초청강연-2

Could Natural Products Confer Inhibition of SARS-CoV-2 Main Protease? *In-silico* Drug Discovery

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In December 2019, the COVID-19 epidemic was discovered in Wuhan, China, and since has disseminated around the world impacting human health for millions.

Herein, *in-silico* drug discovery approaches were utilized to identify potential candidates as Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) main protease (M^{pro}) inhibitors. We investigated several databases including natural and natural-like products (>100,000 molecules), DrugBank database (10,036 drugs), major metabolites isolated from daily used spices (32 molecules), and current clinical drug candidates for the treatment of COVID-19 (18 drugs).

All tested compounds were prepared and screened using molecular docking techniques. Based on the calculated docking scores, the top ones from each project under investigation were selected and subjected to molecular dynamics (MD) simulations followed by molecular mechanics-generalized Born surface area (MM-GBSA) binding energy calculations. Combined long MD simulations and MM-GBSA calculations revealed the potent compounds with prospective binding affinities against M^{pro}. Structural and energetic analyses over the simulated time demonstrated the high stabilities of the selected compounds.

Our results showed that 4-bis([1,3]dioxolo)pyran-5-carboxamide derivatives (natural and natural-like products database), DB02388 and Cobicistat (DB09065) (DrugBank database), salvianolic acid A (spices secondary metabolites) and TMC-310911 (clinical-trial drugs database) exhibited high binding affinities with SARS-CoV-2 M^{pro}. In conclusion, these compounds are up-and-coming anti-COVID-19 drug candidates that warrant further detailed *in vitro* and *in vivo* experimental estimations.