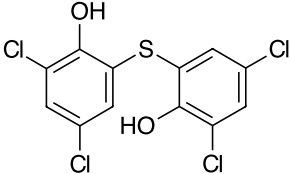
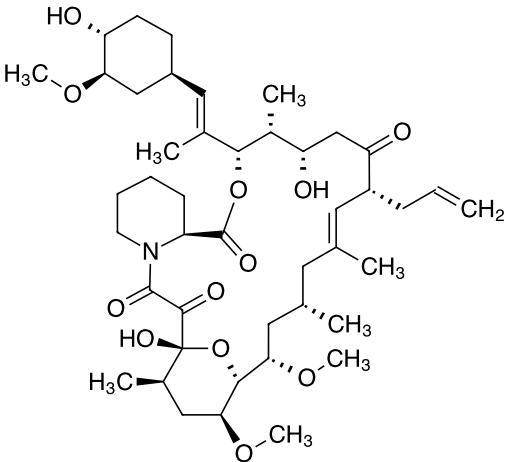
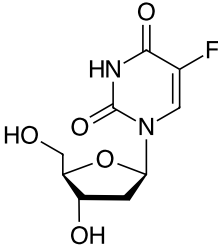
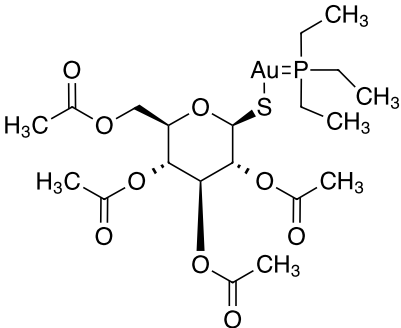
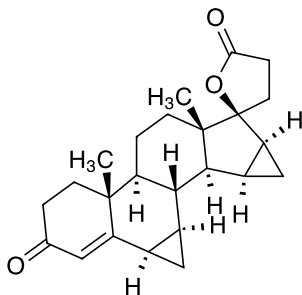


SUPPLEMENTARY TABLES

Table S1. Pharmacology of repositioned compounds.

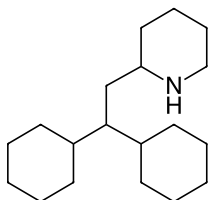
| Compounds | Pharmacology |
|---|---|
| <p>Bithionol [18]</p>  | <ul style="list-style-type: none"> • Halogenated anti-infective agent that is used against trematode and cestode infestations. • Inhibits human soluble adenylyl cyclase |
| <p>Tacrolimus [19]</p>  | <ul style="list-style-type: none"> • Inhibits calcineurin phosphatase activity, thus decreases cytokine production. • Exhibits immunosuppressive activity (more potent than cyclosporine). • Prevents T-lymphocyte activation in response to antigenic or mitogenic stimulation. |
| <p>Floxuridine [20]</p>  | <ul style="list-style-type: none"> • Fluorinated pyrimidine monophosphate analog of 5-fluoro-2'-deoxyuridine-5'-phosphate (FUDR-MP) with antineoplastic activity. • Inhibits thymidylate synthase, thus disrupting DNA synthesis. • Fluorouracil, the metabolized product, incorporates into RNA, which prevents the utilization of uracil in RNA synthesis. |
| <p>Auranofin [21]</p>  | <ul style="list-style-type: none"> • Inhibits the activity of mitochondrial thioredoxin reductase (TrxR) by interacting with selenocysteine within the redox-active domain. • Induces mitochondrial oxidative stress, thus resulting in the induction of apoptosis. • Inhibits the JAK1/STAT3 signaling pathway, hence suppresses the expression of immune factors involved in inflammation. |

Drospirenone [22]



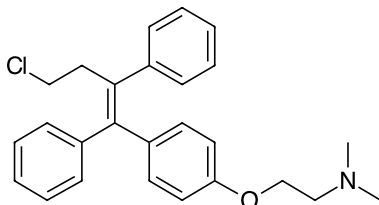
- Possesses progestational and anti-mineralocorticoid activity.
- Binds to the progesterone receptor, resulting in a suppression/inhibition of LH activity and ovulation (oral contraceptive).

Perhexiline [23]



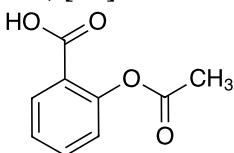
- Binds to the mitochondrial enzyme carnitine palmitoyltransferase (CPT)-1 and CPT-2.
- Shifts myocardial substrate utilization, viz., shifting from long chain fatty acids to carbohydrates via the inhibition of CPT-1 and CPT-2, thus used for the therapy in patients with ischaemia.
- May cause neuropathy and hepatitis.

Toremifene [24]



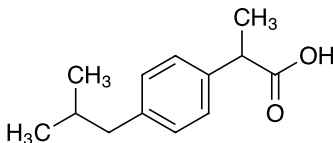
- Selectively modulates estrogen receptors by competitively binds to the receptors, thus interferes with estrogen activity.

