## Supplementary Materials for:

# Repurposed drugs targeting eIF2α-P-mediated translational repression prevent neurodegeneration in mice

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**Supplementary data figures and tables**

Supplementary methods

Supplementary data figures 1-4 and legends

Supplementary data tables 1 (cropped and full) and 2 and legends

## Supplementary methods

### *C. elegans* maintenance

*C. elegans* (N2) were maintained under standard conditions, as outlined by Brenner(Brenner, 1974). Worms were grown on 6cm Petri dishes filled with nematode growth medium (NGM). 200µL of *E. coli* strain OP50 was used as a food source. Worms were transferred to fresh plates every 3-5 days. *C. elegans* was visualized using a dissecting stereomicroscope equipped with a transmitted light source (Leica model M165 FC) with standard 10X eyepieces and objectives which range from 0.6X to 5X (total magnification of 6X to 50X). N2 worms and bacterial strain OP50 were obtained from the *C. elegans* genetics center (CGC) http://cbs.umn.edu/cgc/home.

### *C. elegans* egg extraction

Worms were washed off NGM plates with sterile $H_20$ three days after the last transfer to gather large numbers of gravid hermaphrodites. The collected worms were centrifuged for 1 minute at 1300rpm to pellet them, and the supernatant aspirated. The pellet was re-suspended in a solution of 1ml 5% sodium hypochlorite, 0.5ml 5M sodium hydroxide and water up to 5ml. The sodium hypochlorite solution was vortex/shaken until the worms had dissolved (approximately 5-10 minutes), leaving behind the eggs. As above, the eggs were centrifuged at 1300rpm for 1 minute to collect them, and the supernatant aspirated again. The eggs were washed with 5ml water and re-centrifuged 3-5 times. 1-2µl of eggs were pipetted onto a glass slide and counted to calculate a concentration of eggs. Approximately 100 eggs were pipetted onto each test plate.

### Inducing unfolded proteins in *C. elegans* with tunicamycin

*C. elegans* develop through 4 larval stages (L1-L4) before reaching adulthood (Supplementary Fig. 1A). Tunicamycin is a UPR stressor that induces the formation of unfolded proteins. When administered to *C. elegans*, which have orthologues of the main mammalian UPR, it causes a developmental delay that stalls development at the L3 larval stage in approximately 60% of animals (Richardson *et al.*, 2011). Tunicamycin was added to NGM plates before pouring, at a final concentration of

2μg/ml. Approximately 100 eggs prepared from a *C. elegans* egg extraction were pipetted onto each plate, and allowed to develop for 3 days (the normal generational time of *C. elegans*).

After three days the proportion of worms reaching:

- L4 stage of development or older (i.e. unaffected by tunicamycin)
- L1-L3 stage of development (i.e. developmentally delayed)
- Dead (i.e. killed by the tunicamycin stress)

was counted. This gave a baseline measure of the developmental delay phenotype after tunicamycin treatment in *C. elegans.*

*Screen for possible UPR inhibitors in NINDS custom collection 2 library*

The 1040 compounds of the NINDS custom collection 2 library were screened in *C. elegans* (Supplementary table 1). Approximately 100 eggs extracted as above were placed onto each test plate. Each plate contained 2μg/ml tunicamycin, 20 μM of the drug being tested and a final concentration of 1% dimethyl sulfoxide (DMSO). Control plates contained 2 μg/ml tunicamycin and 1% DMSO, and were included in parallel with drug treated plates during every test session. Each drug was tested in duplicate.

**'UPR inhibition' rating**

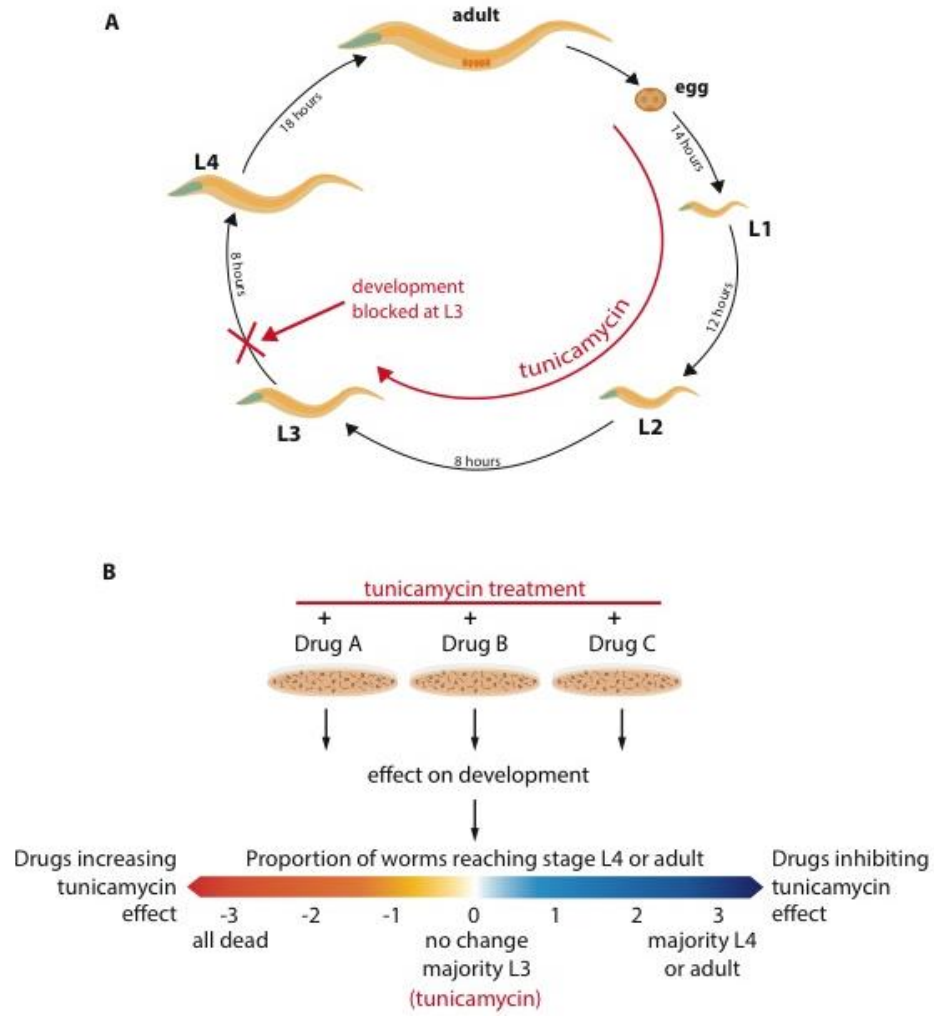
The eggs were allowed to grow for 3 days, after which the plate was scored for -3 and +3 as a rating of "UPR inhibition". A positive score indicated an improvement in the developmental phenotype, a negative score indicated a worsening of the developmental phenotype (with -3 being a plate of dead worms), and a score of 0 indicated there was no change after drug treatment compared to tunicamycin-only treatment (Supplementary Fig. 1B). Any plate that scored +2 or +3 was then counted as for controls: the proportion of worms reaching the following stages were counted for comparison to control and calculation of fold-change in proportion of worms overcoming developmental delay at L3.

- L4 stage of development or older
- L1-L3 stage of development
- Dead

As the number of worms reaching L4 or adulthood varied by approximately 10% on test days, drug-treated plates were compared to controls performed on the same day, with the data expressed as the fold change in the proportion of worms reaching L4 or adulthood (Supplementary Table 1). (Plates with scores between -3 and 1 counted periodically to confirm scoring was accurate). **A hit was defined as a drug that caused a 3-fold or greater increase in the proportion of worms reaching L4 or adulthood**. The 20 hits are recorded in Supplementary table 1_cropped. The data for all compounds are recorded in Supplementary table 1_full.

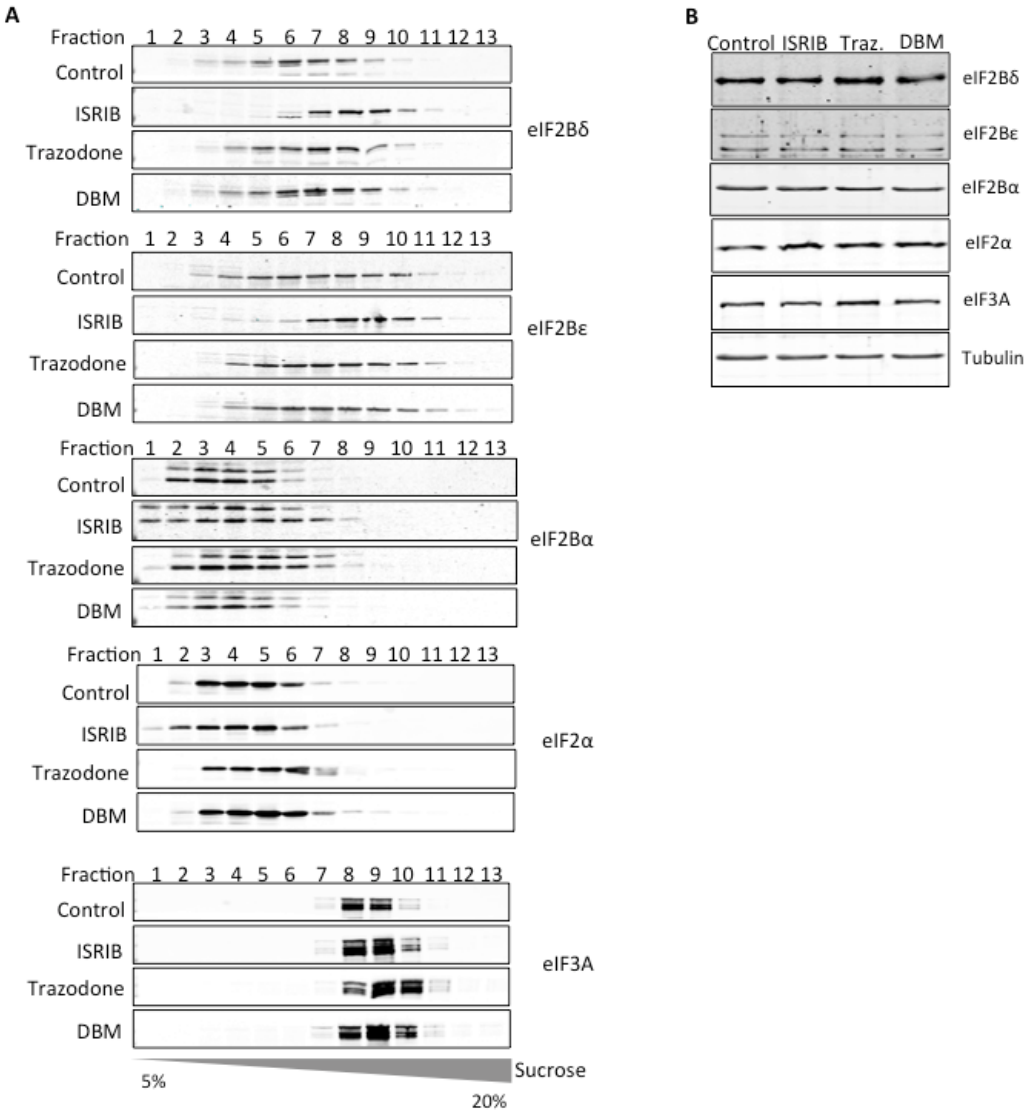
**Sucrose gradient separation of eIF2B subunits**

