Known active compounds used in this article

As COX-2 active compounds, 12 inhibitors and 2 natural ligands were selected. The two natural ligands were arachidonic acid and prostaglandin H2. The 12 inhibitors were diclofenac, etodolac, suprofen, diflunisal, piroxicam, sulindac, indomethacin, ketoprofen, naproxen, nimesulide, rofecoxib, and 1-phenylsulfonamide-3-trifluoromethyl-5-parabromophenylpyrazole.

The names of the thermolysin inhibitors used in the present study are as follows, with the PDB code in parentheses representing the complex structure from which the compound originated: l-benzylsuccinate (1hyt), phenylalanine phosphinic acid - deamino-methyl-phenylalanine (1os0), (6-methyl-3,4-dihydro-2H-chromen-2-Yl) methylphosphonate (1pe5), 2-(4-methylphenoxy) ethylphosphonate - 3-methylbutan-1-amine (1pe7), 2-ethoxyethylphosphonate - 3-methylbutan-1-amine (1pe8), (2-sulfanyl-3-phenylpropanoyl)-Phe-Tyr (1qf0), [2(R,S)-2-sulfanylheptanoyl]-Phe-Ala (1qf1), [(2S)-2-sulfanyl-3-phenylpropanoyl]-Gly-(5-phenylproline) (1qf2), n-(1-(2(R, S)-carboxy-4-phenylbutyl) cyclopentylcarbonyl)- (S)-tryptophan (1thl), (R)-retrothiorphan (1z9g), (S)-thiorphan (1zdp), hydroxamic acid (4tln), phenylalanine phosphinic acid (4tmn), Honh-benzylmalonyl-L-alanylglycine-P-nitroanilide (5tln),

Cbz-Gly^{P}-Leu-Leu ($Zg^{P}Ll$) (5tmn), Cbz-Gly^{P}-(O)-Leu-Leu ($Zg^{P}(O)Ll$) (6tmn), $CH_2CO(N\text{-}OH)Leu\text{-}OCH_3$ (7tln), benzyloxycarbonyl-D-Ala (1kto), benzyloxycarbonyl-L-Ala (1kl6), benzyloxycarbonyl-D-Thr (1kro), benzyloxycarbonyl-L-Thr (1kj0), benzyloxycarbonyl-D-Asp (1ks7), benzyloxycarbonyl-L-Asp (1kkk), benzyloxycarbonyl-D-Glu (1kr6) and benzyloxycarbonyl-L-Glu (1kjp), aspartame, aspartic acid and phenyl alanine.

The names of the GST inhibitors used in the present study are as follows, with the PDB code in parentheses representing the complex structure from which the compound originated: Benzylcysteine - Phenylglycine (10gs), Glutathione - [2,3-Dichloro-4-(2-Methylene-1-Oxobutyl) Phenoxyacetic Acid (11gs), S-Nonyl-Cysteine (12gs), 1-(S-Glutathionyl)-2,4-Dinitrobenzene (18gs), Glutamyl Group - S-(4-Bromobenzyl)Cystine (1aqv), Glutamyl Group - S-(2,3,6-Trinitrophenyl)Cysteine (1aqx), S-Hexylglutathione (1pgt), Cibacron Blue (20gs), Chlorambucil (21gs), Ethacrynic Acid (2gss), (9r,10r)-9-(S-Glutathionyl)-10-Hydroxy-9,10 Dihydrophenanthrene (2pgt), 2-Amino-4- [1- (Carboxymethyl-Carbamoyl)-2-(9-Hydroxy-7 8-Dioxo- 7,8,9,10- Tetrahydro-Benzo [Def] Chrysen-10 Ylsulfanyl) -Ethylcarbamoyl]-Butyric Acid (3pgt).

The names or the SMILES of the HIV protease-1 inhibitors used in the present study are as follows, with the PDB code in parentheses representing the complex structure from which the compound originated:

C1(c2ccc(F)cc2)(SCCS1)CCCN3CCC(c4ccc(Cl)cc4)(O)CC3 (1aid),

c1(OCC2N(S(N(C(C(C2O)O)COc3ccccc3)Cc4ccccc4)(=O)=O)Cc5ccccc5)ccccc1 (1ajv),

C1(N(C(C(C(C(N1Cc2ccccc2)COc3ccccc3)O)O)COc4ccccc4)Cc5ccccc5)=O (1ajx),

[4r-(4alpha,5alpha,6beta,7beta)]-3,3'-[[Tetrahydro-5 6-Dihydroxy-2-Oxo-4,7-Bis(Phenylmethyl)-1h-1,3 Diazepine-1,3(2h)-Diyl] Bis(Methylene)]Bis[N-2 Thiazolylbenzamide (1bv7),

