**Table S1. Antiviral drug candidates for entry inhibition of SARS-CoV-2.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Supplier** | **Catalog #** | **Candidate** **(generic name)** | **Mechanism of action** | **Current indications and remarkable properties** |
|  | ***TMPRSS2 inhibitors*** |  |
| Selleckchem | S2874 | **Camostat mesylate** | * Inhibits serine proteases [[[1](#_ENREF_1)](#_ENREF_1)](#_ENREF_1).
* Prevents TMPRSS2 to activate SARS-CoV-2 spike protein for viral entry [2](#_ENREF_2" \o "Hoffmann, 2021 #145).
 | * Antiproteinuric drug [1](#_ENREF_1).
* Approved for pancreatitis in Japan [2](#_ENREF_2" \o "Hoffmann, 2021 #145).
 |
|  | ***Corticosteroids*** |  |
|  | * Block the initial inflammatory response by inhibiting the production of nitric oxide and eicosanoids that promote vascular permeability and vasodilation. As a result, leukocyte migration to inflamed tissues is decreased [3](#_ENREF_3).
* Modulate events in chronic inflammation by altering/suppressing T cell activation [3](#_ENREF_3).
 | * Immune-mediated diseases, e.g., rheumatoid arthritis, allergies, ulcerative colitis, lupus erythematosus and skin disorders such as psoriasis and dermatitis [3](#_ENREF_3).
 |
| Selleckchem | S4430 | **Cortisol** | * Major glucocorticoid in humans [3](#_ENREF_3).
 | * It has disadvantageous salt retaining properties which distinguishes it from other glucocorticoids [4](#_ENREF_4).
 |
| Sigma-Aldrich | D1756 | **Dexamethasone** | * Possesses 20 to 30 times the binding affinity for glucocorticoid receptors of endogenous cortisol [5](#_ENREF_5).
 | * Treatment for post-operative and chemotherapy-induced nausea and vomiting [5](#_ENREF_5).
 |
| Selleckchem | S2121 | **Ciclesonide** | * Converted in the lower respiratory tract to an active metabolite with 100-fold greater relative glucocorticoid receptor binding affinity than ciclesonide itself [6](#_ENREF_6) [7](#_ENREF_7).
 | * Asthma prevention [7](#_ENREF_7).
 |
| Selleckchem | S1696 | **Prednisone** | * Metabolized in the liver to its active metabolite [8](#_ENREF_8).
 | * First choice in miastenia gravis [8](#_ENREF_8).
* Maintenance therapy for kidney transplant patients [8](#_ENREF_8).
 |
|  | ***Nonsteroidal anti-inflammatory drugs (NSAIDs)*** |  |
|  |  |  | * Inhibit ciclooxygenases (COXs), causing a reduction in the production of prostaglandins at the site of tissue injury and attenuation of the inflammatory cascade [9](#_ENREF_9).
 | * Provide analgesia for mild to moderate pain resulting from surgery, injury, and disease [9](#_ENREF_9).
* Anti-inflammatory properties [9](#_ENREF_9).
 |
| Selleckchem | S1261 | **Ibuprofen** | * Inhibits COX [9](#_ENREF_9).
* Exerts a direct spinal action by blocking the hyperalgesic response induced by activation of spinal glutamate and substance P receptors [9](#_ENREF_9).
 | * Widely used as an analgesic, anti-inflammatory, and antipyretic [10](#_ENREF_10).
 |
| Selleckchem | S1622 | **Licofelone** | * Inhibits COX and lipoxigenase (LOX) [11](#_ENREF_11).
 | * Phase III trials have been successfully completed as a treatment for osteoarthritis[11](#_ENREF_11).
 |
| Selleckchem | S1638 | **Sulindac** | * Converted *in vivo* to an active sulfide compound by liver enzymes [12](#_ENREF_12).
* Inhibits COX [12](#_ENREF_12).
* Modulates Wnt/β-catenin as well as NF-κB signalling that can have repercussion on the invasive behaviour of cancer cells [13](#_ENREF_13).
 | * Relief of signs and symptoms of several arthritic conditions [12](#_ENREF_12).
