

## ABSTRACT

The coronavirus disease 2019 (COVID-19) is a rapidly spreading disease that poses a global challenge in many fields including health and disease management. In this situation, this research serves as a preliminary study by screening potential compounds from natural herbs *Zingiber officinale* (127) and *Syzygium aromaticum* (33) that may act as prophylaxis against COVID-19 by a series of *in silico* studies namely chemical characterization, ADMET prediction, molecular docking, and gene enrichment analysis. Collectively, 155 candidate compounds were predicted for their inhibitory effects against key protein targets (RdRp, Mpro, PLpro, Nucleocapsid, Spike, and ACE2) through molecular docking. In conjunction, gene enrichment analysis was also carried out to provide insight in relevant gene and pathway modulation related to COVID-19 and the immune system. Together, the study has revealed a number of promising compounds including cembrene, caryophyllene oxide,  $\alpha$ -curcumene, germacrene B, and liguloxide which are predicted to possess good inhibition activity towards target proteins and the ability to modulate relevant genes namely IFNG, CD14, TNFRSF1A, GAPDH, HMOX1, and NOS2. Overall, this study proposed that the prophylactic effect may be achieved by 3 layers of preventive action, namely (1) immune system enhancement; (2) suppression of proinflammatory cytokines; and (3) hypoxia symptom management.

Keywords: COVID-19, essential oils, immune system, molecular docking, natural compounds

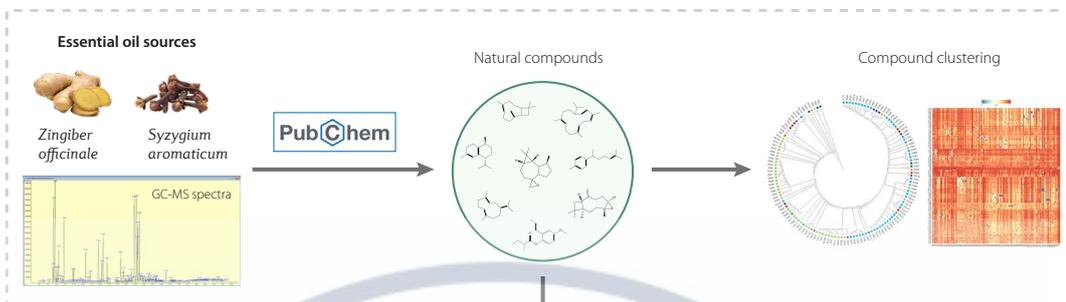
## ABSTRAK

Penyakit virus korona 2019 (COVID-19) adalah penyakit dengan tingkat penyebaran cepat yang menimbulkan tantangan global di berbagai bidang termasuk kesehatan dan manajemen penyakit. Penelitian ini ditujukan sebagai studi pendahuluan dengan menyaring senyawa potensial dari herbal alami *Zingiber officinale* (127) dan *Syzygium aromaticum* (33) yang dapat bertindak sebagai profilaksis terhadap COVID-19 melalui rangkaian studi *in silico* termasuk karakterisasi kimia, prediksi ADMET, docking molekuler, analisis pengayaan gen. Secara keseluruhan, terdapat 155 senyawa kandidat yang diprediksi memiliki efek penghambatan terhadap target protein utama (RdRp, Mpro, PLpro, Nucleocapsid, Spike, dan ACE2) melalui docking molekuler. Bersamaan dengan itu, analisis pengayaan gen juga dilakukan untuk memberikan wawasan tentang modulasi gen dan jalur seluler yang berkaitan dengan COVID-19 dan sistem kekebalan tubuh. Penelitian ini telah mengungkap sejumlah senyawa yang menjanjikan termasuk cembrene, caryophyllene oxide,  $\alpha$ -curcumene, germacrene B, dan liguloxide yang diprediksi memiliki aktivitas penghambatan yang baik terhadap target protein dan kemampuan untuk memodulasi gen yang relevan, yaitu IFNG, CD14, TNFRSF1A, GAPDH, HMOX1, dan NOS2. Telah diusulkan bahwa efek profilaksis dapat dicapai dengan 3 lapis tindakan pencegahan, yaitu (1) peningkatan sistem kekebalan tubuh; (2) penekanan sitokin proinflamasi; dan (3) manajemen gejala hipoksia.

