

Homeopathy should **not** be used or promoted for the treatment of HIV positive patients

Dr D R Walwyn

Conflict of Interest Statement

- I do not sell medicines of any kind
- I work in pharmaceuticals research (iThemba Pharmaceuticals)
 - my professional activities cover drug discovery/development for the treatment of neglected diseases, especially HIV, TB and malaria
- I am interested in all medicines

Framework for Meds Evaluation

- My framework of analysis for all therapeutic interventions (allopathic and TCAM) is :
 - evidence-based efficacy (clinical evidence)
 - proven safety
 - consistent/reliable/measurable quality
 - preferably a clearly established mechanism of action

TCAM = traditional, complementary and alternative medicines

What is the Context?

- Global growth in use of TCAM driven by ...
- Ignorance of the psycho-cognitive aspects of healing (the placebo effect)
 - believing in your practitioner is important
 - believing in yourself (as important)
- The demise of evidence-based decision making and the rise of relativism
 - the age of enlightenment has been dimmed
 - all viewpoints are equally valid

TCAM Use; Significant or Small?

- In USA^{1,2}:
 - overall TCAM usage 38% of adults @ \$34 billion
 - 69% of HIV-infected patients regularly used herbs, vitamins or dietary supplements
 - 45% visited a TCAM provider average of once per month; average out of pocket expenditure \$938 p.a.
 - 81% (of the 68%) believe the therapies were useful
 - 40% of USA citizens are known to use TCAM
- In the South African study³
 - 50 to 60% of PLWH take traditional medicine
 - close to 50% of PLWHA believe traditional remedies are safer than Western medicines
 - 60% believe that herbs control their HIV rather than ARVs
 - 66% believe that they would not be able to live without traditional medicines

¹Fairfield et al Arch Intern Med, 158(9): pp 2257-2264 (1998)

²Bormann et al J. Ass. Nurses AIDS Care, 20(6): pp 468-480 (2009)

³Ramlagan et al, Poster 17th AIDS Conference, Mexico (2008)

What about Homeopathy?

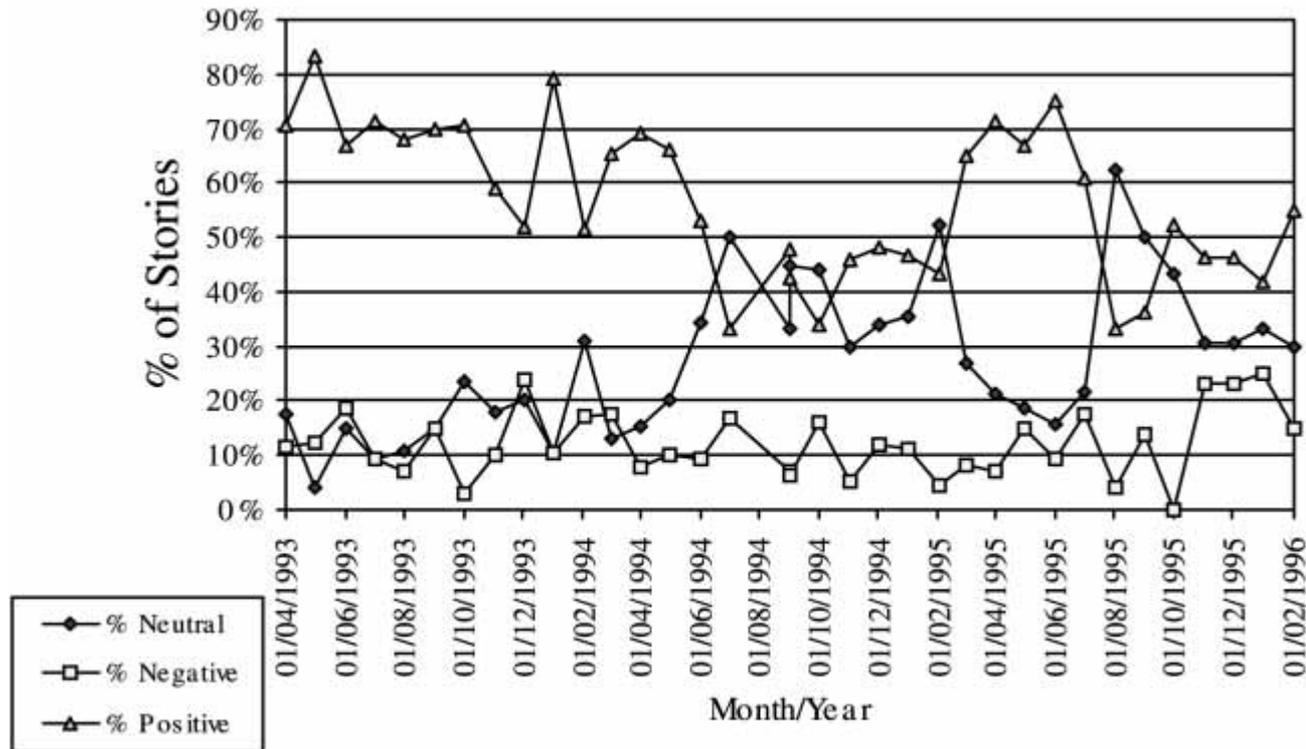
- 300 million people worldwide use homeopathic medicines
- In 1998, proportion of the total population using homeopathy¹
 - France 38%
 - Germany 34%
 - Netherlands 38%
 - USA 12%
- In 2007 in USA²
 - 3.4 million patient visits to homeopaths by 862,000 persons (2.3% of population)
 - out-of-pocket expenditure \$2.9 billion
- Top drugs
 - Sulph, Lyc, Nux V, Calc, Med, Ars,

