# CHAPTER IV

# CONCLUSIONS

Chromatographic separation of *Chaetomium brasiliense*, *C.bostrychodes*, and *C. siamense* led to the isolation of nineteen compounds. Twelve compounds were from *C. brasiliense*. They were four new compounds: mollicellin K **(1.5)**, mollicellin L **(1.6)**, mollicellin M **(1.7)**, and mollicellin N **(1.11)** together with eight known compounds: ergosterol **(1.1)**, 24(*R*)-5α,8α-epidioxyergosta-6-22-dine-3α-ol **(1.2)**, mollicellin H **(1.3)**, mollicellin J **(1.4)**, mollicellin B **(1.8)**, mollicellin C **(1.9)**, mollicellin E **(1.10)**, and mollicellin F **(1.12)**. Seven compounds were isolated from *C. bostrychodes*. They were seven known compounds: ergosterol **(2.1)**, 24(*R*)-5α,8α-epidioxyergosta-6-22-dine-3α-ol **(2.2)**, ergosterylplamitate **(2.3)**, chaetoviridin A **(2.4)**, chaetoviridin F **(2.5)**, chrysophanol **(2.6)** and emodin **(2.7)**. Eight know compounds were isolate from *C. siamense*. They were ergosterol **(3.1)**, 24*(R)*-5α,8α-epidioxyergosta-6-22-dine-3α-ol **(3.2)**, ergosterylplamitate **(3.3)**, cochliodone D **(3.4)**, chaetoviridine A **(3.5)**, chaetoviridin F **(3.6)**, chaetoviridin G **(3.7)** and chrysophanol **(3.8)**.

Among these shown that ergosterol **(1.1, 2.1,** or **3.1)** and 24(*R*)-5α,8α-epidioxyergosta-6-22-dine-3α-ol **(1.2, 2.2,** or **3.2)** were produced from all three *Chaetomium* spp. studied. The four known isolated compounds, ergosterylplamitate **(2.3** or **3.3)**, chaetoviridin A **(2.4** or **3.5)**, chaetoviridin F **(2.5** or **3.6)**, and chrysophanol **(2.6** or **3.8)** were produced from both *C. bostrychodes* and *C. siamense*. Whereas, *C. brasiliense* produced ten specific compounds such as mollicellin H **(1.3)**, mollicellin J **(1.4)**, mollicellin K **(1.5)**, mollicellin L **(1.6)**, mollicellin M **(1.7)**, mollicellin B **(1.8)**, mollicellin C **(1.9)**, mollicellin E **(1.10)**, mollicellin N **(1.11)**, and mollicellin F **(1.12)**. Only emodin **(2.7)** was produced from *C. bostrychodes*. In addition, cochliodone D **(3.4)** and chaetoviridin G **(3.7)** were produced from only *C. siamense* as shown in Table 4.1. The detail of compounds are as follows :-

**Table 4.1** Weight and percentage of compounds from *Chaetomium* spp.

| Compound | 1. *C. brasiliense* mg, (%) | 2. *C. bostrychodes* mg, (%) | 3. *C. siamense* mg, (%) |
|---|---|---|---|
| ergosterol **(1.1)**, **(2.1)**, **(3.1)** | 104 (0.0034%) | 44.6 (0.0387%) | 37.9 (0.0274%) |
| 24(*R*)-5α,8α-epidioxyergosta-6-22-dine-3α-ol **(1.2)**, **(2.2)**, **(3.2)** | 7.4 (0.0025%) | 52 (0.0437%) | 136.2 (0.0454%) |
| mollicellin H **(1.3)** | 14 (0.0047%) | | |
| mollicellin J **(1.4)** | 54 (0.0018%) | | |
| mollicellin K **(1.5)***  | 155.1 (0.0517%) | | |
| mollicellin L **(1.6)*** | 25.2 (0.0083%) | | |
| mollicellin M **(1.7)*** | 7.8 (0.023%) | | |
| mollicellin B **(1.8)** | 67.6 (0.0018%) | | |
| mollicellin C **(1.9)** | 13.2 (0.0045%) | | |
| mollicellin E **(1.10)** | 66.6 (0.022%) | | |
| mollicellin N **(1.11)*** | 16.2 (0.0054%) | | |
| mollicellin F **(1.12)** | 21.3 (0.007%) | | |
| ergosterylplamitate **(2.3)**, **(3.3)** | | 8.7 (0.0073%) | 116.7 (0.0087%) |
| cochliodone D **(3.4)** | | | 13.3 (0.0096%) |
| Chaetoviridin A **(2.4)**,**(3.5)** | | 145.2 (0.0122%) | 983.5 (0.729%) |
| Chaetoviridin F **(2.5)**, **(3.6)** | | 9.5 (0.079%) | 15.5 (0.0115%) |
| Chaetoviridin G **(3.7)** | | | 10.9 (0.0014%) |
| Chrysophanol **(2.6)**, **(3.8)** | | 3.6 (0.0302%) | 2.0 (0.0014%) |
| emodin **(2.7)** | | 9.5 (0.0079%) | |