$3x10^6$ HeLa cells were seeded per treatment. 24h later cells were treated with either DMSO, 1μM ISRIB, 20μM trazodone or 20μM DBM for 1 hour. Cells washed twice with ice-cold PBS, and scraped into ice-cold lysis buffer (50 mM Tris pH 7.5, 400 mM KCl, 4 mM Mg(OAc)2, 0.5% Triton X-100 and EDTA-free protease inhibitor tablets, Roche). The lysates were passed through a 25g needle 10x and clarified at 17,000×g for 20 min at 4°C and the supernatant was then subjected to a high-speed spin at 100,000×g (rcf) (48000rpm) in a TLA120.2 rotor for 30 min at 4°C to pellet the ribosomes. 800ul of the supernatants were then loaded on a 5–20% sucrose gradient and centrifuged in a SW40 rotor for 14 hr at 33,100 rpm 4°C. Gradients run at 0.8ml/min and 13 x 0.8ml fractions were collected per gradient. Protein from fractions was methanol precipitated by adding 9 volumes of methanol to 1 volume of protein, vortexing and precipitation for 2h at -80C. Samples centrifuged at 4400rpm for 1h. Pellets air dried and resuspended in SDS-PAGE loading buffer. Western blotting were performed for inputs and gradient fractions.

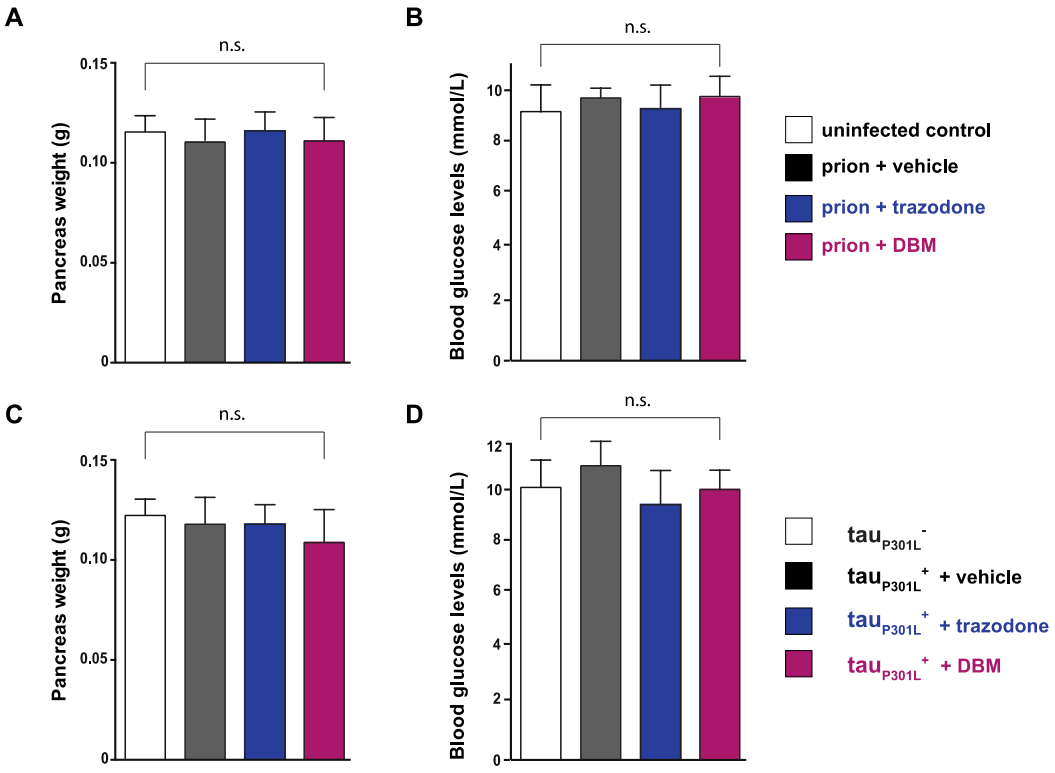



**Supplementary Fig. 1. Primary screen of NINDS library drugs effects on tunicamycin-induced developmental delay phenotype in *C. elegans.*** (**A**) Schematic showing life cycle of *C. elegans*, which consists of four developmental larval stages (L1-L4) before the adulthood is reached, ~ 3 days after eggs hatch. The UPR stressor tunicamycin induces developmental delay and arrest at L3 stage (2). (The nematodes have orthologues of the major components of the mammalian UPR). L1-L3 worms are much smaller than adult (and even L4 larvae) and are easily distinguished by eye. (**B**) Eggs were plated on individual plates with growth medium containing tunicamycin (2μg/ml) and each of the 1040 compounds from the NINDS custom collection 2 library at 20 M concentration. The proportion of adult versus larval worms for each drug was initially scored semi-quantitatively, as a rating of 'UPR inhibition'. Where this was equivalent to tunicamycin treatment, a score of 0 was given. Where the proportion of adult and freely moving worms compared to tunicamycin treatment was increased, a score of +1 (slight increase) +2 (moderate increase) or +3 (most worms adult) was assigned. Where the drug/compound increased the effects of tunicamycin, scores of -1 (some decrease in adult worms), -2 (moderate decrease) or -3 (mostly dead worms) were assigned (full details in Supplementary data table 1). Drugs producing scores of +2 or +3

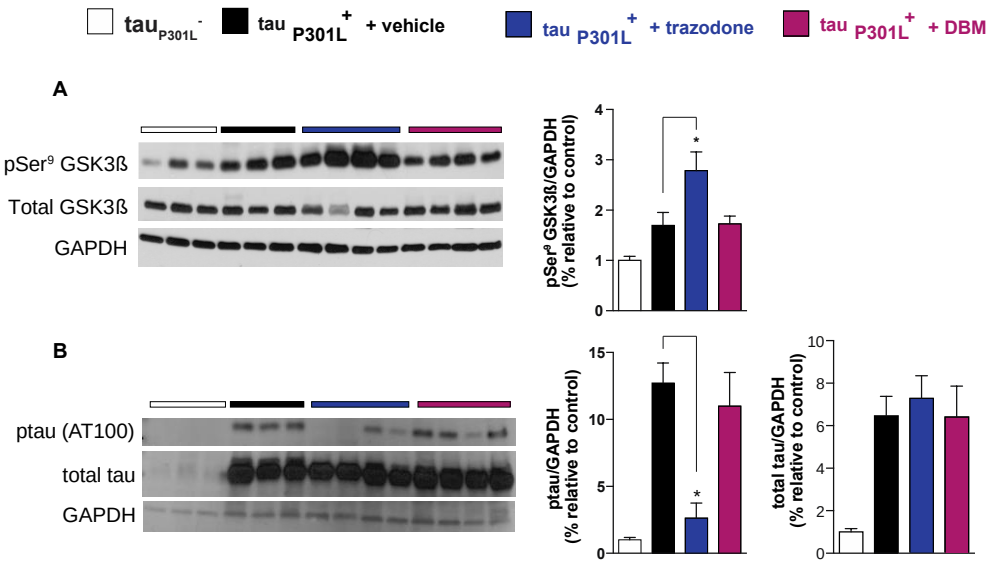
were considered overcoming/inhibiting tunicamycin stress: these plates were further assessed and individual larval and adult forms counted to give a fold increase in adult worms. **Drugs causing a 3-fold or greater increase in the proportion of worms reaching L4 or adulthood were assigned as 'hits' (first 20 compounds in table S1, shown below).** All drugs were tested in duplicate.




**Supplementary figure 2. Sucrose gradient separation shows ISRIB affects eIF2B subunit mass distribution but Trazodone or Dibenzoylmethane do not.** HeLa cells were treated with DMSO (Con), 1μM ISRIB, 20μM trazodone (Traz.) or 20μM DBM for 1 hour. Cells were harvested and clarified lysates were loaded on to 5–20% sucrose gradients and centrifuged for 14 hr at 33,100 rpm. Gradients were run and 13 x 0.8ml fractions were collected per gradient. Proteins were methanol precipitated and resuspended in SDS-PAGE loading buffer. Western blotting was performed for: eIF2B α, δ and ε subunits as well as eIF2α and eIF3a on (A). Gradient fractions and (B). Inputs.