¹Borneman, British Homeopathic Journal 90, 204–213 (2001)

²Nahin et al, National Health Statistics Reports, 18 (2009)

Homeopathy in the Media (USA)

- I am in the minority!



Outline of Argument

- Homeopathy fails in two major respects
 - little or no clinical evidence of benefit for PLWHA
OVER AND ABOVE THE PLACEBO EFFECT
 - its two major premises breach basic principles of medicine/pharmacology
- Lack of regulation of TCAM is a problem

PLWHA = people living with HIV/AIDS

Homeopathy and Clinical Evidence

- Origins of homeopathy date back to 1700s; three hundred years of ‘clinical trials’
 - danger of anecdotal validation
- The placebo effect is real (and not equal to zero)
- Many clinical trials (randomised, double blind, placebo controlled) indicate placebo effect only
 - results are variable and highly dependent on the indication

RDBCT = randomised, double blind, placebo controlled clinical trial

Reviews of Homeopathy Clinical Trials

- Several extensive meta-analysis of published data
 - We have found insufficient evidence that homeopathy is clearly efficacious for any single clinical condition¹
 - 186 trials reviewed, 119 met criteria, 89 adequate data
 - There is some evidence that homeopathic treatments are more effective than placebo; however, the strength of this evidence is low because of the low methodological quality of the trials.²
 - Studies of high methodological quality were more likely to be negative than the lower quality studies. Further high quality studies are needed to confirm these results

¹Linde et al, The Lancet ,350: 884-43 (1997)

²Cucherat et al . European Journal of Clinical Pharmacology, 56: 27–33 (2000).

“Homeopathy Higher than Placebo”

- Cough
- Rheumatoid arthritis
- Cramps
- Agitation
- Notable failures for pain, infectious diseases, osteoarthritis, others

Government Reviews

- 2010 evaluation by the British House of Commons Science and Technology Committee declared
 - homeopathy was no more efficacious than a placebo.
- Australia's National Health and Medical Research Council said
 - although homeopathy was not harmful in its own right, it might pose a risk to patients if safe and efficacious conventional treatments were delayed in favour of homeopathic treatments

Dr Freckleton (Melbourne Barrister)

- Case of Perth woman Penelope Dingle, who died from bowel cancer in 2005 after spending about \$30,000 on unsuccessful homeopathic treatments, including extracts from the venus flytrap plant.
- Homeopaths had used crushed-up pieces of the Berlin Wall to treat depression.
- In the latest edition of the journal Spectrum of Homeopathy, the authors detailed the use of wolf's milk for eczema and bulimia, cheetah's blood for multiple sclerosis and tiger's blood for depression.

