Improving the Efficacy of Amine Containing Medicines: A Computational Approach

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In this computational study, approximately 150 well known medicinal agents, from malaria drugs to cancer treatments, are examined as candidates for improving their efficacy, by increasing their water solubility. Each of these agents contain an amine. As opposed to other approaches, such as liposomes, nanoparticles or proteins, this study will show that a number of drugs can have improved water solubility, thereby offering better treatment efficiency by binding the amine structure to a specific cation in the correct molecular location.   The ratio of the molecules' dipole moment (D; Debye) to molecular volume (V; A^3) or its D/V ratio when unbound compared to the bound complex is used to make the physiological argument.
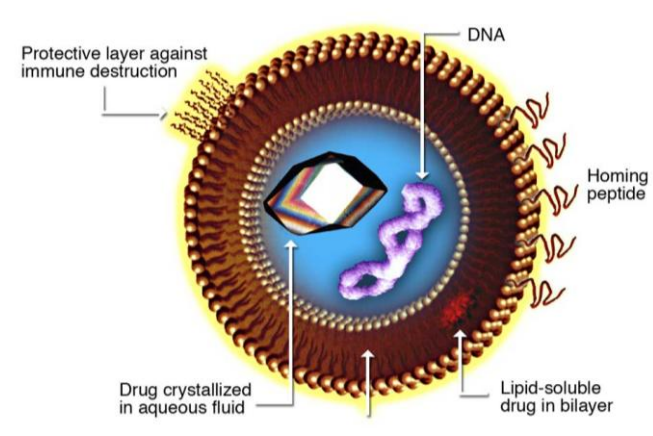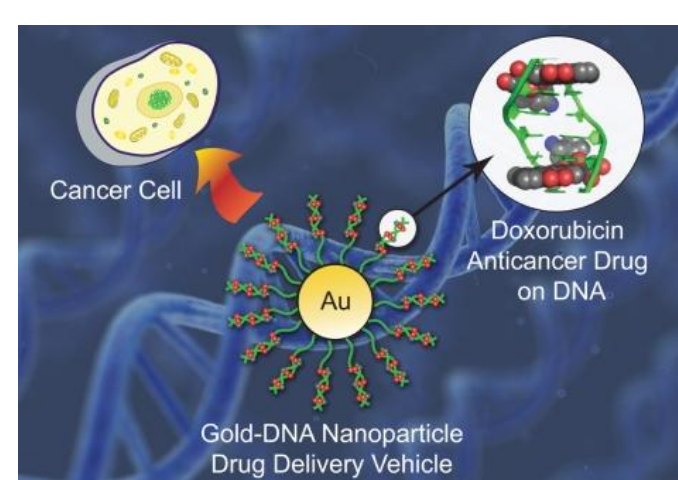
Other Drug Transport Systems:

- **Liposomes**: their natural chemical composition, controllable pharmokinetics, and their ability to protect encapsulated drugs allows for drug delivery across cell membranes.