**Supplementary Fig. 3. Trazodone and DBM do not have pancreatic toxicity.** Daily trazodone and DBM treatment for 6 weeks from 7 w.p.i. in prion infected mice produced (**A**) no reduction in pancreas weights compared to vehicle treatment and untreated controls and (**B**) no change in blood glucose levels, consistent with normal pancreatic histology of both exocrine tissue and islets of Langherhans (Figure 3B, panels i-l). Daily trazodone and DBM treatment for 4 weeks months from 4 months old in Tg4510 mice caused (**C**) no reduction in pancreas weights compared to vehicle treatment and untreated controls and (**D**) no change in blood glucose levels, consistent with normal pancreatic histology of both exocrine tissue and islets of Langherhans (Figure 4B, panels m-p). Bar charts show mean ± SEM




**Supplementary Fig. 4. Trazodone treatment reduces phosphorylated tau in rTg4510 tau$_{301L}$+ mice, by increasing inhibitory phosphorylation on GSK3β.**

(A) Western blots showing that trazodone, but not DBM, increases phosphorylation of GSK3β at pSer9, an inhibitory phosphorylation site. (B) Western blots for ptau levels displayed in Fig. 4E, and associated controls, confirming reduction of ptau seen histologically (Figure 4B, panels k,l), on trazodone but not DBM treatment. This is likely another off-target/unpredicted effect of trazodone. Bar charts show quantitation of ptau and total tau. n = 3-4; all experiments repeated in triplicate. Bar charts show mean ± SEM, *$p$<0.05.

| Molecular Name | UPR inhibition rating | Fold increase in the proportion of worms reaching L4 or older |
|---|---|---|
| 2-THIOURACIL | 3 | 3.36 |
| ACRIFLAVINIUM HYDROCHLORIDE | 3 | 6.17 |
| ATORVASTATIN CALCIUM | 3 | 3.85 |
| AZADIRACHTIN | 3 | 7.75 |
| BROXYQUINOLINE | 3 | 5.14 |
| CHLOROGUANIDE HYDROCHLORIDE (PROGUANIL) | 3 | 4.96 |
| DIALLYL SULFIDE | 3 | 3.49 |
| DIBENZOYLMETHANE | 3 | 4.47 |
| EMODIC ACID | 3 | 3.94 |
| ESTRADIOL VALERATE | 3 | 6.10 |
| ESTRIOL | 3 | 8.50 |
| FLUOCINONIDE | 3 | 6.86 |
| PRISTIMERIN | 3 | 3.17 |
| PROPAFENONE HYDROCHLORIDE | 3 | 5.02 |
| SULINDAC | 3 | 4.97 |
| TANNIC ACID | 3 | 4.21 |
| TRAZODONE HYDROCHLORIDE | 3 | 4.20 |
| TRIFLUOPERAZINE HYDROCHLORIDE | 3 | 3.87 |
| VENLAFAXINE | 3 | 3.85 |
| BIFONAZOLE | 2 | 3.49 |
| GSK2606414 | 3 | 3.28 |
| ISRIB | 2 | 2.05 |

**Supplementary Table 1_cropped. The 20 hits from the primary screen of compounds on tunicamycin-induced developmental delay in *C. elegans***

Compound name, semi-quantitative 'UPR inhibition' rating score and fold increase in the proportion of worms reaching L4 or older are provided for 20 hits out of 1040 compounds. These produced a fold change of 3 or more in worms reaching L4 or adulthood compared to tunicamycin treatment, overcoming tunicamycin-induced developmental delay. Effects of GSK2606414 and ISIRB are added for reference. The insolubility of ISRIB may be preventing it from eliciting a similar effect as GSK2606414. Data on all 1040 compounds is presented in Supplementary data table 1_full.

| Drug | Dosage | Sample time (h) | Plasma mean nmol/ml ± sd | Brain mean nmol/g ± sd | Mean ratio Brain: plasma |
|---|---|---|---|---|---|
| Vehicle | N/A | 2 | NQ | NQ | NQ |
| Trazodone | 40 mg/kg | 2 | 11.1 ± 0.28 | 4.12 ± 0.88 | 0.37 |
| Trazodone | 40 mg/kg | 8 | 5.18 ± 1.05 | 1.33 ± 0.55 | 0.26 |
| Dibenzoylmethane | 0.5% food mixture | 24 | 204 ± 195 | 159 ± 113 | 0.78 |

**Supplementary Table 2. Mean plasma and brain concentrations of trazodone and DBM following oral dosing.** Concentrations of trazodone and DBM in brain and plasma of wild type FVB mice were measured by LC-MS/MS. For trazodone this was at 2 and 8 hours after an intra-peritoneal dose of 40mg/kg trazodone (equivalent to 196mg in human, within normal therapeutic range [23]). For DBM levels were measured 24 hours after ad libitum oral consumption of DBM at 0.5% in food mixture. The mean brain:plasma ratios show that both drugs readily cross the blood-brain barrier, achieving good penetration into brain tissue. NQ = not quantifiable, sd = standard deviation.

**Supplementary Table 1_full. Full results of primary screen of compounds of custom 2 NINDS library on tunicamycin-induced developmental delay in *C. elegans***

| **Supplementary data table 1_full** | | |
|---|---|---|
| **Molecular Name** | **UPR inhibition rating** | **Fold increase in the proportion of worms reaching L4 or older** |
| 2-THIOURACIL | 3 | 3.36 |
| ACRIFLAVINIUM HYDROCHLORIDE | 3 | 6.17 |
| ATORVASTATIN CALCIUM | 3 | 3.85 |
| AZADIRACHTIN | 3 | 7.75 |
| BROXYQUINOLINE | 3 | 5.14 |
| CHLOROGUANIDE HYDROCHLORIDE (PROGUANIL) | 3 | 4.96 |
| DIALLYL SULFIDE | 3 | 3.49 |
| DIBENZOYLMETHANE | 3 | 4.47 |
| EMODIC ACID | 3 | 3.94 |
| ESTRADIOL VALERATE | 3 | 6.10 |
| ESTRIOL | 3 | 8.50 |
| FLUOCINONIDE | 3 | 6.86 |
| PRISTIMERIN | 3 | 3.17 |
| PROPAFENONE HYDROCHLORIDE | 3 | 5.02 |
| SULINDAC | 3 | 4.97 |
| TANNIC ACID | 3 | 4.21 |
| TRAZODONE HYDROCHLORIDE | 3 | 4.20 |
| TRIFLUOPERAZINE HYDROCHLORIDE | 3 | 3.87 |
| VENLAFAXINE | 3 | 3.85 |
| BIFONAZOLE | 2 | 3.49 |
| CLEBOPRIDE MALEATE | 3 | 2.55 |
| MELOXICAM | 3 | 2.10 |
| TETRACHLOROISOPHTHALONITRILE | 3 | 2.83 |
| ACETAZOLAMIDE | 2 | 2.29 |
| ALVERINE CITRATE | 2 | 2.70 |
| AMINOGLUTETHIMIDE | 2 | 2.37 |
| AMITRIPTYLINE HYDROCHLORIDE | 2 | 2.51 |
| APOMORPHINE HYDROCHLORIDE | 2 | 2.22 |
| AZATHIOPRINE | 2 | 2.32 |
| BENZOCAINE | 2 | 2.23 |
| BENZTHIAZIDE | 2 | 2.58 |
| CARBENICILLIN DISODIUM | 2 | 2.03 |
| CARBINOXAMINE MALEATE | 2 | 2.15 |

| | | |
|---|---|---|
| CHLORAMPHENICOL | 2 | 2.64 |
| CHLOROCRESOL | 2 | 3.00 |
| CLIDINIUM BROMIDE | 2 | 2.32 |
| ESTRADIOL CYPIONATE | 2 | 3.00 |
| NITRENDIPINE | 2 | 2.07 |
| PSEUDOEPHEDRINE HYDROCHLORIDE | 2 | 2.82 |
| SULFATHIAZOLE | 2 | 2.66 |
| TETRANDRINE | 2 | 2.05 |
| TRIHEXYPHENIDYL HYDROCHLORIDE | 2 | 2.73 |
| TRYPTOPHAN | 2 | 2.32 |
| ACETYLCARNITINE | 1 | 1.93 |
| ADENOSINE | 1 | 2.01 |
| ALEXIDINE HYDROCHLORIDE | 1 | 1.03 |
| AMIKACIN SULFATE | 1 | 1.68 |
| AMILORIDE HYDROCHLORIDE | 1 | 1.76 |
| AMITRAZ | 1 | 1.62 |
| AMOXICILLIN | 1 | 1.52 |
| BENZANTHRONE | 1 | |
| BENZETHONIUM CHLORIDE | 1 | 1.55 |
| BENZYL ISOTHIOCYANATE | 1 | 1.59 |
| BENZYL PENICILLIN POTASSIUM | 1 | 1.13 |
| BITHIONOL | 1 | 1.93 |
| CEFDINIR | 1 | 1.84 |
| CEFTIBUTEN | 1 | 1.01 |
| CHLORANIL | 1 | |
| CHLOROTRIANISENE | 1 | 1.59 |
| CLOFIBRIC ACID | 1 | 2.07 |
| COLISTIMETHATE SODIUM | 1 | 1.69 |
| CORTISONE ACETATE | 1 | 1.92 |
| CYCLOPENTOLATE HYDROCHLORIDE | 1 | |
| CYCLOPHOSPHAMIDE HYDRATE | 1 | |
| CYTARABINE | 1 | |
| DEMECLOCYCLINE HYDROCHLORIDE | 1 | |
| DESIPRAMINE HYDROCHLORIDE | 1 | |
| DICUMAROL | 1 | |
| DIPHENHYDRAMINE HYDROCHLORIDE | 1 | |
| DYPHYLLINE | 1 | |
| ENALAPRIL MALEATE | 1 | 2.08 |
| ENOXACIN | 1 | 1.51 |
| ERGONOVINE MALEATE | 1 | |
| ESTRADIOL | 1 | 2.08 |
| ETHINYL ESTRADIOL | 1 | |
| FLOXURIDINE | 1 | 2.66 |
| GALLAMINE TRIETHIODIDE | 1 | 1.25 |
| GATIFLOXACIN | 1 | 1.51 |
| GENTIAN VIOLET | 1 | |
| GOSSYPOL | 1 | |
| HALOPERIDOL | 1 | |

