H. Kuo,*2007. New Lignans from the Roots of *Taiwania cryptomerioides* Hayata. *Helv. Chim. Acta*., **90**(4), 738-747.
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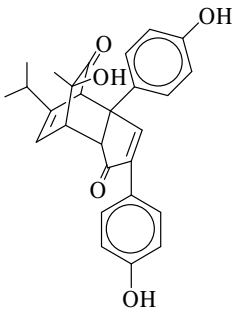

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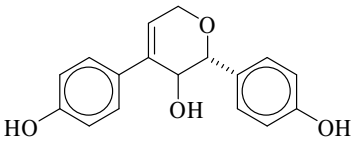

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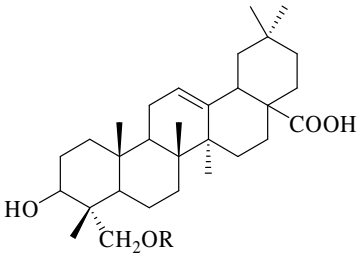

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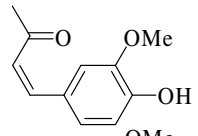

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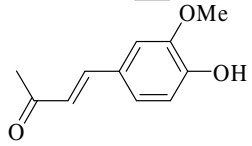
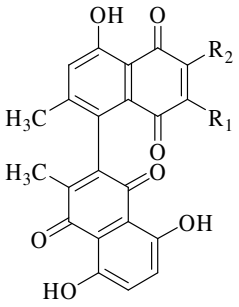
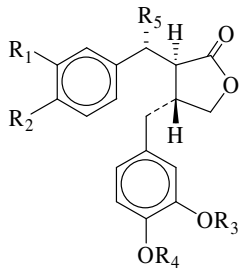
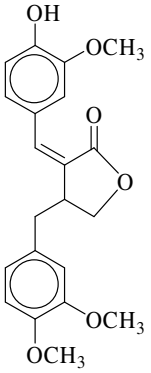




5 R_1= OEt, R_2= H
6 R_1= H, R_2= OEt



7 R_1+ R_2 = OCH_2 , R_3 = R_4 = R_5 = H
8 R_1= H, R_2 = R_5 = OH, R_3 + R_4 = CH_2
9 R_1= R_5 = H, R_2 = OH, R_3 = R_4 = CH_3



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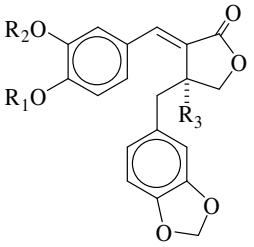
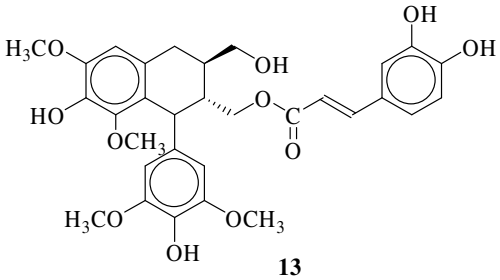


10 R_1+ R_2 = CH_2 , R_3 = OH
11 R_1= R_3 = H, R_2 = CH_3



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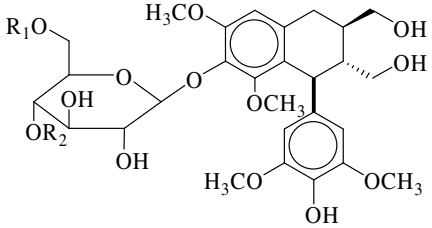
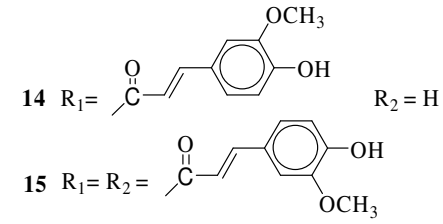
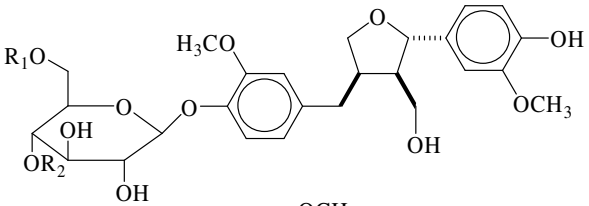
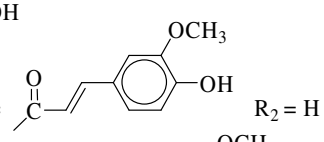




