Supplementary Information

DFT, wave function analyses of protocatechualdehyde, a natural product

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Received 10 January 2025; accepted (revised) 10 June 2026

Table S1: The activity profile as per PASS prediction, their probable function and corresponding citations.

Metabolic Activity	Pa*	Pi*	Function in relation to the protein descriptors	References
Aldehyde oxidase inhibitor	0.954	0.003	Xenobiotic clearance, Hepatoprotective and Anti-cancerous	Barr, J. T., & Jones, J. P. (2011). Inhibition of human liver aldehyde oxidase: implications for potential drug-drug interactions. *Drug metabolism and disposition: the biological fate of chemicals*, *39*(12), 2381–2386. https://doi.org/10.1124/dmd.111.041806
Catechol 1,2-dioxygenase inhibitor	0.935	0.001	Hepatoprotective, especially in alcohol digestion	Guzik, U., Hupert-Kocurek, K., Sitnik, M., &Wojcieszyńska, D. (2013). High activity catechol 1,2-dioxygenase from Stenotrophomonasmaltophilia strain KB2 as a useful tool in cis,cis-muconic acid production. *Antonie van Leeuwenhoek*, *103*(6), 1297–1307. https://doi.org/10.1007/s10482-013-9910-8
Feruloyl esterase inhibitor	0.923	0.003	Antifungal	Crepin VF, Faulds CB, Connerton IF. A non-modular type B feruloyl esterase from Neurosporacrassa exhibits concentration-dependent substrate inhibition. *Biochem J*. 2003;370(Pt 2):417-427. doi:10.1042/BJ20020917
Monodehydroascorbate reductase (NADH) inhibitor	0.92	0.003	Anti- Oxidant, Anti-cancerous	Leterrier M, et al. (2005). "Peroxisomal monodehydroascorbate reductase. Genomic clone characterization and functional analysis under environmental stress conditions". *Plant Physiol*. **138** (4): 2111–23. doi:10.1104/pp.105.066225.
Aspulvinonedimethylallyltransferase inhibitor	0.919	0.005	Anti-cizmatics, anti-fobic, Alzheimer's and Schizophrenia	Imran Ali, DnyaneshwarNighot, Mohammad Nadeem Lone & Arvind Jain (2017) Efficient copper-catalyzedSonogashira coupling reactions and simulation studies, Synthetic Communications, 47:12, 1175-1184, DOI: 10.1080/00397911.2017.1319488
Benzoate 4-monooxygenase	0.914	0.002	Antifungal activity	Korošec, B., Sova, M., Turk, S., Kraševec, N., Novak, M., Lah, L., Stojan, J., Podobnik, B., Berne,

inhibitor				S., Zupanec, N., Bunc, M., Gobec, S. and Komel, R. (2014), Antifungal activity of cinnamic acid derivatives involves inhibition of benzoate 4-hydroxylase (CYP53). J ApplMicrobiol, 116: 955-966. https://doi.org/10.1111/jam.12417
Aspartate-phenylpyruvate transaminase inhibitor	0.903	0.002	ATP synthesis blocker in Cancerous cells	Fahien LA, Smith SE. The enzyme-enzyme complex of transaminase and glutamate dehydrogenase. *J Biol Chem*. 1974;249(9):2696-2703.
L-glucuronate reductase inhibitor	0.88	0.003	Hepato-protective, Antioxidant (Xenobiotic metabolism), pentosuria, Kidney protective, Anti-cancerous	Carole L. Linster and Emile Van Schaftingen. Glucuronate, the precursor of vitamin C, is directly formed from UDP-glucuronate in the liver. FEBS Journal 273 (2006) 1516–1527. doi:10.1111/j.1742-4658.2006.05172.x
Chlordecone reductase inhibitor	0.882	0.007	Xenobiotic metabolism, Anticancer activity	Molowa DT, Shayne AG, Guzelian PS. Purification and characterization of chlordecone reductase from human liver. J Biol Chem. 1986 Sep 25;261(27):12624-7.
CDP-glycerol glycerophosphotransferase inhibitor	0.879	0.014	Antibacterial (especially Bacillus subtilis)	Pooley, H. M., Abellan, F. X., &Karamata, D. (1992). CDP-glycerol: poly(glycerophosphate) glycerophosphotransferase, which is involved in the synthesis of the major wall teichoic acid in Bacillus subtilis 168, is encoded by tagF (rodC). *Journal of Bacteriology*, *174*(2), 646–649. https://doi.org/10.1128/jb.174.2.646-649.1992
Dehydro-L-gluconate decarboxylase inhibitor	0.869	0.004	Antimicrobial, Anti-cancerous and Anti-Oxidants (xenobiotic metabolism)	Kuivanen J, Sugai-Guérios MH, Arvas M, Richard P. A novel pathway for fungal D-glucuronate catabolism contains an L-idonate forming 2-keto-L-gulonate reductase. Sci Rep. 2016 May 18;6:26329. Doi: 10.1038/srep26329. PMID: 27189775; PMCID: PMC4870679.
UGT1A6 substrate	0.863	0.004	Antioxidant, Hepato-protective	N. Hanioka, S. Ozawa, H. Jinno, M. Ando, Y. Saito & J. Sawada (2001) Human liver UDP-glucuronosyltransferase isoforms involved in the glucuronidation of 7-ethyl-10-hydroxy camptothecin, Xenobiotica, 31:10, 687-699, DOI: 10.1080/00498250110057341
Aryl-alcohol dehydrogenase inhibitor	0.86	0.002	Xenobiotic detoxification, Anti Cancerous and production of natural flavours.	Ken, C. F., Chang, C. C., Wen, L., Huang, J. K., & Lin, C. T. (2014). Biochemical characterization of a functional recombinant aryl-alcohol dehydrogenase from Taiwanofunguscamphorata. *Botanical studies*, *55*(1), 14. https://doi.org/10.1186/1999-3110-55-14
Membrane integrity agonist	0.875	0.017	Anticancer therapy, Antimicrobial	Ammendolia, D.A., Bement, W.M. &Brumell, J.H. Plasma membrane integrity: implications for health and disease. *BMC Biol* **19,** 71 (2021). https://doi.org/10.1186/s12915-021-00972-y
Nitrilase inhibitor	0.859	0.002	Defence, detoxification, cyanide detoxification, nitrogen utilization,	Howden AJ, Preston GM (July 2009). "Nitrilase enzymes and their role in plant-microbe interactions". *Microbial Biotechnology*. **2** (4): 441–51. doi:10.1111/j.1751-7915.2009.00111.x.

