

Computational investigation on *Andrographis paniculata* phytochemicals to evaluate their potency against SARS-CoV-2 in comparison to known antiviral compounds in drug trials

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Communicated by Ramaswamy H. Sarma

ABSTRACT

The outbreak due to SARS-CoV-2 (or Covid-19) is spreading alarmingly and number of deaths due to infection is aggressively increasing every day. Due to the rapid human to human transmission of Covid-19, we are in need to find a potent drug at the earliest by ruling-out the traditional time-consuming approach of drug development. This is only possible if we use reliable computational approaches for screening compounds from chemical space or by drug repurposing or by finding the phytochemicals and nutraceuticals from plants as they can be immediately used without the need for carrying out drug-trials to test safety and efficacy. A number of plant products were routinely suggested as drugs in traditional Indian and Chinese medicine. Here using molecular docking approach, and combined molecular dynamics and MM-GBSA based free energy calculations approach, we study the potency of the four selected phytochemicals namely andrographolide (AGP1), 14-deoxy 11,12-didehydro andrographolide (AGP2), neoandrographolide (AGP3) and 14-deoxy andrographolide (AGP4) from *A. paniculata* plant against the four key targets including three non-structural proteins (3L main protease (3CLpro), Papain-like proteinase (PLpro) and RNA-directed RNA polymerase (RdRp)) and a structural protein (spike protein (S)) of the virus which are responsible for replication, transcription and host cell recognition. The therapeutic potential of the selected phytochemicals against Covid-19 were also evaluated in comparison with a few commercially available drugs. The binding free energy data suggest that AGP3 could be used as a cost-effective drug-analog for treating covid-19 infection in developing countries.

ARTICLE HISTORY

Received 20 April 2020
Accepted 27 May 2020

KEYWORDS

SARS-CoV-2; *Andrographis paniculata*; andrographolide; neoandrographolide; RNA-directed RNA polymerase; spike protein; Covid-19

1. Introduction

The current outbreak of highly transmissible fatal pneumonia in human referred as Coronavirus Disease-2019 (Covid-19) has spread globally with over 5.5M confirmed cases and over 340000 deaths worldwide as of 15th April 2020 (Wu, Liu, et al., 2020). Covid-19 is caused by a novel zoonotic pathogenic virus termed as Severe Acute Respiratory Syndrome Coronavirus 2(SARS-CoV-2) which has been first

pandemic potential of SARS-CoV-2 is due to its high human to human transmissible efficiency which makes it difficult to contain (Wu, Zhao, et al., 2020). SARS-CoV-2 has enveloped positive sense single stranded RNA genome and sequence analysis of its 30,000 base-pair genome has evidenced about 14 open reading frames (ORF) (Fehr & Perlman, 2015). The 5' end ORF1a/b codes for polyprotein that are consequently processed by proteolytic cleavage into 16 non-structural and