Supplementary Material

Evaluation of molnupiravir analogues as novel coronavirus (SARS-CoV-2) RNA-dependent RNA polymerase (RdRp) inhibitors – an *in silico* docking and ADMET simulation study

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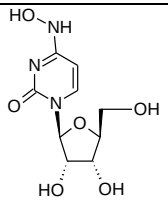
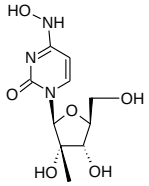
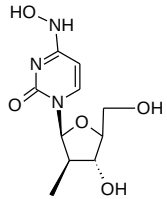
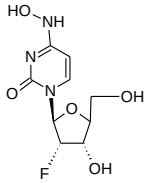
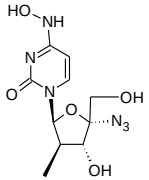
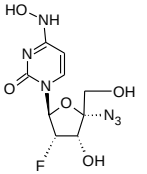
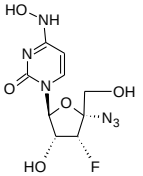
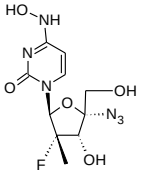
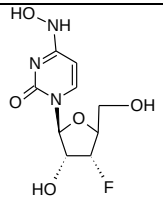
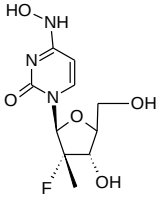
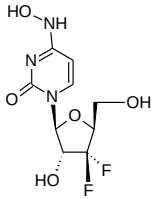
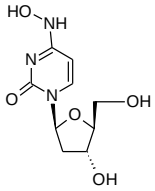
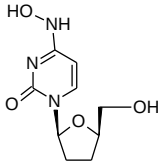
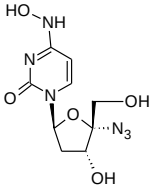
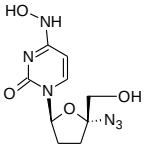
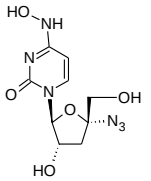
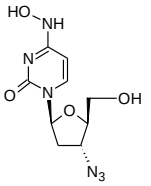
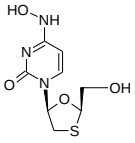
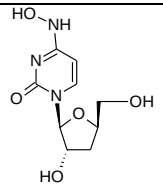
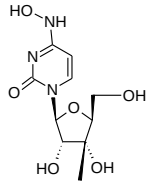
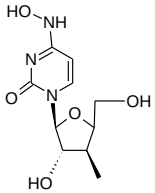
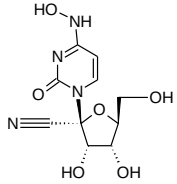
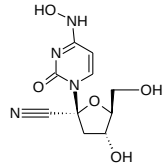
Table S1. Binding energy of compounds **C1-C55**, molnupiravir (**MLN**), monophosphate derivatives both of **C17** and **MLN** into the active site of SARS-CoV-2 RdRp enzyme.

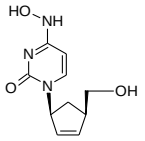
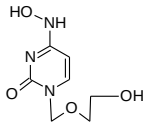
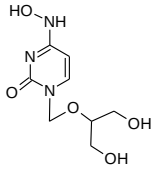
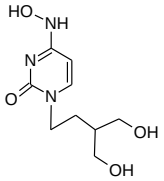
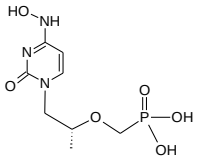
Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C1 (EIDD-2801)		$C_9H_{13}N_3O_6$	-5.7
C2*		$C_{10}H_{15}N_3O_6$	-5.6
C3		$C_{10}H_{15}N_3O_5$	-5.5
C4*		$C_9H_{12}FN_3O_5$	-5.4

