In vitro screening of a FDA approved chemical library reveals potential inhibitors of SARS-CoV-2 replication

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Summary

A novel coronavirus, named SARS-CoV-2, emerged in 2019 from Hubei region in China and rapidly spread worldwide. As no approved therapeutics exists to treat Covid-19, the disease associated to SARS-Cov-2, there is an urgent need to propose molecules that could quickly enter into clinics. Repurposing of approved drugs is a strategy that can bypass the time consuming stages of drug development. In this study, we screened the Prestwick Chemical Library® composed of 1,520 approved drugs in an infected cell-based assay. 90 compounds were identified. The robustness of the screen was assessed by the identification of drugs, such as Chloroquine derivatives and protease inhibitors, already in clinical trials. The hits were sorted according to their chemical composition and their known therapeutic effect, then EC50 and CC50 were determined for a subset of compounds. Several drugs, such as Azithromycine, Opipramol, Quinidine or Omeprazol present antiviral potency with 2<EC50<20µM. By providing new information on molecules inhibiting SARS-CoV-2 replication *in vitro*, this study could contribute to the short-term repurposing of drugs against Covid-19.

Introduction

Human coronaviruses (HCoVs) are enveloped positive-stranded RNA viruses belonging to the *Nidovirales* order that are mostly involved in gastrointestinal and respiratory tract infections. Among them, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) CoVs that emerged in 2002 and 2013 respectively, have been associated with severe human illnesses, such as severe acute respiratory distress syndromes (de Wit et al., 2016). In December 2019, a new coronavirus (SARS-CoV-2) has emerged in the city of Wuhan and quickly spread around the world. SARS-CoV-2 causes in human a viral infection, named COVID-19, which is associated in some patients with severe respiratory diseases and significant mortality rates, in particular in elderly populations (Li et al., 2020). While an unknown fraction (most probably a majority) of infected people remain pauci- or asymptomatic, some require hospitalization, sometimes in intensive care units, which may jeopardise health systems during peak pandemic periods. In such a context, vaccines would represent great tools to prevent or limit virus spread. However, vaccine development is a long process and COVID-19 vaccines will most probably not be concretely available for mass usage, at least during the first wave of the disease. Accordingly, the availability of efficient antiviral drugs would be of utmost interest for the treatment of infected patients and possibly for preventive or preemptive use. Regrettably, the current and unprecedented outbreak of SARS-CoV-2 occurs in an unprepared world, with no firmly established identification of active molecules against beta-coronaviruses (Callaway et al., 2020). There is thus an urgent necessity to provide *hic et nunc* therapeutic solutions to limit viral infection. As the timeframe for a conventional drug development is unrelated to the immediate needs, repurposing of drugs originally developed for other viral infections or therapeutic uses is likely the fastest way to enter clinics. This fast track drug development and validation lead to the initiation of numerous clinical trials for the treatment of Covid19 (Li and De Clercq, 2020) but there is still a need to expand the number of possible drug candidates to treat COVID19 and/or evaluate possible drug combinations to potentiate the antiviral effects (Cheng et al., 2019). Whereas the number of clinical trials cannot be extensively multiplied, libraries of “old” drugs can be screened *in vitro* in medium to high throughput assays. Proof of concepts for drug repositioning against SARS-CoV, MERS-CoV or other viruses in *in vitro* assay already showed the relevance of this strategy (de Wilde et al., 2014; Dyall et al., 2014; Mercorelli et al., 2018). In this study, we screened the 1,520 approved and off-patent drugs of the Prestwick Chemical Library® in a SARS-CoV-2 infection cell-based

assay. The *in vitro* screening identified 90 drugs showing inhibition effect on the viral replication at 10 µM. Hits, selected from different classes of compounds, were then confirmed by EC50 and CC50 determination.

Material and methods

Chemical library

The Prestwick Chemical Library® (hereafter named PCL) is a library of 1,520 off-patent small molecules, mostly approved drugs (FDA, EMA and other agencies). The compounds are provided at a concentration of 10mM in 100% DMSO.

Cell line

VeroE6 (ATCC CRL-1586) cells were grown in minimal essential medium (Life Technologies) with 7.5% heat-inactivated fetal calf serum (FCS), at 37°C with 5% CO^2 with 1% penicillin/streptomycin (PS, 5000U.mL^{-1} and 5000µg.mL^{-1} respectively; Life Technologies) and supplemented with 1% non-essential amino acids (Life Technologies).

Virus strain

SARS-CoV-2 strain BavPat1 was obtained from Pr Drosten through EVA GLOBAL (https://www.european-virus-archive.com/). To prepare the virus working stock, a 25cm^2 culture flask of confluent VeroE6 cells growing with MEM medium with 2.5% FBS (Life Technologies) was inoculated at MOI 0.001. Cell supernatant medium was harvested at the peak of infection and supplemented with 25mM HEPES (Sigma) before being stored frozen in small aliquots at -80°C. All experiments were conducted in BSL3 laboratory.

Antiviral screen

One day prior to infection for the antiviral screening 5×10^4 VeroE6 cells were seeded in 100µL assay medium (containing 2.5% FCS) in 96 well plates. The next day, a single dilution of each compound of the PCL at 10µM final concentration was added to the cells (25µL/well, in 2.5% FCS-containing medium). Six virus control wells were supplemented with 25µL medium (positive controls hereafter named vc) and eight cell control wells were supplemented with 50µL of medium (negative controls, hereafter named nc). Two internal well controls of viral inhibition were added, corresponding to the addition of 10µM arbidol (Sigma) in the infected

cell culture (arbidol controls, hereafter named arb). After 15 min, 25µL of a virus mix diluted in 2.5% FCS-containing medium was added to the wells at MOI 0.002.

Three days after infection, cell supernatant media were discarded and CellTiter-Blue® reagent (Promega) was added following the manufacturer's instructions. Plates were incubated for 2 hours prior recording fluorescence (560/590nm) with a Tecan Infinite 200Pro machine. From the measured OD_{590nm}, the Inhibition Index was calculated as follows: first, cell viability for compounds, vc and arb were calculated: (OD_{590nm} value/mean OD_{590nm} of nc)*100. For vc and arb, mean cell viability were calculated. Then all cell viabilities were normalized by subtracting mean vc. cell viability of the 96 well plates. Finally, Inhibition index was calculated as follows: Inh. Index= normalized cell viability of the compound/normalized cell viability of arb in the same 96 well plate. All compounds with Inhibition index values above 1 were considered as a hit.