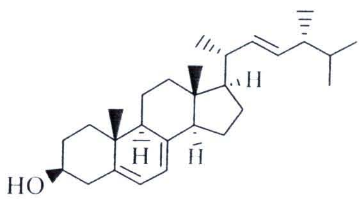
* new compounds

**4.1 *Chaetomium brasiliense***

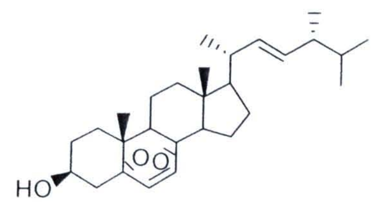
Sequential extraction of air-dried mycelial mats of *C. brasiliense* (300 g) with hexane, EtOAc, and MeOH gave three crude extracts. They were crude hexane 6.8 g (2.27%), crude EtOAc 17.8 g (5.93%), and crude MeOH 20.6 g (6.89%), respectively.

Chromatographic separation of crude extracts from *C. brasiliense* gave twelve compounds, **1.1** – **1.2**. Among these, they were two sterols **1.1** and **1.2** and ten depsidones **1.3** – **1.12**. Their structures were elucidated on the basis of spectroscopic evidences (UV, IR, MS, $^{1}$H NMR, $^{13}$C NMR, DEPT, and 2D NMR) as ergosterol (**1.1**), 24(*R*)-5α,8α-epidioxyergosta-6-22-diene-3β-ol (**1.2**), mollicellin H (**1.3**), mollicellin J (**1.4**), mollicellin K (**1.5**), mollicellin L (**1.6**), mollicellin M (**1.7**), mollicellin B (**1.8**), mollicellin C (**1.9**), mollicellin E (**1.10**), mollicellin N (**1.11**), and mollicelin F (**1.12**). The structures of isolated compounds are shown in Figures 4.1. According to the SciFinder Scholar database 2010, four compounds **1.5**, **1.6**, **1.7** and **1.11** were new compounds. Furthermore, this is the first isolation of six known compounds **1.1, 1.2,** and **1.5** - **1.12** from *C. brasilense.*

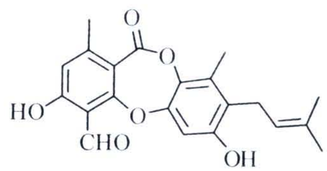
The results of bioactivity assays of these isolated compounds revealed that compounds **1.4** - **1.10** displayed antimalarial activity against *P. falciparum*, with $IC_{50}$ ranging from 1.2 – 1.9 μg/mL. Only **1.5** exhibited antiTB activity against *M. tuberculosis* and potent activity againt *Candida albicans*, as well as cytotoxicity against KB cell lines. However, compounds **1.3**, **1.5, 1.7**, **1.9,** and **1.10,** exhibited significant cytotoxicity against NCI-H187 cell line with $IC_{50}$ values of 3.1, 1.0, 3.9, 0.35, and 0.68 μg/mL, respectively. In addition, compounds **1.5** and **1.7** – **1.12** significant cytotoxicity against five cholangiocarcinoma cell lines with $IC_{50}$ values raning from 2.5 to 15.7 μg/mL. It should be noted that all compounds exhibited $IC_{50}$ values against KKU–100 ranging from 4.5 to 6.5 μg/mL and were more cytotoxic than the control drug ellipticine. Unfortunatly, the results of inhibition of platetet aggregation induced by AA, collagen, ADP and PAF receptor binding, **1.6**, **1.8**, **1.9**, and **1.10** had no effect.



