A summary of drugs targeting enzymes

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System-wise list of drugs acting on Enzymes

Class	Drugs	Mechanism
Autonomic Nervous System		
Anticholinesterases	Physostigmine, Rivastigmine, Tacrine, Dyflos, Malathione, Carbaryl, Propoxur	Acetyl cholinesterase inhibitors
Acetyl cholinesterase reactivators	Pralidoxime, Obidoxime, Diacetyl mono-oxime	Acetyl cholinesterase reactivators
Autocoids		
NSAIDS	Aspirin, Ibuprofen, Nimesulide, Paracetamol	Cyclooxygenase (COX) inhibitor
Anti Gout drugs	Allopurinol, Febuxostat	Xanthine Oxidase inhibitor
Antimetabolites	Methotrexate	Dihydro Folate Reductase inhibitor
Immunomodulators	Leflunomide	Dihydro-orotate dehydrogenase inhibitor
Immunomodulators	Mycophenolate Mofetil	Cytosine monophosphate dehydrogenase inhibitor
Renal system		
Diuretics	Acetazolamide, Dorzolamide, methazolamide	Carbonic Anhydrase inhibitors
Indirect ET Receptor antagonists	Phosphoramidon, CGS 35066	Endothelin Converting Enzyme inhibitors
Antihypertensives	Captopril, Enalapril, Lisinopril	Angiotensin Converting Enzyme Inhibitors
Cardiovascular System		
Bipyridines	Mirinone, Cilostazole	Phosphodiesterase-3-inhibitor

Class	Drugs	Mechanism
Antiplatelet	Dipyridamole	Adenosine deaminase inhibitor Phosphodiesterase inhibitor
Cardiac Glycosides	Digoxin, Digitoxin	Na ⁺ /K ⁺ ATPase inhibitor
Statins	Atorvastatin, Simvastatin, Lovastatin	β -hydroxy β -methylbutyryl-CoA (HMG-CoA) Reductase Inhibitor
Fibrates	Gemfibrozil, Bezafibrate, Fenofibrate	Lipoprotein Lipase Activators
Endocrinology		
Antiestrogens	Letrozole, Anastrozole	Aromatase inhibitor
Antiandrogens	Finasteride, Dutasteride	5- α -Reductase Inhibitor
Erectile dysfunction drugs	Sildenafil, Tadalafil	Phosphodiesterase-5-inhibitor
Antithyroid	PTU, Carbimazole	Thyroid Peroxidase inhibitor
Antidiabetics	Insulin	Tyrosine Kinase activator
Antidiabetics	Sitagliptin, Saxagliptin	Dipeptidyl Peptidase-4 inhibitor
Antidiabetics	Acarbose, Miglitol, Voglibose	α -Glucosidase inhibitor
Antidiabetics Biguanides	Metformin	AMP-activated protein kinase activator
Gastrointestinal tract		
Proton Pump Inhibitors	Omeprazole, Pantoprazole, Lansoprazole, Dexlansoprazole, Rabeprazole, Esomeprazole	H ⁺ /K ⁺ ATPase inhibitor
Central nervous system		
Antimaniac	Lithium	Inosine-5'-monophosphatease (IMPase) inhibitors
Antidepressants Monoamine oxidase (MAO) A Inhibitors	Moclobemide, Clorgyline	Monoamine oxidase (MAO) A inhibitors
Antiparkinsonian Monoamine oxidase (MAO) B Inhibitors	Selegiline	Monoamine oxidase (MAO) B inhibitors

Class	Drugs	Mechanism
Alcohol dehydrogenase Inhibitors	Ethanol	Alcohol dehydrogenase inhibitor
Alcohol dehydrogenase Inhibitors	Fomepizole	Alcohol Dehydrogenase inhibitor
Aldehyde Dehydrogenase Inhibitors	Disulfiram	Aldehyde Dehydrogenase inhibitor
Antiepileptic drugs	Valproate	gamma-Aminobutyric acid (GABA) Transaminase inhibitor
Antiepileptic	Vigabatrin	gamma-Aminobutyric acid (GABA) Transaminase inhibitor
Peripheral decarboxylase Inhibitors	Carbidopa	Dihydroxyphenylalanine (DOPA) decarboxylase inhibitor
Antiparkinsonian Catechol-O-methyltransferase (COMT) Inhibitors	Tolcapone, Entacapone	Catechol-O-methyltransferase (COMT) inhibitors
Haematology		
Parenteral anticoagulants	Heparin	Antithrombin (AT) III activator
Coumarin derivatives	Warfarin	Vitamin K reductase inhibitors
Fibrinolytic Drugs	Streptokinase, Urokinase	Tissue type Plasminogen activators
Platelet Phosphodiesterase inhibitors	Dipyridamol, Cilostazol	Phosphodiesterase III inhibitors
Antibacterials		
β -lactam antibiotic	Penicillins	Bacterial Transpeptidase inhibitors
β -Lactamase inhibitors	Clavulanic acid, Sulbactam	β -Lactamase inhibitors
Fluoroquinolones	ciprofloxacin, gemifloxacin	Topoisomerase DNA Gyrase
Rifamycins	Rifampicin, Rifabutin	Prokaryotic RNA Polymerase inhibitor
Sulfonamides	sulfamethoxazole, Sulfadiazine	Dihydropteroate Synthase inhibitors
Antifungals		

