



The role of herbal medicine in combating antimicrobial resistance

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Synergy

vital in combating AMR

- Medicine increasingly using combination therapies to combat many serious diseases e.g. TB, HIV-AIDS and malaria. The use of drugs in combination means reduced incidence of developing resistance to any of the drugs used.
- Synergy an essential characteristic of herbal medicines. Every plant is an orchestra of chemicals and combinations of herbs used in all herbal traditions e.g. TCM, Tibetan, Ayurveda and Western herbal medicine.
- Herbal synergy occurs at pharmacodynamic (what the drug does to the body) and pharmacokinetic (what the body does to the drug) levels.
- Multi-targeting increases efficacy and reduces

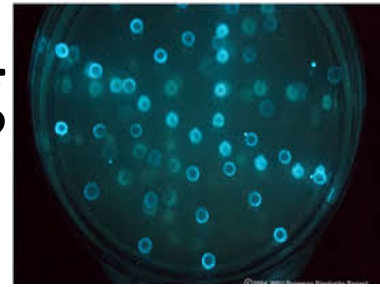
Synergy

Synergy may be combined effort that more than the sum of enhanced result of two working together as cooperative interaction

Mechanisms via which herbal medicines exert antimicrobial effect

- Phytochemical **attack on the bacterial cell wall** e.g. carvacrol - a phenol in oregano and thyme breaches defensive cell membrane enabling the bacteria to be destroyed.
- **Inhibition of enzymes** generated by bacteria for the deactivation of antibiotics e.g. epigallocatechin gallate (EGCg) in green tea and carob. EGCg also shown to damage the cell wall of bacteria... i.e. has a multi-action v bacteria.
- **Disabling the efflux pumping system** developed by bacteria to prevent antibiotics penetrating into the bacteria e.g. baicalein, a cell-permeable flavone, in thyme and *Scutellaria* species reverses MRSA resistance to ciprofloxacin by inhibiting efflux pump.

More mechanisms having antimicrobial effect



- **Inhibiting quorum sensing** i.e. bacterial signalling that enables bacteria to coordinate defence against compounds toxic to the bacteria. Bacteria use quorum sensing to coordinate activity such as biofilm formation, virulence, and antibiotic resistance, based on the local density of the bacterial population. Quorum sensing can occur within a single bacterial species as well as between diverse species.
- Blocking the QS systems helps reduce virulence of bacteria and prevent the formation of biofilms by which bacteria form a protective matrix around their colony and excrete a glue-like substance that can anchor them to all kinds of material – most significantly animal tissue.
- Garlic, ginseng, cranberry and cinnamaldehyde (gives cinnamon its taste) shown to inhibit QS.

Still more mechanisms

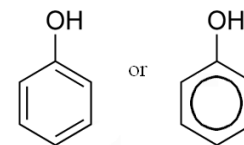
- Essential oils in many medicinal herbs/spices have antifungal effect via **membrane disruption and disruption of mitochondria** e.g. dill, clove and tea tree oil.
- Antiviral effects of herbs and spices shown to function by indirectly suppressing virus proliferation by **regulating the hosts' immune systems** and also by **directly inhibiting virus proliferation** through targeting viral proteins essential for the viral life cycle e.g. *Isatis tinctoria*



Plant chemicals have antibiotic properties



- In general, medicinal plants more effective against gram-positive than gram-negative bacteria.
- Main antibacterial constituents in medicinal plants are phenols. Plants appear to synthesize phenolic compounds in response pathogen and insect attack, UV radiation and wounding.
- Phenols from spices active against *Staph. aureus*, *Bacillus cereus*, *E. coli* & *Salmonella*. Flavonoids are largest group of phenols.



- Non-phenolic constituents of EOs of oregano, clove, cinnamon, garlic, coriander, rosemary and sage effective against gram-positive and gram-negative bacteria.

Ineffective antimicrobials combined with herbs can regain potency

- Berberine (alkaloid found in many plants eg *Berberis vulgaris*) combined with antibiotics levofloxacin and azithromycin recently ineffective v Methicillin-resistant *Staphylococcus aureus* (MRSA) resulted in the reactivation of the antibiotics. (Zuo GY et al 2012)
- Synergistic interaction between EGCg and antimycotics such as amphotericin B and fluconazole has been reported against *C. albicans*. (Hemaiswarya et al 2008)
- *Nigella sativa* and omeprazole compared favourably to triple therapy in eradication of *Helicobacter pylori* in 88 patients with dyspepsia and positive H. pylori test. (Salem et al 2010)

Use of herbal medicine reserves synthetic antibiotics for severe cases

- Many common ailments such as sinus problems, sore throats, simple urinary tract infections and superficial wounds do not necessitate antibiotics in most cases.
- These can be effectively treated with appropriate diet and lifestyle changes and expert botanical medicine care by trained herbalists.



Pelargonium sidoides

root



- Native to South Africa
- Comprehensive systematic review concluded that strong scientific evidence (includes good quality RCTs involving 933 participants) – to support the use of pelargonium for acute bronchitis.
- Good scientific evidence for its use in acute pharyngitis and the common cold. No serious side effects noted.

(Ulbricht C et al 2010)

Ancient medicine for modern times!



- Herbal medicines have been used as antimicrobials for thousands of years, yet remain effective.
- Suggests that bacteria, fungi and viruses have a reduced ability to adapt to a plant derived antimicrobial regime.