

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

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## ABSTRACT

2',4'-Dihydroxy-6'-methoxy-3',5'-dimethylchacone (DMC, **1**) is a natural product derived from the seeds of *Syzygium nervosum* or Ma-kiang. In this research, 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. This compound was chemically modified through conventional reactions to yield four derivatives in moderate to high yields. The potential of the synthesized compounds against the epidermal growth factor receptor (EGFR) was evaluated using an *in silico* molecular docking approach. As a result, 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. These findings provide a promising starting point for further studies on cancer therapies.