Class	Drugs	Mechanism
Imidazoles	Ketoconazole, Miconazole	14- α -sterol demethylase inhibitor
Echinocandins	Caspofungin, Micafungin	1,3- β -d-Glucan synthase inhibitor
Allylamines	Terbinafine	Squalene Epoxidase Inhibitor
Antivirals (Non Retroviral)		
Anti Herpesvirus agents	Acyclovir, Valacyclovir	Viral DNA polymerase inhibitor
Anti Herpesvirus agents	Ganciclovir, Valganciclovir	Viral Phosphotransferase inhibitor
Antiinfluenza	Oseltamivir, Zanamivir	Influenza Neuramidase inhibitor
Anti Hepatitis B drugs	Entecavir, Adefovir	Viral DNA polymerase inhibitor
Anti Hepatitis C drugs	Sofosbuvir	HCV RNA Polymerase inhibitor
Anti Hepatitis C drugs	Simeprevir	HCV NS3 Protease inhibitor
Antiretrovirals		
Nucleoside Reverse-transcriptase inhibitors (NRTI)	Zidovudine, Lamivudine	Viral Reverse Transcriptase inhibitor
Nucleotide Reverse-transcriptase inhibitors (NRTI)	Tenofovir	Viral Reverse Transcriptase inhibitor
Non Nucleoside Reverse-transcriptase inhibitors (NNRTI)	Nevirapine, Efavirenz	HIV 1 Reverse Transcriptase inhibitors
Protease Inhibitors	Saquinavir, Ritonavir, Lopinavir	Virus aspartyl Protease Inhibitor
Integrase Inhibitors	Raltegravir, Elvitegravir	HIV encoded Integrase
Antiprotozoal		
Antiprotozoal drugs	Eflornithine	Ornithine decarboxylase inhibitor
Anticancer drugs		
Antimetabolites	Methotrexate, Pemetrexed	DHFR inhibitors

Class	Drugs	Mechanism
Pyrimidine Analogues	5-FU, Floxuridine	Thymidylate synthase inhibitors
Pyrimidine Analogues	Cytarabine	DNA polymerase inhibitors
Antibiotic anticancer drugs	Bleomycin, Dactinomycin	Topoisomerase II inhibitors
Epipodophyllotoxins	Etoposide, Teniposide	Topoisomerase II inhibitors
Camptothecins	Topotecan, Irinotecan	Topoisomerase I inhibitors
Misc. anticancer drugs	Hydroxyurea	Ribonucleotide Reductase
Proteasome Inhibitors	Bortezomib, Carfilzonib	Proteasome Inhibitors
Histone Deacetylase Inhibitors	Vorinostat	Histone Deacetylase Inhibitors
Signalling Pathways		
Monoclonal antibody EGFR kinase inhibitors	Cetuximab, Necitumumab	epidermal growth factor receptor (EGFR) Kinase inhibitors
Small molecule EGFR Kinase Inhibitor	Erlotinib, Gefitinib, Afatinib	epidermal growth factor receptor (EGFR) Kinase Inhibitors
Small molecule HER2 Kinase inhibitors	Lapatinib, Neratinib	Human epidermal growth factor receptor 2 (HER2) Kinase inhibitors epidermal growth factor receptor (EGFR) inhibitors
Monoclonal Antibody HER2 Kinase inhibitors	Trastuzumab, Pertuzumab	Human epidermal growth factor receptor 2 (HER2) Kinase inhibitors
Platelet derived growth factor inhibitors	Olaratumab	Platelet derived growth factor inhibitors
Mutant B-RAF Kinase Inhibitors	Vemurafenib, Dabrafenib	Mutant B-RAF Kinase Inhibitors
MAP Kinase Inhibitors	Cobimetinib, Trametinib	mitogen-activated protein (MAP) Kinase Inhibitors
Cyclin dependent kinase 4/6 inhibitors	Palbociclib, Abemaciclib	Cyclin dependent kinase 4/6 inhibitors
Anaplastic lymphoma kinase inhibitors	Alectinib, Ceritinib	Anaplastic lymphoma kinase inhibitors
VEGF inhibitor	Bevacizumab, Ramucirumab	Vascular Endothelial Growth Factor (VEGF) inhibitor

