Potential FabI1 Inhibitors of *B. pseudomallei* from the heartwoods of *Mansonia gagei* Drumm.: Biological prediction and molecular docking calculations

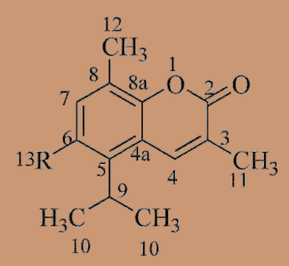
Sasithorn Lorroengsil[1,*], Sirintip Sangsawang[2], Siripen Modmung[2], Somjintana Taweepanich[2], Chan Inntam[2], Pharit Kamsri[3], Auradee Punkvang[3], Jidapa Sangswan[1], Jiraporn Leanpolchareanchai[4], Narisara Chantratita[5], Warinthorn Chavasiri[6], Khomson Suttisintong[7], Prasat Kittakoop[8,9,10], Pornpan Pungpo[2]

[1] Department of Biological Science, Faculty of Science, Ubon Ratchathani University, Ubon Ratchathani 34190, Thailand
[2] Department of Chemistry, Faculty of Science, Ubon Ratchathani University, Ubon Ratchathani 34190, Thailand
[3] Division of Chemistry, Faculty of Science, Nakhon Phanom University, Nakhon Phanom 48000, Thailand
[4] Faculty of Pharmacy, Mahidol University, 10400 Bangkok, Thailand
[5] Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, 10400 Bangkok, Thailand
[6] Department of Chemistry, Faculty of Science, Chulalongkorn University, 10330 Bangkok, Thailand
[7] National Nanotechnology Center, National Science and Technology Development Agency, Thailand Science Park, 12120 Pathumthani, Thailand
[8] Chulabhorn Research Institute, 10210 Bangkok, Thailand
[9] Chulabhorn Graduate Institute, Chemical Biology Program, Chulabhorn Royal Academy, 10210 Bangkok, Thailand
[10] Center of Excellence on Environmental Health and Toxicology (EHT), CHE, Ministry of Education, 10300 Bangkok, Thailand

Introduction

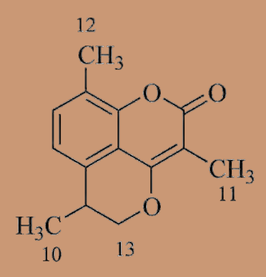
Burkholderia pseudomallei (*B. pseudomallei*) is a Gram-negative soil-dwelling bacillus that causes melioidosis, a frequently fatal infectious disease, in tropical and subtropical regions. Melioidosis is highly endemic in Thailand. Incidence of melioidosis is increasing in Northeast Thailand. Its varied clinical manifestations and resistance to many antibiotics. Therefore, the potential drug to overcome drug resistant is urgently required. This study, biological prediction and molecular docking were applied to identify novel FabI1 inhibitors as anti- *B. pseudomallei* drug from Thai medicinal plant.

Materials and Methods

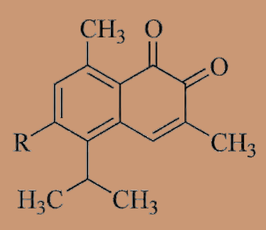


1 R = OCH_3

2 R = OH

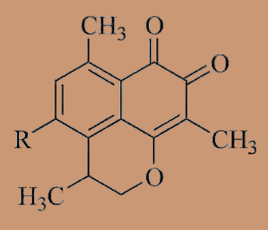


3



4 R = H

5 R = OH



6 R = H

7 R = OH

Reported Structure of Flavans from *Desmos cochinchinensis* → AntibacPred → Molecular docking