* Induction of cholestatic liver injury due to its competitive inhibition of canalicular bile acid transport [14](#_ENREF_14).
 |
| Selleckchem | S2386 | **Celecoxib** | * Selectively inhibits COX-2 [15](#_ENREF_15).
 | * Pain relief in osteoarthritis [15](#_ENREF_15).
* Reduction of precancerous polyps in the colon [16](#_ENREF_16).
* Potentiation of the anticoagulant effects of warfarin. Serious bleeding complications have been reported [17](#_ENREF_17).
 |
|  | ***Other immunomodulators*** |  |
| Selleckchem | S4238 | **Cepharanthine** | * Alkaloid isolated from *Stephania cepharantha* [18](#_ENREF_18).
* Modulates efflux pumps and membrane rigidification [19](#_ENREF_19).
* Reduces inflammation by AMPK activation and NF-κB inhibition [19](#_ENREF_19).
* Inhibits plasma membrane lipid peroxidation and platelet aggregation [20](#_ENREF_20).
* Suppresses cytokine production [20](#_ENREF_20).
 | * Used in Japan since the 1950s to treat leukopenia, snake bites, xerostomia and alopecia areata [19](#_ENREF_19).
* Immunoregulatory, anti-oxidative, -inflammatory, -cancer, -viral and -parasitic properties [19](#_ENREF_19).
 |
| Selleckchem | S4008 | **Pemirolast potassium** | * Stabilizes mast cells [21](#_ENREF_21).
 | * Prevention and relief of ocular manifestations of allergic conjunctivitis [21](#_ENREF_21).
 |
|  | ***For enzymatic deficiencies*** |  |
| Selleckchem | S4680 | **Protilerin** | * Stimulates the release of thyroid-stimulating hormone from the anterior pituitary gland [22](#_ENREF_22).
 | * Stimulation test to diagnose hyperthyroidism [23](#_ENREF_23).
 |
| Sigma-Aldrich | T4425 | **Tetrahydrobiopterin dihydrochloride** | * Essential cofactor required for the synthesis of several neurotransmitters [24](#_ENREF_24).
 | * Tetrahydrobiopterin deficiency (phenylketonuria) [25](#_ENREF_25).
 |
|  | ***Blood regulation*** |  |
| Selleckchem | S5084 | **Carbazochrome sodium sulfonate** | * Reduces capillary permeability [26](#_ENREF_26).
* Hemostatic agent that promotes clotting [27](#_ENREF_27).
 | * Pain relief in refractory chronic prostatitis [26](#_ENREF_26).
* In combination with tranexamic acid for the reduction of perioperative blood loss and inflammatory response [28](#_ENREF_28).
* In combination with vitamin C, vitamin E and lysozyme for the reduction of gingival inflammation in chronic periodontitis [29](#_ENREF_29).
* In combination with procaine results in better efficacy and less adverse effects in treating moderate to massive hemoptysis than vasopressin [30](#_ENREF_30).
 |
| MedChemExpress | HY-B0799 | **Ergoloid mesylates** | * Binds with high affinity to the γ-aminobutyric acid (GABA)A receptor Cl- channel, producing an allosteric interaction with the benzodiazepine site [31](#_ENREF_31).
* Dihydrogenation eliminates vasoconstrictor effects of ergotoxine and enhances its α-adrenoreceptor and 5-hydroxytryptamine (serotonin) receptor antagonist properties [32](#_ENREF_32).
* Inhibits brain-specific phosphodiesterases [32](#_ENREF_32).
 | * Supposed therapeutic effects in depression, confusion, lack of self-care in the elderly, and erectile dysfunction [32](#_ENREF_32).
 |
| Sigma-Aldrich | SML2313 | **Higenamine hydrochloride** | * Alkaloid found in *Aconitum* plant [33](#_ENREF_33).
* Reduces IL-1β-induced inflammation in human nucleus pulposus cells via inhibiting NF-κB signaling pathway [34](#_ENREF_34).
* Protects neuronal cells against oxygen-glucose deprivation/reperfusion (OGD/R)-induced injury by regulating the Akt and Nrf2/HO-1 signaling pathways [35](#_ENREF_35).
