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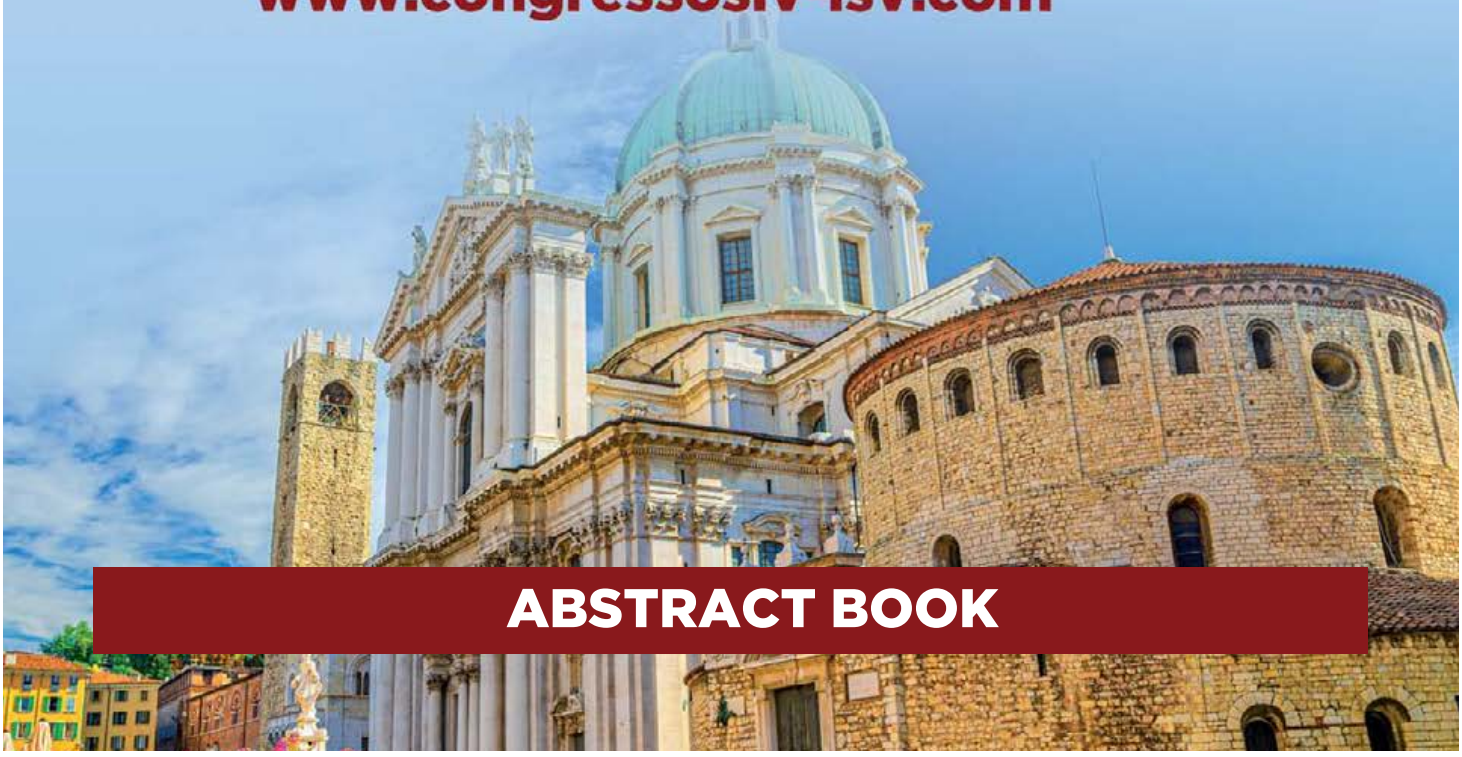

ABSTRACT BOOK

PO 012

STRIGOLACTONES AS BROAD-SPECTRUM ANTIVIRALS AGAINST ß-CORONAVIRUSES THROUGH TARGETING THE MAIN PROTEASE Mpro

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Aim of the Study: The current SARS-CoV-2 pandemic and the likelihood that new coronavirus strains will emerge in the immediate future point out the urgent need to identify new pan-coronavirus inhibitors. Strigolactones (SLs) are a class of plant hormones with multifaceted activities whose role in plant-related fields has been extensively explored. Recently, we proved that SLs also exert an antiviral activity toward herpesviruses, such as human cytomegalovirus (HCMV). Based on this background, this work aimed to ascertain whether SLs might constitute a new class of broad-spectrum compounds against ß-coronaviruses (ß-CoVs).

Methods used: We employed two indole-based SL analogs, named TH-EGO and EDOT-EGO. We assessed the antiviral activity of the compounds against SARS-CoV-2 and the common cold human coronavirus HCoV-OC43, as prototypes of ß-CoVs by standard plaque assay on VERO-E6 and MRC- 5 cells, respectively. By using FLAP implemented in BiOGPS, we then investigate which might be the target of the analyzed SLs; we performed a docking simulation on all the available structures of SARS-CoV-2 proteins present in the Protein Data Bank, and among the highest-scored pockets we noticed the presence of the main protease (M^{pro}) orthosteric site. Therefore, with Gold, we performed a more accurate docking simulation between the compounds and the M^{pro} binding site to obtain ligand poses, and with Glide we simulated a covalent docking to obtain potential adducts. In the end, to strengthen the computational results, we tested the effect of EDOT-EGO and TH-EGO on SARS-CoV-2 M^{pro} activity using an *in-vitro* biochemical assay based on Fluorescence Resonance Energy Transfer (FRET).

Results and Conclusions: Here we show that the synthetic SLs TH-EGO and EDOT-EGO impair ß-CoVs replication, including SARS-CoV-2 and HCoV-OC43. Interestingly, in-silico simulations suggest the binding of SLs in the SARS-CoV-2 main protease (M^{pro}) active site, and this was further confirmed by an *in-vitro* activity assay. Overall, our results highlight the potential efficacy of SLs as broad-spectrum antivirals against ß-CoVs, which may provide the rationale for repurposing this class of hormones for the treatment of COVID-19 patients.