			and plant hormone synthesis	
Ubiquinol-cytochrome-c reductase inhibitor	0.867	0.012	Anti-toxicity, Age regulation and Anti-Cancerous	Casey L. Quinlan, Jason R. Treberg, Martin D. Brand, Chapter 3 - Mechanisms of Mitochondrial Free Radical Production and their Relationship to the Aging Process, Editor(s): Edward J. Masoro, Steven N. Austad, In Handbooks of Aging, Handbook of the Biology of Aging (Seventh Edition), Academic Press, 2011, Pages 47-61, ISBN 9780123786388,
CYP2C12 substrate	0.873	0.018	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-toxicity and Anti cancerous Antioxidants	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C* *Curr Drug Metab. 2006 Dec; 7(8):939-48.*
Alkane 1-monooxygenase inhibitor	0.853	0.004	Antibacterial	Nie, Y., Chi, CQ., Fang, H. *et al.* Diverse alkane hydroxylase genes in microorganisms and environments. *Sci Rep* **4,** 4968 (2014). https://doi.org/10.1038/srep04968
Glutathione thioesterase inhibitor	0.852	0.004	Immune Modulator, Anti-inflammatory, histamine release factor, Anti-cancerous (leukocytes)	Kousaku Murata, Nobuyuki Sato, Hae-ik Rhee, Kunihiko Watanabe & Akira Kimura (1987) Purification and Characterization of Glutathione Thiol Esterase from Saccharomycescerevisiae, Agricultural and Biological Chemistry, 51:7, 1901-1907, DOI: 10.1080/00021369.1987.10868321
GABA aminotransferase inhibitor	0.845	0.003	Anticonvulsants, antiepileptic, antiseizure,	Ciesielski, L.; Simler, S.; Gensburger, C.; Mandel, P.; Taillandier, G.; Benoit-Guyod, J. L.; Boucherle, A.; Cohen-Addad, C.; Lajzerowicz, J. (1979). "GABA transaminase inhibitors". *Advances in Experimental Medicine and Biology*. **123**: 21–41. Doi:10.1007/978-1-4899-5199-1_2. ISBN 978-1-4899-5201-1.
Acylphosphatase inhibitor	0.844	0.002	Calcium metabolism, Anticancer activity	Interaction between acylphosphatase and SERCA in SH-SY5Y cells Cecchi, C.; Liguri, G.; Pieri, A.; Degl' Innocenti, D.; Nediani, C.; Fiorillo, C.; Nassi, P.; Ramponi, G. Molecular and Cellular Biochemistry 211(1-2): 95-102 2000 https://eurekamag.com/research/010/860/010860720.php
G-protein-coupled receptor kinase inhibitor	0.848	0.008	Autoimmune inflammation,	Homan, K. T., & Tesmer, J. J. (2015). Molecular basis for small molecule inhibition of G protein-

			Schizophrenia/bipolar disorder and asthma	coupled receptor kinases. *ACS Chemical Biology*, *10*(1), 246–256. https://doi.org/10.1021/cb5003976
Beta-adrenergic receptor kinase inhibitor	0.848	0.008	Alzheimer's disease, multiple sclerosis, Parkinson's disease and cardiac disorders	Cannavo A, Liccardo D and Koch WJ (2013) Targeting cardiac β-adrenergic signalling via GRK2 inhibition for heart failure therapy. *Front. Physiol.* **4**:264. doi: 10.3389/fphys.2013.00264
Arylacetonitrilase inhibitor	0.845	0.007	Mmandelic acid synthesis	Bhatia SK, Mehta PK, Bhatia RK, Bhalla TC. Optimization of arylacetonitrilase production from Alcaligenes sp. MTCC 10675 and its application in mandelic acid synthesis. Appl Microbiol Biotechnol. 2014 Jan;98(1):83-94. Doi: 10.1007/s00253-013-5288-9. Epub 2013 October 9. PMID: 24104468.
Aldehyde dehydrogenase two substrate	0.837	0.001	Sjögren-Larsson syndrome, Type 2 hyperprolinemia, pyridoxine-dependent seizures, hyperammonemia, γ-hydroxybutyric aciduria, and alcoholic liver disease	Non-P450 aldehyde oxidizing enzymes: the aldehyde dehydrogenase superfamily. *Marchetti SA, Brocker C, Stagos D, Vasiliou V Expert Opin Drug Metab Toxicol. 2008 Jun; 4(6):697-720.*
Testosterone 17beta-dehydrogenase (NADP+) inhibitor	0.85	0.014	Sex Hormones Regulation. Helps in Menopause and Puberty	Boulpaep EL, Boron WF (2005). *Medical Physiology: A Cellular and Molecular Approach* (Updated ed.). Philadelphia, Pa.: Elsevier Saunders. p. 1155. ISBN 978-1-4160-2328-9.
JAK2 expression inhibitor	0.839	0.005	Anticancer activity	Sayyah J, Sayeski PP. Jak2 inhibitors: rationale and role as therapeutic agents in hematologic malignancies. CurrOncol Rep. 2009 Mar;11(2):117-24. Doi: 10.1007/s11912-009-0018-2. PMID: 19216843; PMCID: PMC2805456.
4-Hydroxybenzoate 3-monooxygenase inhibitor	0.829	0.001	Xenobiotic degradation, Environmental bioremediation	Entsch B, Ballou DP, Begley TP (2007-01-01). Wiley Encyclopedia of Chemical Biology. John Wiley & Sons, Inc. doi:10.1002/9780470048672.wecb672. ISBN 9780470048672.
Phenol 2-monooxygenase inhibitor	0.822	0.002	Environmental bioremediation	NAKAGAWA H, TAKEDA Y (1962). "Phenol hydroxylase". Biochim. Biophys. Acta. 62 (2): 423–6. doi:10.1016/0006-3002(62)90275-5
CYP2A substrate	0.824	0.005	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-toxicity and Anti cancerous	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C Curr Drug Metab. 2006 Dec; 7(8):939-48.*
Vomilenine	0.82	0.001	Blood pressure,	Xia, Liqun& Lin, Haili&Staniek, Agata&Panjikar,