* Possesses positive ionotropic and chronotropic, activating slow channel, vascular and tracheal relaxation effects [33](#_ENREF_33).
 | * Collapse, syncope, painful joints, edema, and bronchial asthma treatment in Asian traditional medicine [33](#_ENREF_33).
* Antispasmodic for Raynaud's phenomenon and cold-induced vasoconstriction [36](#_ENREF_36).
* Potential therapeutic effects for diseases like intravertebral disc degeneration [34](#_ENREF_34), heart failure, disseminated intravascular coagulation, ischemia/reperfusion injuries and erectile dysfunction [33](#_ENREF_33).
* Immunomodulatory, anti-inflammatory, -thrombotic, -apoptotic and -oxidative properties [33](#_ENREF_33).
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|  | ***Antidiabetics*** |  |
| Vall d’Hebron Pharmacy Department |  | **Metformin** | * Reduces gluconeogenesis and hepatic glucose production and improves insulin sensitivity by increasing peripheral glucose uptake [37](#_ENREF_37).
* Increases anaerobic glucose metabolism in enterocytes [38](#_ENREF_38).
* Accumulates in the mitochondria to inhibit mitochondrial complex I, leading to increased cytoplasmic ADP:ATP and AMP:ATP ratios. These changes activate AMPK to regulate glucose metabolism [38](#_ENREF_38).
 | * First choice drug for Type 2 diabetes [39](#_ENREF_39).
 |
| Selleckchem | S2542 | **Phenformin** | * Acts on the cell membrane to decrease oxidative phosphorylation [40](#_ENREF_40).
* Produces tissue anoxia [40](#_ENREF_40).
* Increases peripheral glucose uptake (Pasteur Effect) [40](#_ENREF_40).
* Leads to lactic acidosis by inhibition of lactic acid metabolism [40](#_ENREF_40).
 | * Predecessor of metformin with an unacceptably high incidence of lactic acidosis, often fatal [41](#_ENREF_41).
 |
| Vall d’Hebron Pharmacy Department |  | **Vildagliptin** | * Selectively inhibits dipeptidyl peptidase-4 (DPP-4), an enzyme that degrades and inactivates glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), which promote insulin secretion and regulate blood glucose levels [42](#_ENREF_42).
 | * Type 2 diabetes [43](#_ENREF_43).
 |
| Vall d’Hebron Pharmacy Department |  | **Sitagliptin** | * Selectively inhibits DPP-4 [43](#_ENREF_43).
* Elevates GLP-1 levels to increase insulin release after meals and improve glucose tolerance [43](#_ENREF_43).
 | * Type 2 diabetes [43](#_ENREF_43).
 |

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|  | ***Natural compounds - Flavonoids*** |  |
|  | * Possess several anticancer effects: they modulate reactive oxygen species (ROS)-scavenging enzyme activities, participate in arresting the cell cycle, induce apoptosis, autophagy, and suppress cancer cell proliferation and invasiveness [44](#_ENREF_44).
 | * Multiple potential applications.
 |
| Selleckchem | S2320 | **Luteolin** | * Found in a number of dietary sources [45](#_ENREF_45).
 | * Plants rich in luteolin have been used in Chinese traditional medicine for hypertension, inflammatory disorders, and cancer treatment [46](#_ENREF_46).
 |
| Sigma-Aldrich | 94258 | **Eriodictyol** | * Present in citrus fruits and Chinese herbs used in the food industry [47](#_ENREF_47).
* Reduces inflammation by NF-κB blockade [48](#_ENREF_48).
* As opposite to other flavonoids, eriodictyol lacks the C2–C3 double bond responsible to give more inhibitory activity of basal vascular NO release and vascular superoxide formation [49](#_ENREF_49)
 | * Anti-inflammatory, -allergenic, -microbial, -cancer, and -oxidant properties [48](#_ENREF_48).
 |
| Selleckchem | S2391 | **Quercetin** | * Obtained from diverse fruits and vegetables [50](#_ENREF_50).
* Stabilizes basophils and mast cells [50](#_ENREF_50).
* Reduces obesity by increase in AMPK expression [51](#_ENREF_51).
