

# Derivatization of 2',4'-Dihydroxy-6'-Methoxy-3',5'-Dimethylchacone from *Syzygium nervosum* Seeds as Potent EGFR Inhibitors



Kunlanit Suwannajit and Puttinan Meepowpan\*

Department of Chemistry, Faculty of Science, Chiang Mai University, Chiang Mai 50200, Thailand

Corresponding Author's E-mail: puttinan.m@cmu.ac.th



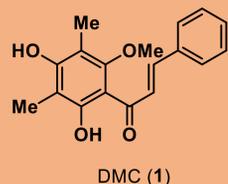
FACULTY OF SCIENCE  
CHIANG MAI UNIVERSITY

## ABSTRACT

### *Syzygium nervosum* or Ma-kiang

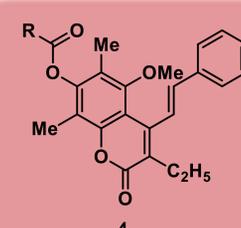
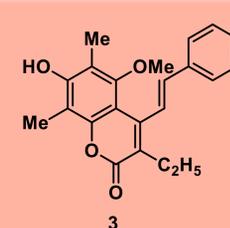
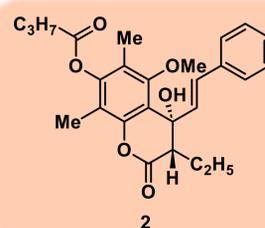


ISOLATION  
AND PURIFICATION



Finding new therapeutic agents is crucial, as cancer remains a serious health concern. To develop new biologically active compounds with potential anticancer properties, DMC (1) was isolated from *S. nervosum* seeds.

### MODIFICATION



Derivatives **3** and **4a** exhibited the highest binding affinities ( $K_D$  from **13.4** to **14.9**  $\mu\text{M}$ ) among the synthesized compounds, suggesting their potential as lead compounds for further *in vitro* investigation.

4a: R =  $\text{CH}_2\text{CH}_3$   
4b: R =  $\text{CHCH}_2$

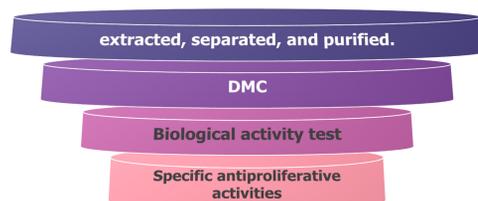
## INTRODUCTION

### Natural Product

### DMC



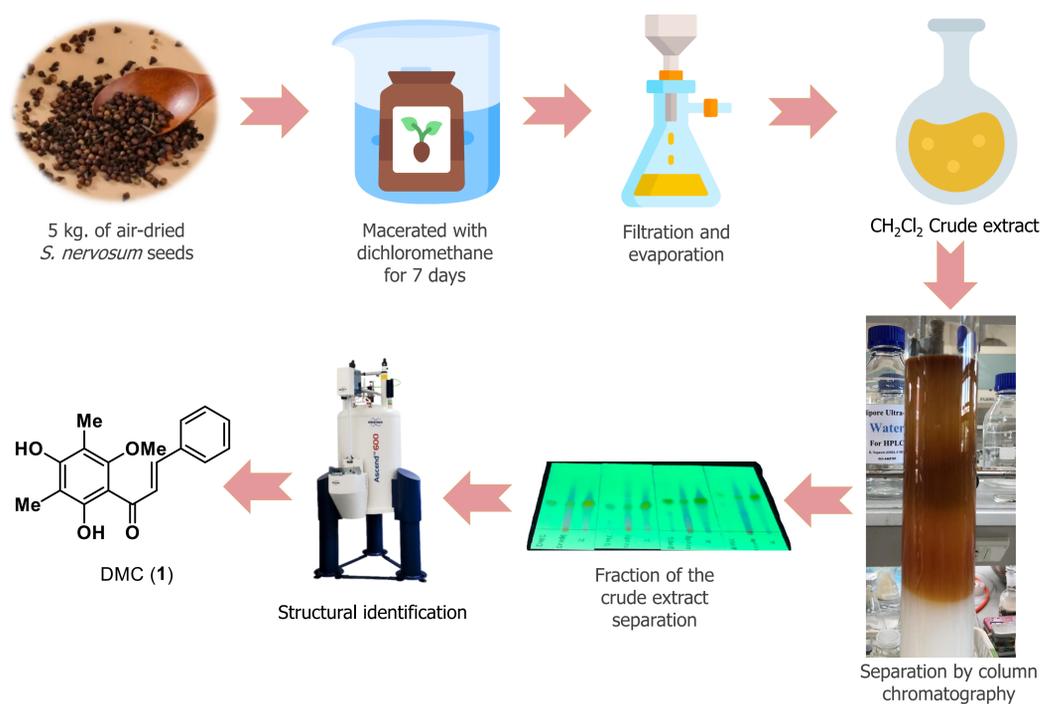
*Syzygium nervosum* A. Cunn. ex DC.  
is in the Myrtaceae family.  
Found in **Southeast Asia**



These finding provide a promising to starting point for further studies on cancer therapies

## EXPERIMENT

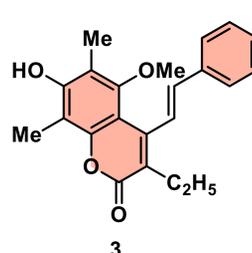
### Extraction, Isolation, Purification and Identification