EC50 and CC50 determination

One day prior to infection, 5×104 VeroE6 cells were seeded in 100µL assay medium (containing 2.5% FCS) in 96 well plates. The next day, seven 2-fold serial dilutions of compounds (0.6µM to 40µM, in triplicate) were added to the cells (25µL/well, in assay medium). Four virus control wells were supplemented with 25µL of assay medium. After 15 min, 25µL of a virus mix diluted in medium was added to the wells. The amount of virus working stock used was calibrated prior to the assay, based on a replication kinetics, so that the replication growth is still in the exponential growth phase for the readout as previously described (Delang et al., 2016; Touret et al., 2019). Four cell control wells (*i.e.* with no virus) were supplemented with 50µL of assay medium. On each plate a control compound (Remdesivir, BLDpharm) was added in duplicate with seven 2-fold serial dilutions (0.16µM to 20µM, in duplicate). Plates were incubated for 2 days at 37°C prior to quantification of the viral genome by real-time RT-PCR. To do so, 100µL of viral supernatant was collected in S-Block (Qiagen) previously loaded with VXL lysis buffer containing proteinase K and RNA carrier. RNA extraction was performed using the Qiacube HT automat and the Cador Pathogen 96 HT kit following manufacturer instruction. Viral RNA was quantified by real-time RT-qPCR (EXPRESS One-Step Superscript™ qRT-PCR Kit, universal Invitrogen using 3.5µL of RNA and 6.5µL of RT qPCR mix and standard fast cycling parameters, *i.e.*, 10min at 50°C, 2 min at 95°C, and 40 amplification cycles (95°C for 3 sec followed by 30sec at 60°C). Quantification was provided by four 2 log serial dilutions of an appropriate T7-generated synthetic RNA standard of known quantities (10^2 to 10^8 copies). RT-qPCR reactions were performed on

QuantStudio 12K Flex Real-Time PCR System (Applied Biosystems) and analyzed using QuantStudio 12K Flex Applied Biosystems software v1.2.3. Primers and probe sequences, which target SARS-CoV-2 N gene, were: Fw: GGCCGCAAATTGCACAAT ; Rev : CCAATGCGCGACATTCC ; Probe: FAM-CCCCCAGCGCTTCAGCGTTCT-BHQ1. The 50% and 90% effective concentrations (EC50, EC90; compound concentration required to inhibit viral RNA replication by 50% and 90%) were determined using logarithmic interpolation as previously described (Touret et al., 2019). For the evaluation of the CC50 (the concentration that reduces the total cell number by 50%), the same culture conditions were set as for the determination of the EC50, without addition of the virus, and cell viability was measured using CellTiter Blue® (Promega) as previously described for the screening. CC50 was determined using logarithmic interpolation. All data obtained were analyzed using Graph pad prism 7 software (Graph pad software). All graphical representations were also performed on Graph pad prism 7 software.

Results and discussion

We developed a HTS SARS-CoV-2 replication inhibition assay based on the measurement of the cell viability 3 days after cell infection with a MOI of 0.002. Prior to the screening, we evaluated the antiviral effect of arbidol, a broad spectrum antiviral compounds that blokes the viral entry of many enveloped viruses (Blaising et al., 2014). In our experimental conditions, we demonstrated that 10µM arbidol limit the SARS-CoV-2 infection leading to around 70-90% cell viability, with a EC50 of 10.7µM. This compound was next used as reference compounds in order to calculate the inhibition index (Inh. Index).

We next tested the Prestwick Chemical Library® (PCL®) composed of 1,520 approved drugs at a final concentration of 10µM. The cell viability was determined and we calculated the relative value of inhibition potency compared to arbidol. Among the 1,520 compounds of the PCL®, 90 compounds showed equal or more potent inhibition than arbidol with an Inh. Index ≥ 1 (5.85 % positive hits) (Fig.1), and the mean Inh. Index of the library was 0.28 (Table 1 of the supplemental data). As the threshold for the selection is arbitrary, the raw data for each compound of the PCL® is presented in the supplemental data, in order to allow the scientific community to further analyse the results and possibly rescue molecules of interest.

Among the selected hits, we first identified drugs previously demonstrated to inhibit *in vitro* the SAR-CoV2 replication. Accordingly, Chloroquine and Hydroxychloroquine (Liu et al., 2020; Wang et al., 2020; Yao et al., 2020) were shown to limit SARS-CoV-2 replication with

a Inh. Index of 1.35 and 1.43 respectively. In addition to chloroquine derivatives, two hits are also currently evaluated in different clinical trials, namely Darunavir and Azythromycine. These observations assessed the robustness of the screening assay. In order to further consolidate the results provided by the assay, EC50 was determined on a set of selected compounds. Whereas the screening relied on the quantification of cytopathic effect (CPE) using CellTiter Blue® providing qualitative information on the viral infection, EC50 determination were based on the quantification of the viral genome by Real-Time RT-PCR (Touret et al., 2019). For this assay Remdesivir was used as a control compound for validation, with an EC50 of 1.6µM (Table 1), a value in agreement with previously published data (Wang et al., 2020).

From the 90 selected hits (Table 2), some were arbitrary removed after visual inspection of their initial therapeutic use or strong side effects (ophthalmic treatment, topical administration, teratogenic effect …). The compounds were organised in 12 groups by structural similarity and/or therapeutic class including ten steroids (mainly sex steroids used for endocrine therapy and corticosteroids with anti-inflammatory properties), two prostaglandins (both PGE1 displaying a variety of pharmacologic actions such as vasodilatator for one and anti-ulcer for the other), two proton pump inhibitors (PPIs used as anti-ulcer agents), two antiretrovirals (HIV anti-protease and anti-integrase), twelve antibacterial drugs (including fluoroquinolone, oxazolidinone, macrolide and beta-lactam derivatives among others), fifteen cardiovascular drugs (antiarrhythmic, vasodilatator and antihypertensive agents including ion channel blockers, an angiotensin converting enzyme inhibitor (ACE), angiotensin II receptor inhibitors, and beta-adrenergic receptor blockers), two opioids plus sixteen non-opioid CNS drugs (that display a variety of pharmacologic actions such as antipsychotic, antidepressant, antiparkinsonian, anti-alzheimer…), six neuromuscular-blocking drugs (including muscle relaxant and local anesthesic agents), three respiratory system drugs (mostly used as a bronchodilator in the treatment of asthma and COPD), three allergy medications (with antihistaminic and antiemetic properties), three antiparasitic drugs (more specifically antimalarial agents), and fourteen unrelated drugs (used in ophthalmology, dermatology and other isolated pathologies).

Interestingly, based on the SARS-Cov-2 infection cycle, one can infer that some of the identified molecules may inhibit specific steps of the virus replication cycle. This is illustrated for example by Candesartan, Olmesartan and Ambrisentan which interfer with angiotensin pathways, that play a key role in virus entry as the SARS-CoV2 Spike protein is known to bind to the cellular Angiotensin Converting Enzyme 2 receptor (ACE2) (Kuster et al., 2020; Lan et

al., 2020). We also noted that 4 compounds (Omeprazole, Vonoprazan, Chloroquine diphosphate and Hydroxychloroquine sulfate) have been demonstrated to increase the pH of endosomial/golgian pathway either by inhibiting ATPase proton pomp, or by buffering the pH. We can thus expect that such endosomial pH modification would limit the processing of the Spike protein by endosomal proteases and in turn bloke the virus entry mediated by membrane fusion process. Finally, we also identified Darunavir, a HIV protease inhibitor might interfere with viral polyprotein processing during the replication cycle. This analysis identified at least three possible steps of the viral infection that can be targeted by approved drugs.

We next aimed at determining the EC50 of 16 drugs selected from the different groups. Whereas EC50 could be determined for 10 of them (Table 1, Fig 2), low to no antiviral effect (EC50 ≥ 40µM) was observed for Darunavir, Levalbuterol, Olmesartan, Ambrisentan and Ranolazine. As the compounds are selected from a screening based on the inhibition of the SARS-CoV-2-mediated CPE, we cannot exclude that these compounds have no antiviral effect but rather protect the cells from CPE. In addition Artenimol was rejected as it showed toxicity at 20µM concentration, in the same range of the antiviral effect. In conclusion, the screening of the approved compounds identified a set of molecules showing inhibition on SARS-CoV-2 *in vitro* replication. Some of these experimentally selected candidates, with EC50 at the 2-20 µM range may provide information to guide the choice for downstream experiments and validation, or initiate medicinal chemistry projects to find more potent derivatives.