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|---|---|---|
| HEXACHLOROPHENE | 1 | |
| HUPERZINE A | 1 | 1.53 |
| HYDROCHLOROTHIAZIDE | 1 | |
| HYDROCORTISONE ACETATE | 1 | |
| HYDROXYPROGESTERONE CAPROATE | 1 | |
| ISOSORBIDE DINITRATE | 1 | 1.40 |
| ISOXICAM | 1 | 1.22 |
| LASALOCID SODIUM | 1 | 1.62 |
| LEVOFLOXACIN | 1 | 1.60 |
| LINCOMYCIN HYDROCHLORIDE | 1 | 1.27 |
| LOSARTAN | 1 | 1.46 |
| MEDROXYPROGESTERONE ACETATE | 1 | 1.18 |
| METHIONYL-LEUCYLPHENYLALANINE ACETATE | 1 | 2.19 |
| MINOXIDIL | 1 | |
| MORIN | 1 | 1.33 |
| MOXALACTAM DISODIUM | 1 | 1.71 |
| MOXIFLOXACIN HYDROCHLORIDE | 1 | 2.21 |
| NEOSTIGMINE BROMIDE | 1 | 1.24 |
| NIMESULIDE | 1 | 1.35 |
| NITROFURANTOIN | 1 | 1.91 |
| NORFLOXACIN | 1 | |
| NORTRIPTYLINE | 1 | 1.59 |
| ORPHENADRINE CITRATE | 1 | 1.37 |
| OXOTREMORINE SESQUIFUMARATE | 1 | |
| OXYBENZONE | 1 | 1.33 |
| PAROMOMYCIN SULFATE | 1 | 2.25 |
| PEFLOXACINE MESYLATE | 1 | 1.50 |
| PENICILLAMINE | 1 | 1.23 |
| PHENAZOPYRIDINE HYDROCHLORIDE | 1 | 1.58 |
| PURPURIN | 1 | |
| S-(1,2-DICARBOXYETHYL)GLUTATHIONE | 1 | 1.99 |
| SACCHARIN | 1 | 1.91 |
| SALSOLINE | 1 | |
| SILIBININ | 1 | |
| SODIUM beta-NICOTINAMIDE ADENINE DINUCLEOTIDE PHOSPHATE | 1 | |
| SPIRAMYCIN | 1 | |
| SULCONAZOLE NITRATE | 1 | 1.74 |
| SULFISOXAZOLE | 1 | 1.52 |
| SULPIRIDE | 1 | 1.75 |
| TUAMINOHEPTANE SULFATE | 1 | 1.38 |
| VERATRIDINE | 1 | |
| ZOLMITRIPTAN | 1 | 1.76 |
| 1- (2-METHOXYPHENYL)PIERAZINE HYDROCHLORIDE | 0 | |
| 1-BENZYLOXYCARBONYLAMINOPHENETHYL CHLOROMETHYL KETONE | 0 | |

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|---|---|---|
| 1-METHYLXANTHINE | 0 | |
| 1-PHENYLBIGUANIDE HYDROCHLORIDE | 0 | |
| 1,2-DIMETHYLHYDRAZINE HYDROCHLORIDE | 0 | |
| 1,3-DIPROPYL-8-CYCLOPENTYLXANTHINE [DPCPX] | 0 | |
| 18alpha-GLYCYRRHETINIC ACID | 0 | |
| 1R,2S-PHENYLPROPYLAMINE | 0 | |
| 1R,9S-HYDRASTINE | 0 | |
| 1S,2R-PHENYLPROPANOLAMINE HYDROCHLORIDE | 0 | |
| 2-(2,6-DIMETHOXYPHENOXYETHYL)AMINOMETHYL-1,4-BENZODIOXANE HYDROCHLORIDE (WB 4101) | 0 | |
| 2-MERCAPTOBENZOTHIAZOLE | 0 | |
| 2,3-DIHYDROXY-6,7-DICHLOROQUINOXALINE | 0 | |
| 2,6-DI-t-BUTYL-4-METHYLPHENOL | 0 | |
| 3-AMINOPROPANESULPHONIC ACID | 0 | |
| 3-ISOBUTYL-1-METHYLXANTHINE (IBMX) | 0 | |
| 3-METHYL-1-PHENYL-2-PYRAZOLIN-5-ONE (MCI-186) | 0 | |
| 3-METHYLXANTHINE | 0 | |
| 3,3'-DIINDOLYLMETHANE | 0 | |
| 3,5-DINITROCATECHOL (OR-486) | 0 | |
| 4-NAPHTHALIMIDOBUTYRIC ACID | 0 | |
| 4'-DEMETHYLEPIPODOPHYLLOTOXIN | 0 | |
| 5-AMINOPENTANOIC ACID HYDROCHLORIDE | 0 | |
| 5-CHLOROINDOLE-2-CARBOXYLIC ACID | 0 | |
| 5-FLUORO-5'-DEOXYURIDINE | 0 | |
| 5-FLUOROINDOLE-2-CARBOXYLIC ACID | 0 | |
| 5-NITRO-2-PHENYLPROPYLAMINOBENZOIC ACID [NPPB] | 0 | |
| 6-AMINONICOTINAMIDE | 0 | |
| 6,7-DICHLORO-3-HYDROXY-2-QUINOXALINECARBOXYLIC ACID | 0 | |
| 6alpha-METHYLPREDNISOLONE ACETATE | 0 | |
| 7-CHLOROKYNURENIC ACID | 0 | |
| 7-NITROINDAZOLE | 0 | |
| 8-CYCLOPENTYLTHEOPHYLLINE | 0 | |
| 9-AMINO-1,2,3,4-TETRAHYDROACRIDINE HYDROCHLORIDE | 0 | |

| | | |
|---|---|---|
| ABRINE (L) | 0 | |
| ACEBUTOLOL HYDROCHLORIDE | 0 | |
| ACETAMINOPHEN | 0 | 1.29 |
| ACETAMINOSALOL | 0 | |
| ACETANILIDE | 0 | |
| ACETOHYDROXAMIC ACID | 0 | 1.16 |
| ACETYL TYROSINE ETHYL ESTER | 0 | |
| ACETYL-L-LEUCINE | 0 | |
| ACETYLCHOLINE | 0 | |
| ACETYLCYSTEINE | 0 | 0.87 |
| ACETYLGLUCOSAMINE | 0 | |
| ACETYLTRYPTOPHAN | 0 | |
| ACETYLTRYPTOPHANAMIDE | 0 | |
| ACEXAMIC ACID | 0 | |
| ACIVICIN | 0 | |
| ACONITINE | 0 | |
| ACYCLOVIR | 0 | |
| AESCULIN | 0 | |
| AGMATINE SULFATE | 0 | |
| AJMALINE | 0 | |
| AKLAVINE HYDROCHLORIDE | 0 | |
| AKLOMIDE | 0 | |
| ALAPROCLATE | 0 | |
| ALFLUZOCIN | 0 | |
| ALLANTOIN | 0 | |
| ALLOPURINOL | 0 | |
| ALLOXAN | 0 | |
| ALMOTRIPTAN | 0 | |
| alpha-CYANO-3-HYDROXYCINNAMIC ACID | 0 | |
| alpha-TOCHOPHERYL ACETATE | 0 | |
| ALTHIAZIDE | 0 | |
| ALTRETAMINE | 0 | |
| AMANTADINE HYDROCHLORIDE | 0 | |
| AMBROXOL HYDROCHLORIDE | 0 | |
| AMCINONIDE | 0 | |
| AMINACRINE | 0 | |
| AMINOCYCLOPROPANECARBOXYLIC ACID | 0 | |
| AMINOHIPPURIC ACID | 0 | |
| AMINOHYDROXYBUTYRIC ACID | 0 | |
| AMINOLEVULINIC ACID HYDROCHLORIDE | 0 | |
| AMINOPHENAZONE | 0 | |
| AMINOPTERIN | 0 | |
| AMINOPYRIDINE | 0 | |
| AMINOSALICYLATE SODIUM | 0 | |
| AMINOTHIAZOLE | 0 | |

| | | |
|---|---|---|
| AMIODARONE HYDROCHLORIDE | 0 | |
| AMLODIPINE BESYLATE | 0 | |
| AMODIAQUINE DIHYDROCHLORIDE | 0 | |
| AMOXAPINE | 0 | |
| AMPHOTERICIN B | 0 | 0.91 |
| AMPICILLIN SODIUM | 0 | |
| AMPROLIUM | 0 | 0.92 |
| ANDROSTERONE SODIUM SULFATE | 0 | |
| ANISINDIONE | 0 | |
| ANISODAMINE | 0 | |
| ANISOMYCIN | 0 | |
| ANTAZOLINE PHOSPHATE | 0 | |
| ANTHRAQUINONE | 0 | |
| ANTIPYRINE | 0 | |
| APIGENIN | 0 | |
| APRAMYCIN | 0 | |
| ARECOLINE HYDROBROMIDE | 0 | |
| ASPARTAME | 0 | |
| ASPIRIN | 0 | |
| ASTEMIZOLE | 0 | |
| ATENOLOL | 0 | |
| ATOVAQUONE | 0 | |
| ATRACTYLOSIDE POTASSIUM | 0 | |
| ATROPINE | 0 | |
| AVOBENZONE | 0 | |
| AVOCADYNE | 0 | |
| AVOCADYNONE ACETATE | 0 | |
| AZACITIDINE | 0 | |
| AZAPERONE | 0 | |
| AZASERINE | 0 | |
| AZELAIC ACID | 0 | |
| AZELASTINE HYDROCHLORIDE | 0 | |
| AZITHROMYCIN | 0 | |
| AZLOCILLIN SODIUM | 0 | |
| AZOBENZENE | 0 | |
| BACAMPICILLIN HYDROCHLORIDE | 0 | |
| BAICALEIN | 0 | |
| BENAZEPRIL HYDROCHLORIDE | 0 | |
| BENDROFUMETHIAZIDE | 0 | |
| BENFLUOREX HYDROCHLORIDE | 0 | |
| BENSERAZIDE HYDROCHLORIDE | 0 | 1.23 |
| BENZALKONIUM CHLORIDE | 0 | |
| BEPRIDIL HYDROCHLORIDE | 0 | 1.22 |
| BERBAMINE HYDROCHLORIDE | 0 | |
| BERBERINE CHLORIDE | 0 | |
| BERGAPTEN | 0 | |
| beta-PELTATIN | 0 | |
| BETAMIPRON | 0 | |