DBPCT, HIV and Homeopathy

- Evaluation of the immuno-modulatory role of homeopathy in HIV¹
 - four arms
 - 50 subjects stage II and III (two arms, two groups per arm)
 - 190 days on individualised treatment
 - Elevation of CD4+ T cells seen in stage III (400 to 500)
 - no viral loads

¹Rastogi et al, British Homeopathic Journal , 88: 49-57 (1999)

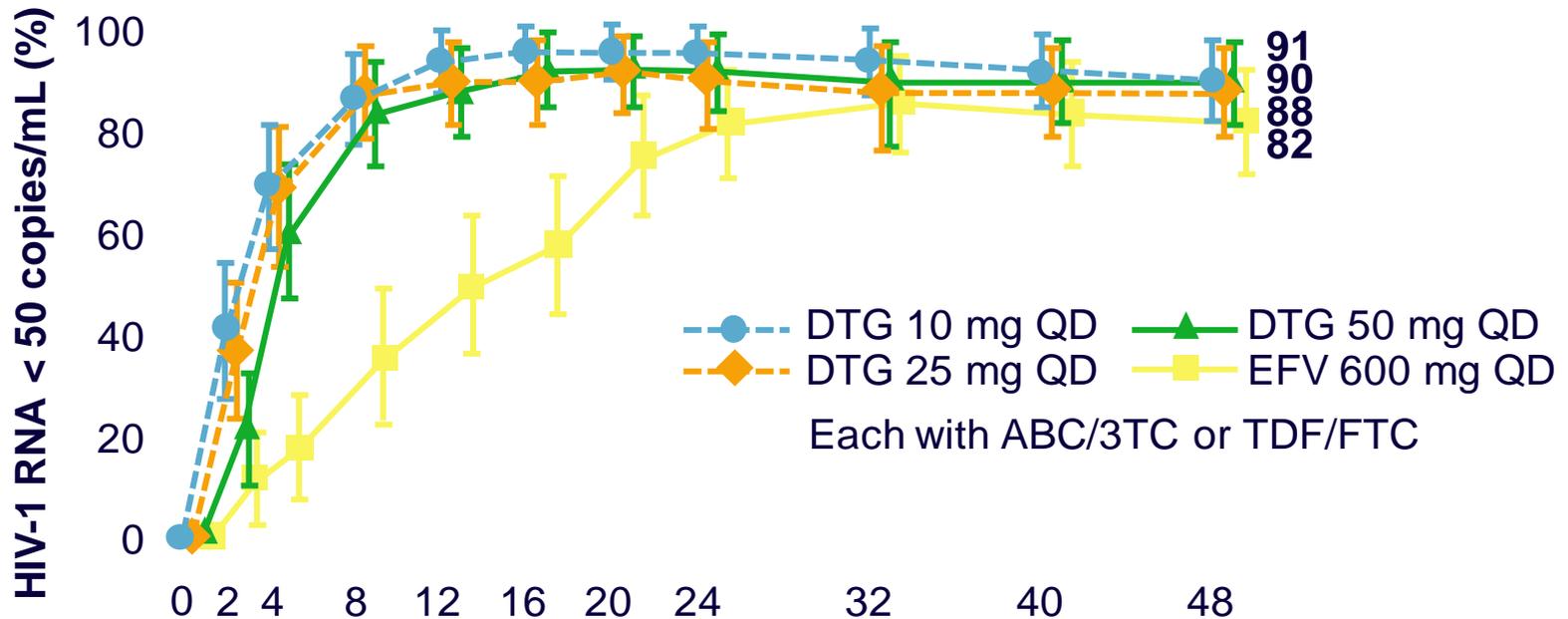


Non-Individualised Treatment

- A randomized placebo-controlled study during 1995-1997 to ascertain the treatment efficacy involved 39 people prescribed homeopathic medicines (Amyle Nitricum-30CH and Azadirachta indica-6X)
- The individuals also underwent physical and breathing exercises, besides half ounce of honey and 30 grams to 50 grams of moong dal (green gram) sprouts in their daily regimen.
- At the end of each month, the individuals tested remained “asymptomatic”
- No viral loads or CD4 (accepted surrogate markers for anti-HIV efficacy)!

Allopathic Medicine Trials

- Is this really too difficult for homeopaths (weeks to viral load below 50 with dolutegravir)?