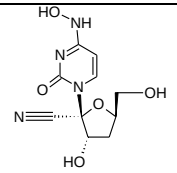
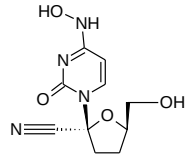
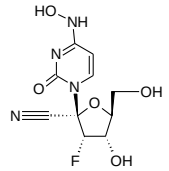
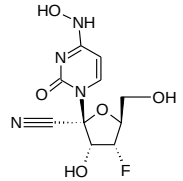
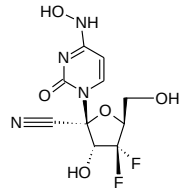
Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C31		$C_{10}H_{14}N_6O_5$	-5.5
C32*		$C_9H_{11}FN_6O_5$	-6.5
C33		$C_9H_{11}FN_6O_5$	-5.8
C34		$C_{10}H_{13}FN_6O_5$	-6.3

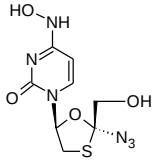
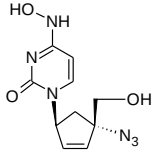
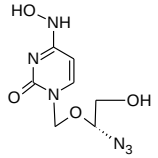
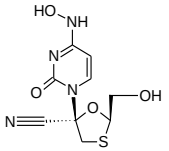
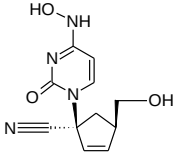
Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C5		$C_9H_{12}FN_3O_5$	-5.7
C6*		$C_{10}H_{14}FN_3O_5$	-5.7
C7		$C_9H_{11}F_2N_3O_5$	-5.8
C8*		$C_9H_{13}N_3O_5$	-5.7
C9*		$C_9H_{13}N_3O_4$	-5.8

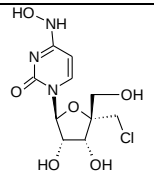
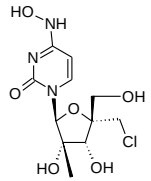
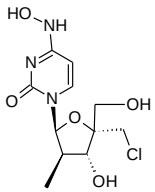
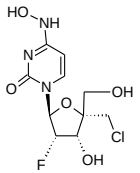
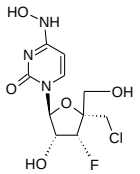
Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C35		$C_9H_{12}N_6O_5$	-5.8
C36		$C_9H_{12}N_6O_4$	-5.2
C37		$C_9H_{12}N_6O_5$	-5.9
C38*		$C_9H_{12}N_6O_4$	-5.7
C39*		$C_8H_{11}N_3O_4S$	-5.4

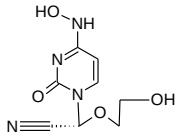
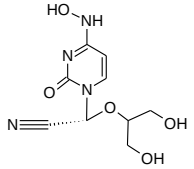
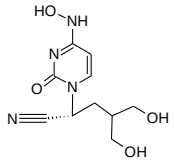
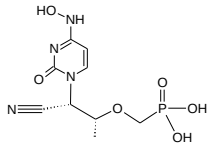
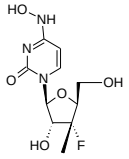
Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C10*		$C_9H_{13}N_3O_5$	-6.0
C11		$C_{10}H_{15}N_3O_6$	-6.0
C12		$C_{10}H_{15}N_3O_5$	-6.0
C13*		$C_{10}H_{12}N_4O_6$	-6.6
C14		$C_{10}H_{12}N_4O_5$	-6.4

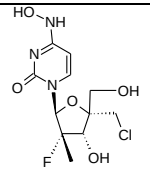
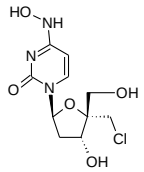
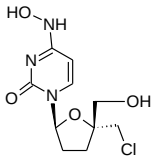
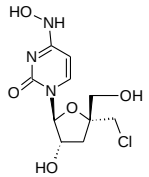
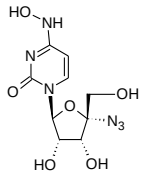
Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C40		$C_{10}H_{13}N_3O_3$	-5.5
C41		$C_7H_{11}N_3O_4$	-5.0
C42		$C_8H_{13}N_3O_5$	-4.8
C43		$C_9H_{15}N_3O_4$	-5.2
C44		$C_8H_{14}N_3O_6P$	-5.9