- **Nanoparticles**: can deliver drugs that would not normally be able to cross certain membranes in vivo. They can also target the drugs towards specific cells and organs.
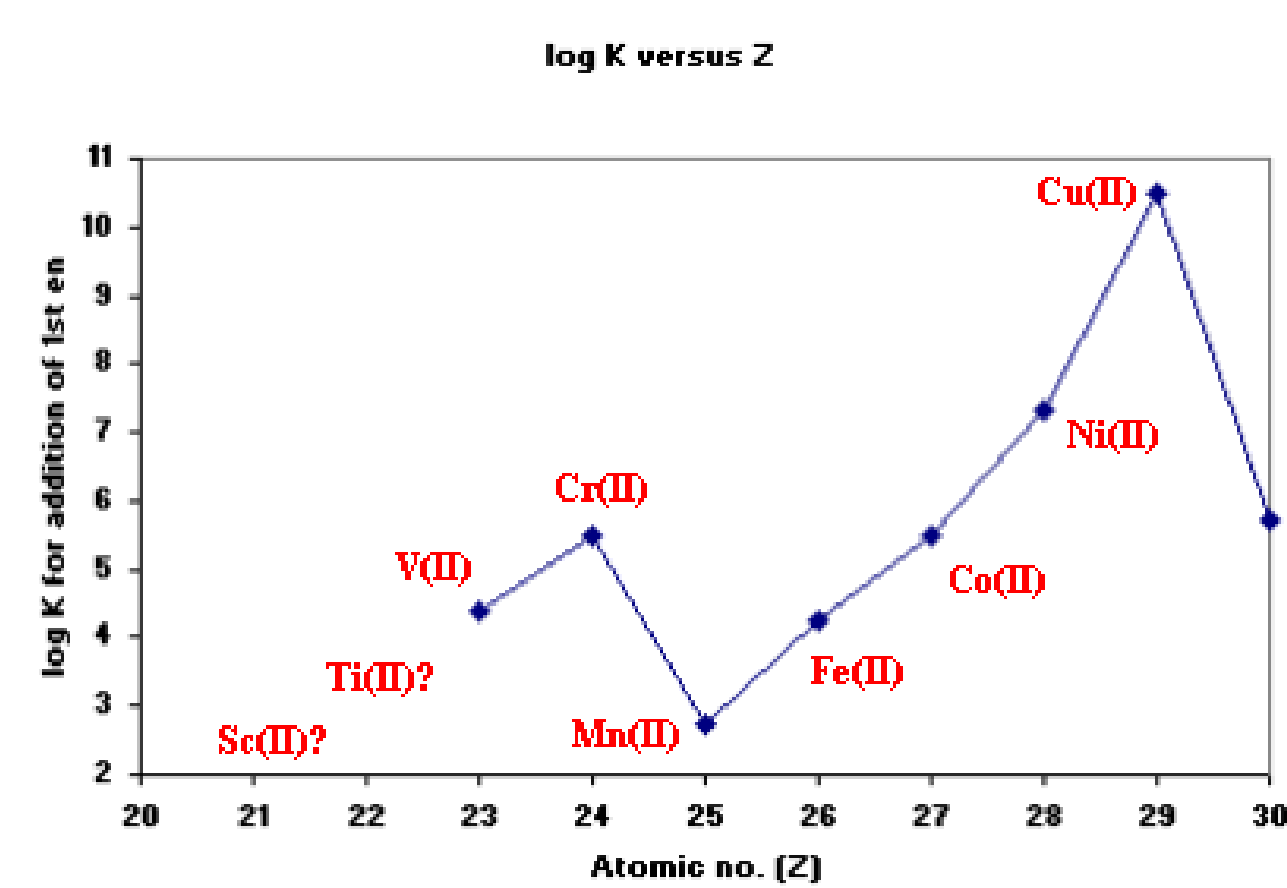

