**RdRp-SOF and –remdesivir molecular interaction and simulation**

The binding pockets residues like Asp623, Thr680, Thr687 and Asp760 were involved in polar contact formation with remdesivir. Pi-interactions of Arg553, Asp623, Arg624 and Ser681 with a functional group of ligands stabilized the ligand binding (Figure S1A). Similarly, SOF formed multiple H-bonds with Thr556, Asp-623, Arg-624 and Ser-628. Besides this, Cys622 was involved in Pi-sulfur interaction with aromatic groups and Asp623 formed attractive interaction with a charged group of the ligand (Figure S1B). RdRp, Remdesivir and SOF showed RMSD in range of 0.1 to 0.4 nm (Figure S1C and D).

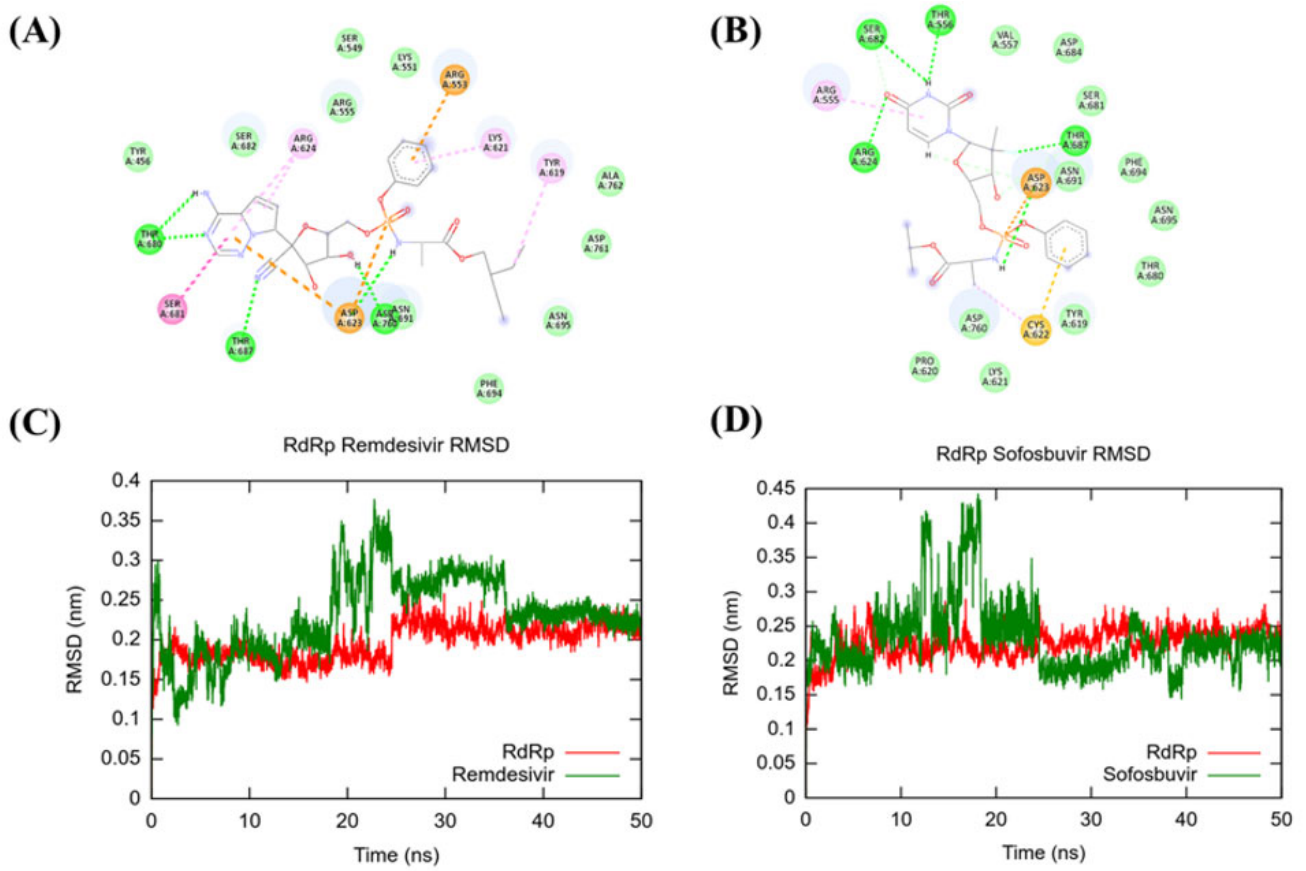


**Figure S1.** Molecular interactions of RdRp with (**A**) Remdesivir (**B**) SOF. RMSD of RdRp in complex with (**C**) Remdesivir (**D**) SOF upon 50ns similar.

