Tea Tree Oil and Staphylococcal Sepsis

Prof. Thomas V. Riley, University of Western Australia

A Webber Training Teleclass

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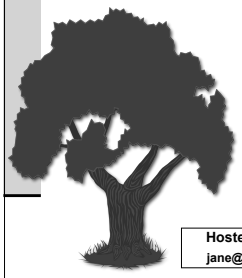

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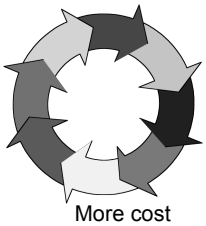
Increasing resistance means:

Higher antibiotic doses are required



More resistance

More side effects

More cost

Alternative approaches

- *Naturally-occurring antimicrobial agents*
  Phytomedicines (plant-based remedies in the form of teas, extracts and oils) are a multimillion dollar industry worldwide.
  - Medicinal plants
  - Essential oils
  - Garlic
  - Honey
- *Bacteriophage therapy*
  Bacterial viruses are making a comeback.
- *Probiotic therapy*
  Probiotic therapy uses a live microbial food supplement to beneficially affect the host.

Naturally-occurring antimicrobials

- garlic
- qinghaosu
- cranberries
- honey
- tea tree oil
- "Dysentery bush" (*Grewia retusifolia*)
- "Jelly leaf" (*Sida rhombifolia*)
- "Quinine tree" (*Alstonia constricta*)
- "Caustic bush" (*Sarcostemma australe*)

Medicinal plants

- Antimicrobial activity of plant extracts many applications:
  - raw and processed food preservation
  - pharmaceuticals
  - alternative medicines

- Over 2700 plants active against *S. aureus* and MRSA (Mahady GB *Curr Pharm Design* 2005; 11: 2405-27))
  - eg berberine is a naturally occurring isoquinolone alkaloid present in a number of plants eg *Coptis chinensis* and *Berberis vulgaris*
  - *S. aureus* MIC of 25 μg/mL

Medicinal plants

- Extracts of *Hypericum perforatum*, commonly known as St John's Wort, are also active against MRSA
- Historically, St John's Wort has been used to treat skin and wound infections
- Active component appears to be hyperforin, a phloroglucin
- More work is required on safety, particularly in relation to interactions with conventional medication.

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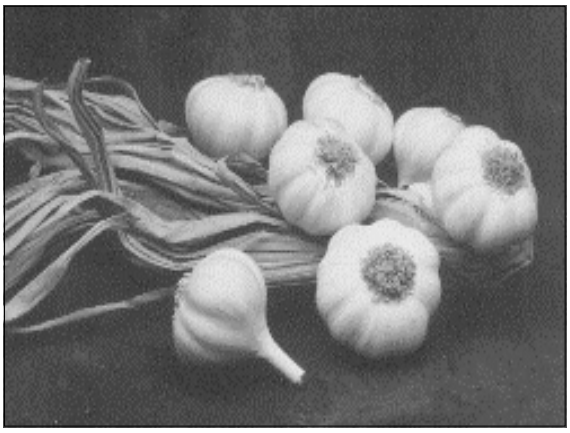

Garlic (*Allium sativum*)

- First recorded use in 3000BC by the Sumerians – widely cultivated then
- Used by Egyptian pyramid builders
- The Romans extolled the virtues of garlic as did the Greeks including Hippocrates
- 1st evidence as antimicrobial from plague in France in 1721 – macerated garlic and wine
- Juice used by French and English in WW I to treat infected wounds

(Harris *et al. Appl Microbiol Biotech* 2001; 57: 282-6)

Garlic

- Antimicrobial properties attributed to allicin which is produced from alliin (alliinase)
- Di-allyl tri- & tetra-sulphides very potent and µg amounts effective in vitro
- Active against many Gram +ve (incl. MRSA) & -ve bacteria, and fungi including dermatophytes
- Mode of action still being debated

Garlic anti-MRSA activity in vivo

(Tsao *et al. J Antimicrob Chemother* 2003; 52: 974-80)

- Previously shown anti-MRSA activity of serum from humans who had eaten garlic
- Infected BALB/cA mice with MRSA and treated with garlic extract, DAS & DADS p.o. (vanc)
- DAS & DADS at high conc. killed mice
- All 3 inhibited growth of MRSA in a dose dependant manner
- All 3 suppressed infection induced elevation of fibrinolectin and IL-6
- Significant antioxidant protection

Honey

- Long recorded history of use
- Antibacterial activity against a range of organisms: *Staph aureus* (incl. MRSA), *E.coli*, *Pseudomonas*, enterococci and *H.pylori*
- Activity attributed to high osmolarity, low pH, presence of H_2O_2 but there is something else (UMF)
- Renewed interest in wound care

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Topical honey for diabetic foot ulcers

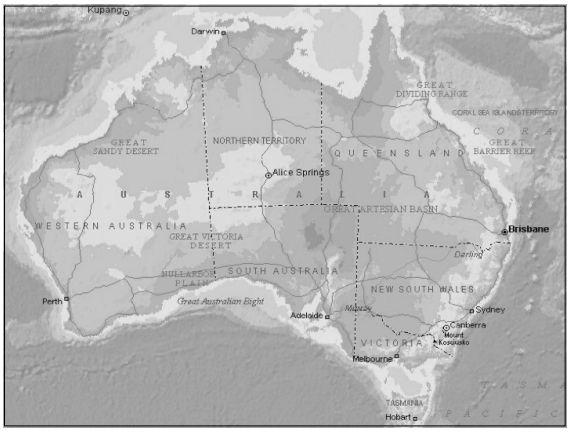
Eddy JJ, Gideonsen MD. *J Fam Prac* 2005; 54: 533-5