- **Proteins**: proteins ,such as albmunin, facilitate uptake of the drug and offer a degree of selectivity. Abraxane is albumin-bound paclitaxel, which is used to treat breast cancer.
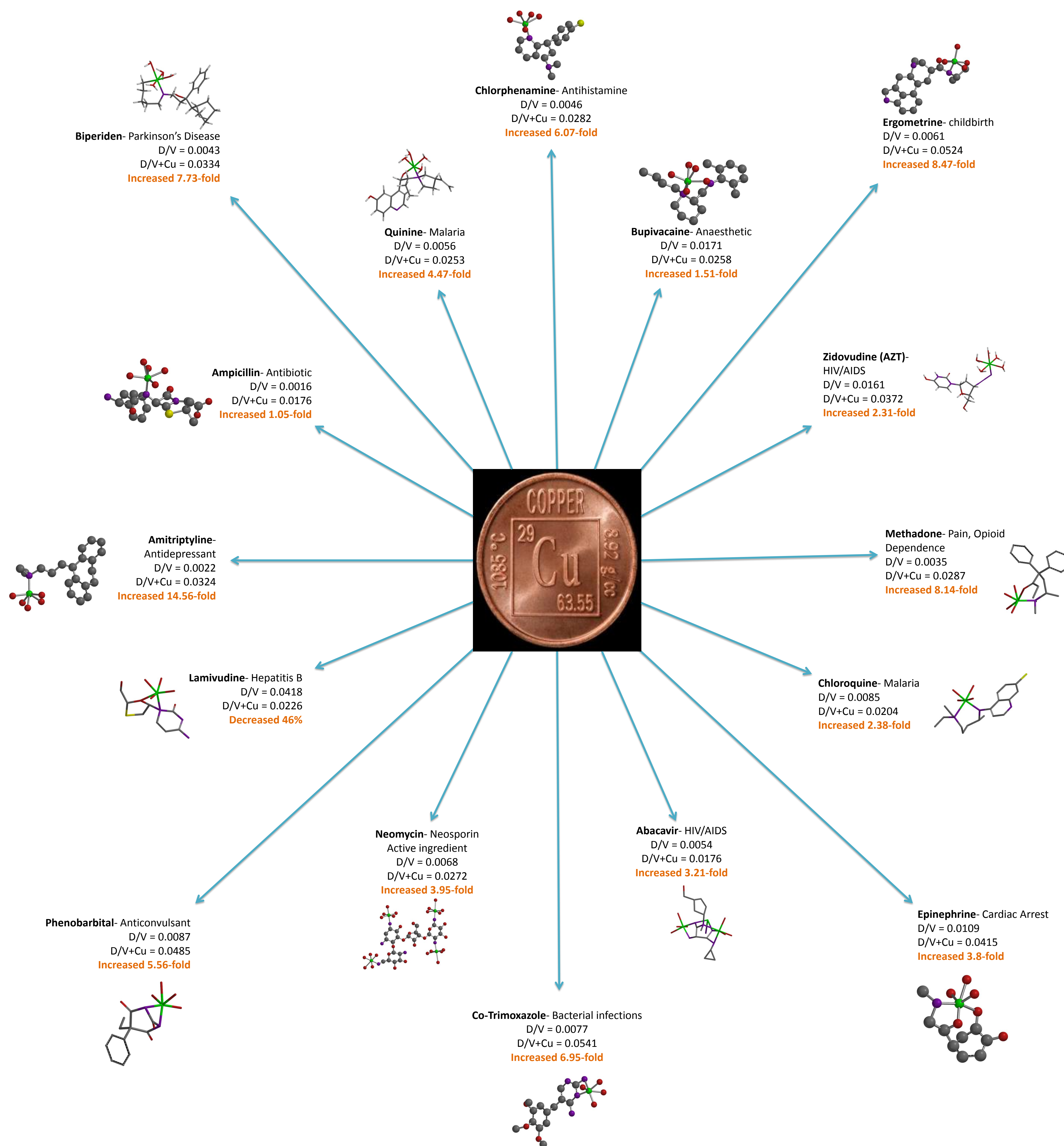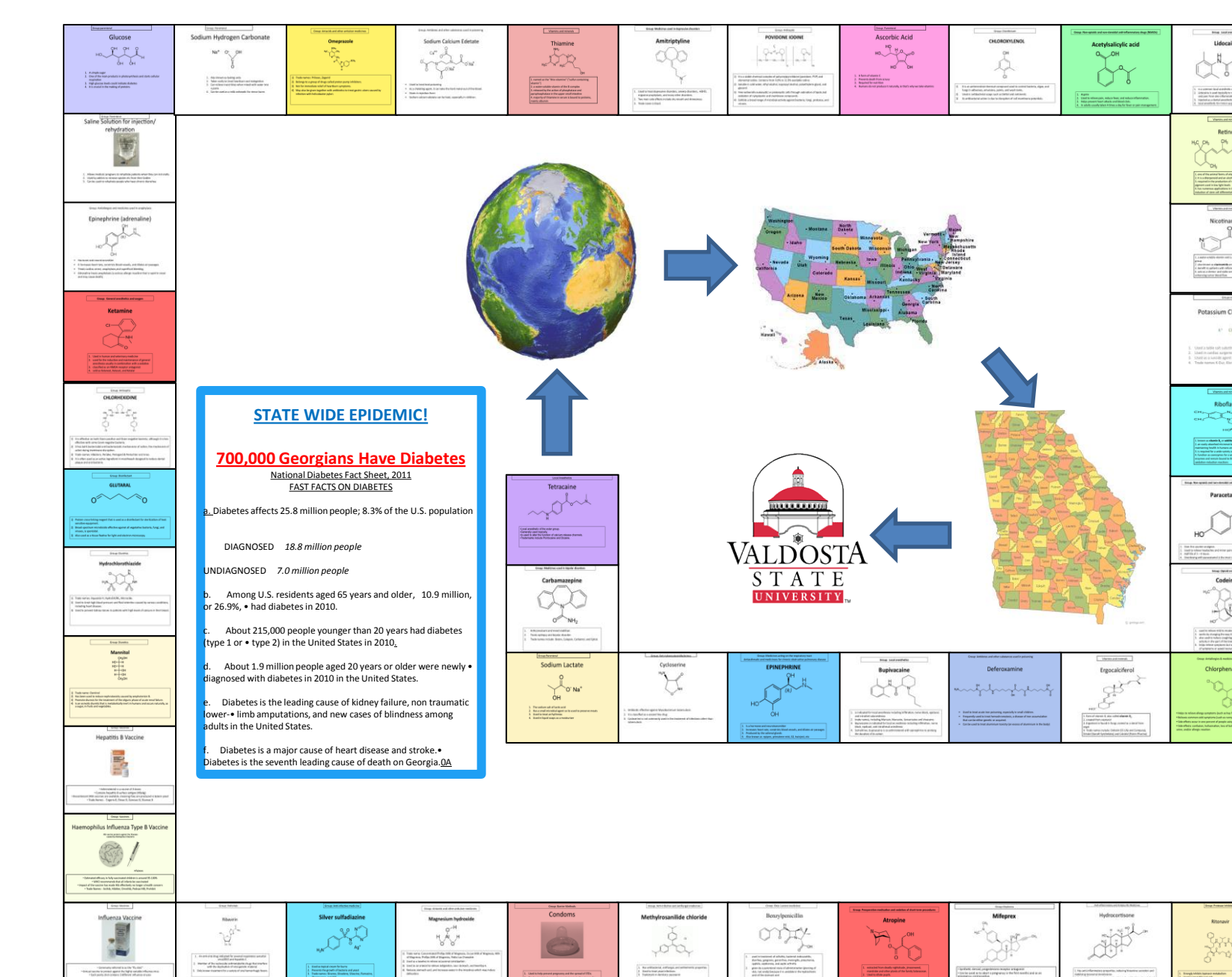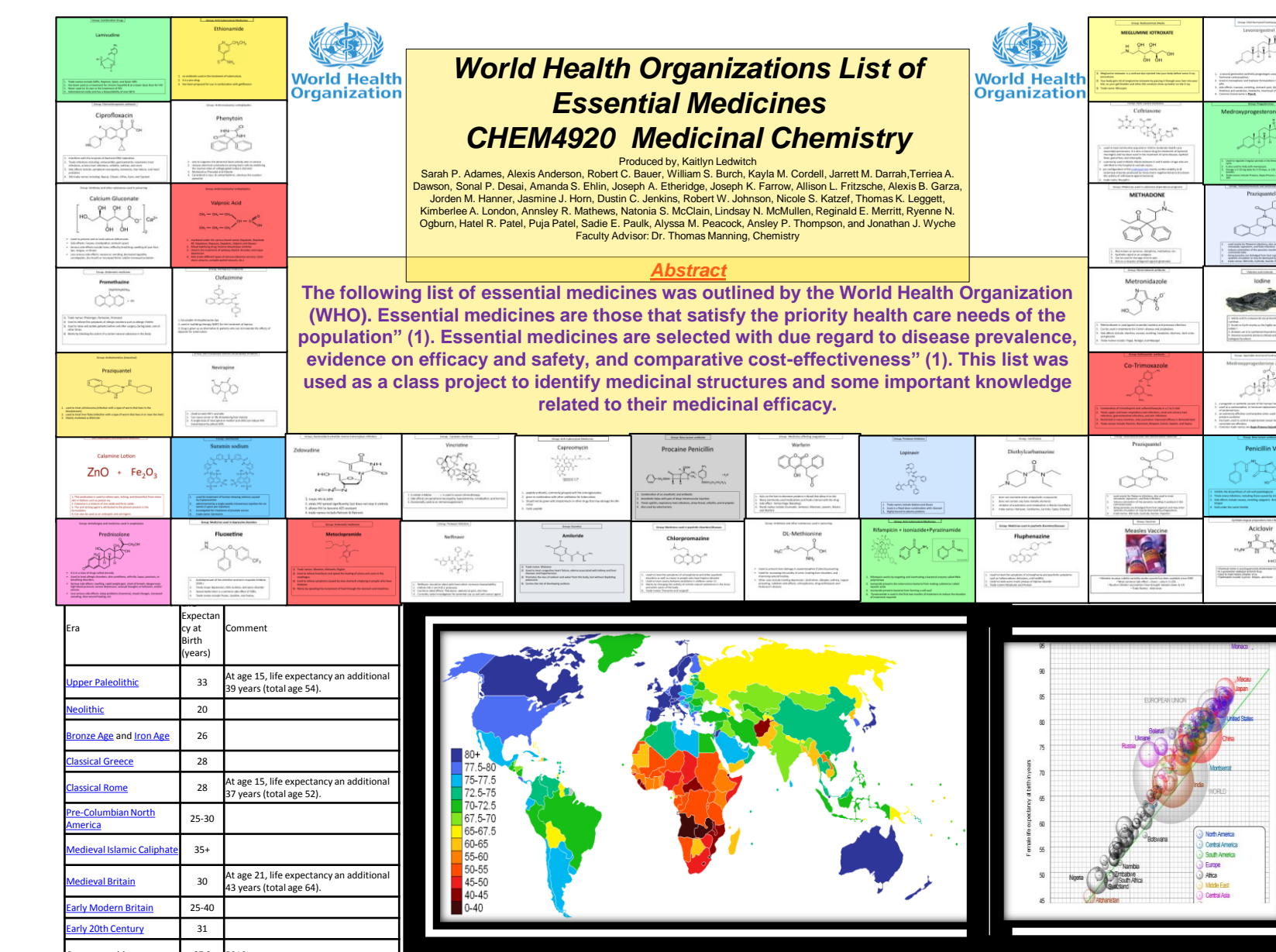