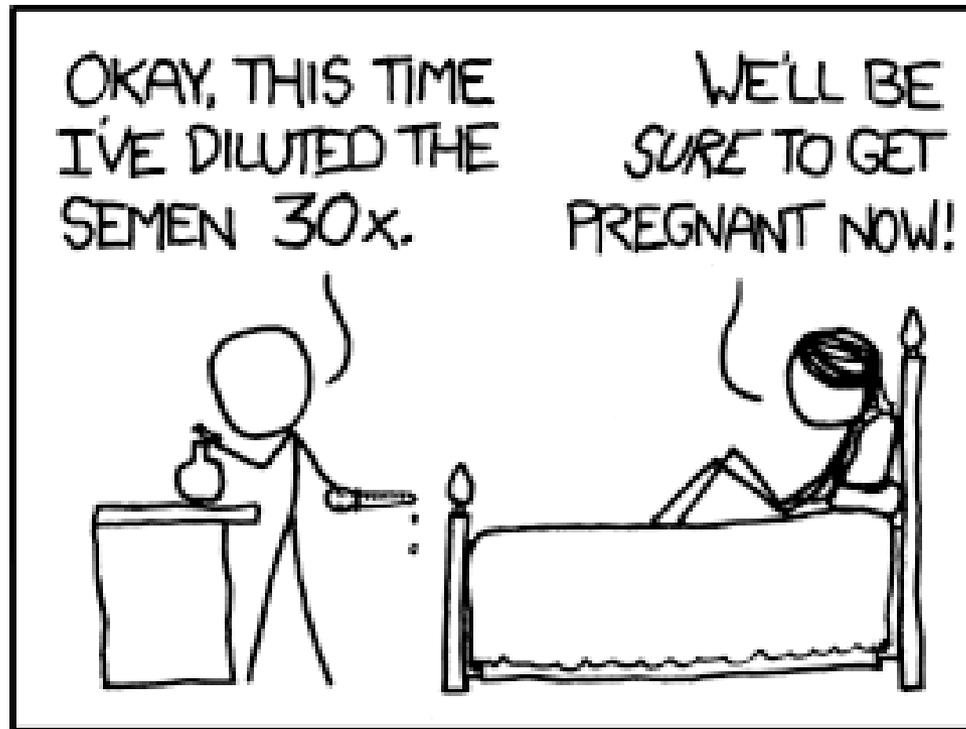
Homeopathy and HIV

- Good patient healthcare provider relationship can improve health outcomes!
- High levels of depression/hopelessness among HIV positive patients
- Advice on diet/lifestyle is essential
- .. but, healthcare is more than just sensible advice and compassion

Homeopathy and Pharmacokinetics

- Two basic principles (“similars” and “potencies”) unproven, neither is there a plausible hypothesis
- Similars:
 - patients with particular signs and symptoms can be cured if given a drug that produces the same signs in a healthy individual
- Potencies or theory of infinitesimals:
 - the more dilute, the more powerful the remedy, described as ‘potentisation’ (Hahnemann)
 - some remedies 30C (thirty times a 1 in 100 dilution)
 - at 12C, one litre of water would contain only ‘0.6’ molecule!
 - conflicts with standard PK principles including dose response curves