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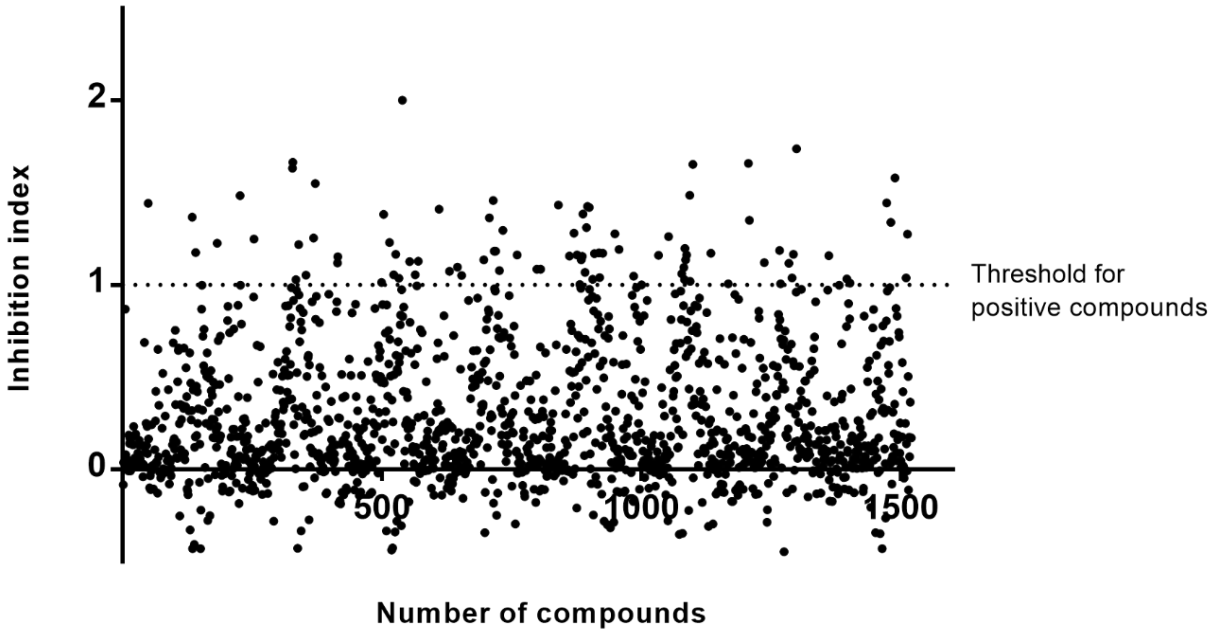
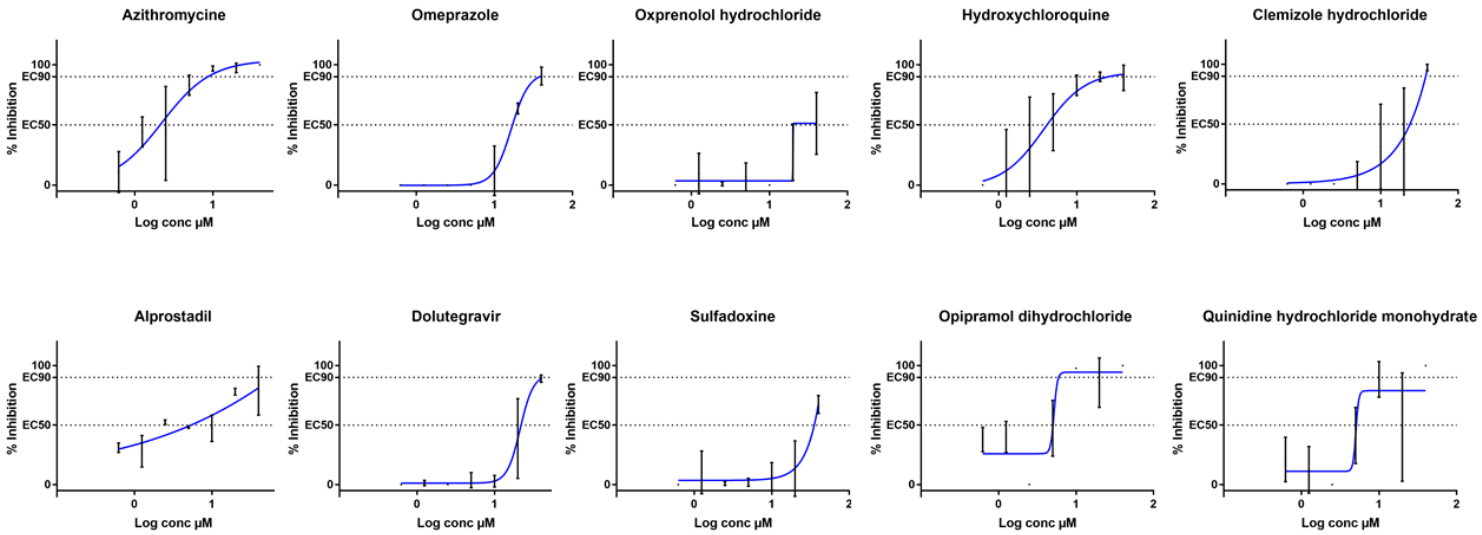


293

294 **Figure 1:** Screening of 1,520 clinically approved compounds from Prestwick Chemical Library® and
295 hits selection**.** The threshold was based on the *in vitro* antiviral potency of arbidol at 10µM.

296



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299 **Figure 2**: Dose response curves of selected compounds from the hits and control compounds.
300 EC50: 50% inhibition, EC90: 90% inhibition. Compounds concentrations are in presented in
301 log scale for logarithmic interpolation.

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303

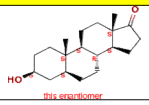
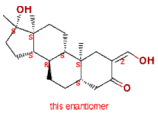
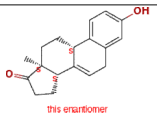
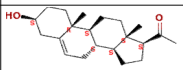
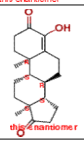
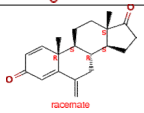
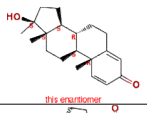
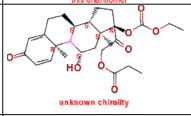
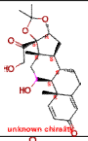
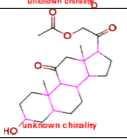
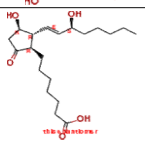
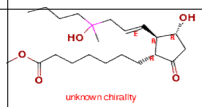
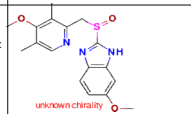
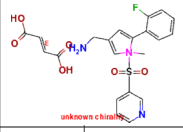
	EC50	EC90	CC50	SI
Azithromycine	**2,12**	**8,65**	**>40**	**>19**
Omeprazole	**17,06**	**38,01**	**>40**	**>2,35**
Oxprenolol hydrochloride	**20,22**	**>40**	**>40**	**>2**
Hydroxy-chloroquine	**4,17**	**25,49**	**>40**	**>10**
Clemizole hydrochloride	**23,94**	**38,23**	**>40**	**>1,7**
Alprostadil	**5,39**	**62,40**	**>40**	**>7,4**
Dolutegravir	**22,04**	**42,81**	**>40**	**>1,8**
Sulfadoxine	**35,37**	**45,11**	**>40**	**>1,13**
Opipramol dihydrochloride	**5,05**	**5,97**	**>40**	**>7,9**
Quinidine hydrochloride monohydrate	**5,11**	**>40**	**>40**	**>7,8**
Arbidol	**10,7**	**15,2**	**>40***	**>3,7**
Remdesivir 5 exp	**1,65±0,79**	**2,52±0,81**	**n.d**	**n.d**