Why Copper?

Compared to other first-row transition metal ions, the octahedral Cu(II) ion is much more stable when bound to a ligand containing nitrogen. Binding Cu(II) to the amine group of a drug often times increases its water solubility, thus improving the efficacy of the drug.

log K versus Z

Biperiden- Parkinson's Disease
D/V = 0.0043
D/V+Cu = 0.0334
Increased 7.73-fold

Chlorphenamine- Antihistamine
D/V = 0.0046
D/V+Cu = 0.0282
Increased 6.07-fold

Ergometrine- childbirth
D/V = 0.0061
D/V+Cu = 0.0524
Increased 8.47-fold

Quinine- Malaria
D/V = 0.0056
D/V+Cu = 0.0253
Increased 4.47-fold

Bupivacaine- Anaesthetic
D/V = 0.0171
D/V+Cu = 0.0258
Increased 1.51-fold

Ampicillin- Antibiotic
D/V = 0.0016
D/V+Cu = 0.0176
Increased 1.05-fold

Zidovudine (AZT)- HIV/AIDS
D/V = 0.0161
D/V+Cu = 0.0372
Increased 2.31-fold

Amitriptyline- Antidepressant
D/V = 0.0022
D/V+Cu = 0.0324
Increased 14.56-fold

Methadone- Pain, Opioid Dependence
D/V = 0.0035
D/V+Cu = 0.0287
Increased 8.14-fold

Lamivudine- Hepatitis B
D/V = 0.0418
D/V+Cu = 0.0226
Decreased 46%

Chloroquine- Malaria
D/V = 0.0085
D/V+Cu = 0.0204
Increased 2.38-fold

Neomycin- Neosporin Active ingredient
D/V = 0.0068
D/V+Cu = 0.0272
Increased 3.95-fold

Abacavir- HIV/AIDS
D/V = 0.0054
D/V+Cu = 0.0176
Increased 3.21-fold

Phenobarbital- Anticonvulsant
D/V = 0.0087
D/V+Cu = 0.0485
Increased 5.56-fold

Epinephrine- Cardiac Arrest
D/V = 0.0109
D/V+Cu = 0.0415
Increased 3.8-fold

Co-Trimoxazole- Bacterial infections
D/V = 0.0077
D/V+Cu = 0.0541
Increased 6.95-fold

World Health Organization List of Essential Medicines- Approximately 140/320 drugs contain an amine group.