C(N(Cc1ncccc1)C)(=O)NC(C(=O)NC(C(C(C(NC(=O)C(C(C)C)NC(N(Cc2ncccc2)C)=O)Cc3ccccc3)(O)O)(F)F)Cc4ccccc4)C(C)C (1dif),

C(N1C(C(=O)NC(C)(C)C)CSC1)(=O)C(C(NC(=O)C(NC(=O)COc2[c]3[c](cncc3)ccc2)CSC)Cc4ccccc4)O (1hpx),

C(=O)(C(NC(=O)C(CC(C)C)N)CCC(=O)N)NC(C(=O)NC(C(=O)O)CO)CCC(=O)O (1hte),

C(=O)(C1C(SC(C(C(=O)NCc2ccccc2)NC(=O)Cc3ccccc3)N1)(C)C)NC(Cc4ccccc4)CO (1htf),

c12c(cccc1)NC(=N2)CNC(=O)CC(C(NC(=O)C3C(SC(C(C(=O)NCc4ccccc4)NC(=O)C

c5ccccc5)N3)(C)C)Cc6ccccc6)O (1htg), 2-Phosphoglycolic Acid (1hvi), C1(N(C(C(C(C(N1Cc2c[c]3[c](cc2)cccc3)Cc4ccccc4)O)O)Cc5ccccc5)Cc6c[c]7[c](cc6)cccc7)=O (1hvr), 2-Carbonylquinoline - Phenylalaninol Group -Decahydro-1-Methylisoquinoline-2-Carbonyl - Tertiary-Butylamino Group (1hxb), Ritonavir (1hxw), Naphthyloxyacetyl - Cyclohexyl Ala-Psi(Choh-Choh)-Val -2-Aminomethyl-Pyridine (1ivp), 2-Carbonylquinoline - Phenylalanylmethane -3-(Carboxyamide (2-Carboxyamide-2-Tertbutylethyl)) Penta (1jld), C1(N(C(C(C(C(N1Cc2ccc(cc2)CO)Cc3ccccc3)O)O)Cc4ccccc4)Cc5ccc(cc5)CO)=O (1mes), Tertiary-Butoxyformic Acid - Phenylalaninol Group - Dimethylamine -Phenylalaninol Group - Tertiary-Butoxyformic Acid (1odw), (5r,6r)-2,4-Bis-(4-Hydroxy-3-Methoxybenzyl)-1,5dibenzyl-3-Oxo-6-Hydroxy-1,2,4-Triazacycloheptane (1pro), C1(C(=C(C=C(O1)C(Cc2ccccc2)CC)O)C(c3cc(ccc3)NC(=O)CCNC(=O)OC(C)(C)C)C4CC4)=O (2upj), N,N-Bis- (2(R)-Hydroxy-1 (S)-Indanyl-2,6- (R,R) -Diphenylmethyl-4-Hydroxy-1,7-Heptandiamide (4hpv).

The following compounds are the antagonists of the histamine H1 receptor: astemizole, cetirizine, chlorpheniramine, clemastine, cyprohrptadine, diphenhydramine, homochlorcyclizine, mequitazine, olopatadine, and promethazine.

The following compounds are the agonists of the adrenaline beta receptor: clenbuterol、dobutamine, epinephrine, fenoterol, isoprenaline, mabuterol, methylephedrine, norepinephrine, procatelol, salbutamol, terbutaline, and trimetoquinol.

The following compounds are the antagonists of the adrenaline beta receptor: alprenolol, arotinolol, atenolol, betaxolol, bisoprolol, bopindolol, carteolol, metoprolol, nadlol, pindolol, propranolol, tilisolol, and timolol.

The following compounds are the antagonists of the serotonin receptor: azasetron, (1-{2-[(methelsulfonyl)amino]ethyl}-4-piperidyl)methyl 1-methylindoline-3-carboxylate, granisetron, ketanserin, mesulergine, ondansetron, ramosetron, tropisetron, and cyclohexy-N-{2-[4-(2-methoxyphenyl)piperazinyl]ethyl}-N-(2-pyridyl)carboxamide.

The following compounds are the agonists of the dopamine D2 receptor: apomorphine, bromocriptine, denopamine, dobutamine, quinpirole, and 1-phenyl-1H,2H,3H,4H,5H-benzo[d]azepine-7,8-diol.