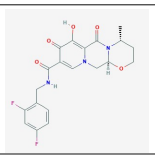
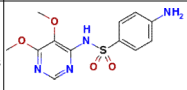
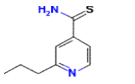
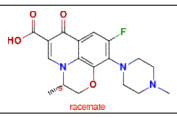
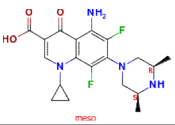
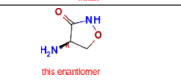
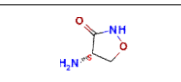
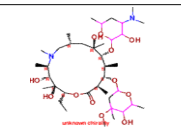
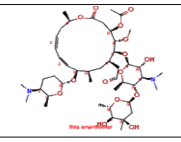
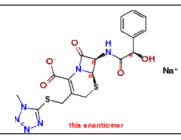
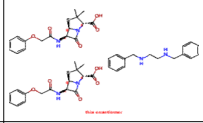
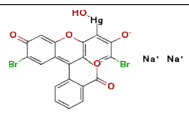
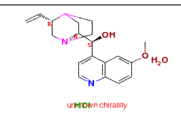
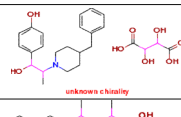
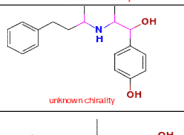
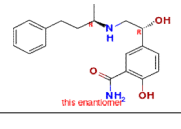
304

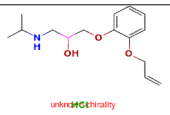
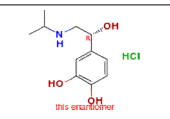
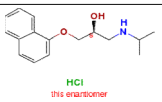
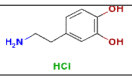
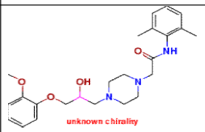
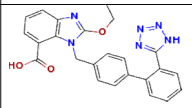
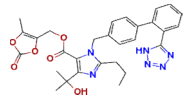
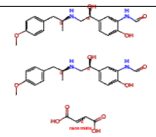
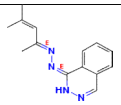
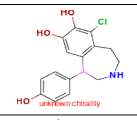
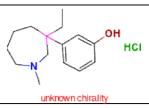
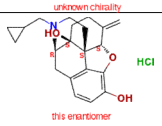
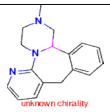
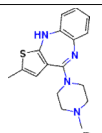
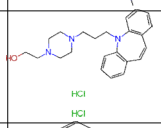
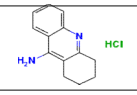
305 **Table 1**: Antiviral activity of selected compounds from the hits and control compounds. EC50:
306 50% inhibition, EC90: 90% inhibition, CC50:50% cytotoxicity and SI: selectivity index. n.d:
307 not determined. All value are in µM. *From (Haviernik et al., 2018)

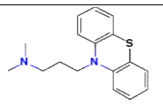
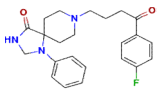
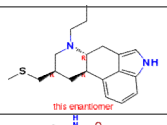
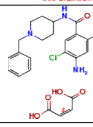
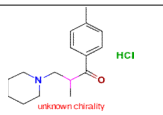
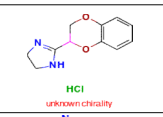
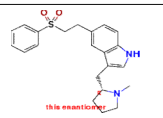
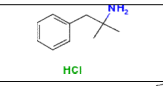
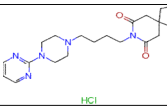
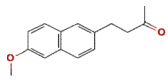
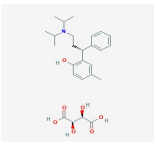
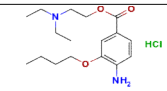
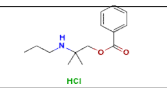
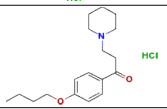
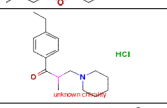
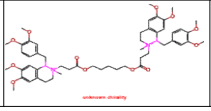
308 **Table2**: Inhibition index and detailed description of the 90 hit compounds. The compounds
309 are organized in functional and/or structural class.

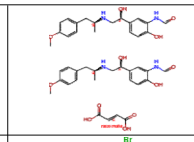
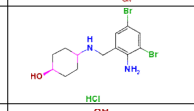
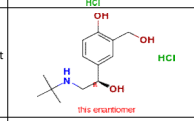
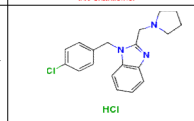
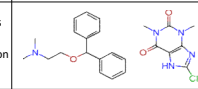
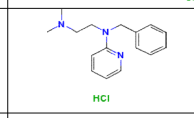
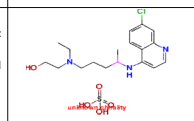
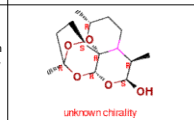
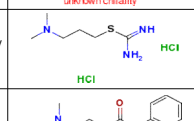
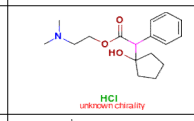
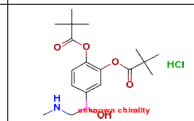
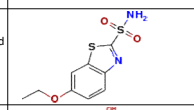
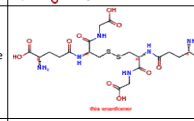
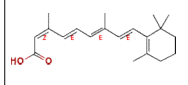
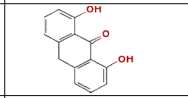
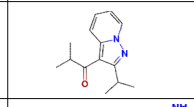
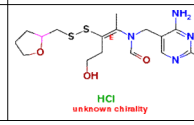
310