Kata kunci: COVID-19, docking molekuler, minyak atsiri, senyawa alami, sistem imun

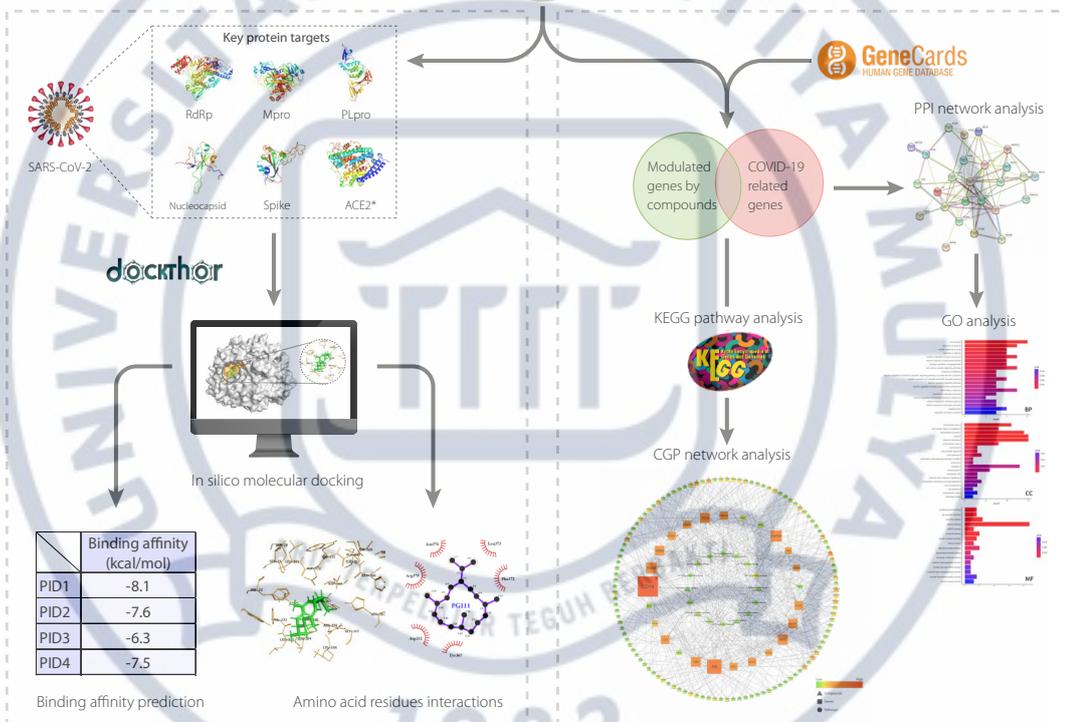
# GRAPHICAL ABSTRACT

## Step 1: Chemical characterisation and clustering

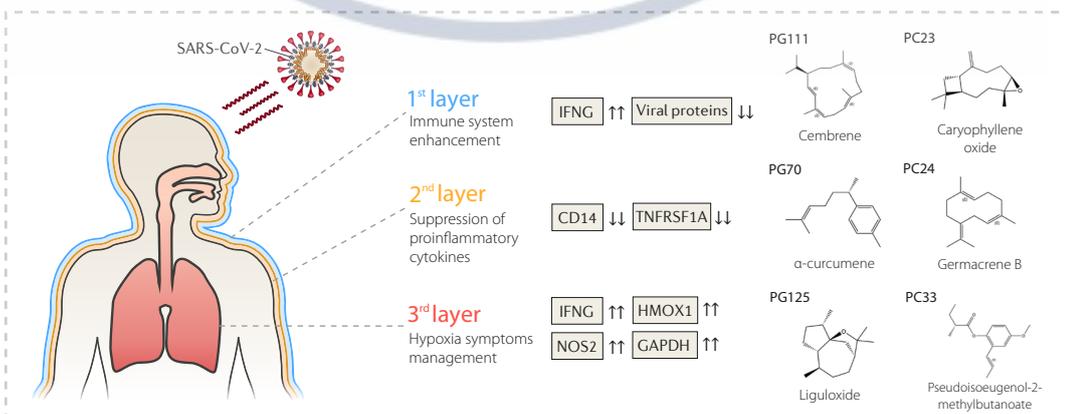


## Step 2: Molecular docking

## Step 3: Enrichment analysis



## Step 4: Prophylactic strategy generation



\* Host protein receptor, not strictly from SARS-CoV-2