## Potential energy plots for simulated complexes

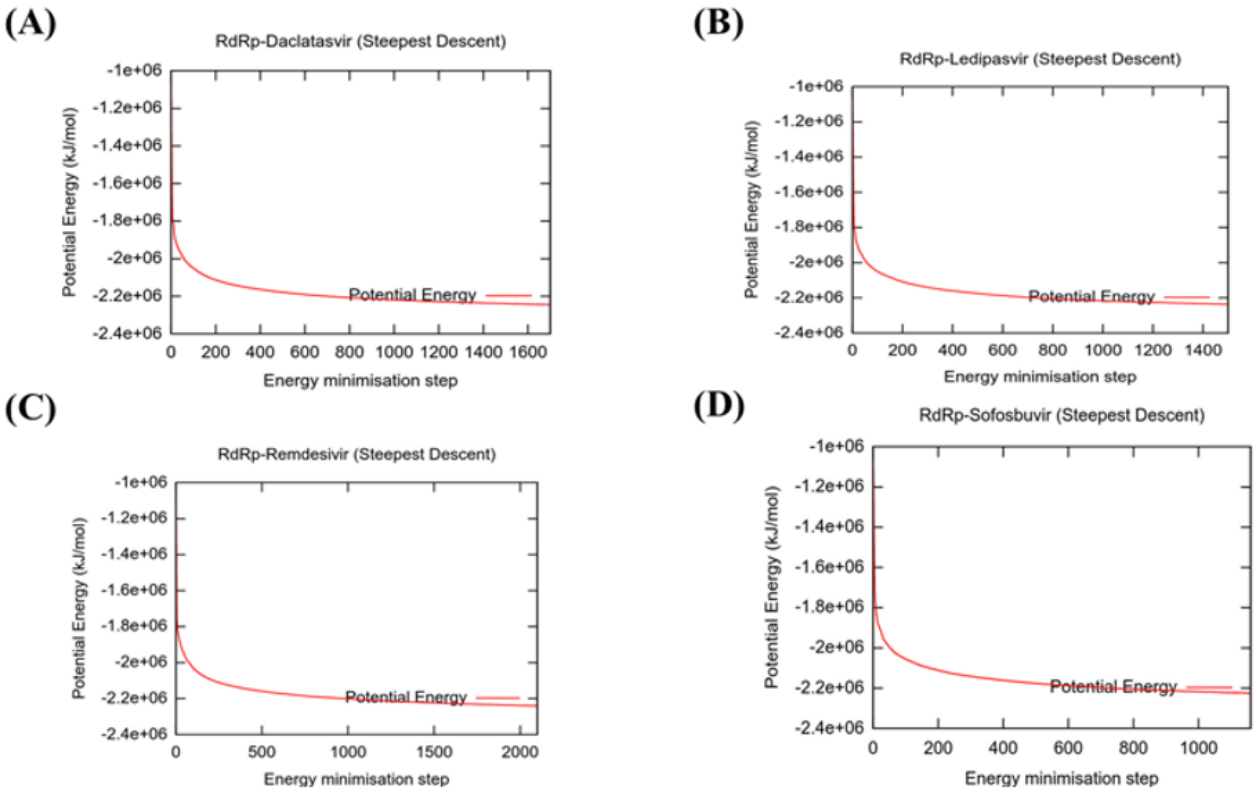


**Figure S2.** Potential energy plots for RdRp in complex with (**A**) DCV (**B**) LDP (**C**) Remdesivir and (**D**) SOF after 50 ns simulation.

**Table S1.** Binding score and predicted affinity of selected ligands against RdRp of SARS-CoV-2.

| Ligand | Binding Score (Kcal/mol) | Binding Affinty (−log10(KD\|Ki)) |
|---|---|---|
| Remdesvir | −8.2 | 11.6 |
| Ledipasvir | −9.4 | 93.6 |
| Daclatasvir | −7.8 | 24.3 |
| Sofosbuvir | −7.6 | −25.4 |