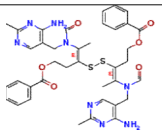
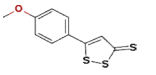
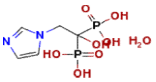
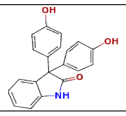
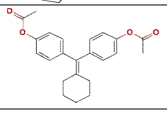
Plate Number / Position Number	Inhibition index	Chemical name	Biological properties	Structure	CAS numbe	Approved by	Patent Ref	Therapeutic class	Therapeutic effect	Target type	Target name
06D11	1.07	Epiandrosterone	metabolite and a precursor of testosterone and estradiol with hypolipidemic and anabolic property, it has a role as an androgen and a human metabolite		481-29-8	no	US 2783252	Endocrinology	Anabolic		
16G10	1.74	Oxymetholone	orally active synthetic anabolic steroid and a 17alpha-methylated derivative of dihydrotestosterone, with androgenic activity, Indicated in the treatment of anemias caused by deficient red cell production and also used to treat osteoporosis / HIV/AIDS wasting syndrome and blocks Entry of Ebola Virus in HTS		434-07-1	FDA	DE 1070632	Endocrinology	Anabolic	Nuclear receptors	Androgen receptor
11E11	1.28	Equilin	naturally occurring steroid with estrogenic activity obtained from the urine of pregnant mares. For the treatment of moderate to severe vasomotor symptoms associated with the menopause, atrophic vaginitis, osteoporosis, hypoestrogenism due to hypogonadism, castration, primary ovarian failure, breast cancer (for palliation only), and advanced androgen-dependent carcinoma of the prostate (for palliation only)		474-86-2	EMA	US 2221340	Endocrinology			
07G07	1.66	Pregnenolone	endogenous steroid hormone synthesized from cholesterol, which can act either as a neuroactive steroid or as a prohormone for progestogens, mineralocorticoids, glucocorticoids, androgens, estrogens, and the neuroactive steroids		145-13-1	Not FDA but OTC	US 2221826	Endocrinology	Anabolic		
14D08	1.37	Formestane	synthetic steroidal substance with antineoplastic activity. Formestane binds irreversibly to and inhibits the enzyme aromatase, thereby blocking the conversion of cholesterol to pregnenolone and the peripheral aromatization of androgenic precursors into estrogens		566-48-3	EMA	WO 1990010462	Endocrinology	Antineoplastic	Coenzyme	Cytochrome P450 19A1
08D06	1.09	Exemestane	synthetic androgen analogue. For the treatment of advanced breast cancer in postmenopausal women whose disease has progressed following tamoxifen therapy (Antineoplastic Agents) / blocks entry of Ebola Virus in HTS		107868-30-	FDA	BE 0905067	Endocrinology	Antineoplastic	Coenzyme	Cytochrome P450 19A1
18C04	1.13	Methandrostenolone	orally-effective anabolic steroid, this compound stimulates anabolism and inhibit catabolism (withdrawn in most countries)		72-63-9	JAN	US4177267	Endocrinology	Anabolic	Nuclear receptor	androgen receptor
14A05	1.37	Prednicarbate	synthetic non-halogenated double-ester derivative of the corticosteroid prednisolone with anti-inflammatory, antipruritic and vasoconstrictive properties. Treatment of atopic dermatitis, Treatment of dermatomycosis (dermatology, topical use)		73771-04-7	FDA	US 4242334	Metabolism	Anti-Inflammatory	Nuclear receptors	Glucocorticoid receptor
16H10	1.58	Desonide	a synthetic glucocorticosteroid for topical use, with anti-inflammatory activity.		638-94-8	FDA	US 2990401	Dermatology	Antipsoriatic	Nuclear receptors	
13E02	1.00	Alfadolone	a corticosteroid hormone that affect neuronal excitability (neurosteroid) and induces general anesthesia		23930-37-2	EMA	EP 0236280	Central Nervous System	Anesthetic	Ionotropic receptor	GABAa receptor
13F09	1.06	Alprostadil	prostaglandin E1 (PGE1) which displays a variety of pharmacologic actions. Alprostadil is a potent vasodilator, bronchodilation, erectile dysfunction... Clinical trials for Respiratory Distress Syndrome		745-65-3	FDA	CA 894250	Cardiovascular	Erectile dysfunction treatment	GPCR	Prostaglandin receptor
14F04	1.03	Misoprostol	synthetic prostaglandine E1 (PGE1) analogue, reduces the risk of NSAID induced gastric ulcers and has also oxytocic properties		59122-46-2	FDA	US 3965143	Metabolism	Antiulcer	GPCR	Prostaglandin receptor
07B04	1.25	Omeprazole	benzimidazole with selective and irreversible proton pump inhibition activity. Treatment of gastroesophageal reflux disease (GERD), peptic ulcers, erosive esophagitis, Zollinger-Ellison syndrome, and eosinophilic esophagitis (Antiulcer Agents) / inhibition of HIV-1 RT-RNase H and Hepatitis C Virus in HTS		73590-58-6	FDA	EP 0005129	Gastroenterology	Antiulcer	Enzyme	H+/K+ ATPase
19F05	1.17	Vonoprazan	pyrrole used in form of the fumarate for the treatment of gastroduodenal ulcer and erosive Esophagitis (Proton pump inhibitors)		881681-00-	JAN	CN105566295A	Gastroenterology	Antiulcer	Pump	H+ K+ ATPase
13E07	1.15	Darunavir	HIV PROTEASE INHIBITOR that is used in the treatment of AIDS and HIV INFECTIONS		635728-49-	FDA	WO 1994004492	Infectiology	Antiviral	Enzyme	Human immunodeficiency virus type 1 protease

16E09	1.17	Dolutegravir	integrase strand-transfer inhibitor (INSTI), with activity against human immunodeficiency virus type 1 (HIV-1) infection (antiretroviral)		1051375-16-	FDA	WO 2009082819	Infectiology	Antiviral	Enzyme	HIV integrase
14F05	1.12	Sulfadoxine	broad-spectrum sulfanilamide and a synthetic analog of para-aminobenzoic acid (PABA) with bacteriostatic and antimalarial properties. Also indicated for the treatment of Plasmodium falciparum malaria in those patients in whom chloroquine resistance is suspected.		2447-57-6	FDA	IL 36409	Infectiology	Antibacterial	Enzyme	Dihydropteroate synthase
13D07	1.14	Prothionamide	thioamide derivative with antitubercular activity. Clinical trial to study antiretroviral (HIV) and tuberculosis medications in pregnant women and their infants		14222-60-7	EMA	FR 2091338	Infectiology	Antibacterial	Enzyme	enoyl-acyl ACP reductase
13G07	1.19	Levofloxacin	broad-spectrum, third-generation fluoroquinolone antibiotic and optically active L-isomer of ofloxacin with antibacterial activity. Levofloxacin is used to treat bacterial conjunctivitis, sinusitis, chronic bronchitis, community-acquired pneumonia and pneumonia caused by penicillin-resistant strains of Streptococcus pneumoniae, skin and skin structure infections, complicated urinary tract infections and acute pyelonephritis.	 racemate	100986-85-	FDA	US5053407A	Infectiology	Antibacterial	Enzyme	DNA gyrase
15D07	1.18	Enoxacin	oral broad-spectrum fluoroquinolone antibacterial agent, inhibit the growth or reproduction of bacteri used in the treatment of urinary tract infections		84294-96-2	FDA	US 4352803	Infectiology	Antibacterial	Protein	Cytochrome P-450 CYP1A2
15E07	1.03	Sparfloxacin	fluoroquinolone antibiotic used in the treatment of bacterial infections, used in the treatment of tuberculosis. It has a controversial safety profile, withdrawn from the U.S. market due to a high incidence of phototoxicity	 meso	110871-86-	FDA	EP 0221463	Infectiology	Antibacterial	Enzyme	Bacterial DNA gyrase
14E07	1.42	D-cycloserine	analogue of the amino acid D-alanine with broad-spectrum antibiotic and glycinergic activities, Used in combination with up to 5 other drugs as a treatment for Mycobacterium avium complex (MAC) and is also used to treat tuberculosis (TB)	 this enantiomer	68-41-7	FDA	US 2773878	Infectiology	Antibacterial	Enzyme	Peptidoglycan synthesis
14E10	1.42	L-Cycloserine	An antibiotic isolated from Erwinia uredovora. It has a role as an anticonvulsant, an EC 2.3.1.50 (serine C-palmitoyltransferase) inhibitor and an anti-HIV agent	 this enantiomer	339-72-0	FDA	US 2773878	Infectiology	Antibacterial		
15F04	1.49	Azithromycin	an azalide, derived from erythromycin, and a member of a subclass of macrolide antibiotics with bacteriocidal and bacteriostatic activities. Macrolides stop bacterial growth by inhibiting protein synthesis and translation, treating bacterial infections. Azithromycin has additional immunomodulatory effects and has been used in chronic respiratory inflammatory diseases for this purpose / clinical trial for anti-viral effects of Azithromycin in Patients With Asthma and COPD		83905-01-5	FDA	BE 0892357	Infectiology	Antibacterial	Ribosome	50S unit
19H04	1.28	Acetyl spiramycin	antibiotic substance classified in the erythromycin-carbomycin group (macrolide) to treat toxoplasmosis and various other infections of soft tissues		24916-51-6	JAN	US3795669	Infectiology	Antibacterial	Ribosome	50S ribosome
17B04	1.05	Cefamandole sodium salt	beta-lactam, second-generation cephalosporin antibiotic with bactericidal activity, It has a role as an antibacterial drug	 this enantiomer	30034-03-8	FDA, EMA	US3855213	Infectiology	Antibacterial	protein	Penicillin-binding protein
13G09	1.01	Benzathine	benzylpenicillin antibiotic		5928-84-7	FDA	US 2627491	Metabolism	Antibacterial	Enzyme	Peptidoglycan synthesis
10G08	1.12	Merbromin disodium salt	topical antiseptic (mercurochrome)		129-16-8	EMA	US 2951766	Infectiology	Antibacterial		
04D11	1.41	Quinidine hydrochloride monohydrate	antiarrhythmic agent to prevent ventricular arrhythmias. Antiarrhythmic and antimalarial effects / Inhibitor of Hepatitis C Virus (HCV) in HTS		6151-40-2	FDA	US 1615843	Cardiovascular	Antiarrhythmic	Enzyme	Heme polymerase
04H02	1.16	Ifenprodil tartrate	Excitatory Amino Acid Antagonists, inhibitor of the NMDA receptor, vasodilatator. Adrenergic alpha-antagonists are used in the treatment of hypertension, vasospasm, peripheral vascular disease, shock, and pheochromocytoma / inhibitors of binding or entry into cells for Lassa Virus and for Marburg Virus, blocks Entry of Ebola Virus in HTS		23210-58-4	EMA	US 3509164	Cardiovascular	Vasodilator	GPCR	Adrenergic receptors
11F03	1.26	Nylidrin	β2 adrenoreceptor agonist that acts as a vasodilator / indicated in conditions like arteriosclerosis		447-41-6	EMA	US 4188404	Cardiovascular	Vasodilator	GPCR	Adrenergic Beta receptors
19E10	1.28	Dilevalol	salicylamide derivative that is a non-cardioselective blocker of beta-adrenergic receptors, used for treatment of hypertension, cardiac arrhythmias, angina pectoris, glaucoma, migraine headaches, and anxiety.		75659-07-3	FDA	EP 9702	Cardiovascular	Antihypertensive	GPCR	beta-2 adrenergic