| | | |
|---|---|---|
| BETULINIC ACID | 0 | |
| BEZAFIBRATE | 0 | |
| BIOTIN | 0 | |
| BISACODYL | 0 | 0.79 |
| BOVINOCIDIN (3-nitropropionic acid) | 0 | |
| BRETYLIUM TOSYLATE | 0 | |
| BROMHEXINE HYDROCHLORIDE | 0 | |
| BROMOPRIDE | 0 | |
| BROMPHENIRAMINE MALEATE | 0 | |
| BUCLADESINE | 0 | |
| BUDESONIDE | 0 | |
| BUMETANIDE | 0 | |
| BUPROPION | 0 | |
| BUTACAINE | 0 | |
| BUTAMBEN | 0 | |
| CACODYLIC ACID | 0 | |
| CALCEIN | 0 | |
| CAMPTOTHECIN | 0 | |
| CANDESARTAN CILEXTIL | 0 | |
| CANRENOIC ACID, POTASSIUM SALT | 0 | |
| CANRENONE | 0 | |
| CAPSANTHIN | 0 | |
| CAPTOPRIL | 0 | |
| CARBADOX | 0 | |
| CARBENOXOLONE SODIUM | 0 | |
| CARBETAPENTANE CITRATE | 0 | |
| CARBIMAZOLE | 0 | |
| CARBOPLATIN | 0 | |
| CARISOPRODOL | 0 | |
| CARMOFUR | 0 | |
| CARNITINE HYDROCHLORIDE | 0 | |
| CARPROFEN | 0 | |
| CARVEDILOL TARTRATE | 0 | |
| CEFACLOR | 0 | |
| CEFADROXIL | 0 | |
| CEFAMANDOLE NAFATE | 0 | |
| CEFAZOLIN SODIUM | 0 | |
| CEFDITORIN PIVOXIL | 0 | |
| CEFMETAZOLE SODIUM | 0 | |
| CEFOPERAZONE SODIUM | 0 | |
| CEFOTAXIME SODIUM | 0 | 1.39 |
| CEFOXITIN SODIUM | 0 | |
| CEFUROXIME SODIUM | 0 | |
| CELASTROL | 0 | |
| CELECOXIB | 0 | |
| CEPHALEXIN | 0 | |
| CEPHALORIDINE | 0 | |
| CEPHARANTHINE | 0 | |

| | | |
|---|---|---|
| CEPHRADINE | 0 | |
| CETRIMONIUM BROMIDE | 0 | |
| CETYLPYRIDINIUM CHLORIDE | 0 | 1.46 |
| CEVADINE | 0 | |
| CHAULMOSULFONE | 0 | |
| CHLORMADINONE ACETATE | 0 | |
| CHLORMEZANONE | 0 | |
| CHLOROACETOXYQUINOLINE | 0 | |
| CHLOROPHYLLIDE Cu COMPLEX Na SALT | 0 | |
| CHLOROTHIAZIDE | 0 | |
| CHLOROXINE | 0 | |
| CHLOROXYLENOL | 0 | |
| CHLORPHENIRAMINE (S) MALEATE | 0 | 0.64 |
| CHLORPROPAMIDE | 0 | |
| CHLORTHALIDONE | 0 | 1.06 |
| CHRYSANTHEMIC ACID | 0 | |
| CHRYSIN | 0 | |
| CILOSTAZOL | 0 | |
| CIMETIDINE | 0 | |
| CINEOLE | 0 | |
| CINNARAZINE | 0 | |
| CISPLATIN | 0 | |
| CITICOLINE | 0 | |
| CITIOLONE | 0 | |
| CITRININ | 0 | |
| CITROPTEN | 0 | |
| CLARITHROMYCIN | 0 | |
| CLEMASTINE | 0 | 0.77 |
| CLINDAMYCIN HYDROCHLORIDE | 0 | 0.96 |
| CLOBETASOL PROPIONATE | 0 | |
| CLOMIPRAMINE HYDROCHLORIDE | 0 | |
| CLOPERASTINE HYDROCHLORIDE | 0 | |
| CLOPIDOL | 0 | |
| CLOTRIMAZOLE | 0 | |
| CLOZAPINE | 0 | |
| COLCHICEINE | 0 | |
| COLCHICINE | 0 | 1.48 |
| COLFORSIN | 0 | |
| CONVALLATOXIN | 0 | |
| CORALYNE CHLORIDE | 0 | |
| COTININE | 0 | 0.90 |
| CREATININE | 0 | |
| CRESOL | 0 | 0.84 |
| CROMOLYN SODIUM | 0 | |
| CROTAMITON | 0 | |
| CRUSTECDYSONE | 0 | |
| CURCUMIN | 0 | |
| CYCLIZINE | 0 | |

| | | |
|---|---|---|
| CYCLOBENZAPRINE HYDROCHLORIDE | 0 | |
| CYCLOCREATINE | 0 | |
| CYCLOHEXIMIDE | 0 | |
| CYCLOLEUCINE | 0 | |
| CYCLOSERINE | 0 | |
| CYCLOSPORINE | 0 | |
| CYPROTERONE | 0 | |
| CYSTAMINE DIHYDROCHLORIDE | 0 | |
| CYTISINE | 0 | |
| D-PHENYLALANINE | 0 | |
| DANAZOL | 0 | |
| DAPSONE | 0 | |
| DEGUELIN(-) | 0 | |
| DELTALINE | 0 | |
| DERACOXIB | 0 | |
| DESMETHYLDIHYDROCAPSAICIN | 0 | |
| DESOXYCORTICOSTERONE ACETATE | 0 | |
| DEXAMETHASONE | 0 | |
| DEXAMETHASONE SODIUM PHOSPHATE | 0 | |
| DEXPROPRANOLOL HYDROCHLORIDE | 0 | |
| DEXTROMETHORPHAN HYDROBROMIDE | 0 | |
| DIAZOXIDE | 0 | |
| DIBENZOTHIOPHENE | 0 | |
| DICLOFENAC SODIUM | 0 | |
| DIENESTROL | 0 | |
| DIETHYLCARBAMAZINE CITRATE | 0 | |
| DIETHYLSTILBESTROL | 0 | |
| DIETHYLTOLUAMIDE | 0 | |
| DIFLUNISAL | 0 | |
| DIGITOXIN | 0 | |
| DIHYDROJASMONIC ACID, METHYL ESTER | 0 | |
| DIHYDROSTREPTOMYCIN SULFATE | 0 | |
| DILTIAZEM HYDROCHLORIDE | 0 | |
| DIMETHADIONE | 0 | |
| DINITOLMIDE | 0 | 1.04 |
| DIOXYBENZONE | 0 | |
| DIPHENYLPYRALINE HYDROCHLORIDE | 0 | |
| DIPLOSALSALATE | 0 | |
| DIPYRIDAMOLE | 0 | |
| DIPYRONE | 0 | |
| DIRITHROMYCIN | 0 | |
| DISOPYRAMIDE PHOSPHATE | 0 | |
| DOPAMINE HYDROCHLORIDE | 0 | |
| DOXEPIN HYDROCHLORIDE | 0 | |
| DOXYCYCLINE HYDROCHLORIDE | 0 | |
| DOXYLAMINE SUCCINATE | 0 | |
| DROPERIDOL | 0 | |
| DROPROPIZINE | 0 | |

| | | |
|---|---|---|
| DYCLONINE HYDROCHLORIDE | 0 | |
| EBSELEN | 0 | |
| ECONAZOLE NITRATE | 0 | |
| EDROPHONIUM CHLORIDE | 0 | |
| ELAIDYLPHOSPHOCHOLINE | 0 | |
| ELLAGIC ACID | 0 | |
| EMETINE | 0 | |
| EPHEDRINE (1R,2S) HYDROCHLORIDE | 0 | |
| ERGOCALCIFEROL | 0 | |
| ERYTHROMYCIN ESTOLATE | 0 | |
| ESERINE | 0 | |
| ESTRADIOL ACETATE | 0 | |
| ESTRADIOL DIACETATE | 0 | |
| ESTRADIOL METHYL ETHER | 0 | |
| ESTRADIOL PROPIONATE | 0 | |
| ESTRADIOL-3-SULFATE, SODIUM SALT | 0 | |
| ESTRIOL BENZYL ETHER | 0 | |
| ESTRIOL METHYL ETHER | 0 | |
| ESTRONE | 0 | |
| ESTRONE ACETATE | 0 | |
| ESTRONE HEMISUCCINATE | 0 | |
| ETANIDAZOLE | 0 | |
| ETHAMBUTOL HYDROCHLORIDE | 0 | |
| ETHAVERINE HYDROCHLORIDE | 0 | |
| ETHIONAMIDE | 0 | |
| ETHISTERONE | 0 | |
| ETHOPROPAZINE HYDROCHLORIDE | 0 | |
| ETHYL 1-BENZYL-3-HYDROXY-2-OXO[5H]PYRROLE-4-CARBOXYLATE | 0 | |
| ETHYLNOREPINEPHRINE HYDROCHLORIDE | 0 | |
| ETODOLAC | 0 | |
| EUCATROPINE HYDROCHLORIDE | 0 | |
| EUGENOL | 0 | |
| EZETIMIBE | 0 | |
| FAMCICLOVIR | 0 | |
| FAMOTIDINE | 0 | |
| FENBENDAZOLE | 0 | |
| FENBUFEN | 0 | |
| FENBUTYRAMIDE | 0 | |
| FENDILINE HYDROCHLORIDE | 0 | |
| FENOFIBRATE | 0 | |
| FENOPROFEN | 0 | |
| FENOTEROL HYDROBROMIDE | 0 | |
| FENSPIRIDE HYDROCHLORIDE | 0 | |
| FIPEXIDE HYDROCHLORIDE | 0 | |
| FLUDROCORTISONE ACETATE | 0 | |
| FLUFENAMIC ACID | 0 | |