The following compounds are the antagonists of the dopamine D2 receptor: benperidol, chlorpromazine, clozapine, fluphenazine, haloperidol, metiapine, molindone, primozide, prochlorperazine, promazine, spiperone, sulpiride, thioproperazine, thioridazine, and trazodone.

g(ε) distribution

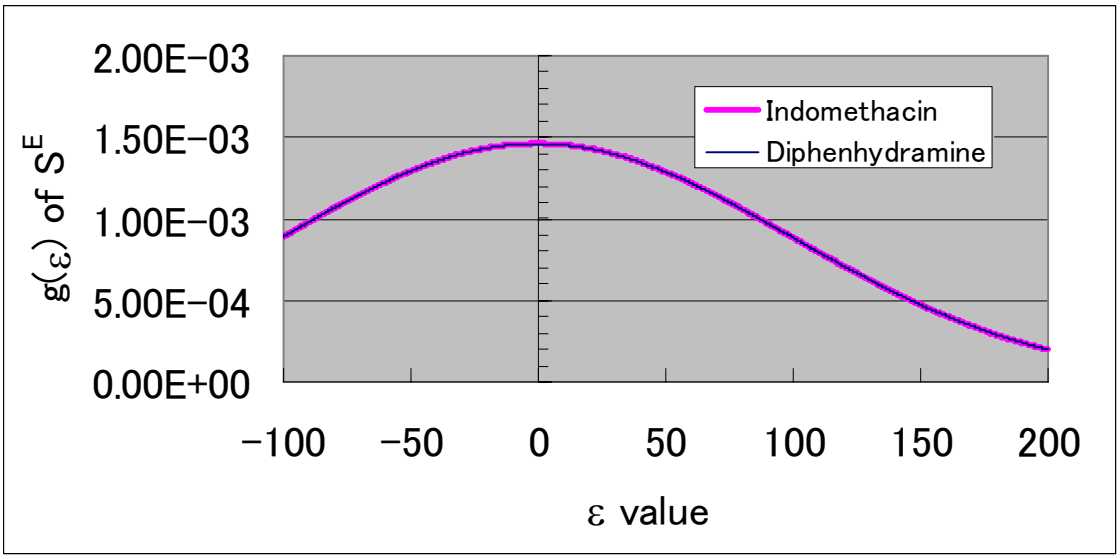


Figure 1 g(ε) distribution of matrix S^E with c=0.01

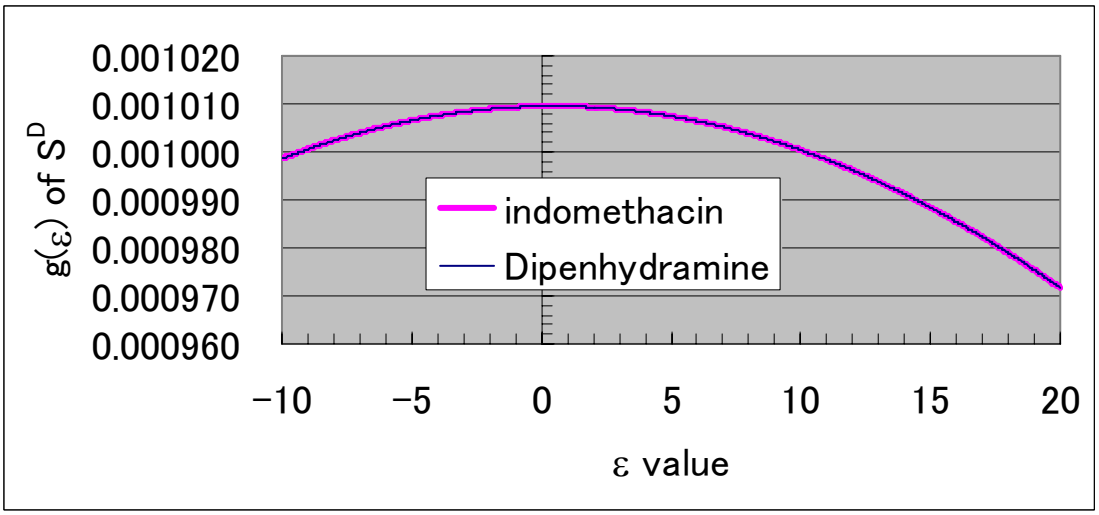
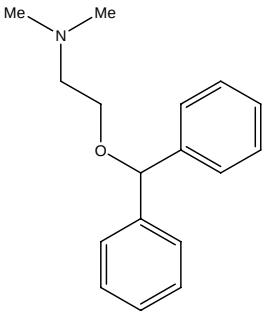
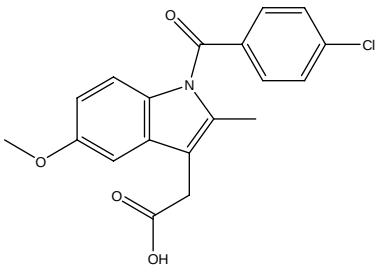


Figure 2 g(ε) distribution of matrix S^D with c=0.00005



Dipenhydramine



Indomethacin