14B08	1.63	Oxprenolol hydrochloride	lipophilic, nonselective beta-adrenergic receptor antagonist with anti-arrhythmic, anti-anginal and antihypertensive activities, used in the treatment of hypertension, angina pectoris, arrhythmias, and anxiety / inhibitors of DENV, HCV, Ebola virus in HTS		6452-73-9	FDA	FR 1463034	Cardiovascular	Antianginal	GPCR	Adrenergic beta receptor
14F08	1.16	Cyclopentolate hydrochloride	synthetic catechol compound and potent beta adrenergic agonist with peripheral vasodilator, bronchodilator, and cardiac stimulating / medication used for the treatment of bradycardia, heart block, and rarely for as asthma		5984-95-2	FDA	US 2868691	Cardiovascular	Bronchodilator	GPCR	Adrenergic receptors
14E02	1.06	(S)-(-)-Propranolol hydrochloride	A β-adrenergic receptor antagonist, betablocker used for hypertension (angiotensive inhibitor) / inhibitors of binding or entry into cells for Marburg Virus in HTS		4199-10-4	FDA	GB 0994918	Cardiovascular	Antianginal	GPCR	Adrenergic beta receptor
15C03	1.05	Dopamine hydrochloride	a monoamine compound with positive inotropic activity, mimics the effects of stimulating postganglionic adrenergic sympathetic nerves, increases heart rate and force, thereby increasing cardiac output		62-31-7	FDA	DE 247906	Cardiovascular	Antihypertensive	GPCR	Adrenergic Beta 1 receptors
14F03	1.01	Ranolazine	piperazine derivative with anti-anginal and potential antineoplastic activities. Ranolazine is indicated for the treatment of chronic angina		95635-55-5	FDA	EP 0126449	Cardiovascular	Antianginal	Not identified	Alters the intracellular sodium level
15C07	1.17	Candesartan	benzimidazole-derived angiotensin II receptor antagonist prodrug with antihypertensive activity. Candesartan is an angiotensin II receptor blocker used widely in the therapy of hypertension and heart failure. Treatment of hypercholesterolaemia, Treatment of hypertension		139481-59-	FDA	US 5196444	Cardiovascular	Antihypertensive	GPCR	Angiotensin II receptor type 1
15G05	1.12	Olmesartan	synthetic imidazole derivative prodrug with an antihypertensive property, used in the treatment of acute or chronic vascular hypertension. Agent that antagonizes angiotensin II type 1 receptor		144689-63-	FDA	EP 0503785	Cardiovascular	Antihypertensive	GPCR	Angiotensin II receptor type 1
15D05	1.46	Ambrisentan	endothelin receptor antagonist used in the therapy of pulmonary arterial hypertension (PAH)		177036-94-	FDA	DE 4313412	Cardiovascular	Antihypertensive	GPCR	Endothelin receptor A
15G11	1.04	Fosinopril	Fosinopril is an angiotensin-converting enzyme (ACE) inhibitor used in the therapy of hypertension and heart failure.		98048-97-6	FDA	US 4337201	Cardiovascular	Antihypertensive	Enzyme	Angiotensin-converting enzyme
19B02	1.55	Budralazine	member of phthalazines vasodilatator and treatment of acute or chronic vascular hypertension		36798-79-5	JAN	EP0085840	Cardiovascular	Vasodilator	Receptor	adrenergic receptor
16D07	1.08	Fenoldopam	benzazepine derivative with vasodilatory and antihypertensive properties . Drug used in the treatment of acute or chronic vascular hypertension and also used to cause dilation of the blood vessels		67227-56-9	FDA	US 4160765	Cardiovascular	Antihypertensive	GPCR	Dopaminergic D1 receptor
13E05	1.14	Meptazinol	hydrochloride 3-phenylazepane derivative narcotic antagonist with analgesic properties (opioid / narcotic), it is used for the control of moderate to severe pain / block Entry of Ebola Virus and HCMV in HTS		59263-76-2	EMA	DE 1941534	Central Nervous System	Analgesic	GPCR	Opioid receptors
15F10	1.66	Nalmefene hydrochloride	a naltrexone analogue with opioid antagonistic property, Agents inhibiting the effect of narcotics on the central nervous system (alcohol and gambling dependence)		58895-64-0	FDA	US 4567185	Central Nervous System		GPCR	Opioid receptors
07H07	1.03	Mirtazapine	synthetic tetracyclic derivative of the piperazino-azepines with antidepressant activity, used off-label for a variety of conditions including panic disorder, generalized anxiety disorder, dysthymia, and sexual disorders		61337-67-5	FDA	US 4062848	Central Nervous System	Antidepressant	GPCR	Catecholaminergic receptors
11E02	1.16	Olanzapine	thienobenzodiazepine with antipsychotic, antinausea, and antiemetic activities. Olanzapine is an atypical antipsychotic that is used currently in the treatment of schizophrenia and bipolar illness, also used to prevent nausea or vomiting		132539-06-	FDA	US 4115568	Central Nervous System	Antipsychotic	GPCR	Serotoninergic 5-HT receptors
09D04	1.05	Opipramol dihydrochloride	A tricyclic antidepressant with actions similar to Amitriptyline / inhibitor of binding or entry into cells for Marburg Virus and for Marburg Virus, blocks Entry of Ebola Virus		909-39-7	EMA	FR 1271971	Central Nervous System	Antidepressant	GPCR	Sigma receptors
05A10	1.44	Tacrine hydrochloride	an aminoacridine derivative with cognitive stimulating property, acetylcholinesterase inhibitor. It was the first centrally acting cholinesterase inhibitor approved for the treatment of Alzheimer's disease (central and peripheral anti-inflammatory effects)		1684-40-8	FDA	EP 0328535	Central Nervous System	CNS Stimulant	Enzyme	Acetylcholinesterase