14 R_1= R_2 = H

15 R_1= R_2 =





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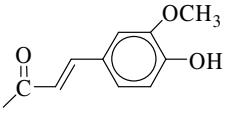

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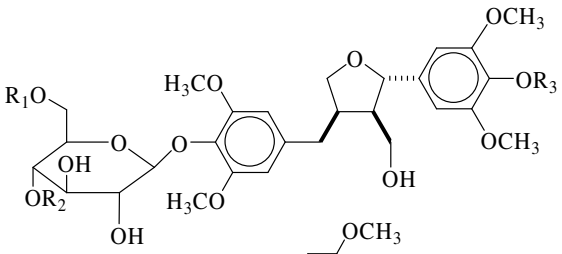
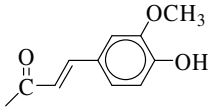
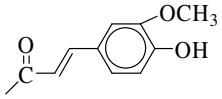
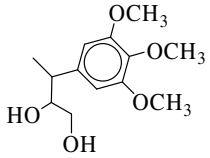
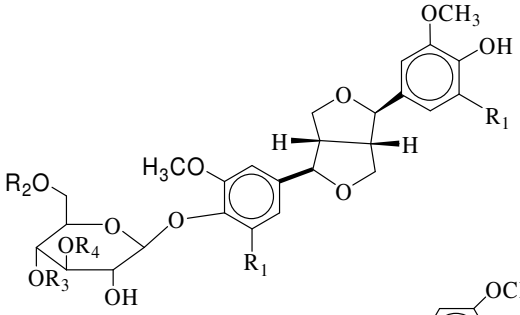
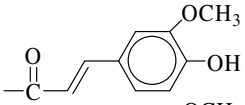
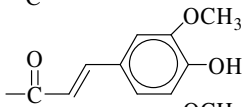


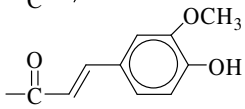
18 $R_1 = R_2 =$  $R_3 = H$

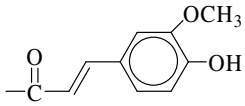
19 $R_1 = R_2 =$  $R_3 =$ 

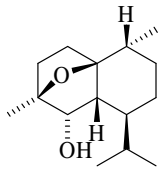


20 $R_1 = R_3 = R_4 = H$, $R_2 =$ 

21 $R_1 = R_4 = H$, $R_2 = R_3 =$ 

22 $R_1 = R_3 = H$, $R_2 = R_4 =$ 

23 $R_1 = OCH_3$, $R_2 = R_3 =$ 



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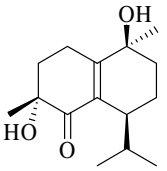

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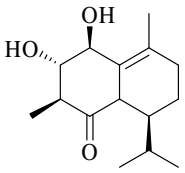

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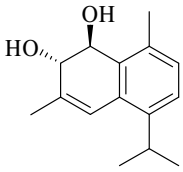

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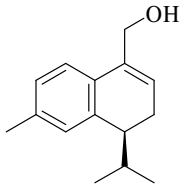

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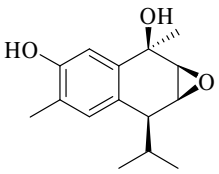

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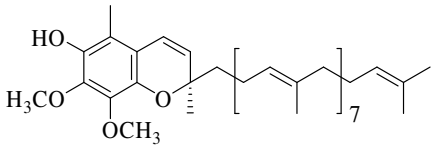

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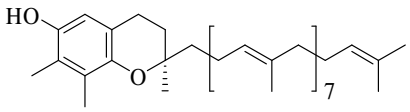

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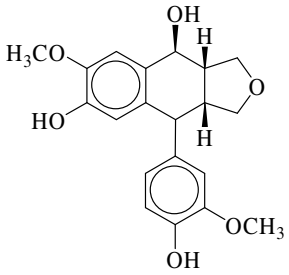

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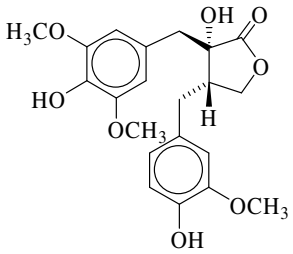

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