

Abstract

A substantial global public health concern has been raised due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak in 2019. Flavonoids were reported to possess anti-SARS-CoV-2 properties by targeting 3-Chymotrypsin Like protease (3CLpro) which is the main enzyme involved in the life cycle of SARS-CoV-2. *Zingiber zerumbet* (bitter ginger) is a plant native to Indonesia and is also known by the name of "*lempuyang*". The rhizome part of bitter ginger was reported to contain several flavonoids such as kaempferol and quercetin, which are reported to possess promising 3CLpro inhibitory effects. Thus, the main objective of the study was to investigate the anti-SARS-CoV-2 properties of the bitter ginger rhizome extract. The constituents in the extract were characterized using the UPLC-ESI-MS followed by *in silico* studies and *in vitro* inhibition bioassay. Through UPLC-ESI-MS/MS qualitative analysis, kaempferol, quercetin, and several of its derivatives were identified in the crude extract. The compounds were found to have high predicted binding with a binding affinity of between -7.5 to -8.7 kcal/mol. The IC_{50} of the bitter ginger rhizome crude extract was 0.3 mg/ml. Therefore, this study emphasized the potential of bitter ginger rhizome extract as a SARS-CoV-2 3CLpro inhibitor. More studies in relation to the pharmacological action, metabolism, safety, and efficacy of the bitter ginger rhizome extract is required to further investigate its potential. The results are aimed to provide a foundation for further research on the development of COVID-19 treatments using herbal materials native to Indonesia.

Keywords: 3CLpro, Anti SARS-CoV-2, COVID-19, Bitter Ginger, Flavonoid