09F04	1.16	Promazine hydrochloride	a phenothiazine derivative with antipsychotic and antiemetic properties, older medication used to treat schizophrenia. Drug used to prevent nausea or vomiting / inhibitors of binding or entry into cells for Marburg Virus, blocks Entry of Ebola Virus in HTS		53-60-1	FDA	US 2519886	Central Nervous System	Antipsychotic	GPCR	Dopaminergic receptors
04E09	1.09	Spiperone	a dopaminergic antagonist, a serotonergic antagonist, an alpha-adrenergic antagonist, an antipsychotic agent and a psychotropic drug, recommended in the treatment of Schizophrenia / inhibits nucleocapsid/RNA interactions in Rift Valley Fever Virus, Inhibitor of binding or entry into cells for Lassa Virus, blocks Entry of Ebola Virus in HTS		749-02-0	PMDA Japan	US 3155669	Central Nervous System	Antipsychotic	GPCR	Dopaminergic D2 receptor
04F06	1.05	Pergolide mesylate	semi-synthetic ergot derivative and a dopamine agonist with antiparkinson property / block Entry of Ebola Virus in HTS		66104-23-2	FDA	US 4166182	Central Nervous System	Antiparkinsonian	GPCR	Dopaminergic receptors
05F11	1.05	Clebopride maleate	Drugs used to prevent nausea orvomiting / blocks Entry of Ebola Virus in HTS		84370-95-6	EMA	US 4138492	Central Nervous System	Antiemetic		
16C03	1.04	Donepezil hydrochloride	piperidine derivative with neurocognitive-enhancing activity, improves neurocognitive function in Alzheimer's disease / blocks Entry of Ebola Virus in HTS		120011-70-	FDA	AU 8818216	Central Nervous System	Anti-Alzheimer	Enzyme	Acetylcholinesterase
17E06	1.17	Tolperisone hydrochloride	centrally acting muscle relaxant that has been used for the symptomatic treatment of spasticity and muscle spasm, used also for the treatment of a variety of clinical conditions that have in common only the presence of skeletal muscle hyperactivity		3644-61-9	EMA, JAN	US6500455	Central Nervous System	Muscle relaxant	Protein	Voltage-gated calcium channel
12E07	1.16	Idazoxan hydrochloride	benzodioxane-linked imidazole that has alpha-2 adrenoceptor antagonist activity, investigated as an antidepressant. More recently, under investigation as treatment in schizophrenia		79944-56-2	EMA	WO1989001774	Central Nervous System	Antiparkinsonian	Transmembrane receptor	kappa receptor
14B09	1.67	Ondansetron hydrochloride	competitive serotonin type 3 receptor antagonist. It is effective in the treatment of nausea and vomiting caused by cytotoxic chemotherapy drugs, and has reported anxiolytic and neuroleptic properties		103639-04-	FDA	US 4695578	Central Nervous System	Antianemic	Ionotropic receptor	Serotoninergic 5-HT3 receptor
19A03	1.23	Eletriptan	role as a serotonergic agonist, a vasoconstrictor agent and a non-steroidal anti-inflammatory drug treatment of migraine headaches / blocks Entry of Ebola Virus in HTS		143322-58-	FDA	US5545644	Central Nervous System	Antimigraine	GPCR	5-HT1b receptor
15B10	1.22	Phentermine hydrochloride	a sympathomimetic amine with central nervous system (CNS) stimulant and appetite depressant properties (treatment of obesity)		1197-21-3	FDA	US 2408345	Central Nervous System	Anti-obesity	GPCR	Catecholaminergic receptors
15A02	1.18	Buspirone hydrochloride	an anxiolytic agent chemically and pharmacologically unrelated to benzodiazepines, barbiturates, or other sedative/hypnotic drugs		33386-08-2	FDA	US 3717634	Central Nervous System	Anxiolytic	GPCR	Serotoninergic 5-HT receptors
12C10	1.01	Nabumetone	naphthylalkanone and non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, antipyretic and analgesic activities, used in therapy of chronic arthritis		42924-53-8	FDA	EP 0003643	Central Nervous System	Analgesic	Enzyme	Cyclooxygenase
16G04	1.17	Tolterodine tartrate	benzhydryl compound (Detrol) and a muscarinic receptor antagonist possessing both antimuscarinic and antispasmodic properties, used in the treatment of urinary incontinence		209747-05-	FDA	EP 0325571	Neuromuscular	Muscle relaxant	GPCR	Muscarinic M2 / M3 receptors
01F08	1.19	Benoxinate hydrochloride	ester-based local anaesthetic used especially in ophthalmology and otolaryngology. It has a role as a local anaesthetic and a topical anaesthetic / block Entry of Ebola Virus in HTS		5987-82-6	FDA	US 3957996	Neuromuscular	Local anesthetic	Ion channel	Na+
14C05	1.23	Meprylcaine hydrochloride	benzoate ester local anesthetic with stimulant properties that is structurally related to dimethocaine		956-03-6	no	US 4024223	Neuromuscular	Local anesthetic	Ion channel	Voltage-gated Na+ channel
04C05	1.12	Dyclonine hydrochloride	an unclassified compound with local anesthetic effect (throat spray) / blocks Entry of Ebola Virus		536-43-6	FDA	US 2771391	Neuromuscular	Local anesthetic	Ion channel	Voltage-gated Na+ channel
18B09	1.26	Eperisone HCl	antispasmodic drug used as vasodilatator and muscle relaxant agent, also used to prevent seizures / blocks Entry of Ebola Virus, Inhibitors of binding or entry into cells for Marburg Virus in HTS		56839-43-1	JAN	EP0083108A2	Neuromuscular	Muscle relaxant	Ion channel	Sodium channels
16H02	1.34	Cisatracurium besylate	non-depolarizing skeletal muscle relaxant of the benzylisoquinolinium class, used as muscle relaxant during anesthesia		64228-79-1	FDA	US 4179507	Neuromuscular	Muscle relaxant	Ion channel	Nicotinic receptors