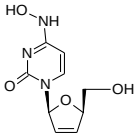
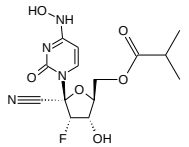
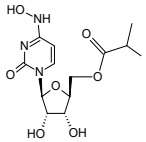
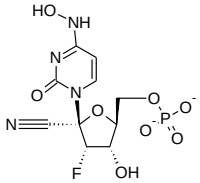
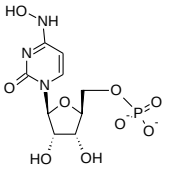
Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C15		$C_{10}H_{12}N_4O_5$	-6.4
C16		$C_{10}H_{12}N_4O_4$	-5.6
C17		$C_{10}H_{11}FN_4O_5$	-7.3
C18		$C_{10}H_{11}FN_4O_5$	-6.5
C19		$C_{10}H_{10}F_2N_4O_5$	-6.7

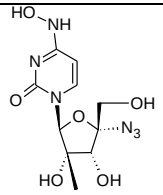
Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C45		$C_8H_{10}N_6O_4S$	-5.5
C46		$C_{10}H_{12}N_6O_3$	-5.5
C47		$C_7H_{10}N_6O_4$	-5.4
C48		$C_9H_{10}N_4O_4S$	-6.5
C49		$C_{11}H_{12}N_4O_3$	-5.9

Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C20		$C_{10}H_{14}ClN_3O_6$	-5.7
C21		$C_{11}H_{16}ClN_3O_6$	-5.7
C22		$C_{11}H_{16}ClN_3O_5$	-5.6
C23*		$C_{10}H_{13}ClFN_3O_5$	-5.7
C24		$C_{10}H_{13}ClFN_3O_5$	-6.1

Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C50		$C_8H_{10}N_4O_4$	-5.6
C51		$C_9H_{12}N_4O_5$	-5.5
C52		$C_{10}H_{14}N_4O_4$	-5.7
C53		$C_9H_{13}N_4O_6P$	-6.3
C54		$C_{10}H_{14}FN_3O_5$	-5.9

Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C25		$C_{11}H_{15}ClFN_3O_5$	-5.7
C26		$C_{10}H_{14}ClN_3O_5$	-5.8
C27		$C_{10}H_{14}ClN_3O_4$	-5.9
C28		$C_{10}H_{14}ClN_3O_5$	-6.2
C29		$C_9H_{12}N_6O_6$	-5.5

Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C55*		$C_9H_{11}N_3O_4$	-5.5
C17_PD		$C_{14}H_{17}FN_4O_6$	-6.9
MLN		$C_{13}H_{19}N_3O_7$	-6.0
C17_MP		$C_{10}H_{10}FN_4O_8P$	-6.8
MLN_MP		$C_9H_{12}N_3O_7$	-6.3

Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)
C30		$C_{10}H_{14}N_6O_6$	-6.4

Compounds	Structure	Molecular Formula	Binding Energy (Kcal/mol)

* These compounds were reported in the literature.

Table S2. List of molecular properties (physico-chemical, lipophilicity, water solubility, drug likeness) of all compounds by using online webserver SwissADME.