| | | |
|---|---|---|
| FLUMEQUINE | 0 | |
| FLUMETHAZONE PIVALATE | 0 | |
| FLUNISOLIDE | 0 | |
| FLUOROMETHOLONE | 0 | |
| FLUOROURACIL | 0 | |
| FLUOXETINE | 0 | |
| FLUPHENAZINE HYDROCHLORIDE | 0 | |
| FLURANDRENOLIDE | 0 | |
| FLUTAMIDE | 0 | 1.14 |
| FOLIC ACID | 0 | |
| FORMESTANE | 0 | |
| FOSCARNET SODIUM | 0 | |
| FOSFOMYCIN | 0 | |
| FOSFOSAL | 0 | |
| FUREGRELATE SODIUM | 0 | |
| FUROSEMIDE | 0 | |
| FUSIDIC ACID | 0 | |
| GABOXADOL HYDROCHLORIDE | 0 | |
| GALANTHAMINE HYDROBROMIDE | 0 | |
| GAMBOGIC ACID | 0 | |
| gamma-AMINOBUTYRIC ACID | 0 | |
| GEDUNIN | 0 | |
| GEMFIBROZIL | 0 | |
| GEMIFLOXACIN MESYLATE | 0 | |
| GENETICIN | 0 | |
| GINKGOLIC ACID | 0 | |
| GLAFENINE | 0 | |
| GLICLAZIDE | 0 | |
| GLUCONOLACTONE | 0 | |
| GLUCOSAMINE HYDROCHLORIDE | 0 | |
| GLUTATHIONE | 0 | |
| GLYBURIDE | 0 | |
| GLYCYLLEUCYLPHENYLALANINE | 0 | |
| GRISEOFULVIN | 0 | |
| GUAIFENESIN | 0 | |
| GUANABENZ ACETATE | 0 | |
| GUANIDINE CARBONATE | 0 | |
| GUVACINE HYDROCHLORIDE | 0 | |
| HALAZONE | 0 | |
| HALCINONIDE | 0 | |
| HARMALINE | 0 | |
| HARMALOL HYDROCHLORIDE | 0 | |
| HARMINE | 0 | |
| HARMOL HYDROCHLORIDE | 0 | |
| HECOGENIN | 0 | |
| HEXAMETHONIUM BROMIDE | 0 | |
| HEXESTROL | 0 | |
| HEXETIDINE | 0 | |

| | | |
|---|---|---|
| HEXYLRESORCINOL | 0 | |
| HISTAMINE DIHYDROCHLORIDE | 0 | |
| HOMATROPINE BROMIDE | 0 | |
| HOMATROPINE METHYLBROMIDE | 0 | |
| HYCANTHONE | 0 | |
| HYDROCORTISONE | 0 | |
| HYDROCORTISONE BUTYRATE | 0 | |
| HYDROCORTISONE HEMISUCCINATE | 0 | |
| HYDROFLUMETHIAZIDE | 0 | |
| HYDROQUINIDINE | 0 | |
| HYDROQUINONE | 0 | |
| HYDROXYCHLOROQUINE SULFATE | 0 | |
| HYDROXYTACRINE MALEATE | 0 | |
| HYDROXYUREA | 0 | |
| HYOSCYAMINE | 0 | |
| IBUPROFEN | 0 | |
| ICARIIN | 0 | |
| IMIDACLOPRID | 0 | |
| IMIPRAMINE HYDROCHLORIDE | 0 | |
| INDAPAMIDE | 0 | |
| INDOLE-2-CARBOXYLIC ACID | 0 | |
| INDOLE-3-CARBINOL | 0 | |
| INDOMETHACIN | 0 | |
| INDOPROFEN | 0 | |
| IODIPAMIDE | 0 | |
| IODOQUINOL | 0 | |
| IOPANIC ACID | 0 | |
| IPRATROPIUM BROMIDE | 0 | |
| IPRONIAZID SULFATE | 0 | |
| IRBESARTAN | 0 | |
| ISOBUTYLMETHYLXANTHINE | 0 | |
| ISOLIQUIRITIGENIN | 0 | |
| ISONIAZID | 0 | |
| ISOPROPAMIDE IODIDE | 0 | |
| ISOPROTERENOL HYDROCHLORIDE | 0 | |
| ISORESERPINE | 0 | |
| ISOXSUPRINE HYDROCHLORIDE | 0 | |
| JUGLONE | 0 | |
| KAINIC ACID | 0 | |
| KANAMYCIN SULFATE | 0 | |
| KETOCONAZOLE | 0 | |
| KETOPROFEN | 0 | |
| KETOROLAC TROMETHAMINE | 0 | |
| KETOTIFEN FUMARATE | 0 | |
| KINETIN | 0 | |
| KOJIC ACID | 0 | |
| KYNURENIC ACID | 0 | |
| L-LEUCYL-L-ALANINE | 0 | |

| | | |
|---|---|---|
| L-PHENYLALANINOL | 0 | |
| LABETALOL HYDROCHLORIDE | 0 | |
| LACTULOSE | 0 | |
| LAPACHOL | 0 | |
| LEUCINE ENKEPHALIN | 0 | |
| LEUCOVORIN CALCIUM | 0 | |
| LEVODOPA | 0 | |
| LEVONORDEFRIN | 0 | |
| LIDOCAINE HYDROCHLORIDE | 0 | |
| LIOTHYRONINE SODIUM | 0 | |
| LISINOPRIL | 0 | |
| LOBELINE HYDROCHLORIDE | 0 | |
| LOMEFLOXACIN HYDROCHLORIDE | 0 | |
| LOPERAMIDE HYDROCHLORIDE | 0 | |
| LORATADINE | 0 | |
| LOVASTATIN | 0 | |
| LOXAPINE SUCCINATE | 0 | |
| LUPININE | 0 | |
| LYSYL-TYROSYL-LYSINE ACETATE | 0 | |
| MADECASSIC ACID | 0 | |
| MAFENIDE HYDROCHLORIDE | 0 | |
| MEBENDAZOLE | 0 | |
| MEBEVERINE HYDROCHLORIDE | 0 | |
| MEBHYDROLIN NAPHTHALENESULFONATE | 0 | |
| MECAMYLAMINE HYDROCHLORIDE | 0 | |
| MECHLORETHAMINE | 0 | |
| MECLIZINE HYDROCHLORIDE | 0 | |
| MECLOCYCLINE SULFOSALICYLATE | 0 | |
| MECLOFENAMATE SODIUM | 0 | |
| MEFENAMIC ACID | 0 | |
| MEFEXAMIDE | 0 | |
| MEFLOQUINE | 0 | |
| MEGESTROL ACETATE | 0 | |
| MELATONIN | 0 | |
| MEMANTINE HYDROCHLORIDE | 0 | |
| MENADIONE | 0 | |
| MENTHOL(-) | 0 | |
| MEPENZOLATE BROMIDE | 0 | |
| MEPHENESIN | 0 | |
| MEPHENTERMINE SULFATE | 0 | |
| MEPIVACAINE HYDROCHLORIDE | 0 | |
| MERBROMIN | 0 | |
| MERCAPTAMINE HYDROCHLORIDE | 0 | |
| MERCAPTOPURINE | 0 | |
| MESNA | 0 | |
| METAMPICILLIN SODIUM | 0 | |
| METAPROTERENOL | 0 | |
| METARAMINOL BITARTRATE | 0 | |

| | | |
|---|---|---|
| METAXALONE | 0 | |
| METERGOLINE | 0 | |
| METHACHOLINE CHLORIDE | 0 | |
| METHACYCLINE HYDROCHLORIDE | 0 | |
| METHAZOLAMIDE | 0 | |
| METHENAMINE | 0 | |
| METHICILLIN SODIUM | 0 | |
| METHIMAZOLE | 0 | |
| METHOCARBAMOL | 0 | |
| METHOTREXATE | 0 | |
| METHOXAMINE HYDROCHLORIDE | 0 | |
| METHOXSALEN | 0 | |
| METHSCOPOLAMINE BROMIDE | 0 | |
| METHYLBENZETHONIUM CHLORIDE | 0 | |
| METHYLDOPA | 0 | |
| METHYLERGONOVINE MALEATE | 0 | |
| METHYLPREDNISOLONE | 0 | |
| METHYLTHIOURACIL | 0 | |
| METOCLOPRAMIDE HYDROCHLORIDE | 0 | |
| METOLAZONE | 0 | |
| METOPROLOL TARTRATE | 0 | |
| METRONIDAZOLE | 0 | |
| MEXAMINE | 0 | |
| MICONAZOLE NITRATE | 0 | |
| MIDODRINE HYDROCHLORIDE | 0 | |
| MIGLITOL | 0 | |
| MILTEFOSINE | 0 | |
| MIMOSINE | 0 | |
| MINAPRINE HYDROCHLORIDE | 0 | |
| MITOXANTHRONE HYDROCHLORIDE | 0 | |
| MIZORIBINE | 0 | |
| MODAFINIL | 0 | |
| MOLSIDOMINE | 0 | |
| MONENSIN SODIUM | 0 | |
| MONOCROTALINE | 0 | |
| MORANTEL CITRATE | 0 | |
| MYCOPHENOLIC ACID | 0 | |
| N (g)-NITRO-L-ARGININE | 0 | |
| N- (9-FLUORENYLMETHOXYCARBONYL)-L-LEUCINE | 0 | |
| N-ACETYLNEURAMIC ACID | 0 | |
| N-ACETYLPROLINE | 0 | |
| N-AMINOHEXYL-5-CHLORO-1-NAPTHALENESULFONAMIDE HYDROCHLORIDE | 0 | |
| N-CHLOROETHYL-N-ETHYL-2'-METHYLBENZYLAMINE HYDROCHLORIDE | 0 | |
| N-FORMYLMETHIONYL- | 0 | |

| | | |
|---|---|---|
| LEUCYLPHENYLALANINE | | |
| N-FORMYLMETHIONYLPHENYLALANINE | 0 | |
| N-HISTIDYL-2-AMINONAPHTHALENE (betaNA) | 0 | |
| N-HYDROXYMETHYLNICOTINAMIDE | 0 | |
| N,N-HEXAMETHYLENEAMILORIDE | 0 | |
| NABUMETONE | 0 | |
| NADOLOL | 0 | |
| NALBUPHINE HYDROCHLORIDE | 0 | |
| NALIDIXIC ACID | 0 | |
| NALOXONE HYDROCHLORIDE | 0 | |
| NALTREXONE HYDROCHLORIDE | 0 | |
| NAPHAZOLINE HYDROCHLORIDE | 0 | |
| NAPROXEN(+) | 0 | |
| NAPROXOL | 0 | |
| NARASIN | 0 | |
| NARINGENIN | 0 | |
| NARINGIN | 0 | |
| NATEGLINIDE | 0 | |
| NEFOPAM | 0 | |
| NEOHESPERIDIN DIHYDROCHALCONE | 0 | |
| NEOMYCIN SULFATE | 0 | |
| NEROL | 0 | |
| Ng-METHYL-L-ARGININE ACETATE | 0 | |
| NICARDIPINE HYDROCHLORIDE | 0 | |
| NICERGOLINE | 0 | |
| NICOTINE DITARTRATE | 0 | |
| NICOTINYL TARTRATE | 0 | |
| NIFENAZONE | 0 | |
| NIGERICIN SODIUM | 0 | |
| NILUTAMIDE | 0 | |
| NIMODIPINE | 0 | |
| NIPECOTIC ACID | 0 | |
| NITROFURAZONE | 0 | |
| NITROMIDE | 0 | |
| NOMIFENSINE MALEATE | 0 | |
| NOREPINEPHRINE | 0 | |
| NORETHINDRONE ACETATE | 0 | |
| NORETHYNODREL | 0 | |
| NORGESTREL | 0 | |
| NORHARMAN | 0 | |
| NOSCAPINE HYDROCHLORIDE | 0 | |
| NOVOBIOCIN SODIUM | 0 | |
| NYLIDRIN HYDROCHLORIDE | 0 | |
| NYSTATIN | 0 | |

