molecules

MDPI

Supporting information

Drug Repurposing for Influenza Virus Polymerase Acidic (PA) Endonuclease Inhibitor

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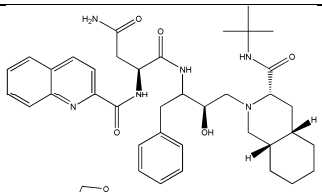
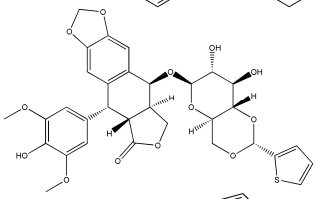
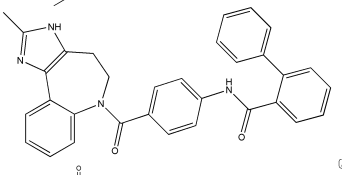
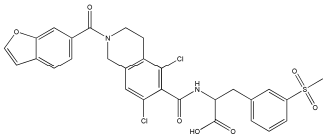
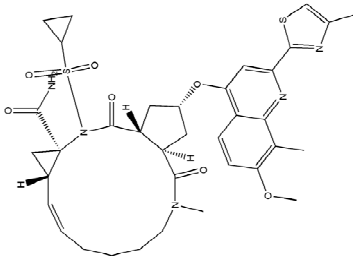
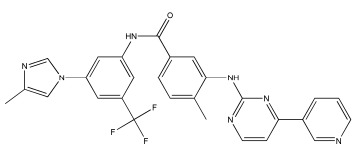
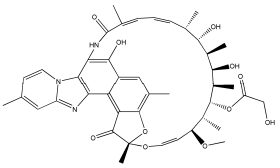
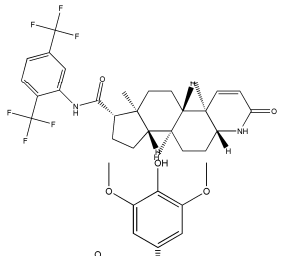
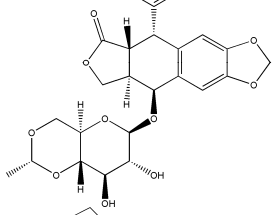
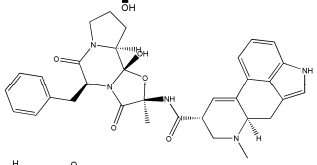
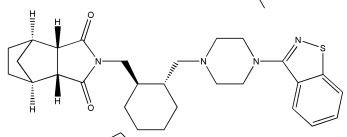
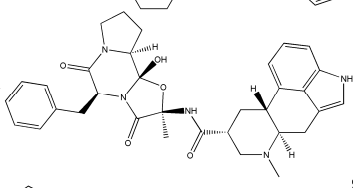
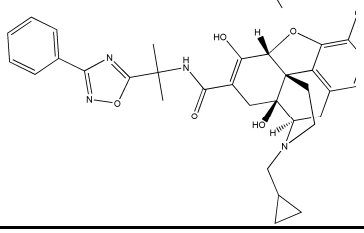
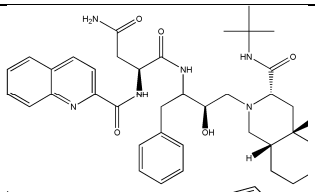
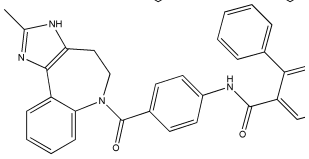
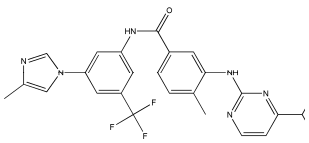
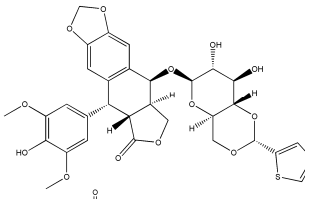
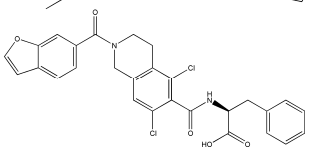
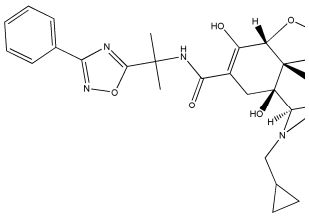
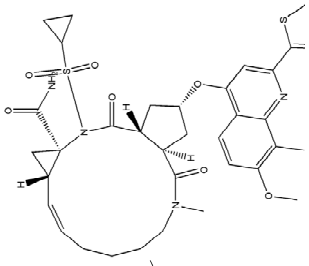
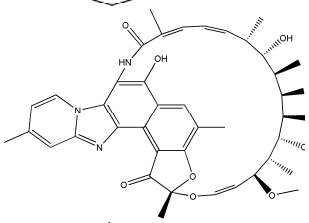
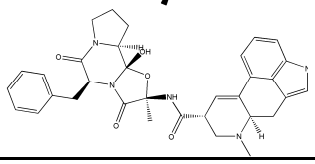
Table S1. The properties and energy score of the potential PAN inhibitors.