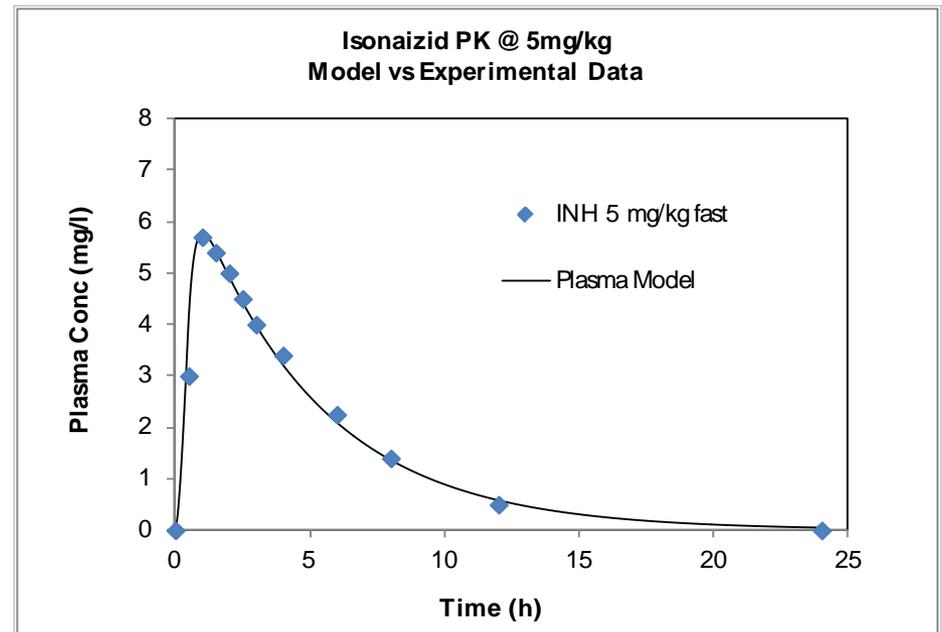
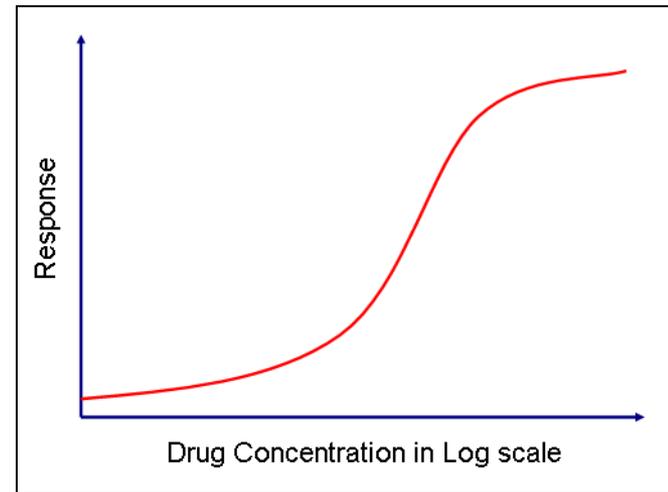
Infinitesimals and Infertility



BELIEF IN HOMEOPATHY IS NOT,
EVOLUTIONARILY, SELECTED FOR.

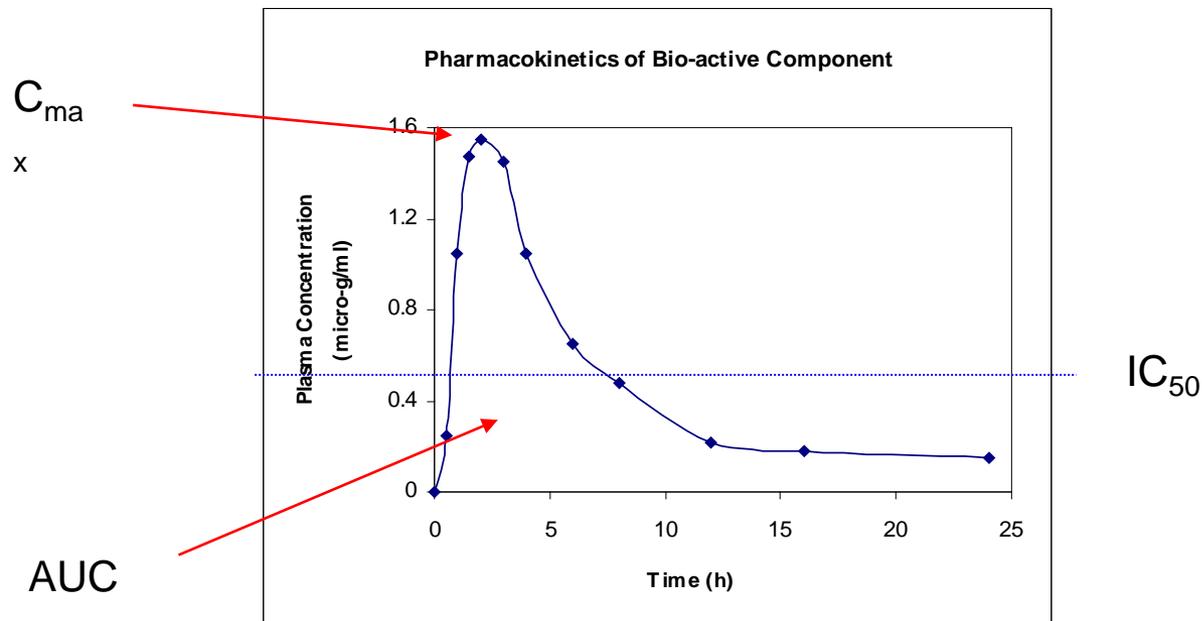
Pharmacokinetics – A Primer

- Dose response curve
 - correlation between dose and pharmacological response
 - the more dilute, the lower the effect of the medicine
- Plasma level-time curve
 - C_{max} , t_{max} , AUC



What Makes an Effective Drug?

