

ABSTRACT

The coronavirus disease 2019 (COVID-19) is a highly infectious disease that still endangers the lives of many people worldwide. In an effort to develop preventive strategies, this research serves as a preliminary study by screening a vast number of natural compounds from *Cymbopogon citratus* Stapf. (lemongrass) and *Piper betle* L. (betel) essential oils to generate prophylactic measures against COVID-19 by a series of *in silico* studies, namely chemical characterization, ADMET prediction, molecular docking and gene enrichment analysis. In total, six targets (RdRp, Mpro, PLpro, Nucleocapsid, Spike, and ACE2) and 186 natural compounds were predicted through molecular docking study. The gene enrichment analysis revealed that the integrated-actions of the compounds may modulate several COVID-19 related genes and are involved in numerous pathways in association to the pathogenesis and body's immune system. Among the most promising molecules, geranylinalool, isoeugenyl phenylacetate, terpinen-4-ol acetate, and precocene II have been predicted to possess good inhibitory effects against SARS-CoV-2 related targets and modulate the key important genes including IFNG, CD14, TNFRSF1A, GAPDH, HMOX1, and NOS2. Taken together, three layers of prophylactic mechanisms by lemongrass and betel essential oil compounds were proposed against COVID-19: (1) immune system enhancement; (2) suppression of proinflammatory cytokines; (3) hypoxia symptoms management. This research will provide a basis for further investigation of *in vitro*, pre-clinical and clinical trials of selected compounds against COVID-19.

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

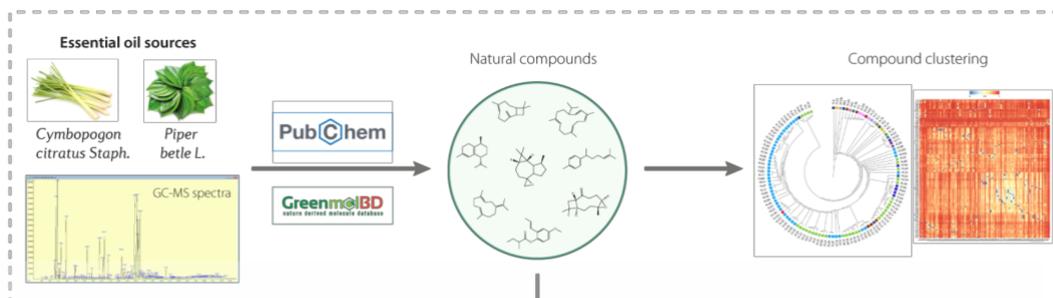
ABSTRAK

Penyakit virus corona 2019 (COVID-19) adalah penyakit yang sangat menular dan masih membahayakan kehidupan masyarakat di seluruh dunia. Dalam upaya pengembangan strategi pencegahan, penelitian ini bertujuan sebagai studi pendahuluan dengan menyaring sejumlah senyawa alami minyak atsiri dari *Cymbopogon citratus* Stapf. (sereh) dan *Piper betle* L. (sirih) untuk menghasilkan perlindungan terhadap COVID-19 melalui serangkaian studi *in silico*, diantaranya adalah karakterisasi kimia, prediksi ADMET, docking molekuler, dan analisis pengayaan gen. Enam target (RdRp, Mpro, PLpro, Nucleocapsid, Spike dan ACE2) dan 186 senyawa alami diprediksi melalui studi docking molekuler. Analisis pengayaan gen menunjukkan aksi dari senyawa-senyawa alami secara terintegrasi dapat memodulasi beberapa gen yang berkaitan dengan COVID-19 dan terlibat dalam berbagai jalur pensinyalan berkaitan dengan patogenesis COVID-19 dan sistem kekebalan tubuh. Beberapa molekul yang paling menjanjikan diantaranya adalah geranylinalool, isoeugenyl phenylacetate, terpinen-4-ol acetate, dan precocene II diprediksi memiliki efek penghambatan terhadap target terkait SARS-CoV-2 dan memodulasi gen-gen yang memiliki peran penting, diantaranya IFNG, CD14, TNFRSF1A, GAPDH, HMOX1, dan NOS2. Secara keseluruhan, senyawa dari minyak atsiri serai dan sirih diusulkan memiliki tiga lapis mekanisme terhadap COVID-19: (1) peningkatan sistem kekebalan tubuh; (2) penekanan sitokin proinflamasi; (3) menjaga gejala hipoksia. Penelitian ini akan menjadi dasar untuk investigasi lebih lanjut pada uji *in vitro*, pre klinis dan uji klinis dari senyawa terpilih terhadap COVID-19.