Chemical name	Structure	Energy* (kcal/mol)	M_{wt}	Chemical Formula	Summary
Saquinavir		−10.8	670.8	C38H50N6O5	HIV protease inhibitor used in combination with other antiretroviral agents for the treatment of HIV-1 with advanced immunodeficiency.
Teniposide		−10.1	656.7	C32H32O13S	Cytotoxic drug used as an adjunct for chemotherapy induction in the treatment of refractory childhood acute lymphoblastic leukemia.
Conivaptan		−10	498.6	C32H26N4O2	Antidiuretic hormone inhibitor used to raise serum sodium levels.
Lifitegrast		−10	615.5	C29H24Cl2N2O7S	Medication used to treat dry eye disease.
Simeprevir		−9.9	749.9	C38H47N5O7S2	Direct-acting antiviral agent that inhibits HCV NS3/4A protease to treat chronic hepatitis C virus (HCV) infection in adults with HCV genotype 1 or 4.
Nilotinib		−9.8	529.5	C28H22F3N7O	Kinase inhibitor used for the chronic phase treatment of Chronic Myeloid Leukemia (CML) that is Philadelphia chromosome-positive and for the treatment of CML that is resistant to therapy containing imatinib.

Rifaximin		−9.8	785.9	C43H51N3O11	Rifamycin-based non-systemic antibiotic used for the treatment of gastrointestinal bacterial infections, such as traveler's diarrhea and irritable bowel syndrome, and reduction in overt hepatic encephalopathy recurrence in adults.
Dutasteride		−9.7	528.5	C27H30F6N2O2	Antiandrogenic compound that is used for the treatment of symptomatic benign prostatic hyperplasia (BPH) in adult males by inhibiting 5-alpha reductase.
Etoposide		−9.7	588.6	C29H32O13	Podophyllotoxin derivative used to treat testicular and small cell lung tumors.
Ergotamine		−9.6	581.7	C33H35N5O5	Alpha-1 selective adrenergic agonist vasoconstrictor used to treat migraines with or without aura and cluster headaches.
Lurasidone		−9.5	492.7	C28H36N4O2S	Atypical antipsychotic used to treat schizophrenia and depressive episodes associated with bipolar I disorder.
Dihydroergotamine		−9.5	583.7	C33H37N5O5	Ergot alkaloid used in the acute treatment of migraine headaches and cluster headaches.
Naldemedine		−9.5	570.6	C32H34N4O6	Opioid antagonist used to treat opioid-induced constipation.

* Affinity binding energy of virtual screening results by AutoDock vina program.

Table S2. The properties and energy score of the potential PAN-I38T endonuclease inhibitors.