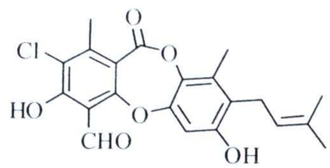
1.1



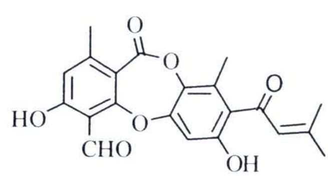
1.2



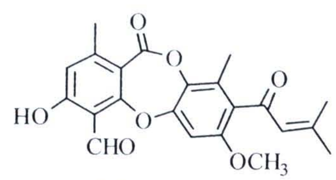
1.3



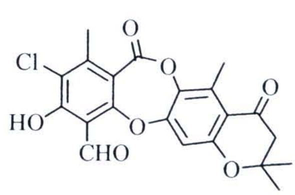
1.4



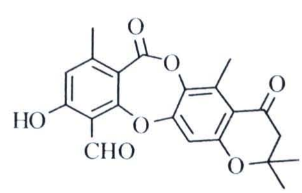
1.5



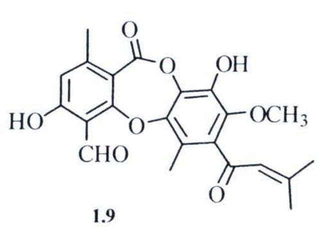
1.6



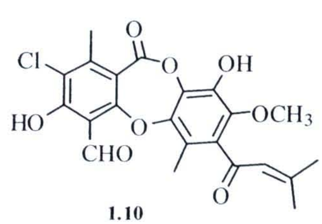
1.7



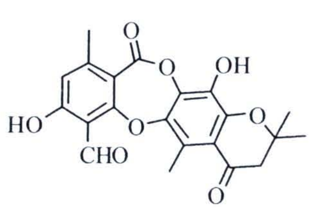
1.8



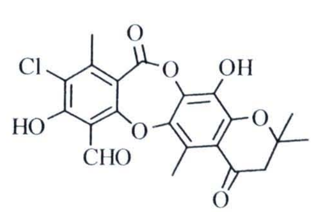
1.9



1.10



1.11



1.12

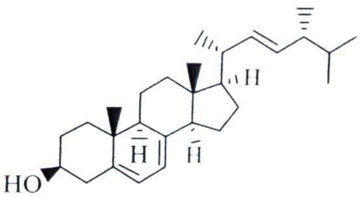
**Figure 4.1** The isolated compounds from *C. brasiliense.*

### 4.2 *Chaetomium bostrychodes*

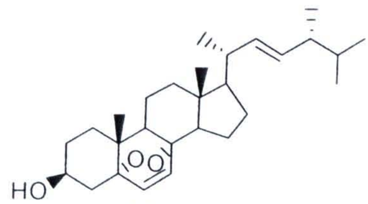
Sequential extraction of air-dried mycelial mats of *C. bostrychodes* (119 g) with hexane, EtOAc, and MeOH gave three crude extracts. They were crude hexane 1.5 g (1.26%), crude EtOAc 2.1 g (1.76%), and crude MeOH 4.5 g (3.78%).

Chromatographic separation of crude extracts from *C. bostrychodes* gave seven compounds, **2.1** – **2.7**. Among these, they were three sterols **2.1, 2.2**, and **2.3**, two azaphilones **2.4** and **2.5**, and two hydroxyanthraquinones **2.6** and **2.7.** Their structures were elucidated on the basis of spectroscopic evidences (IR, $^{1}$H NMR, and $^{13}$C NMR) as ergosterol (**2.1**), 24(*R*)-5α,8α-epidioxyergosta-6-22-diene-3β-ol (**2.2**), ergosterylplamitate (**2.3**), chaetoviridin A (**2.4**), chaetoviridin F (**2.5**), chrysophanol (**2.6**), and emodin **(2.7).** The structures of isolated compounds is shown in Figures 4.2. According to the SciFinder Scholar database 2010, all of these compounds are the first isolation from *C. bostrychodes*.

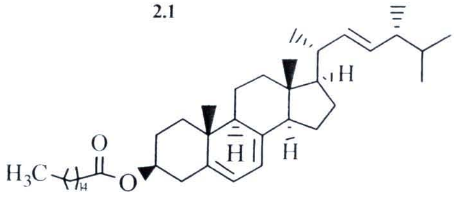
THE NATIONAL RESEARCH COUNCIL OF THAILAND RESEARCH LIBRARY