15H04	1.44	Formoterol	fumarate eformoterol, is a long-acting β2 agonist (LABA) used as a bronchodilator in the management of asthma and COPD (inhalation) (also reduces mediator substance release in inflammatory cells)		43229-80-7	FDA	DE 2305092	Respiratory	Antiasthmatic	GPCR	Adrenergic beta-2 receptor
05E07	1.08	Ambroxol hydrochloride	breaks up phlegm, used in the treatment of respiratory diseases associated with viscid or excessive mucus (expectorant)		23828-92-4	EMA	US 3536713	Respiratory	Expectorant		
14E05	1.31	Levalbuterol hydrochloride	a relatively selective sympathomimetic beta-2 adrenergic receptor agonist with bronchodilator activity (inhalation) used in the treatment of asthma and chronic obstructive pulmonary disease (inhibits the release of inflammatory mediators from mast cells)		50293-90-8	FDA	US 5399765	Respiratory	Antiasthmatic	GPCR	Adrenergic beta-2 receptor
03G08	1.01	Clemizole hydrochloride	an orally bioavailable histamine H1 antagonist, with potential anti-tumor and anti-allergic activities / clinical trial (phase 1 in 2010) for HCV treatment and Inhibitors of binding or entry into cells for Marburg Virus, blocks Entry of Ebola Virus in HTS phase 1 HCV and		1163-36-6	EMA	US 3117910	Allergology	Antibacterial	GPCR	Histaminergic H1 receptor
04C06	1.15	Dimenhydrinate	first-generation histamine antagonist with anti-allergic activity, This prevents histamine-induced bronchoconstriction, vasodilation, increased capillary permeability, also used for treatment or prevention of motion sickness or symptoms of nausea and dizziness		523-87-5	FDA	US 2499058	Allergology	Antiemetic	GPCR	Histaminergic H1 receptor
15E10	1.17	Tripelennamine hydrochloride	an ethylenediamine derivative with an antihistaminergic property, agent used to treat allergic reactions		154-69-8	FDA	US 2406594	Allergology	Antihistaminic	GPCR	Histaminergic H1 receptor
07G09	1.35	Chloroquine diphosphate	a quinoline compound with antimalarial and anti-inflammatory properties (non-steroidal) / inhibitor of binding or entry into cells for Marburg Virus, blocks Entry of Ebola Virus in HTS		50-63-5	FDA	US 2233970	Metabolism	Anti-inflammatory	Enzyme	Heme polymerase
08E11	1.43	Hydroxychloroquine sulfate	synthetic derivative of quinolyl with chemotherapeutic and antibiotic properties. Hydroxychloroquine Sulfate acts against erythrocytic malarial parasites with anti-inflammatory properties and is also used in the treatment of rheumatoid arthritis and lupus erythematosus / block Entry of Ebola Virus in HTS		747-36-4	FDA	US 2546658	Metabolism	Antimalarial	Receptor	Toll-like receptors
18H11	1.04	Artenimol	indicated for the treatment of uncomplicated Plasmodium falciparum malaria , given in coinfection with HIV / Inhibitors of binding or entry into cells for Lassa Virus and for Marburg Virus in HTS		81496-81-3	DRAP	US 20100226943	Infectiology	Antimalarial	Cell	Ferriprotoporphyrin
13C04	1.38	Dimaprit dihydrochloride	histamine H2 receptor agonist that is often used to study the activity of histamine and its receptors		23256-33-9	no	US 4126670	Ophthalmology	Antiglaucoma	GPCR	Histaminergic H2 receptor
14F06	1.14	Cyclopentolate hydrochloride	an anticholinergic drug. Administered in the eye (collyre), cyclopentolate hydrochloride blocks the acetylcholine receptor		5870-29-1	FDA	US 2554511	Ophthalmology	Mydriatic	GPCR	Cholinergic receptors
08H03	1.01	Dipivefrin hydrochloride	a prodrug of epinephrine, and is used to treat open-angle glaucoma (collyre)		64019-93-8	FDA	US 3809714	Ophthalmology	Antiglaucoma		
16C10	2.10	Ethoxzolamide	a sulfonamide and carbonic anhydrase (CA) inhibitor with diuretic and anti-glaucoma activity (collyre). It is used in the treatment of glaucoma and as a diuretic / reduces the secretion of H+ ions		452-35-7	FDA	US 3323999	Ophthalmology	Antiglaucoma	Enzyme	Carbonic anhydrase I
17D04	1.30	Oxiglutatione	oxidized disulfide form of glutathione (GSH) with potential protective activity		27025-41-8	FDA, JAN	US6470894	Ophthalmology	Antidote	Enzyme	Glutathione reductase
04B07	1.49	Isotretinoin	naturally-occurring retinoic acid with potential antineoplastic activity, a vitamin A derivative used in the treatment of severe acne and some forms of skin, head and neck cancer also treatment of neuroblastoma, teratogene		4759-48-2	FDA	US 4464394	Dermatology	Keratolytic		
15D10	1.18	Anthralin	anthraquinone derivative, anti-psoriatic and anti-inflammatory Anthralin, used topically in the treatment of psoriasis, dermatoses, and alopecia areata, it is also used in biomedical research due to its effect on EGFR autophosphorylation		1143-38-0	EMA	US 3450820	Dermatology	Antipsoriatic		
15F05	1.02	Ibudilast	pyrazolopyridine orally bioavailable inhibitor of cyclic nucleotide phosphodiesterase (PDE), with anti-(neuro)inflammatory, vasorelaxant, bronchodilator, analgesic, neuroprotective, potential anti-tumor activities. Treatment of multiple sclerosis, asthma, cerebrovascular disease, and also treatment of amyotrophic lateral sclerosis		50847-11-5	JAN	US 3850941	Metabolism	Anti-inflammatory	Enzyme	Phosphodiesterase 4
13E08	1.39	Fursultiamine hydrochloride	disulfide derivative, medication used to treat thiamine deficiency		2105-43-3	Japan, Pakistan, Indonesia, South Korea	US 3278537	Metabolism	Anti-Alzheimer	Enzyme	Vitamin

19C05	1.06	Bisbentiamine	O-benzoyl thiamine disulfide or vitamin B1 disulfide derivative, used for thiamine deficiency		2667-89-2	JAN	US3284298A	Metabolism	Antianemic		
15B05	1.03	Anethole-trithione	drug used in the treatment of dry mouth. It is listed as being studied in the treatment of cancer.		532-11-6	EMA	DE 855865	Metabolism	Choleretic	Enzyme	72 kDa type IV collagenase
16E10	1.04	Zoledronic acid hydrate	synthetic imidazole bisphosphonate analog of pyrophosphate with anti-bone-resorption activity, used for the treatment of malignancy-related hypercalcemia, osteitis deformans and osteoporosis		165800-06-6	FDA	AU 8781453	Oncology	Antiosteoporetic	Enzyme	Farnesyl diphosphate synthase
19C11	1.13	Oxyphenisatin	Oxyphenisatine is a member of indoles used as laxative agent		125-13-3	FDA	US6900044	Gastroenterology	Laxative	Not identified	Peristalsis
19D11	1.16	Cyclofenil	nonsteroidal selective estrogen receptor modulator (SERM) medication which is used as a gonadotropin stimulant or ovulation inducer and in menopausal hormone therapy in women to treat menstrual disturbances and anovulatory infertility		2624-43-3	EMA	US4729999	Endocrinology	anti-estrogen	Receptor	Estrogen receptor beta

Legend

- steroids
- prostaglandins
- proton pump inhibitors
- antivirals
- antibacterial drugs
- cardiovascular drugs
- opioids
- nonopioid CNS drugs
- neuromuscular drugs
- respiratory system drugs
- allergy medications
- antiparasitic drugs