| | | |
|---|---|---|
| OCTOPAMINE HYDROCHLORIDE | 0 | |
| OFLOXACIN | 0 | |
| OLEANDOMYCIN PHOSPHATE | 0 | |
| OLMESARTAN MEDOXOMIL | 0 | |
| ORLISTAT | 0 | |
| OUABAIN | 0 | |
| OXACILLIN SODIUM | 0 | |
| OXAPROZIN | 0 | |
| OXCARBAZEPINE | 0 | |
| OXFENDAZOLE | 0 | |
| OXICONAZOLE NITRATE | 0 | |
| OXIDOPAMINE HYDROCHLORIDE | 0 | |
| OXYMETAZOLINE HYDROCHLORIDE | 0 | |
| OXYPHENBUTAZONE | 0 | |
| OXYPHENCYCLIMINE HYDROCHLORIDE | 0 | |
| OXYQUINOLINE HEMISULFATE | 0 | |
| OXYTETRACYCLINE | 0 | |
| p-CHLOROPHENYLALANINE | 0 | |
| PAEONOL | 0 | |
| PALMATINE | 0 | |
| PALMATINE CHLORIDE | 0 | |
| PAPAVERINE HYDROCHLORIDE | 0 | |
| PARACHLOROPHENOL | 0 | |
| PARAROSANILINE PAMOATE | 0 | |
| PARAXANTHINE | 0 | |
| PATULIN | 0 | |
| PENICILLIN V POTASSIUM | 0 | |
| PENTAMIDINE ISETHIONATE | 0 | |
| PENTETRAZOL | 0 | |
| PENTOLINIUM TARTRATE | 0 | |
| PEONIFLORIN | 0 | |
| PERHEXILINE MALEATE | 0 | |
| PERICIAZINE | 0 | |
| PERILLIC ACID (-) | 0 | |
| PERILLYL ALCOHOL | 0 | |
| PERINDOPRIL ERBUMINE | 0 | |
| PERPHENAZINE | 0 | |
| PERUVOSIDE | 0 | |
| PHENACETIN | 0 | |
| PHENELZINE SULFATE | 0 | |
| PHENETHYL CAFFEATE (CAPE) | 0 | |
| PHENINDIONE | 0 | |
| PHENIRAMINE MALEATE | 0 | |
| PHENOXYBENZAMINE HYDROCHLORIDE | 0 | |
| PHENYLALANYLTYROSINE | 0 | |
| PHENYLBUTYRATE SODIUM | 0 | |
| PHENYLEPHRINE HYDROCHLORIDE | 0 | |
| PHENYLMERCURIC ACETATE | 0 | |

| | | |
|---|---|---|
| PHENYTOIN SODIUM | 0 | |
| PHLORIDZIN | 0 | |
| PHYSCION | 0 | |
| PHYSOSTIGMINE SALICYLATE | 0 | |
| PICROPODOPHYLLOTOXIN | 0 | |
| PICROTOXININ | 0 | |
| PILOCARPINE NITRATE | 0 | |
| PIMOZIDE | 0 | |
| PIMPINELLIN | 0 | |
| PINACIDIL | 0 | |
| PINDOLOL | 0 | |
| PIOGLITAZONE HYDROCHLORIDE | 0 | |
| PIPERACILLIN SODIUM | 0 | |
| PIPERIDOLATE HYDROCHLORIDE | 0 | |
| PIPERINE | 0 | |
| PIRACETAM | 0 | |
| PIRENZEPINE HYDROCHLORIDE | 0 | |
| PIROMIDIC ACID | 0 | |
| PIROXICAM | 0 | |
| PODOFILOX | 0 | |
| POMIFERIN | 0 | |
| POTASSIUM p-AMINOBENZOATE | 0 | 0.93 |
| PRALIDOXIME MESYLATE | 0 | |
| PRAMOXINE HYDROCHLORIDE | 0 | |
| PRAVASTATIN SODIUM | 0 | |
| PRAZIQUANTEL | 0 | |
| PREDNISOLONE | 0 | |
| PREDNISOLONE ACETATE | 0 | |
| PREDNISONE | 0 | |
| PREGABALIN | 0 | |
| PREGNENOLONE | 0 | |
| PRIDINOL METHANESULFONATE | 0 | |
| PRILOCAINE HYDROCHLORIDE | 0 | |
| PRIMAQUINE DIPHOSPHATE | 0 | |
| PRIMIDONE | 0 | |
| PROADIFEN HYDROCHLORIDE | 0 | |
| PROBENECID | 0 | |
| PROBUCOL | 0 | |
| PROCAINAMIDE HYDROCHLORIDE | 0 | |
| PROCHLORPERAZINE EDISYLATE | 0 | |
| PROCYCLIDINE HYDROCHLORIDE | 0 | |
| PROGESTERONE | 0 | |
| PROGLUMIDE | 0 | |
| PROMAZINE HYDROCHLORIDE | 0 | |
| PROMETHAZINE HYDROCHLORIDE | 0 | |
| PRONETALOL HYDROCHLORIDE | 0 | |
| PROPANTHELINE BROMIDE | 0 | |
| PROPRANOLOL HYDROCHLORIDE | 0 | |

| | | |
|---|---|---|
| PROPYLTHIOURACIL | 0 | |
| PROTHIONAMIDE | 0 | |
| PROTOPORPHYRIN IX | 0 | |
| PROTOVERATRINE B | 0 | |
| PUROMYCIN HYDROCHLORIDE | 0 | |
| PYRANTEL PAMOATE | 0 | |
| PYRAZINAMIDE | 0 | |
| PYRIDOSTIGMINE BROMIDE | 0 | |
| PYRILAMINE MALEATE | 0 | |
| PYRIMETHAMINE | 0 | |
| PYRITHYLDIONE | 0 | |
| PYRVINIUM PAMOATE | 0 | |
| QUASSIN | 0 | |
| QUERCETIN | 0 | |
| QUERCITRIN | 0 | |
| QUINACRINE HYDROCHLORIDE | 0 | |
| QUINALIZARIN | 0 | |
| QUINAPRIL HYDROCHLORIDE | 0 | |
| QUINIDINE GLUCONATE | 0 | |
| QUININE SULFATE | 0 | |
| QUINOLINIC ACID | 0 | |
| RACEPHEDRINE HYDROCHLORIDE | 0 | |
| RAMIFENAZONE | 0 | |
| RANITIDINE | 0 | |
| RESORCINOL | 0 | |
| RESORCINOL MONOACETATE | 0 | |
| RESVERATROL | 0 | |
| RETINOL | 0 | |
| RETINYL ACETATE | 0 | |
| RETINYL PALMITATE | 0 | |
| RHAPONTIN | 0 | |
| RIBOFLAVIN | 0 | |
| RIFAMPIN | 0 | |
| RILUZOLE | 0 | |
| RITODRINE HYDROCHLORIDE | 0 | |
| ROFECOXIB | 0 | |
| RONIDAZOLE | 0 | |
| ROSIGLITAZONE | 0 | |
| ROSMARINIC ACID | 0 | |
| ROSOLIC ACID | 0 | |
| ROSUVASTATIN | 0 | |
| ROTENONE | 0 | |
| ROXITHROMYCIN | 0 | |
| RUTILANTINONE | 0 | |
| S-METHYL-L-THIOCITRULLINE ACETATE | 0 | |
| SAFROLE | 0 | |
| SALICYL ALCOHOL | 0 | |
| SARAFLOXACIN HYDROCHLORIDE | 0 | |

| | | |
|---|---|---|
| SCOPOLAMINE HYDROBROMIDE | 0 | |
| SECURININE | 0 | |
| SEMUSTINE | 0 | |
| SENNOSIDE A | 0 | |
| SERTRALINE HYDROCHLORIDE | 0 | |
| SIBUTRAMINE HYDROCHLORIDE | 0 | |
| SILDENAFIL | 0 | |
| SINOMENINE | 0 | |
| SISOMICIN SULFATE | 0 | |
| SNAP (S-NITROSO-N-ACETYLPENICILLAMINE) | 0 | |
| SODIUM DEHYDROCHOLATE | 0 | |
| SPAGLUMIC ACID | 0 | |
| SPARTEINE HYDROIODIDE | 0 | |
| SPARTEINE SULFATE | 0 | |
| SPECTINOMYCIN HYDROCHLORIDE | 0 | |
| SPERMIDINE TRIHYDROCHLORIDE | 0 | |
| SPIPERONE | 0 | |
| SPIRONOLACTONE | 0 | |
| STREPTOMYCIN SULFATE | 0 | |
| STRYCHNINE | 0 | |
| SULFABENZAMIDE | 0 | |
| SULFACHLORPYRIDAZINE | 0 | |
| SULFADIAZINE | 0 | |
| SULFADIMETHOXINE | 0 | |
| SULFAGUANIDINE | 0 | |
| SULFAMERAZINE | 0 | |
| SULFAMETER | 0 | |
| SULFAMETHAZINE | 0 | |
| SULFAMETHIZOLE | 0 | |
| SULFAMETHOXAZOLE | 0 | |
| SULFAMETHOXYPYRIDAZINE | 0 | |
| SULFANILAMIDE | 0 | |
| SULFAPHENAZOLE | 0 | |
| SULFAPYRIDINE | 0 | |
| SULFASALAZINE | 0 | |
| SULFINPYRAZONE | 0 | |
| SULOCTIDIL | 0 | |
| SUPROFEN | 0 | |
| SUPROFEN METHYL ESTER | 0 | |
| SUXIBUZONE | 0 | |
| TAMOXIFEN CITRATE | 0 | |
| TARGININE HYDROCHLORIDE | 0 | |
| TEGASEROD MALEATE | 0 | |
| TELENZEPINE HYDROCHLORIDE | 0 | |
| TELITHROMYCIN | 0 | |
| TENIPOSIDE | 0 | |
| TENOXICAM | 0 | |
| TERBUTALINE HEMISULFATE | 0 | |