glucosyltransferase inhibitor			diabetics	Santosh &Ruppert, Martin &Hilgers, Petra &Williardt, Jörg&Rajendran, Chitra& Wang, Meitian&Warzecha, Heribert&Jäger, Volker &Stöckigt, Joachim. (2014). Ligand structures of synthetic deoxa-pyranosylamines with raucaffricine and strictosidine glucosidases provide structural insights into their binding and inhibitory behaviours. Journal of enzyme inhibition and medicinal chemistry. 30. 1-7. 10.3109/14756366.2014.949252.
Uroporphyrinogen-III synthase inhibitor	0.821	0.003	Porphyria	A porphomethene inhibitor of uroporphyrinogen decarboxylase causes porphyria cutaneatarda John D. Phillips, Hector A. Bergonia, Christopher A. Reilly, Michael R. Franklin, James P. Kushner Proceedings of the National Academy of Sciences Mar 2007, 104 (12) 5079-5084; DOI: 10.1073/pnas.0700547104
Glucose oxidase inhibitor	0.827	0.009	Biosensor of Glucose, Diabetes	SATOSHI NAKAMURA, YASUYUKI OGURA, Mode of Inhibition of Glucose Oxidase by Metal Ions, The Journal of Biochemistry, Volume 64, Issue 4, October 1968, Pages 439–447, https://doi.org/10.1093/oxfordjournals.jbchem.a128915
CYP2E1 substrate	0.821	0.005	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-toxicity and Anti cancerous	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C* *Curr Drug Metab. 2006 Dec; 7(8):939-48.*
CYP2E substrate	0.82	0.005	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-toxicity and Anti cancerous	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C* *Curr Drug Metab. 2006 Dec; 7(8):939-48.*
Threonine aldolase inhibitor	0.817	0.004	Protein synthesis	Remesh SG, Ghatge MS, Ahmed MH, Musayev FN, Gandhi A, Chowdhury N, di Salvo ML, Kellogg GE, Contestabile R, Schirch V, Safo MK. Molecular basis of E. coli L-threonine aldolase catalytic inactivation at low pH.Biochim Biophys Acta. 2015 Apr;1854(4):278-83. doi: 10.1016/j.bbapap.2014.12.023. Epub 2015 January 2. PMID: 25560296; PMCID: PMC4323617.

CYP2A6 substrate	0.816	0.005	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-toxicity and Anti cancerous	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C* *Curr Drug Metab. 2006 Dec; 7(8):939-48.*
UGT1A9 substrate	0.814	0.004	Colorectal cancer, metastatic gastrointestinal stromal tumours, and hepatocellular carcinoma, antipyretic, analgesic, anti-inflammatory and anti-diabetic	UGT1A9 Substrates (no date) Drugbank.com. Available at: https://go.drugbank.com/categories/DBCAT003966 (Accessed: July 15, 2022).
Methylenetetrahydrofolate reductase (NADPH) inhibitor	0.825	0.015	Mental and emotional stability	MTHFR gene (October 1, 2019) Medlineplus.gov. Available at: https://medlineplus.gov/genetics/gene/mthfr/ (Accessed: July 15, 2022).
MMP9 expression inhibitor	0.812	0.003	anti-metastatic therapy, angiogenesis (Tumor)	Webb, A.H., Gao, B.T., Goldsmith, Z.K. *et al.* Inhibition of MMP-2 and MMP-9 decreases cellular migration and angiogenesis in vitro models of retinoblastoma. *BMC Cancer* **17,** 434 (2017). https://doi.org/10.1186/s12885-017-3418-y
Aryl-acrylamide inhibitor	0.812	0.004	Nervous response	George ST, Balasubramanian AS. The aryl acylamidases and their relationship to cholinesterases in human serum, erythrocyte and liver. Eur J Biochem. 1981 Dec;121(1):177-86. doi: 10.1111/j.1432-1033.1981.tb06447.x. PMID: 7035166.
Orcinol 2-monooxygenase inhibitor	0.806	0.001	Oxidoreductase	Otha Y, Ribbons DW (1970). "Crystallization of orcinol hydroxylase from Pseudomonas putida". FEBS Lett. 11 (3): 189–192. doi:10.1016/0014-5793(70)80525-7
Sugar-phosphatase inhibitor	0.816	0.014	Type 2 Diabetes Treatment	Niels Westergaard& Peter Madsen (2001) Glucose-6-phosphatase inhibitors for the treatment of Type 2 diabetes, Expert Opinion on Therapeutic Patents, 11:9, 1429-1441, DOI: 10.1517/13543776.11.9.1429
Aldehyde dehydrogenase one substrate	0.802	0	Sjögren-Larsson syndrome, Type 2 hyperprolinemia, pyridoxine-dependent seizures, hyperammonemia, γ-hydroxybutyric aciduria, and alcoholic liver disease	Non-P450 aldehyde oxidizing enzymes: the aldehyde dehydrogenase superfamily. *Marchetti SA, Brocker C, Stagos D, Vasiliou V Expert Opin Drug Metab Toxicol. 2008 Jun; 4(6):697-720.*