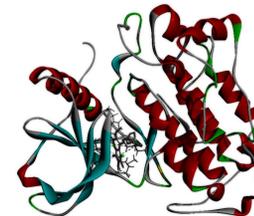
## RESULTS

### *in silico* molecular docking approach

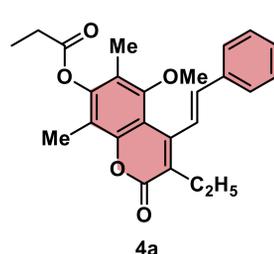
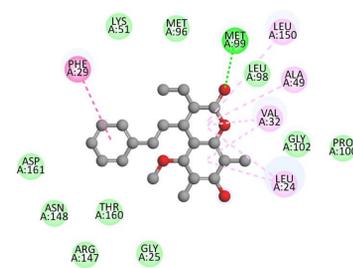
### Derivatives **3** and **4a** exhibited the highest binding affinities



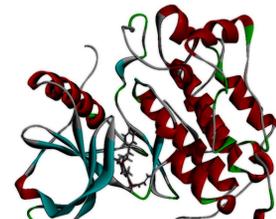
Docking



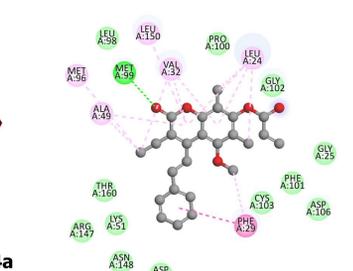
Protein binding with derivative **3**



Docking



Protein binding with derivative **4a**

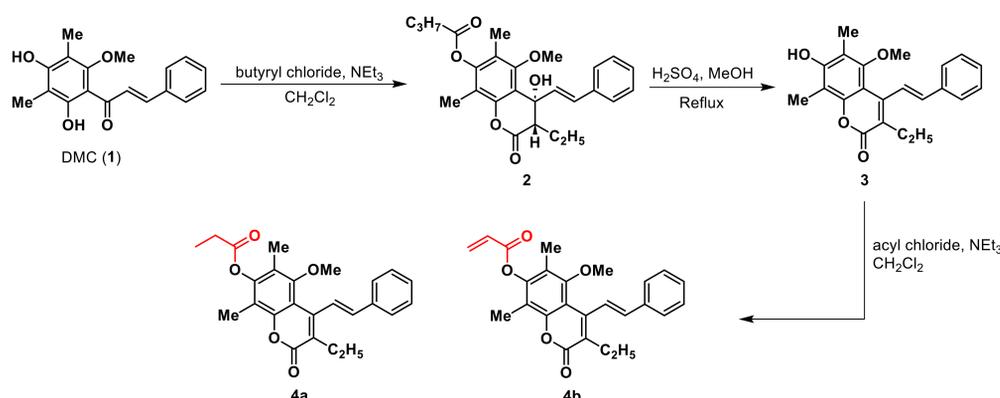


### Binding affinities

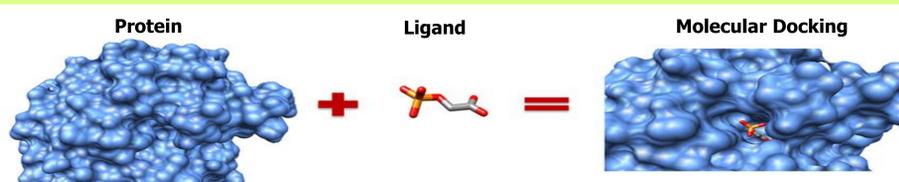
Table 1 Predicted binding affinities of DMC derivatives on EGFR receptor

Derivative	Affinity (kcal/mol)	Intramol (kcal/mol)	CNN pose score	CNN affinity	$K_D$ ( $\mu\text{M}$ )
3	-8.88	0.22	0.8396	6.828	14.8
4a	-8.19	-0.19	0.6876	6.928	11.8

### Synthesis of DMC derivatives



### Molecular Docking



## CONCLUSION

2',4'-Dihydroxy-6'-methoxy-3',5'-dimethylchacone (DMC,1), A natural substance, is made from *Syzygium nervosum* or Ma-kiang seeds. Finding new therapeutic molecules is essential to this study because cancer is still an important health issue. In order to create new biologically active substances that might have anticancer effects, **DMC (1)** was extracted from *S. nervosum* seeds. Conventional processes were used to chemically modify this molecule, producing four derivatives in moderate to high yields. Using an *in silico* molecular docking technique, the synthetic drugs potential against the epidermal growth factor receptor (EGFR) was assessed. Consequently, among the produced compounds, derivatives **3** and **4a** showed the highest binding affinities ( $K_D$  ranging from **11.3** to **11.8**  $\mu\text{M}$ ), indicating their potential as lead compounds for additional *in vitro* research. These results offer a promising starting point for further studies on cancer therapies.

## ACKNOWLEDGEMENTS

I would also like to thank: Assoc. Prof. Dr. Puttinan Meepowpan (Special Problem Adviser), Member of Organic Synthesis Research Laboratory (OSRL-CMU), Chiang Mai University, THAILAND and Department of Chemistry, Faculty of science, Chiang Mai University.

## REFERENCES

- Utama, K.; Khamto, N.; Meepowpan, P.; Aobchey, P.; Kantapan, J.; Sringarm, K.; Roytrakul, S.; Sangthong, P. *Molecules* **2022**, *27*, 1154.
- Khamto, N.; Chaichuang, L.; Rithchumpon, P.; Phupong, W.; Bhoopong, P.; Tateing, S.; Pompimon, W.; Semakul, N.; Chomsri, N.; Meepowpan, P. *RSC Adv.* **2021**, *50*, 31433-31447.