Chemical name	Structure	Energy* (kcal/mol)	M_{wt}	Chemical Formula	Summary
Saquinavir		−10.3	670.8	C38H50N6O5	HIV protease inhibitor used in combination with other antiretroviral agents for the treatment of HIV-1 with advanced immunodeficiency.
Conivaptan		−10.1	498.6	C32H26N4O2	Antidiuretic hormone inhibitor used to raise serum sodium levels.
Nilotinib		−10	529.5	C28H22F3N7O	Kinase inhibitor used for the chronic phase treatment of Chronic Myeloid Leukemia (CML) that is Philadelphia chromosome-positive and for the treatment of CML that is resistant to therapy containing imatinib.
Teniposide		−9.9	656.7	C32H32O13S	Cytotoxic drug used as an adjunct for chemotherapy induction in the treatment of refractory childhood acute lymphoblastic leukemia.
Lifitegrast		−9.9	615.5	C29H24Cl2N2O7S	Medication used to treat dry eye disease.
Naldemedine		−9.9	570.6	C32H34N4O6	Opioid antagonist used to treat opioid-induced constipation.
Simeprevir		−9.9	749.9	C38H47N5O7S2	Direct-acting antiviral agent that inhibits HCV NS3/4A protease to treat chronic hepatitis C virus (HCV) infection in adults with HCV genotype 1 or 4.
Rifaximin		−9.9	785.9	C43H51N3O11	Rifamycin-based non-systemic antibiotic used for the treatment of gastrointestinal bacterial infections, such as traveler's diarrhea and irritable bowel syndrome, and reduction of overt hepatic encephalopathy recurrence in adults.
Ergotamine		−9.7	581.7	C33H35N5O5	Alpha-1 selective adrenergic agonist vasoconstrictor used to treat migraines with or without aura and cluster headaches.

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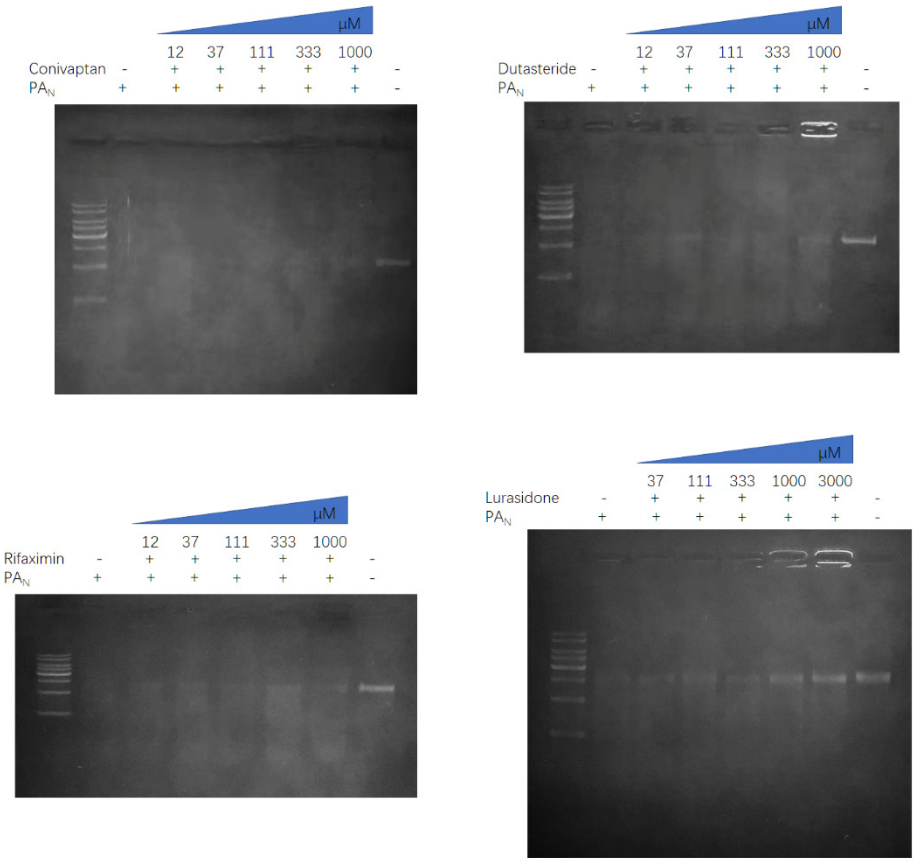

Figure S1. Compounds inhibition for the endonuclease activity of PA$_N$. Different concentrations of conivaptan (0–333μM), dutasteride (0–1000μM), rifaximin (0–1000μM), and lurasidone (0–3000μM) incubated with the PA and substrate ssDNA for 1 h at 37 °C.