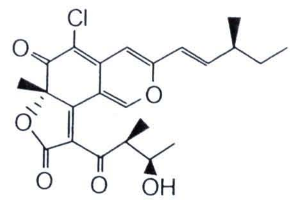
2.1



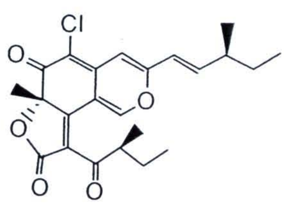
2.2



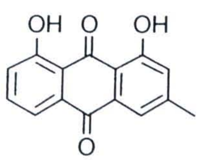
2.3



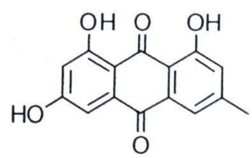
2.4



2.5



2.6



2.7

**Figure 4.2** The isolated compounds from *C. bostrychodes*.

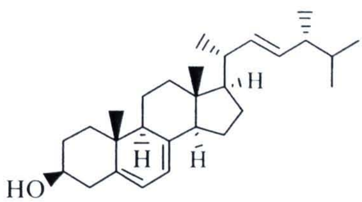
### 4.3 *Chaetomium siamense*

Sequential extraction of air-dried mycelial mats of *C. siamense* (135 g) with hexane, EtOAc, and MeOH gave three crude extracts. The extracts were crude hexane 3.6 g (2.66%), crude EtOAc 4.9 g (3.62%), and crude MeOH 7.6 g (5.62%).

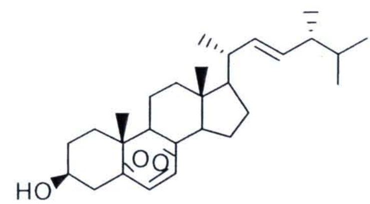
Chromatographic separation of crude extracts from *C. siamense* gave eight compounds, **3.1** – **3.8**. Among these, they were three sterols **3.1, 3.2**, and **3.3**, one bis-spiro-azaphilone **3.4,** three azaphilones **3.5**, **3.6**, and **3.7**, and one hydroxyanthraquinones **3.8**. Their structures were elucidated on the basis of spectroscopic evidences (IR, $^{1}$H NMR, and $^{13}$C NMR) as ergosterol (**3.1**), 24(*R*)-5α,8α-epidioxyergosta-6-22-diene-3β-ol (**3.2**), ergosterylplamitate (**3.3**), cochliodone D (**3.4**), chaetoviridin A (**3.5**), chaetoviridin F (**3.6**), chaetoviridin G

(**3.7**), and chrysophanol (**3.8**). The structures of isolated compounds is shown in Figures 4.2. According to the SciFinder Scholar database 2010, all of these compounds are the first isolation from *C. siamense*.

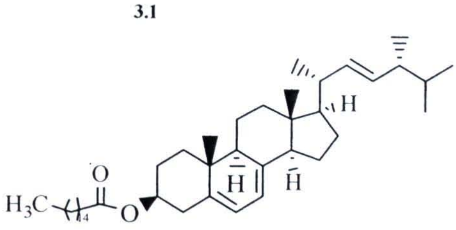
In conclusion, the stuctures of four new compounds, mollicellins K-N **(1.5, 1.6, 1.7,** and **1.8)** could challenge the organic chemists in term of synthesis and structure modification. Finally, the finding of this study should provide some interesting topics for researchers in related fields. Research such as biosynthesis, bioactivity mechanism, toxicology, and the development of the utility of these bioactive compounds should be studied.



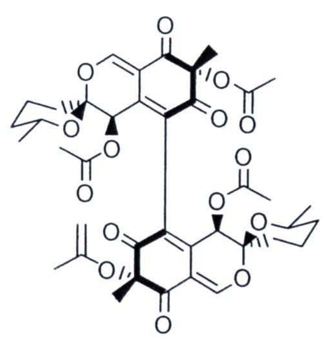
**3.1**



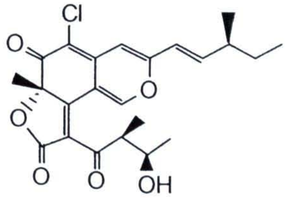
**3.2**



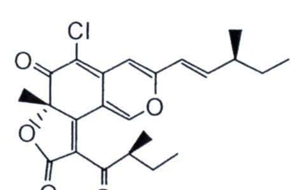
**3.3**



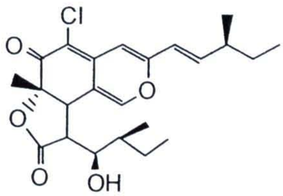
**3.4**



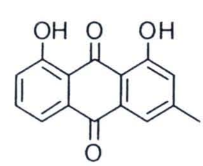
**3.5**



**3.6**



**3.7**



**3.8**

**Figure 4.3** The isolated compounds from *C. siamense*