Aspirin
(Acetylsalicylic acid) [25]



- Non-steroidal anti-inflammatory agent.
- Binds to/acetylates serine residues in cyclooxygenases.
- Decreased synthesis of prostaglandin, platelet aggregation, and inflammation.

Ibuprofen [26]

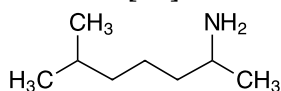


- An anti-inflammatory drug possessing anti-inflammatory, analgesic, and antipyretic activities.
- Inhibits cyclo-oxygenase I and II, thus results in a decreased prostaglandin synthesis.

Human glycogen synthase kinase 3 (GSK-3) inhibitors:
Tideglusib,
TDZD-8,
DIP-3.18

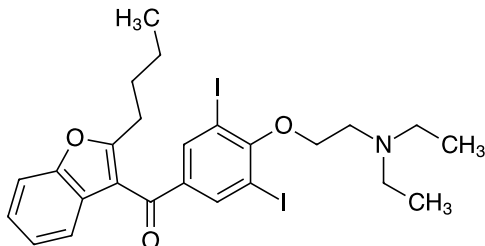
- Not available

Octodrine [27]



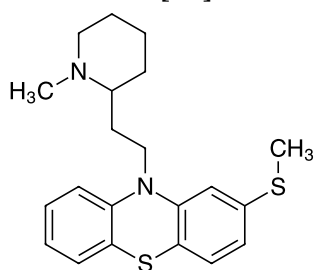
- Small molecule agonist of the estrogen related receptor (ERR) signaling pathway from Tox21 library screening.

Amiodarone [28]



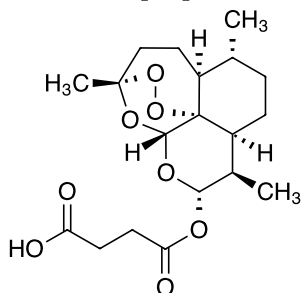
- A class III antiarrhythmic agent possessing antiarrhythmic and vasodilatory activities.
- Blocks the myocardial calcium, potassium and sodium channels, thus resulting in prolongation of the cardiac action potential and refractory period.

Thioridazine [29]



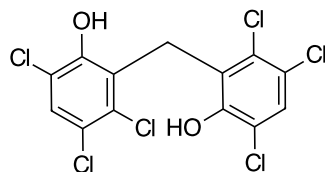
- Binds to dopamine receptors, thus blocking the actions of dopamine or other agonists.

Artesunate [30]



- Anti-malarial, anti-shistosomiasis, antiviral, and potential anti-neoplastic drug.
- Forms reactive oxygen species (ROS) and carbon-centered radicals, which damage parasitic organisms.
- Induces DNA breakage, arrests the cell cycle (G1 and G2/M phases), inhibits cell proliferation, and induces apoptosis via mitochondrial and caspase signal transduction pathways.

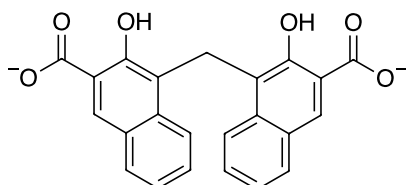
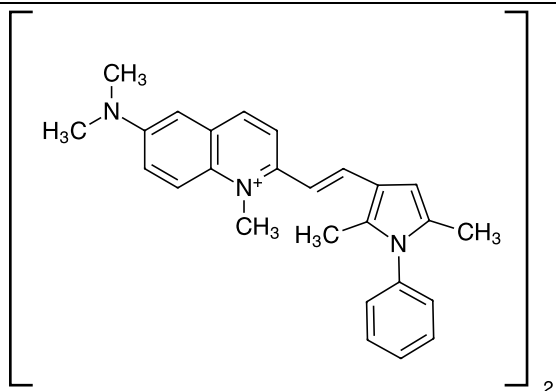
Hexachlorophene [31]



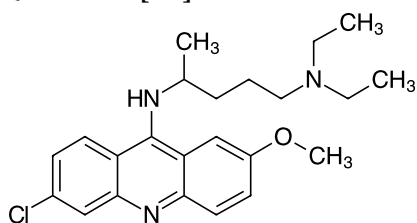
- A chlorinated bisphenol antiseptic agent with bacteriostatic activity.
- Active against gram-positive organisms, (Less effective against gram-negative bacteria).

Pyrvinium pamoate [32]

- Anti-parasitic agent (Used therapeutically for treating helminthiasis)

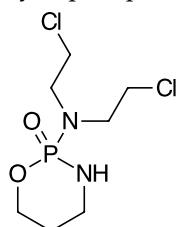


Quinacrine [33]



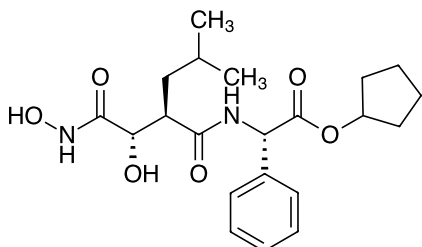
- Potential antineoplastic and antiparasitic agent.
- Inhibits the transcription/activity of nuclear factor-kappaB (NF-kappaB), thus inducing/restoring the expression of tumor suppressor p53, p53-dependent apoptotic pathways, tumor cell apoptosis, etc.