| | | |
|---|---|---|
| TETRACAINE HYDROCHLORIDE | 0 | |
| TETRACYCLINE HYDROCHLORIDE | 0 | |
| TETRAHYDROPALMATINE | 0 | |
| TETRAHYDROZOLINE HYDROCHLORIDE | 0 | |
| Tfa-VAL-TYR-VAL-OH | 0 | |
| THEOBROMINE | 0 | |
| THEOPHYLLINE | 0 | |
| THIABENDAZOLE | 0 | |
| THIAMPHENICOL | 0 | |
| THIMEROSAL | 0 | |
| THIOCTIC ACID | 0 | |
| THIOGUANINE | 0 | |
| THIORIDAZINE HYDROCHLORIDE | 0 | |
| THIOTEPA | 0 | |
| THIOTHIXENE | 0 | |
| THYROXINE | 0 | |
| TIAPRIDE HYDROCHLORIDE | 0 | |
| TIMOLOL MALEATE | 0 | |
| TINIDAZOLE | 0 | |
| TIOXOLONE | 0 | |
| TODRALAZINE HYDROCHLORIDE | 0 | |
| TOLAZAMIDE | 0 | |
| TOLBUTAMIDE | 0 | |
| TOLFENAMIC ACID | 0 | |
| TOLMETIN SODIUM | 0 | |
| TOMATINE | 0 | |
| TOPIRAMATE | 0 | |
| TORSEMIDE | 0 | |
| TRANDOLAPRIL | 0 | |
| TRANEXAMIC ACID | 0 | |
| TRANILAST | 0 | |
| TRANYLCYPROMINE SULFATE | 0 | |
| TRETINON | 0 | |
| TRIACETIN | 0 | |
| TRIADIMEFON | 0 | |
| TRIAMCINOLONE | 0 | |
| TRIAMCINOLONE ACETONIDE | 0 | |
| TRIAMCINOLONE DIACETATE | 0 | |
| TRIAMTERENE | 0 | |
| TRICHLORMETHIAZIDE | 0 | |
| TRIMEDLURE | 0 | |
| TRIMEPRAZINE TARTRATE | 0 | |
| TRIMETHOBENZAMIDE HYDROCHLORIDE | 0 | |
| TRIMETHOPRIM | 0 | |
| TRIOXSALEN | 0 | |
| TRIPROLIDINE HYDROCHLORIDE | 0 | |
| TRISODIUM ETHYLENEDIAMINE TETRACETATE | 0 | |

| | | |
|---|---|---|
| TROLEANDOMYCIN | 0 | |
| TROPICAMIDE | 0 | |
| TRYPTAMINE | 0 | |
| TULOBUTEROL | 0 | |
| TYLOSIN TARTRATE | 0 | |
| TYROTHRICIN | 0 | |
| URETHANE | 0 | |
| URSODIOL | 0 | |
| USNIC ACID | 0 | |
| VALDECOXIB | 0 | |
| VALERYL SALYCILATE | 0 | |
| VALPROATE SODIUM | 0 | |
| VALSARTAN | 0 | |
| VANCOMYCIN HYDROCHLORIDE | 0 | |
| VERAPAMIL HYDROCHLORIDE | 0 | |
| VERATRINE SULFATE | 0 | |
| VESAMICOL HYDROCHLORIDE | 0 | |
| VIDARABINE | 0 | |
| VINBURNINE | 0 | |
| VINCAMINE | 0 | |
| VINPOCETINE | 0 | |
| XANTHURENIC ACID | 0 | |
| XYLAZINE | 0 | |
| XYLOMETAZOLINE HYDROCHLORIDE | 0 | |
| YOHIMBINE HYDROCHLORIDE | 0 | |
| ZAPRINAST | 0 | |
| ZIDOVUDINE [AZT] | 0 | |
| ZOMEPIRAC SODIUM | 0 | |
| ZOXAZOLAMINE | 0 | |
| 1R-CAMPHOR | -1 | |
| ACETOSYRINGONE | -1 | |
| ACETYLGLUTAMIC ACID | -1 | |
| ADRENALINE BITARTRATE | -1 | |
| AMYGDALIN | -1 | |
| ARTEMISININ | -1 | |
| BACITRACIN | -1 | |
| BACLOFEN | -1 | |
| BENZTROPINE | -1 | |
| BETAMETHASONE | -1 | |
| BETHANECHOL CHLORIDE | -1 | |
| BUSULFAN | -1 | |
| CAFFEINE | -1 | |
| CAPREOMYCIN SULFATE | -1 | |
| CARBAMAZEPINE | -1 | |
| CARMUSTINE | -1 | |
| CEPHALOTHIN SODIUM | -1 | |
| CHLOROQUINE DIPHOSPHATE | -1 | |
| CHLORZOXAZONE | -1 | |

| | | |
|---|---|---|
| CICLOPIROX OLAMINE | -1 | |
| CINOXACIN | -1 | 0.58 |
| CLOMIPHENE CITRATE | -1 | 0.58 |
| CLONIDINE HYDROCHLORIDE | -1 | |
| CLOXYQUIN | -1 | |
| DEFEROXAMINE MESYLATE | -1 | |
| DEQUALINIUM CHLORIDE | -1 | |
| DEXAMETHASONE ACETATE | -1 | |
| DIBUCAINE HYDROCHLORIDE | -1 | |
| DIGOXIN | -1 | |
| DIMENHYDRINATE | -1 | |
| DISULFIRAM | -1 | |
| EXALAMIDE | -1 | |
| FLURBIPROFEN | -1 | |
| GUANETHIDINE SULFATE | -1 | |
| HYDRALAZINE HYDROCHLORIDE | -1 | |
| HYDROXYZINE PAMOATE | -1 | |
| LANSOPRAZOLE | -1 | |
| N- (3-TRIFLUOROMETHYLPHENYL)PIPERAZINE HYDROCHLORIDE (TFMPP) | -1 | |
| N-ACETYLASPARTIC ACID | -1 | |
| NIACIN | -1 | |
| NIFEDIPINE | -1 | |
| NIMUSTINE | -1 | |
| PINOCEMBRIN | -1 | |
| RIFAXIMIN | -1 | |
| SALICIN | -1 | |
| SALINOMYCIN, SODIUM | -1 | |
| SECNIDAZOLE | -1 | |
| TROXERUTIN | -1 | |
| VALYLTRYPTOPHAN | -1 | 0.68 |
| 6-AMINOCAPROIC ACID | -2 | 0.72 |
| ACRISORCIN | -2 | |
| ADIPHENINE HYDROCHLORIDE | -2 | |
| beta-CAROTENE | -2 | 0.22 |
| BETA-PROPIOLACTONE | -2 | |
| BUPIVACAINE HYDROCHLORIDE | -2 | |
| CARBACHOL | -2 | 0.63 |
| CEFTRIAXONE SODIUM | -2 | 0.00 |
| CHLORPROMAZINE | -2 | |
| CLOFOCTOL | -2 | 0.58 |
| CLOPIDOGREL SULFATE | -2 | |
| CLOXACILLIN SODIUM | -2 | |
| DIHYDROJASMONIC ACID | -2 | |
| ETHOSUXIMIDE | -2 | |
| FLUNARIZINE HYDROCHLORIDE | -2 | |
| FURAZOLIDONE | -2 | |

| | | |
|---|---|---|
| LEFUNOMIDE | -2 | |
| LEVAMISOLE HYDROCHLORIDE | -2 | |
| LYSYLPHENYLALANYLTYROSINE | -2 | |
| MAPROTILINE HYDROCHLORIDE | -2 | |
| MEDRYSONE | -2 | |
| METHAPYRILENE HYDROCHLORIDE | -2 | |
| METHIOTHEPIN MALEATE | -2 | |
| METHOXYAMINE HYDROCHLORIDE | -2 | |
| NAFCILLIN SODIUM | -2 | |
| NORCANTHARIDIN | -2 | |
| PACLITAXEL | -2 | |
| RAUWOLSCINE HYDROCHLORIDE | -2 | |
| SALICYLAMIDE | -2 | |
| TOLAZOLINE HYDROCHLORIDE | -2 | |
| VULPINIC ACID | -2 | |
| AMIPRILOSE | -3 | |
| CEPHAPIRIN SODIUM | -3 | |
| CIPROFLOXACIN | -3 | |
| d[-Arg-2]KYOTORPHAN ACETATE | -3 | |
| NAFRONYL OXALATE | -3 | |
| PENTOXIFYLLINE | -3 | |
| PYRITHIONE ZINC | -3 | |
| SELAMECTIN | -3 | |
| TRIMIPRAMINE MALEATE | -3 | |
| DICLOXACILLIN SODIUM | N/A | N/A |
| GENTAMICIN SULFATE | N/A | N/A |
| HETACILLIN POTASSIUM | N/A | N/A |
| PHENOTHRIN | N/A | N/A |
| PIPERAZINE | N/A | N/A |
| ROXARSONE | N/A | N/A |
| STREPTOZOSIN | N/A | N/A |
| SULFACETAMIDE | N/A | N/A |
| TOLNAFTATE | N/A | N/A |
| ANTHRALIN | N/A | N/A |
| CHLORAMPHENICOL HEMISUCCINATE | N/A | N/A |
| CHLORTETRACYCLINE HYDROCHLORIDE | N/A | N/A |

**Supplementary Table 1_full. Results of primary screen of compounds of custom 2 NINDS library on tunicamycin-induced developmental delay in *C. elegans***

Compound name, semi-quantitative 'UPR inhibition' rating score and fold increase in the proportion of worms reaching L4 or older are provided for all 1040 compounds. Compounds are listed according to rank with highest scoring first. For these, the fold-change in adults reaching adulthood compared to controls was calculated and is shown. The 20 compounds that produced a fold change of 3 or more in worms reaching L4 or adulthood compared to tunicamycin and hence overcoming tunicamycin-induced developmental delay are in blue font and appear at the top of the table. Some compounds were detrimental to the health of the OP50 food source, affecting the results, and were therefore not counted. These are marked at the bottom of the table in red.