Natural agents against SARS-CoV-2

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is distinctly infective, and there is an ongoing effort to find a cure for this pandemic. Unlikely, no certified drugs to efficiently inhibit the virus were identified and the development of *de-novo* medicines requires approximately 10 years of research. Therefore, the repurposing of natural products could be an effective strategy to handle the SARS-CoV-2 infection. A combined *in silico* workflow to identify novel drug candidates against SARS-CoV-2 was applied. Thus, the characterization of the druggable binding pockets including both orthosteric and allosteric sites of SARS-CoV-2 non-structural proteins (nsp) were adopted for the structure-based virtual screening. Around three million of small molecules were used to select compounds interacting with SARS-CoV-2 nsp proteins. Several scaffolds were clustered for their best multi-targeting profile against the binding pockets of the analysed SARS-CoV-2 druggable targets. Interestingly, the indole derivatives resulted as promising *hits* by our computational protocol, emphasizing its role in designing and discovering the much-awaited anti-SARS CoV-2 therapy. Among the clinical trials actually recruited, some natural compounds are ongoing to examine their potential role to prevent and to treat the COVID-19 infection. Many natural scaffolds, including alkaloids, terpenes, flavonoids, and benzoquinones, were investigated by *in silico*, *in vitro*, and *in vivo* approaches. Despite the large data set obtained by computational approach, experimental evidences in most cases are not available. To fill this gap, further efforts to validate these results are required. This project was carried out in collaboration with Net4Science Academic Spin-Off, (www.net4science.com) and Associazione CRISEA (www.crisea.it).