Cyclophosphamide [34]



- An alkylating agent possessing antineoplastic and immunosuppressive activities.
- The metabolized product phosphoramidate mustard binds to and crosslinks DNA and RNA, thus resulting in the inhibition of DNA replication and protein synthesis.

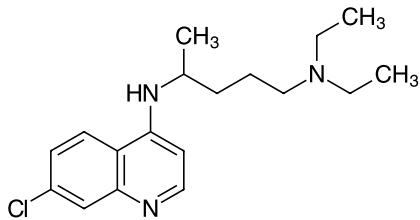
Tosedostat [35]



- An inhibitor of aminopeptidases (M1 family) possessing antineoplastic activity.
- Inhibits protein synthesis and enhances cancer cell death via the increase of Noxa (proapoptotic protein) level.

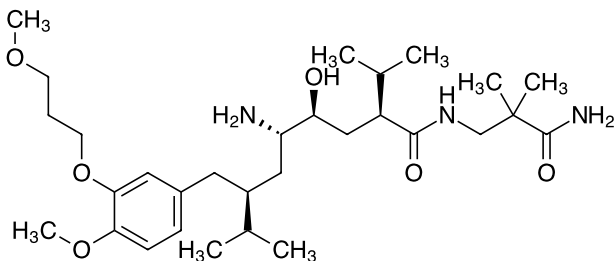
Chloroquine [36]

- An antimalarial, anti-inflammatory drug.
- Inhibits heme polymerase in parasites, thus accumulating toxic heme within the parasitic cell.



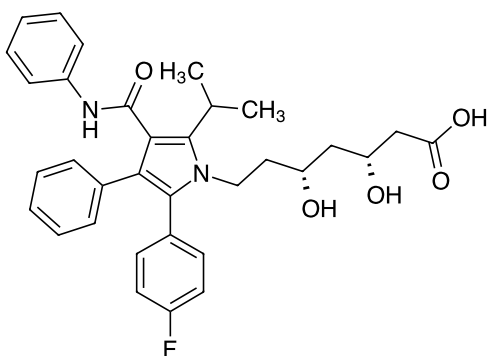
- May interfere with nucleic acid biosynthesis.
- Possesses chemosensitizing and radiosensitizing activities in cancer cell.

Aliskiren [37]



- Non-peptide renin inhibitor with antihypertensive activity.
- Selectively binds to the S3 sub-pocket of renin, thus preventing arterial vasoconstriction and inhibiting aldosterone production.

Atorvastatin [38]



- A lipid-lowering agent.
- Competitively inhibits hepatic hydroxymethyl-glutaryl coenzyme (HMG-CoA) reductase, thus lowers the levels of plasma cholesterol and lipoprotein levels.
- Modulates immune responses.

P21-activated protein kinase inhibitor

- Not available
-

Table S2. Examples of chemosensitizers targeting antioxidant or cell wall systems in fungi previously determined in the model yeast *Saccharomyces cerevisiae*.¹

| Compounds | Antioxidant targets⁵ | Cell wall targets⁵ | References |
|----------------------------------|--|--------------------------------------|-------------------|
| Octyl gallate | <i>yap1Δ</i> | <i>slt2Δ, bck1Δ</i> | [69] |
| <i>trans</i> -Cinnamaldehyde | <i>sod1Δ, sod2Δ</i> | ND ² | [59] |
| 2-Hydroxy-5-methoxy-benzaldehyde | <i>sod1Δ, sod2Δ</i> | ND ² | [59] |
| 2-Hydroxy-4-methoxy-benzaldehyde | ND ² | <i>slt2Δ, bck1Δ</i> | [70] |
| 3,5-Dimethoxy-benzaldehyde | <i>sod1Δ, sod2Δ, glr1Δ</i> | <i>slt2Δ, bck1Δ</i> | [59,70] |
| 2,5-Dimethoxy-benzaldehyde | <i>sod1Δ, sod2Δ</i> | <i>slt2Δ, bck1Δ</i> | [59,70] |
| 2,3-Dihydroxy-benzaldehyde | <i>sod1Δ, sod2Δ, glr1Δ</i> | ND ² | [76] |
| 4-Methoxybenzoic acid | ND ² | <i>slt2Δ, bck1Δ</i> | [70] |

¹Functions of gene products: Sod1, Cytosolic superoxide dismutase; Sod2, Mitochondrial superoxide dismutase; Glr1, Glutathione reductase; Slr2, MAPK of cell wall integrity system; Bck1, MAPKKK of cell wall integrity system.

²Not determined