- Low IC_{50}
- High *in vivo* absorption (C_{max} relative to dose) and metabolic stability (AUC) (see concentration-time curve)

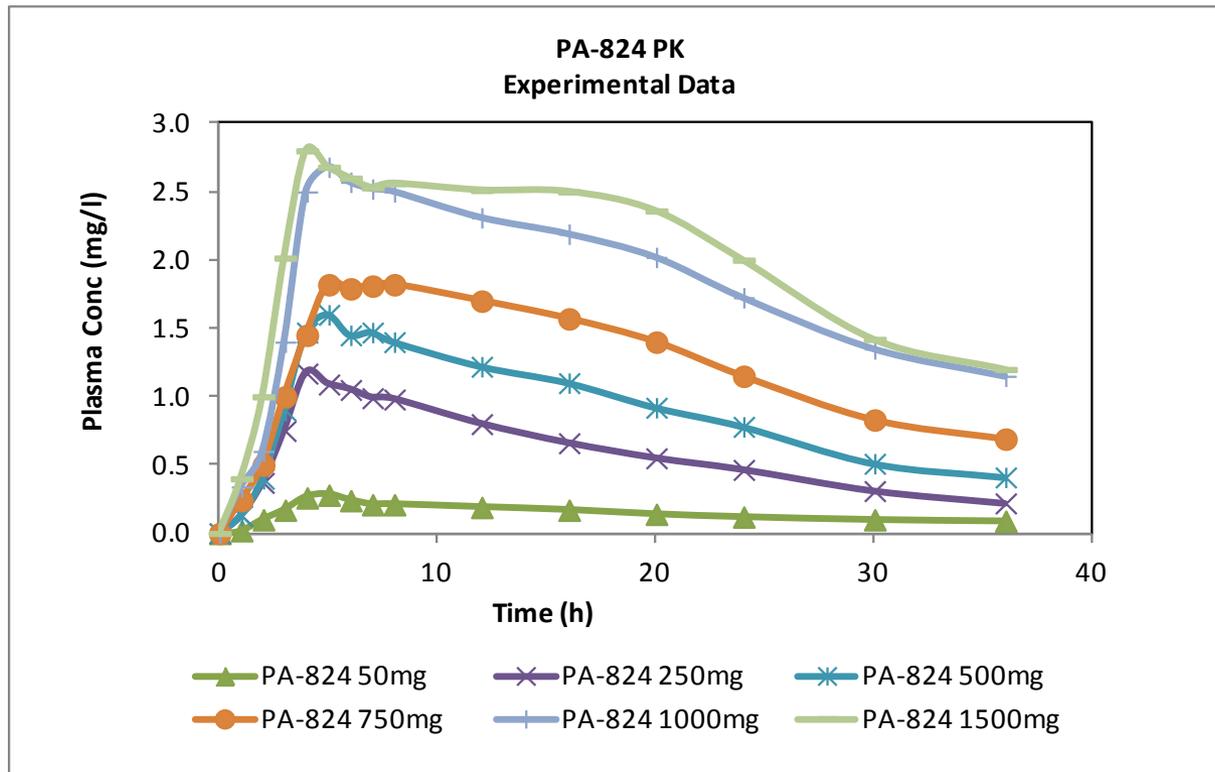


General Properties of Medicines

- 'small molecules' (MW < 600)
- relatively insoluble in water (bind to hydrophobic proteins)
- highly active ($IC_{50} < 0.1 \mu\text{M}$)
- bioavailability > 25%
- typical dose 25 to 600 mg per day

PA-824

- Experimental TB drug with saturation PK



¹Ginsberg et al, Antimicrobial Agents and Chemo, 3720–3725 (2009)

Rilpirivine

- Rilpirivine IV once per week¹
- C_{\max} is proportional to the dose

Dose (mg)	C_{\max} (ng/ml)
300	52
600	98
1200	155

¹Presentation from Jackson et al ,CROI (2012)

The Active Ingredient in Homeopathy

- Even the most hyper-sensitive analytical techniques have failed to detect an active ingredient in the most 'powerful' homeopathic medicines
 - many attempts to prove the hypothesis of potentisation but all have failed
 - the active ingredient is even more extreme if one considers plasma concentrations
 - Search the literature for PK and homeopathy; what do you find?
- The active ingredients vary from sodium sulphate(!) to plant extracts

Herbal Extracts (Echinacea, etc)

- Typical dose ~ 10 drops = 500mg
 - Concentration ~ 1% = 5 mg plant extract
 - Active ingredients 0.1 to 1% of total (no dilution!)
= 5 to 50 μg
 - @ 50 μg , 100% bioavailability & volume of distribution 5 litres, plasma concentration is 0.02 μM
 - Most natural products have $\text{IC}_{50} > 1 \mu\text{M}$
- in general, natural products are insufficiently active to exert a biological effect (not drug-like)

Time for a Cup of Coffee!