2-Hydroxyquinoline 8-monooxygenase inhibitor	0.805	0.005	Coumarine Pathway, Treatment of prostate cancer, renal cell carcinoma and leukaemia	KüpeliAkkol E, Genç Y, Karpuz B, Sobarzo-Sánchez E, Capasso R. Coumarins and Coumarin-Related Compounds in Pharmacotherapy of Cancer. Cancers (Basel). 2020 Jul 19;12(7):1959. doi: 10.3390/cancers12071959. Torres Pazmiño DE, Winkler M, Glieder A, Fraaije MW. Monooxygenases as biocatalysts: Classification, mechanistic aspects and biotechnological applications. J Biotechnol. 2010 Mar;146(1-2):9-24. doi: 10.1016/j.jbiotec.2010.01.021. Epub 2010 February 2. PMID: 20132846.
Alcohol dehydrogenase (NADP+) inhibitor	0.801	0.003	Peptic Ulcer and gastrointestinal infections, Antibacterial (Helicobacter pylori)	Alka K, Windle HJ, Cornally D, Ryan BJ, Henehan GT. A short chain NAD(H)-dependent alcohol dehydrogenase (HpSCADH) from Helicobacter pylori: a role in growth under neutral and acidic conditions. Int J Biochem Cell Biol. 2013 Jul;45(7):1347-55. doi: 10.1016/j.biocel.2013.04.006
Succinate-semialdehyde dehydrogenase [NAD(P)+] inhibitor	0.798	0.002	Neural disorders and liver disorders	Bernocchi G, Barni S. Methodological problems in the histochemical demonstration of succinate semialdehyde dehydrogenase activity. Histochem J. 1983 Dec;15(12):1161-76. doi: 10.1007/BF01002737. PMID: 6643116.
Bisphosphoglycerate phosphatase inhibitor	0.802	0.006	Anaemia, Congenital heart disease	Mulquiney, P. J., Bubb, W. A., &Kuchel, P. W. (1999). Model of 2,3-bisphosphoglycerate metabolism in the human erythrocyte based on detailed enzyme kinetic equations: in vivo kinetic characterization of 2,3-bisphosphoglycerate synthase/phosphatase using 13C and 31P NMR. *The Biochemical Journal*, *342 Pt 3*(Pt 3), 567–580.
NADPH-cytochrome-c2 reductase inhibitor	0.8	0.006	Anti- Cancerous (Preventing the cancerous cells not to respire by retarding Respiratory electron transport), Iron metabolism regulator	Sabo DJ, Orlando JA (1968). "Isolation, purification, and some properties of reduced nicotinamide adenine dinucleotide phosphate-cytochrome C2 reductase from Rhodopseudomonasspheroides". *J. Biol. Chem*. **243** (13): 3742–9. PMID 4385431.
NADPH peroxidase inhibitor	0.804	0.012	Anti-oxidation	Sirokmány G, Geiszt M. The Relationship of NADPH Oxidases and Heme Peroxidases: Fallin' in and Out. Front Immunol. 2019 March 5;10:394. doi: 10.3389/fimmu.2019.00394.
Phosphatase inhibitor	0.795	0.003	Antifungal, Anti-toxic, antibiotic, antagonistic to hepatic tumours, tumorigenesis in tissues like skin and gut	Shenolikar, S. (1995). *Protein phosphatase regulation by endogenous inhibitors. Seminars in Cancer Biology, 6(4), 219–227.*
Glucan endo-1,6-beta-glucosidase inhibitor	0.798	0.008	Anti-diabetic	National Center for Biotechnology Information (2022). PubChem Enzyme Summary for Enzyme 3.2.1.75, Glucan endo-1,6-beta-glucosidase (EC 3.2.1.75). Retrieved July 22, 2022 from