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

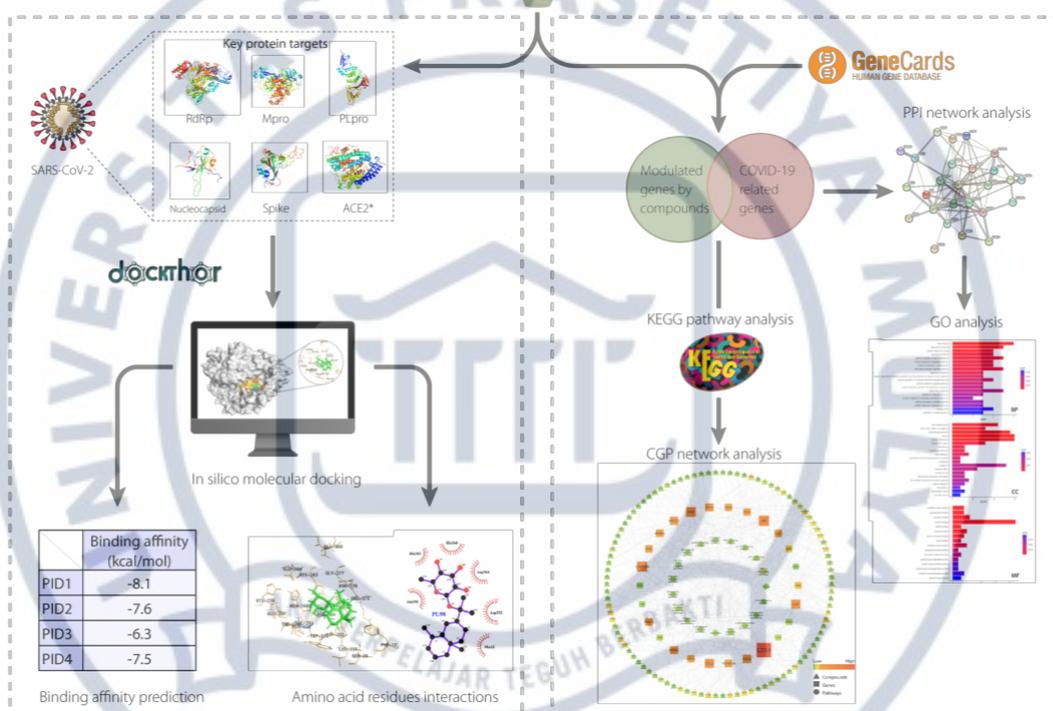
GRAPHICAL ABSTRACT

Step 1: Chemical characterisation and clustering

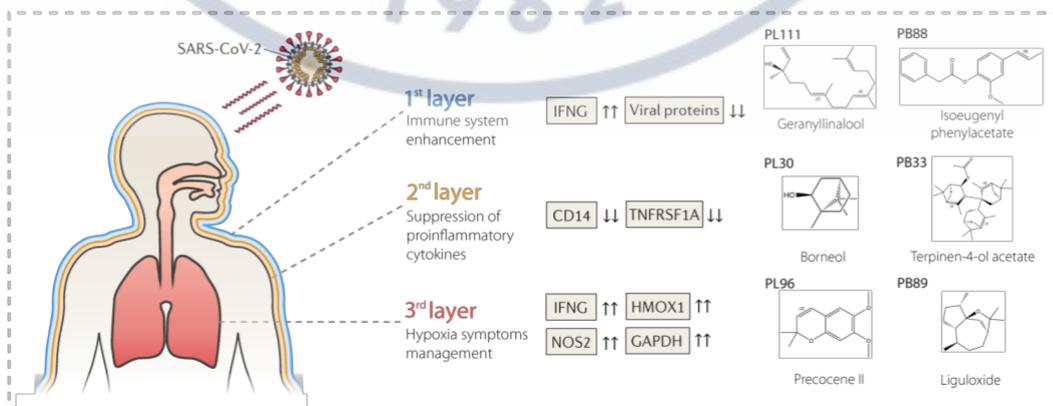


Step 2: Molecular docking

Step 3: Enrichment analysis



Step 4: Prophylactic strategy generation



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