* Inhibits histone deacetylase 1 and DNA methyltransferase 1 [51](#_ENREF_51).
 | * Antioxidative, -inflammatory, -platelet, -apoptotic, -invasive and -angiogenic properties [51](#_ENREF_51).
* Nephro-, gastro-, angio-, cardio- and chondroprotective properties [52](#_ENREF_52).
 |
| Selleckchem | S2007 | **Myricetin** | * Found in tea, berries, fruits, vegetables, and the plant *Diospyros lotus* [53](#_ENREF_53).
* Inhibits thrombin with an IC50 value of 56 μM [54](#_ENREF_54).
* Inhibits the production of proinflammatory mediators through the suppression of NF-κB and STAT1 activation and induction of Nrf2-mediated HO-1 expression in LPS-stimulated RAW264.7 macrophages [55](#_ENREF_55).
 | * *Diospyros lotus* is traditionally used in diabetes, diarrhea, tumor, and hypertension treatment [55](#_ENREF_55).
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|  | ***Natural compounds - Others*** |  |
| Selleckchem | S2326 | **Glycyrrhizin** | * Triterpenoid saponin found as the major active constituent in licorice root [56](#_ENREF_56).
* Shows anti-inflammatory and antioxidant activities [57](#_ENREF_57).
* Stimulates endogenous production of interferons [57](#_ENREF_57).
* Induces melanogenesis through cAMP signaling [58](#_ENREF_58).
 | * Bronchitis, gastritis, and jaundice alleviation in traditional medicine [56](#_ENREF_56).
 |
| Selleckchem | S4646 | **Indirubin** | * Found in a variety of plants, marine mollusks, bacteria, and human urine, and produced in mammals’ intestine [59](#_ENREF_59).
* Inhibits several cyclin-dependent kinases and glycogen synthase kinase 3 [59](#_ENREF_59).
* May suppress lipopolysaccharides-induced inflammation via Toll-like receptor 4 abrogation mediated by the NF-κB and MAPK signaling pathways [60](#_ENREF_60).
 | * Chronic myelogenous leukemia treatment in Chinese traditional medicine [59](#_ENREF_59).
* Indirubin in Lindioil ointment for psoriasis topical treatment [61](#_ENREF_61).
 |
| MedChemExpress | HY-N0453 | **Hypericin** | * Produces primary photosensitization [62](#_ENREF_62).
* Shows selective activity against viruses, both *in vitro* and *in vivo*, including Herpes simplex (HSV)-1 and -2 [63](#_ENREF_63).
 | * Non-melanoma skin cancer topical treatment [62](#_ENREF_62).
 |
|  | ***Antimicrobials*** |  |
| Sigma-Aldrich | 90527 | **Hydroxychloroquine** | * Inhibits pH-dependent viral fusion/replication [1](#_ENREF_1).
* Prevents viral envelope glycoprotein as well as host receptor protein glycosylation [1](#_ENREF_1).
* Prevents virion assembly in endoplasmic reticulum-Golgi intermediate compartment–like structure [1](#_ENREF_1).
* Inhibits TLR-7/9–dependent inflammatory responses [1](#_ENREF_1).
 | * Malaria [64](#_ENREF_64).
* Rheumatoid arthritis [64](#_ENREF_64).
* Systemic lupus erythematosus [64](#_ENREF_64).
 |
| Sigma-Aldrich | M2140 | **Monocaprin** | * Safe functional emulsifier in food industry [65](#_ENREF_65).
* May be a potential preservative independent of pH, acting by disruption of the cell wall and plasma membrane of fungi [65](#_ENREF_65).
 | * Hydrogel formulations have *in vitro* microbicidal activity against HIV and HSV, *Chlamydia trachomatis* and *Neisseria gonorrhoeae* [66](#_ENREF_66).
* In combination with doxycycline as a potential treatment ofherpes labialis [67](#_ENREF_67).
 |
| Sigma-Aldrich | I8898 | **Ivermectin** | * GABA receptor agonist [68](#_ENREF_68).