- 79 yr old man with type 2 diabetes mellitus
- 14 months of care (US$390,000)
- MRSA, VRE, *Pseudomonas*

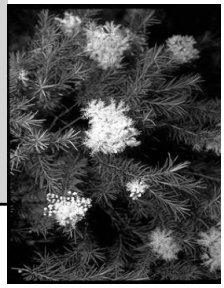
3 weeks

3 months

12 months



Tea tree oil



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Tea tree (*Melaleuca alternifolia*) oil

- pale yellow, viscous fluid
- approximately 100 components
- Mainly terpenes, sesquiterpenes and related alcohols
- compositional levels may vary
- partly regulated by the international standard for 'tea tree' oil (ISO 4730)
- 7 components - 80-90% of the whole oil

Components of tea tree oil

- terpinen-4-ol
- 1,8-cineole
- δ-terpineol
- α-terpinene
- δ-terpinene
- terpinolene
- ρ-cymene
- linalool

Can tea tree (*Melaleuca alternifolia*) oil prevent MRSA?

"The experimental evidence supporting the use of tea tree oil as a prophylactic for MRSA is compelling,……."

Anderson & Fennessy *Med J Aust* 2000; 173: 489.

MIC/MBC (%) of TTO against skin organisms

Organism (n)	MIC 90	MBC 90
Corynebacterium spp. (10)	2	2
Micococcus spp. (11)	0.5	6
CNS (60)	1	6
E.coli (113)	0.25	0.25
K.pneumoniae (14)	0.25	0.25
S.marcescens (11)	0.25	0.25
S.aureus (163)	0.5	2

Potential for resistance to develop

- Low - due to nature, degree and multiplicity of effects
- TTO multicomponent
- Likely to be several different mechanisms
- Gross effects, many non-specific affecting membrane
- Strong argument for use against multi-resistant organisms

Formulation issues

- Formulation of TTO into products requires careful consideration
- Many excipients/surfactants inactivate TTO
- Must test final product
- Things to avoid: SLS, sorbelene, plus many others

In vivo pilot study

- 30 patients – 15 in each group, random allocation
- 4% tto nasal ointment & 5% tto body wash for minimum of 3 d
- 2% mupirocin & Triclosan body wash
- Swabbed at 2 and 4 days post-treatment
- ITT analysis

In vivo pilot study

- control regime clearance 2/15 (13%)
- tto clearance 5/15 (33%)
- 95% CI 0.49 to -0.12, p=0.235

Caelli *et al. J Hosp Infect* 2000; 46: 236-237.

Decolonisation study

Standard

- 2% mupirocin tds 5 days ant. nares
- 4% chlorhexidine once a day/5days
- 1% silver sulfadiazine once a day/5days

Tea tree

- 10% tea tree cream tds 5 days ant. nares
- 5% tea tree body wash once a day/5days
- 10% tea tree cream once a day/5days

Dryden *et al. J Hosp Infect* 2004; 56: 283-286.

Presence or absence of MRSA after 14 days

Treatment	MRSA negative	MRSA positive	Total
Standard	56	58	114
Tea tree	46	64	110
Total	102	122	224

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MRSA carriage and clearance at different sites

	Std total	Std cl (%)	TT total	TT cl (%)
Nose	74	58 (78)	76	36 (47)
Throat	34	16 (47)	36	10 (28)
Axilla	4	2 (50)	14	8 (57)
Groin	14	4 (29)	10	8 (80)
Wound	26	8 (31)	34	16 (47)

Treatment of impetigo with tea tree oil

- In Southern Africa the prevalence of impetigo in school children is 36%
- Particular problem in humid and economically deprived areas
- Situation likely to be similar in Australia
- Tea tree oil a possible alternative

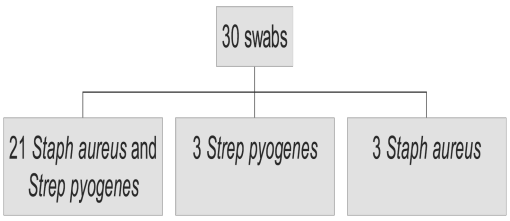
Tea tree oil - impetigo

- Study design: before and after
- Study population: all children at Touwsranten & Wildernesshoogte Primary Schools
- Sample population: all children with impetigo as of 1 January 2000 (max. 30 children)
- Definitions of impetigo:
  - Local infection of superficial skin layers
  - Superficial vesicles, broken and/or unbroken
  - Denuded surface covered with honey-coloured crusts

Tea tree oil - impetigo

- Lesions quantified and qualified
- Parental consent for intervention
- Treatment for 7 days with 6% TTO cream:
  - 0800h, teacher
  - 1300h, teacher
  - 1800h, parent
- Repeat examination at 7 and 10 days
- Conventional medication for failures

Microbiology results



Treatment results

- Pre-treatment lesion average 15 mm
- 17/30 (57%) healed at 10 days
- 12/13 lesions < or = in size (average 10 mm)
- Only 1 lesion larger in a case with scabies also
- Isolates from 2nd set of swabs were typed by pulsed field gel electrophoresis (PFGE)
- Of the 10 *Staph aureus* isolated from repeat swabs, 5 were a different PFGE type
- This suggests possible reinfection rather than failure of therapy

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Why haven't these treatment options been widely explored further?

- Often no obvious protection for a pharmaceutical company – no patent!
- Many companies that produce these products don't understand healthcare
- Many trying to take advantage of interest
- Too many unsubstantiated claims
- No good regulatory processes in place
- Poor quality products
- Clinical trials expensive
- Safety issues

Conclusions

- "Natural" & alternative therapies are viewed favourably by patients
- Less side effects than antibiotics
- Some problems relating to quality
- Lack of good data
- Worthwhile exploring further as adjunctive or replacement therapy
- Government involvement necessary