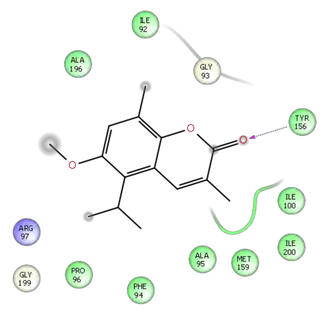
Conclusions

- Six compounds, Mansorin B, Mansorin C, Mansonone C, Mansonone G, Mansonone E and Mansonone H were identified as potential FabI1 Inhibitors of *B. pseudomallei* based on anti-bacterial prediction and molecular docking calculations.
- All compounds were active against resistant-B. pseudomallei with the prediction value ranging from 0.0329 to 0.2859.
- Mansorin B was highest binding affinity with -4.93 kcal/mol for binding in FabI1 binding site.
- The crucial interaction is hydrogen bond interaction of an oxygen carbonyl on Mansorin B with hydroxyl (OH) of Tyr156 sidechain.

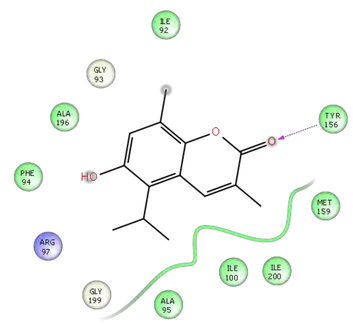
Results

Table 1 Predicted biological property and docking score of natural products in FabI1 binding site

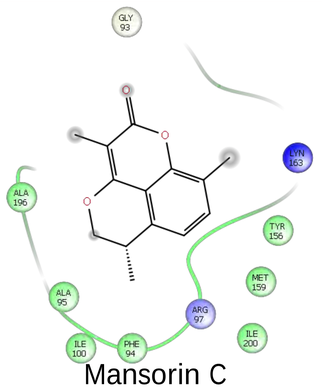
Cpd.	Name	*Burkholderia pseudomallei*	RESISTANT *Burkholderia pseudomallei*	Docking score (kcal/mol)
1	Mansorin A	-	-	-4.82
2	Mansorin B	-	0.0329	-4.93
3	Mansorin C	0.2803	0.2812	-4.06
4	Mansonone C	-	0.0677	-4.15
5	Mansonone G	-	0.0930	-4.53
6	Mansonone E	0.2656	0.2649	-4.33
7	Mansonone H	0.1093	0.2859	-3.41



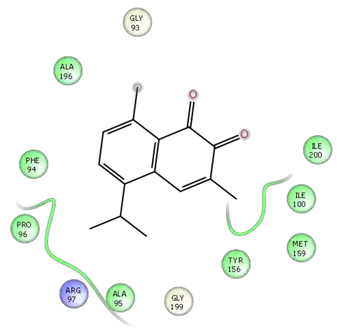
Mansorin A



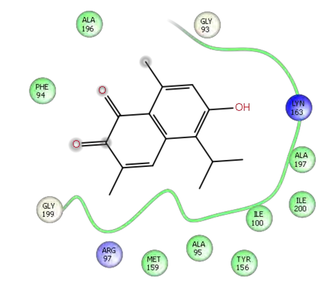
Mansorin B



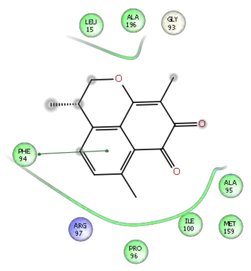
Mansorin C



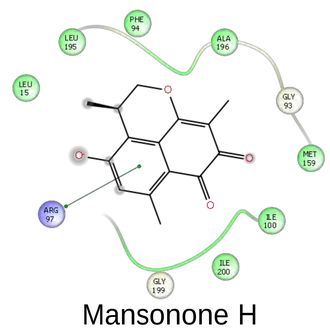
Mansonone C



Mansonone G



Mansonone E



Mansonone H

Figure 1. Binding mode and binding interactions of natural products in FabI1 binding site

Acknowledgements

- Faculty of Science, Ubon Ratchathani University
- National Electronics and Computer Technology Center (NECTEC)