Compound	Physicochemical Properties					Lipophilicity	Water solubility	Drug Likeness	
	MW (g/mol)	nON	nOHN	nRot	TPSA (Å²)	$LogP_{o/w}$ *(consensus)*	LogS *(ESOL)*	Lipinski Rule nviol	Muegge Rule nviol
C1 (EIDD-1931)	259.22	7	5	3	137.07	-1.82	-0.48	0	0
C2	273.24	7	5	3	137.07	-2.03	0.02	0	1
C3	257.24	6	4	3	116.84	-0.86	-0.66	0	0
C4	261.21	7	4	3	116.84	-0.98	-1.14	0	0
C5	261.21	7	4	3	116.84	-0.93	-0.79	0	0
C6	275.23	7	4	3	116.84	-1.14	-0.64	0	0
C7	279.20	8	4	3	116.84	-1.05	-0.36	0	0
C8	243.22	6	4	3	116.84	-1.37	-0.24	0	0
C9	227.22	5	3	3	96.61	-0.44	-0.45	0	0
C10	243.22	6	4	3	116.84	-1.36	0.04	0	1
C11	273.24	7	5	3	137.07	-1.79	0.02	0	1
C12	257.24	6	4	3	116.84	-1.12	-0.31	0	0
C13	284.23	8	5	3	160.86	-2.27	0.01	0	2
C14	268.23	7	4	3	140.63	-1.54	-0.18	0	1
C15	268.23	7	4	3	140.63	-1.56	-0.18	0	1
C16	252.23	6	3	3	120.40	-1.19	-0.36	0	0
C17	286.22	8	4	3	140.63	-1.31	-0.31	0	1
C18	286.22	8	4	3	140.63	-1.34	-0.31	0	1
C19	304.21	9	4	3	140.63	-1.02	-0.57	0	0
C20	307.69	7	5	4	137.07	-1,31	-025	0	1
C21	321.71	7	5	4	137.07	-1.14	-0.45	0	1
C22	305.71	6	4	4	116.84	-0.45	-1.13	0	0
C23	309.68	7	4	4	116.84	-0.54	-0.91	0	0
C24	309.68	7	4	4	116.84	-0.70	-0.57	0	0
C25	323.71	7	4	4	116.84	-0.51	-1.11	0	0
C26	291.69	6	4	4	116.84	-0.88	-0.78	0	0
C27	275.69	5	3	4	96.61	-0.16	-0.96	0	0
C28	291.69	6	4	4	116.84	-0.78	-0.43	0	0
C29	300.23	10	5	4	186.82	-1.99	-0.44	1	1
C30	314.25	10	5	4	186.82	-1.68	-0.63	1	1
C31	298.26	9	4	4	166.59	-0.95	-1.32	1	1
C32	302.22	10	4	4	166.59	-1.11	-1.10	1	1
C33	302.22	10	4	4	166.59	-1.34	-0.75	1	1
C34	316.25	10	4	4	166.59	-0.70	-1.29	1	1
C35	284.23	9	4	4	166.59	-1.03	-0.96	1	1
C36	268.23	8	3	4	146.36	-0.46	-1.14	0	0
C37	284.23	9	4	4	166.59	-1.15	-0.62	1	1
C38	268.23	8	3	4	146.36	-0.99	-1.01	0	0
C39	245.26	5	3	3	121.91	-0.59	-0.80	0	0
C40	223.23	4	3	3	87.38	-0.11	-0.67	0	0
C41	201.18	5	3	5	96.61	-0.99	0.15	0	0
C42	231.21	6	4	6	116.84	-1.46	0.46	0	1
C43	229.23	5	4	6	107.61	-0.81	0.09	0	0
C44	279.19	7	4	6	143.72	-1.46	0.25	0	1
C45	286.27	8	3	4	171.66	-0.45	-1.28	0	1
C46	264.24	7	3	4	137.13	0.34	-1.23	0	0
C47	242.19	8	3	6	146.36	-1.01	-0.64	0	0
C48	270.27	6	3	3	145.70	-0.78	-0.49	0	0
C49	248.24	5	3	3	111.17	-0.69	-0.65	0	0
C50	226.19	6	3	5	120.40	-1.29	0.15	0	1
C51	256.22	7	4	6	140.63	-1.78	0.45	0	1

Compound	Physicochemical Properties					Lipophilicity	Water solubility	Drug Likeness	
	MW (g/mol)	**nON**	**nOHN**	**nRot**	**TPSA (Å²)**	**$LogP_{o/w}$ *(consensus)***	**LogS *(ESOL)***	**Lipinski Rule nviol**	**Muegge Rule nviol**
C52	254.24	6	4	6	131.40	-1.23	0.08	0	1
C53	304.20	8	4	6	167.51	-1.84	0.23	0	2
C54	275.23	7	4	3	116.84	-0.72	-0.29	0	1
C55	225.20	5	3	3	96.61	-0.63	-0.27	0	0
MLN	329.31	8	4	6	143.14	-0.88	-0.83	0	0
C17-PD	356.31	9	3	6	146.70	-0.31	-1.17	0	0

Abbreviations: C: compound; MW: Molecular weight; nON: Number of hydrogen acceptors; nOHN: Number of hydrogen donors; nRot: Number of rotatable bonds; TPSA: Topological polar surface area, LogPo/w: Octanol-water partition coefficient; LogS (ESOL): Estimating aqueous solubility from molecular structure; MLN: Molnupiravir, ***C17-PD****: prodrug form of compound* ***C17****.*