- widely consumed herbal medicine (or toxin?)
 - 100 mg caffeine in a cup of coffee
 - plasma levels of caffeine reach about 5 mg/l = 25 μ M
 - caffeine IC_{50} 5 to 500 μ M
- coffee can have a pharmacological effect based on a plausible mechanism of action

Chinese Traditional Medicines

- In China, the number of people who use TCMs is three times the whole population of America, so there's plenty of people in the world that use them quite happily already!?
 - study has shown limited bioavailability of active ingredients¹
- Jeremy Nicholson²: “the microbiome produces lots of molecules, many which are drug like. So things that influence the microbiome can basically act by changing (the signalling in) your metabolic processes and that is a pretty new discovery”
- Many ingredients in traditional herbal medicines cannot be absorbed by the human gut. Could our microbial inhabitants do for us what we can't do ourselves?
 - Biotransformations
 - Cellular excretions and signalling

¹James Mitchell Crow, Nature, 480, pp S88–S89 (2011)

²Nicholson, Nature podcast (2011)

HIV and Mechanism of Action

- HIV is a virus which causes AIDS
- HIV targets immune cell which carry CD4 receptors (T cells and others)
- Resultant death of these cells causes immune deficiency
- Pathogenesis to AIDS is slow, although initial T cell reduction is rapid
- Elite controllers and LTNP exist!

HAART

- Antiretrovirals follow the classic allopathic medicine model
 - known mechanism of action (various)
 - optimised initially for *in vitro* efficacy
 - then developed to ensure *in vivo* efficacy and safety
 - clinical trials with appropriately designed surrogate markers

Lack of Regulation is a Problem

- Unorthodox practices abound in the TCAM sector
- Even registered homeopaths show little respect for the biomedical evidence and information about HIV
- Compounds the legacy issues around HIV and its treatment (the garlic and beetroot cadre)

Homeopaths on the subject of HIV/AIDS

- From various internet sites:
 - “the only medicine an HIV/AIDS patient needs is his own powerful immune system”
 - “the true treatment of all derangements involves addressing the disorder at the subtle dynamic level instead of mere gross palliation”
- Dr Peter Chappell (developed PC1)
 - I don't reveal the whole process and that is a cause of concern and debate within the team that now works with PC remedies.

Chappell 2 (2010)

- “C Resonances are made by imprinting specific information into water, which has the ability to memorize and store information, as is the case with all homeopathic remedies diluted beyond Avogadro’s number. “
- “The information regarding the totality of the symptoms of a disease and its role and purpose is gathered from a range of sources. This information is synthesized into a totality and imprinted into water by a proprietary process. “
- “Pure water containing some 96% medical alcohol as a preservative, in sealed dropper bottles, is used in the manufacturing process and these bottles stay closed during the whole process.”

Summary

- Homeopathy for the treatment of HIV lacks both clinical evidence and a plausible hypothesis
- Homeopathy for the treatment of HIV co-morbidities lacks evidence and/or are inferior to allopathic treatments
- The two central principles of homeopathy (similars and potencies) are illogical
- Homeopathy is best described as a belief system rather than a system of medicine

Homeopathy should NOT be used or promoted for the treatment of HIV-positive patients

From Noam Bar!

- I've seen (in Maun) homeopathy being very effective in treating:
 - the emotional effects of being HIV positive
 - physical symptoms that relate to the infection
 - side effects from conventional treatment (nausea, diarrhea, peripheral neuropathy, liver deficiency, fatigue etc)
- I've also seen homeopathy help patients who have not reached the threshold of needing antiretroviral treatment. By keeping patients healthy and balanced homeopathy might slow disease processes down but it **CANNOT REPLACE ANTI-RETROVIRALS IF YOU NEED THEM.**