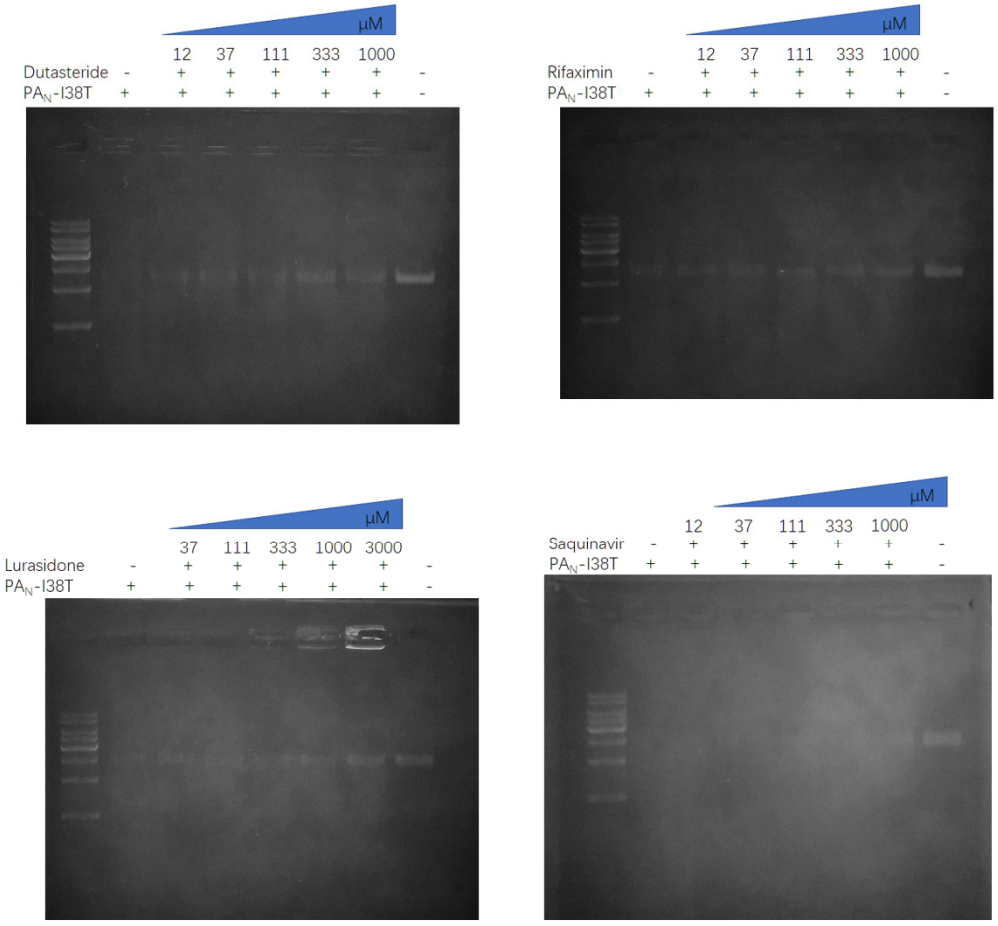

Figure S2. Compounds inhibition for the endonuclease activity of PAN-I38T. Different concentrations of dutasteride (0–1000μM), rifaximin (0–1000μM), saquinavir (0–1000μM), and lurasidone (0–3000μM) incubated with the PAN-I38T and substrate ssDNA for 1h at 37 °C.