Class	Drugs	Mechanism
Bruton Tyrosine Kinase inhibitors	Ibrutinib	Bruton Tyrosine Kinase inhibitors
PI3K inhibitors	Idelalisib	Phosphatidylinositol-4,5-Bisphosphate-3 K inhibitors
Immunomodulators		
Lymphocyte signalling Inhibitors	Cyclosporine, Tacrolimus	Calcineurin Inhibitors
Lymphocyte signalling Inhibitors	Sirolimus, Everolimus	mammalian target of rapamycin (mTOR) inhibitors
Antimetabolites	Mycophenolate Mofetil	Inosine-5'-monophosphate (IMP) Dehydrogenase II Inhibitors
Immune cell Adhesion Inhibitors	Natalizumab	α -4-integrins inhibitor

Microsomal Enzyme Inducers & Inhibitors

CYP	Substrates	Inducers	Inhibitors
1A2	Acetaminophen, clomipramine, theophylline, warfarin	Charcoal-broiled foods, grilled meat, rifampin, smoking	ciprofloxacin
2A6	Coumarin, tobacco nitrosamines, nicotine	Efavirenz, phenobarbital	ketoconazole
2B6	cyclophosphamide, ifosfamide, irinotecan	Carbamazepine, phenobarbital, rifampin	fluoxetine, fluvoxamine, ketoconazole,
2C9	phenytoin, tolbutamide, warfarin	barbiturates, rifabutin, rifampin	cimetidine, fluconazole, erythromycin
2C19	clopidogrel, diazepam, omeprazole	barbiturates, rifampin	fluconazole
2D6	chlorpheniramine, codeine, desipramine, fluoxetine, fluvoxamine, haloperidol, imipramine, morphine, oxycodone paroxetine, tricyclic antidepressants	Unknown	fluoxetine, quinidine

CYP	Substrates	Inducers	Inhibitors
2E 1	Acetaminophen, enflurane, ethanol, halothane	Ethanol	disulfiram
3A4	amlodipine, astemizole, cisapride, cyclosporine, ethinyl estradiol, nifedipine, nifedipine, nimodipine, terfenadine	barbiturates, carbamazepine, phenytoin, rifampin, St. John's wort	clarithromycin,, diltiazem, erythromycin, fluconazole, grapefruit juice, ketoconazole, ritonavir, verapamil

Newly Approved Drugs acting on enzymes

Generic Name	Date	Mechanism	Treatment
upadacitinib	August 16, 2019	Janus kinase 1 (JAK) inhibitor	Rheumatoid Arthritis
fedratinib	August 16, 2019	highly selective JAK2 inhibitor	Myelofibrosis
entrectinib	August 15, 2019	selective tyrosine kinase inhibitor	ROS 1 positive NSCLC
pexidartinib	August 2, 2019	tyrosine kinase inhibitor	Tenosynovial Giant Cell Tumor
bevacizumab-bvzr	June 27, 2019	VEGF inhibitor	multiple types of cancer
alpelisib	May 24, 2019	kinase inhibitor	Postmenopausal women, and men, with HR positive, HER2-negative, breast cancer.

References

- Brunton L, Knollmann B, Hilal-Dandan R. Goodman & Gilman's. 13th ed. New York, N.Y.: McGraw-Hill Education LLC.; 2018.
- Katzung B. Basic & clinical pharmacology. 14th ed. McGraw-Hill Education; 2018.
- Tripathi K. Essentials of medical pharmacology. 7th ed. New Delhi, India: Jaypee Brothers; 2013.
- Sharma H, Sharma K. Sharma & Sharma's principles of pharmacology. 3rd ed. Hyderabad: Paras Medical Publisher; 2017.
- Murray R. Harper's illustrated biochemistry. 31st ed. New York: McGraw-Hill Medical; 2018.
- Kenakin T. Pharmacology in drug discovery. Amsterdam: Academic Press; 2012, Chapter 6, Enzymes as drug targets, Pages 105-124
- Alexander SP, Fabbro D, Kelly E, Marrion NV, Peters JA, Faccenda E, Harding SD, Pawson AJ, Sharman JL, Southan C, Davies JA. The concise guide to PHARMACOLOGY 2017/18: Enzymes. British journal of pharmacology. 2017 Dec;174:S272-359.
- Ramsay R, Tipton K. Assessment of enzyme inhibition: a review with examples from the development of monoamine oxidase and cholinesterase inhibitory drugs. Molecules. 2017;22(7):1192.

- New FDA Approved Drugs for 2019 | CenterWatch [Internet]. Centerwatch.com. 2019 [cited 2 September 2019]. Available from: <https://www.centerwatch.com/drug-information/fda-approved-drugs/>