				https://pubchem.ncbi.nlm.nih.gov/protein/EC:3.2.1.75.
Linoleate diol synthase inhibitor	0.793	0.006	Oxidoreductase	Brodowsky ID, Hamberg M, Oliw EH (1992). "A linoleic acid (8R)-dioxygenase and hydroperoxide isomerase of the fungus Gaeumannomyces graminis. Biosynthesis of (8R)-hydroxylinoleic acid and (7S,8S)-dihydroxylinoleic acid from (8R)-hydroperoxylinoleic acid". J. Biol. Chem. 267 (21): 14738–45.
CYP2B6 substrate	0.793	0.008	Xenobiotic clearance, Hepatoprotective and Anti-cancerous	Hedrich WD, Hassan HE, Wang H. Insights into CYP2B6-mediated drug-drug interactions. Acta Pharm Sin B. 2016 Sep;6(5):413-425. doi: 10.1016/j.apsb.2016.07.016. Epub 2016 August 9. PMID: 27709010; PMCID: PMC5045548.
Antiseborrheic	0.802	0.019		
Aminomuconate-semialdehyde dehydrogenase inhibitor	0.783	0.002	Depression and Neurodegenerative disease states such as Alzheimer's, Parkinson's, and Huntington's diseases.	Yang Y, Davis I, Ha U, Wang Y, Shin I, Liu A. A Pitcher-and-Catcher Mechanism Drives Endogenous Substrate Isomerization by a Dehydrogenase in Kynurenine Metabolism. J Biol Chem. 2016 Dec 16;291(51):26252-26261. doi: 10.1074/jbc.M116.759712.
CYP2J substrate	0.8	0.021	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-toxicity and Anti cancerous	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C* *Curr Drug Metab. 2006 Dec; 7(8):939-48.*
Trans-acenaphthene-1,2-diol dehydrogenase inhibitor	0.784	0.005	Oxidoreductase	Hopkins RP, Drummond EC, Callaghan P (1973). "Dehydrogenation of trans-acenaphthene-1,2-diol by liver cytosol preparations". Biochem. Soc. Trans. 1: 989–991.
Ribulose-phosphate 3-epimerase inhibitor	0.786	0.009	Regulation of carbon fixation in plants	Akana J, Fedorov AA, Fedorov E, Novak WR, Babbitt PC, Almo SC, Gerlt JA (Feb 2006). "D-Ribulose 5-phosphate 3-epimerase: functional and structural relationships to members of the ribulose-phosphate binding (beta/alpha)8-barrel superfamily". Biochemistry. 45 (8): 2493–503. doi:10.1021/bi052474m. PMID 16489742.
Alkenylglycerophosphocholine hydrolase inhibitor	0.795	0.018	Platelet-activating factor; Cardiovascular, renal, neuronal, pulmonary, immunological disorders and in shock	Heterogeneous platelet-activating factor (PAF) receptors and calcium increase in platelets and macrophages. *Centemeri C, Colli S, Tosarello D, Ciceri P, Nicosia S* *BiochemPharmacol. 1999 Feb 1; 57(3):263-71.*
Glutamyl endopeptidase II inhibitor	0.783	0.012	Anti-inflammatory, immune booster, Antibacterial and Anti-sepsis	Dubin G (2002-07-01). "Extracellular proteases of Staphylococcus spp". *Biological Chemistry*. **383** (7–8): 1075–86. doi:10.1515/BC.2002.116.
Monophenol	0.773	0.003	Skin protective	Lee SH, Baek K, Lee JE, Kim BG. I am using

monooxygenase inhibitor				tyrosinase as a monophenol monooxygenase: A combined strategy for effective inhibition of melanin formation. Biotechnol Bioeng. 2016 Apr;113(4):735-43. doi: 10.1002/bit.25855.
Alcohol dehydrogenase substrate	0.771	0.002	Hepatoprotective, Anti-cancerous	Kesheng Wang, Liang Wang, Chapter 20 - Genes Associated with Alcohol Withdrawal, Editor(s): Vinood B. Patel, Molecular Aspects of Alcohol and Nutrition, Academic Press, 2016, Pages 247-259, ISBN 9780128007730, https://doi.org/10.1016/B978-0-12-800773-0.00020-3.
Succinate-semialdehyde dehydrogenase inhibitor	0.771	0.002	Anti-tumor	Rustin, P., Munnich, A. & Rötig, A. Succinate dehydrogenase and human diseases: new insights into a well-known enzyme. Eur J Hum Genet 10, 289–291 (2002). https://doi.org/10.1038/sj.ejhg.5200793
Phosphomevalonate kinase inhibitor	0.768	0.001	Sterol biosynthesis	Heidrun Karlic, Franz Varga, Mevalonate Pathway, Editor(s): Paolo Boffetta, Pierre Hainaut, Encyclopedia of Cancer (Third Edition), Academic Press, 2019, Pages 445-457, ISBN 9780128124857, https://doi.org/10.1016/B978-0-12-801238-3.65000-6.
Aspartyl aminopeptidase inhibitor	0.77	0.003	Anti- Malarial	Sherwin Wilk, Chapter 353 - Aspartyl Aminopeptidase, Editor(s): Neil D. Rawlings, Guy Salvesen, Handbook of Proteolytic Enzymes (Third Edition), Academic Press, 2013, Pages 1570-1573, ISBN 9780123822192, https://doi.org/10.1016/B978-0-12-382219-2.00354-9.
CYP2C substrate	0.777	0.011	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-toxicity and Anti cancerous	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C* *Curr Drug Metab. 2006 Dec; 7(8):939-48.*
Fatty-acyl-CoA synthase inhibitor	0.771	0.006	Fatty acid biosynthesis	Gipson P, Mills DJ, Wouts R, Grininger M, Vonck J, Kühlbrandt W (May 2010). "Direct structural insight into the substrate-shuttling mechanism of yeast fatty acid synthase by electron cryomicroscopy". Proc. Natl. Acad. Sci. U.S.A. 107 (20): 9164–9. Bibcode:2010PNAS..107.9164G. doi:10.1073/pnas.0913547107
Ferredoxin-nitrite reductase inhibitor	0.761	0.002	Nitrogen assimilation	Hanke, G. T.; Kimata-Ariga, Y.; Taniguchi, I.; Hase, T. (2004). "A Post Genomic Characterization of Arabidopsis Ferredoxins". Plant Physiology. 134 (1): 255–264. doi:10.1104/pp.103.032755
Arylsulfatase sulfotransferase inhibitor	0.766	0.009	Chronic inflammation, cancer metastasis, and HIV and herpes virus	Eli Chapman, Sheng Ding, Peter G. Schultz, and Chi-Huey Wong. A Potent and Highly Selective Sulfotransferase