* Exerts toxicity in parasites by blocking the post-synaptic transmission of nerve impulses [68](#_ENREF_68).
 | * Broad-spectrum anti-parasite medication [69](#_ENREF_69).
* First choice treatment for onchocerciasis [69](#_ENREF_69).
 |
| Vall d’Hebron Pharmacy Department |  | **Nitrofurantoin** | * Bacterial intracellular nitroreductases produce the active form of the drug [70](#_ENREF_70).
* Intermediate metabolites bind to bacterial ribosomes and inhibit bacterial enzymes involved in the synthesis of DNA, RNA, and bacterial wall protein synthesis [70](#_ENREF_70).
 | * Uncomplicated urinary tract infections resistant to other antibiotics [71](#_ENREF_71).
 |
| Fisher Scientific | 10387340 | **Lauric acid** | * Found in vegetal oils [72](#_ENREF_72).
* Disrupts the cell membrane of gram-positive bacteria by physicochemical processes [72](#_ENREF_72).
* Interferes with bacterial cell signal transduction and gene transcription processes [72](#_ENREF_72).
* Activates TLR4 signaling [73](#_ENREF_73).
 | * Main antiviral and antibacterial substance found in human breast milk [74](#_ENREF_74).
 |

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| Selleckchem | S3132 | **Sulfamethoxazole** | * A sulfonamide derivative. Sulfonamides have a bacteriostatic effect by inhibiting bacterial folic acid synthesis [75](#_ENREF_75).
 | * In combination with trimethoprim for urinary tract infections, otitis media, chronic bronchitis, *Shigella* and enterotoxigenic *Escherichia coli* infections [76](#_ENREF_76).
* Prophylaxis of *Pneumocystis jirovecii* pneumonia in patients with HIV/AIDS [77](#_ENREF_77).
* High rates of adverse drug reactions in subjects infected by HIV [78](#_ENREF_78).
 |
| Selleckchem | S2302 | **Sulfamerazine** | * A sulfonamide derivative [75](#_ENREF_75).
 | * Bronchitis, prostatitis, and urinary tract infections [79](#_ENREF_79).
* Combined with a folate antagonist, sulfonamides are indicated among others in toxoplasmosis and malaria [80](#_ENREF_80).
 |
| Vall d’Hebron Pharmacy Department |  | **Tazobactam** | * Class A β-lactamase inhibitor [81](#_ENREF_81).
 | * Extension of antibiotic’s spectrum of activity [81](#_ENREF_81).
* Increase in β-lactamic antibiotic stability against bacterial β-lactamases [81](#_ENREF_81).
 |
| Selleckchem | S1784 | **Vidarabine** | * Purine nucleoside analogue [80](#_ENREF_80).
* Competitively inhibits DNA-dependent DNA polymerases of some DNA viruses approximately 40 times more than those of host cells [80](#_ENREF_80).
 | * The degree of maximal resistance to vidarabine is 4-fold, much lower than the 100-fold resistance to acyclovir with similar DNA-polymerase resistant mutations [80](#_ENREF_80).
* No longer used due to toxicity issues as well as the discovery of more potent and safer compounds such as acyclovir, which today is widely prescribed for HSV [82](#_ENREF_82).
 |
| Sigma-Aldrich | M1765 | **Monolaurin** | * Solubilizes the lipids and phospholipids in the envelope of pathogenic viruses and bacteria causing the disintegration of their envelopes [74](#_ENREF_74).
 | * Inactivation to some extent of HIV, measles, HSV-1, vesicular stomatitis, Visna virus, and cytomegalovirus [74](#_ENREF_74).
 |
| Sigma-Aldrich | PHR1949 | **Sodium lauryl sulfate** | * Ionic detergent that rapidly disrupts biological membranes [83](#_ENREF_83).
 | * Inhibition of the formation of several bacterial biofilms [84](#_ENREF_84).
 |
| Selleckchem | S1915 | **Valaciclovir**  | * Purine nucleoside analogue [80](#_ENREF_80).
* Rapidly and extensively converted to aciclovir by first-pass metabolism [85](#_ENREF_85).
 | * Highly active against Herpes simplex and Herpes zoster [85](#_ENREF_85).
 |

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