				Inhibitor Journal of the American Chemical Society 2002 124 (49), 14524-14525 DOI: 10.1021/ja021086u
Cis-1,2-dihydro-1,2-dihydroxy naphthalene dehydrogenase inhibitor	0.76	0.004	Oxidoreductase	Jouanneau Y, Meyer C. Purification and characterization of an arene cis-dihydrodiol dehydrogenase endowed with broad substrate specificity toward polycyclic aromatic hydrocarbon dihydrodiols. Appl Environ Microbiol. 2006 Jul;72(7):4726-34. doi: 10.1128/AEM.00395-06.
UDP-N-acetylglucosamine 4-epimerase inhibitor	0.764	0.009	Cell adhesion to the extracellular matrix, chronic inflammation and cancer metastasis and the sperm-egg recognition	Katharine A Winans, Carolyn R Bertozzi, An Inhibitor of the Human UDP-GlcNAc 4-Epimerase Identified from a Uridine-Based Library: A Strategy to Inhibit O-linked Glycosylation, Chemistry & Biology, Volume 9, Issue 1,2002, Pages 113-129, ISSN 1074-5521, https://doi.org/10.1016/S1074-5521(02)00093-5.
Pyridoxamine-pyruvate transaminase inhibitor	0.754	0	Seborrhoea(dermatitis-like eruption), atrophic glossitis with ulceration, angular cheilitis, conjunctivitis, intertrigo, and neurologic symptoms of somnolence, confusion, and neuropathy	Wada H, Snell EE (January 1962). "Enzymatic transamination of pyridoxamine. II. Crystalline pyridoxamine-pyruvate transaminase". *The Journal of Biological Chemistry*. **237**: 133–7.
Nicotinic alpha6beta3beta4alpha 5 receptor antagonist	0.77	0.017	Muscle relaxant in anaesthesia	Rang, H. P. (2003). Pharmacology. Edinburgh: Churchill Livingstone. ISBN 0-443-07145-4. Page 149
Skin irritation, inactive	0.755	0.005		
Phosphatidylserine decarboxylase inhibitor	0.756	0.006	Cell cycle signalling, apoptosis	Voelker DR. Phosphatidylserine decarboxylase. Biochim Biophys Acta. 1997 Sep 4;1348(1-2):236-44. doi: 10.1016/s0005-2760(97)00101-x. PMID: 9370338.
Aminobutyraldehyde dehydrogenase inhibitor	0.751	0.004	Putrescine degradation pathway	Identification of Escherichia coli K12 YdcW protein as a gamma-aminobutyraldehyde dehydrogenase. Samsonova NN, Smirnov SV, Novikova AE, Ptitsyn LR. FEBS Lett. 579, 4107-12, (2005).
Corticosteroid side-chain-isomerase inhibitor	0.751	0.005	Ketol-aldol interconversion	Monder C, Marandici A. Corticosteroid side-chain isomerase in the circulatory system. Steroids. 1991 Jan;56(1):12-6. doi: 10.1016/0039-128x(91)90108-8. PMID: 2028477.
CYP1A1 substrate	0.75	0.006	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C* *Curr Drug Metab. 2006 Dec; 7(8):939-48.*

			cigarette smoke, Anti-toxicity and Anti cancerous	
3-Hydroxybenzoate 6-monooxygenase inhibitor	0.751	0.007	Antimicrobial	Sucharitakul J, Wongnate T, Montersino S, van Berkel WJ, Chaiyen P. Reduction kinetics of 3-hydroxybenzoate 6-hydroxylase from Rhodococcusjostii RHA1. Biochemistry. 2012 May;51(21):4309-4321. DOI: 10.1021/bi201823c.
CYP2B substrate	0.752	0.008	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-toxicity and Anti cancerous	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C* *Curr Drug Metab. 2006 Dec; 7(8):939-48.*
CYP2C8 substrate	0.751	0.008	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-toxicity and Anti cancerous	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C* *Curr Drug Metab. 2006 Dec; 7(8):939-48.*
Peroxidase inhibitor	0.747	0.008	Antimicrobial, anti-inflammatory, Cardiovascular disease (CVD) including coronary artery disease, congestive heart failure, arterial hypertension, pulmonary arterial hypertension, peripheral arterial disease, myocardial ischemia/reperfusion-related injury, stroke, cardiac arrhythmia and venous thrombosis	Ndrepepa G. Myeloperoxidase - A bridge linking inflammation and oxidative stress with cardiovascular disease. ClinChimActa. 2019 Jun;493:36-51. doi: 10.1016/j.cca.2019.02.022. Epub 2019 February 21. PMID: 30797769.
Taurine dehydrogenase inhibitor	0.758	0.02	Diseases of muscle, the central nervous system, and the cardiovascular system, mitochondrial disease, mitochondrial encephalopathy, lactic acidosis, stroke-like	Schaffer S, Kim HW. Effects and Mechanisms of Taurine as a Therapeutic Agent. BiomolTher (Seoul). 2018 May 1;26(3):225-241. doi: 10.4062/biomolther.2017.251.

			episodes (MELAS), diabetes, arthritis	
2,3-Dihydroxyindole 2,3-dioxygenase inhibitor	0.741	0.003	Insect repellent	Fujioka M, Wada H (1968). "The bacterial oxidation of indole". Biochim. Biophys. Acta. 158 (1): 70–8. doi:10.1016/0304-4165(68)90073-1
Glyoxylate oxidase inhibitor	0.737	0.003	Hyperoxaluria, Kidney stones,	Bourhis JM, Vignaud C, Pietrancosta N, Guéritte F, Guénard D, Lederer F, Lindqvist Y. Structure of human glycolate oxidase in complex with the inhibitor 4-carboxy-5-[(4-chlorophenyl)sulfanyl]-1,2,3-thiadiazole. ActaCrystallogr Sect F StructBiolCrystCommun. 2009 December 1;65(Pt 12):1246-53. doi: 10.1107/S1744309109041670. Epub 2009 November 27. PMID: 20054120; PMCID: PMC2802872.
CYP1A substrate	0.741	0.009	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-toxicity and Anti cancerous	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C* *Curr Drug Metab. 2006 Dec; 7(8):939-48.*
2-Dehydropantoate 2-reductase inhibitor	0.743	0.012	Biosynthesis of Vitamin B5 and fatty acid metabolism	King HL Jr, Dyar RE, Wilken DR (August 10, 1974). "Ketopantoyl lactone and ketopantoic acid reductases: Characterization of the reactions and purification of two forms of ketopantoyl lactone reductase". J. Biol. Chem. 249 (15): 4689–4695.
Phosphopantothenoylcysteine decarboxylase inhibitor	0.733	0.003	Biosynthesis of Vitamin B5 and fatty acid metabolism	Brown GM (1958). "Requirement of cytidine triphosphate for the biosynthesis of phosphopantetheine". J. Am. Chem. Soc. 80 (12): 3161. doi:10.1021/ja01545a062.
Acetylcholine neuromuscular blocking agent	0.732	0.004	Muscle relaxants are mainly used in muscle paralysis treatment	Caldwell JE. Clinical limitations of acetylcholinesterase antagonists. J Crit Care. 2009 Mar;24(1):21-8. doi: 10.1016/j.jcrc.2008.08.003. Epub 2009 January 17. PMID: 19272535.
Anesthetic general	0.733	0.005		
Malate dehydrogenase (acceptor) inhibitor	0.73	0.004	Liver and heart injury reducers are also a biomarker	Jean P. Dzoyem, Victor Kuete, Jacobus N. Eloff, 23 - Biochemical Parameters in Toxicological Studies in Africa: Significance, Principle of Methods, Data Interpretation, and Use in Plant Screenings, Editor(s): Victor Kuete, Toxicological Survey of African Medicinal Plants, Elsevier, 2014, Pages 659-715, ISBN 9780128000182, https://doi.org/10.1016/B978-0-12-800018-2.00023-6

5-O-(4-coumaroyl)-D-quinate 3'-monooxygenase inhibitor	0.741	0.015	Cytochrome Activator, Secondary Metabolite Synthesis, Anti toxicity and Anti- Cancerous	Kuhnl, T.; Koch, U.; Heller, W.; Wellmann, E.: Chlorogenic acid biosynthesis: Characterization of a light-induced microsomal 5-O-(4-coumaroyl)-D-quinate/shikimate 3'-hydroxylase from carrot (Daucuscarota L.) cell suspension cultures. Arch. Biochem. Biophys., 258, 226–232 (1987)
Steroid N-acetylglucosaminyltransferase inhibitor	0.729	0.004	Anticancer treatment	Huang, Xiaomin& Liu, Ting & Wang, Qiongyao& Zhu, Weiliang&Meng, Hui &Guo, Linlang& Wei, Ting & Zhang, Jian. (2017). Inhibition of N-acetylglucosaminyltransferase V enhances the cetuximab-induced radiosensitivity of nasopharyngeal carcinoma cells, likely through EGFR N-glycan alterations. Glycobiology. 27. 10.1093/glycol/cwx046.
Thioredoxin inhibitor	0.73	0.007	Anticancer and tumor	Zhang J, Xu Q, Yang H-Y, Yang M, Fang J and Gao K (2021) Inhibition of Thioredoxin Reductase by Santamarine Conferring Anticancer Effect in HeLa Cells. Front. Mol. Biosci. 8:710676. doi: 10.3389/fmolb.2021.710676
Sulfite reductase inhibitor	0.729	0.006	Anti-tobacco and anti-nicotine metabolism	Naumann M, Hubberten H-M, Watanabe M, Hänsch R, Schöttler MA and Hoefgen R (2018) Sulfite Reductase Co-suppression in Tobacco Reveals Detoxification Mechanisms and Downstream Responses Comparable to Sulfate Starvation. Front. Plant Sci. 9:1423. doi: 10.3389/fpls.2018.01423
3-Phytase inhibitor	0.727	0.005	Antifungal and Antibacterial	Vikas Kumar, Amit K. Sinha, Chapter 3 - General aspects of phytases, Editor(s): Carlos SimõesNunes, Vikas Kumar, Enzymes in Human and Animal Nutrition, Academic Press, 2018, Pages 53-72, ISBN 9780128054192, https://doi.org/10.1016/B978-0-12-805419-2.00003-4.
Respiratory analeptic	0.734	0.012	Depression, Attention Deficit Hyperactivity Disorder (ADHD), anti-convulsants, restlessness, and respiratory depression.	Young, Simon; Campbell, Ryan (January 2015). "Central nervous system stimulants: basic pharmacology and relevance to anaesthesia and critical care". *Anaesthesia & Intensive Care Medicine*. **16** (1): 21–25. doi:10.1016/j.mpaic.2014.10.005.
CYP1A2 substrate	0.725	0.008	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-toxicity and Anti cancerous	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C* *Curr Drug Metab. 2006 Dec; 7(8):939-48.*

Nicotinamidase inhibitor	0.72	0.003	In the treatment of Tuberculosis	Seiner DR, Hegde SS, Blanchard JS. Kinetics and inhibition of nicotinamidase from Mycobacterium tuberculosis. Biochemistry. 2010 Nov 9;49(44):9613-9. Doi: 10.1021/bi1011157. PMID: 20879713; PMCID: PMC3029496.
MAP kinase stimulant	0.717	0.005	Breast and prostate tumours and Lung cancers. Also, in Coffin-Lowry syndrome	Cargnello M, Roux PP. Activation and function of the MAPKs and their substrates, the MAPK-activated protein kinases. MicrobiolMolBiol Rev. 2011 Mar;75(1):50-83. doi: 10.1128/MMBR.00031-10. Erratum in: MicrobiolMolBiol Rev. 2012 Jun;76(2):496. PMID: 21372320; PMCID: PMC3063353.
Tyrosine-ester sulfotransferase inhibitor	0.712	0.002	leukocyte adhesion, hemostasis and chemokine signalling	John W Kehoe, Carolyn R Bertozzi, Tyrosine sulfation: a modulator of extracellular protein-protein interactions, Chemistry & Biology, Volume 7, Issue 3, 2000, Pages R57-R61, ISSN 1074-5521, https://doi.org/10.1016/S1074-5521(00)00093-4.
Gamma-guanidino butyraldehyde dehydrogenase inhibitor	0.715	0.007	Hepatoprotective and kidney-protective	Yorifuji T, Koike K, Sakurai T, Yokoyama K (1986). "4-Aminobutyraldehyde and 4-guanidinobutyraldehyde dehydrogenases for arginine degradation in Pseudomonas putida". Agric. Biol. Chem. 50 (8): 2009–2016. doi:10.1271/bbb1961.50.2009
Membrane permeability inhibitor	0.733	0.026	Cardioprotection, Myocardial ischemia-reperfusion injury inhibitor, Skin disorders treatment	Morin D, Assaly R, Paradis S, Berdeaux A. Inhibition of mitochondrial membrane permeability as a putative pharmacological target for cardioprotection. *Curr Med Chem*. 2009;16(33):4382-4398. doi:10.2174/092986709789712871
CYP2A3 substrate	0.707	0.003	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-toxicity and Anti cancerous	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C Curr Drug Metab. 2006 Dec; 7(8):939-48.*
Apoptosis agonist	0.718	0.013		
CYP2J2 substrate	0.727	0.027	Respiratory problems solver, detoxification and activation of environmental pollutants, including industrial chemicals, therapeutic agents, and chemicals in cigarette smoke, Anti-	Xenobiotic-metabolizing enzymes in human lung. *Zhang JY, Wang Y, Prakash C Curr Drug Metab. 2006 Dec; 7(8):939-48.*

			toxicity and Anti cancerous	
Mucomembranous protector	0.739	0.039	Anti-ulcer and oesophagal protective, antioxidant	Bijo Mathew, Jerad Suresh, S. Anbazhagan, N. Chidambaranathan, Discovery of some novel imines of 2-amino, 5-thio, 1,3,4-thiadiazole as mucomembranous protector. Synthesis, antioxidant activity and in silico PASS approach, Journal of Saudi Chemical Society, Volume 20, Supplement 1,2016, Pages S426-S432, ISSN 1319-6103, https://doi.org/10.1016/j.jscs.2013.01.002.
Aldehyde dehydrogenase three substrate	0.697	0	Sjögren-Larsson syndrome, Type 2 hyperprolinemia, pyridoxine-dependent seizures, hyperammonemia, γ-hydroxybutyric aciduria, and alcoholic liver disease	Non-P450 aldehyde oxidizing enzymes: the aldehyde dehydrogenase superfamily. *Marchetti SA, Brocker C, Stagos D, Vasiliou V Expert Opin Drug Metab Toxicol. 2008 Jun; 4(6):697-720.*
Chymosin inhibitor	0.731	0.036	Regulation of the coagulation of blood	Neal A. Bringe, J.E. Kinsella, Inhibition of Chymosin and the Coagulation of Para-Casein Micelles by Anions, Journal of Dairy Science, Volume 69, Issue 4, 1986, Pages 965-970, ISSN 0022-0302, https://doi.org/10.3168/jds.S0022-0302(86)80489-1.
Acrocylindropepsin inhibitor	0.731	0.036	Antifungal, Insulin regulation	Uchino F, Kurono Y, Doi S (1967). "Purification and some properties of crystalline acid protease from *Acrocylindrium* sp". *Agric. Biol. Chem*. **31**: 428–434. doi:10.1271/bbb1961.31.428.
Saccharopepsin inhibitor	0.731	0.036	Antifungal	Cronin NB, Badasso MO, J Tickle I, et al. X-ray structures of five renin inhibitors bound to saccharopepsin: exploration of active-site specificity. *J Mol Biol*. 2000;303(5):745-760. doi:10.1006/jmbi.2000.4181
Fusarinine-C ornithinesterase inhibitor	0.71	0.021	Electrostatic stabilizer, Alcohol level regulator	Petersen EI, Valinger G, Sölkner B, Stubenrauch G, Schwab H. A novel esterase from Burkholderia gladioli, which shows high deacetylation activity on cephalosporins, is related to beta-lactamases and DD-peptidases. Journal of Biotechnology. 2001 Jul;89(1):11-25. DOI: 10.1016/s0168-1656(01)00284-x.

***Pa** - Percentage of Activity; **Pi** - Percentage of inactivity