Tea Tree Oil and Staphylococcal Sepsis
Prof. Thomas V. Riley, University of Western Australia
A Webber Training Teleclass

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 osmolality, low pH, presence of H₂O₂ but there is something else (UMF)
- Renewed interest in wound care

Hosted by Jane Barnet  jane@webbertraining.com
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Topical honey for diabetic foot ulcers

- 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

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……..”


Components of tea tree oil

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

MIC/MBC (%) of TTO against skin organisms

<table>
<thead>
<tr>
<th>Organism (n)</th>
<th>MIC 90</th>
<th>MBC 90</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corynebacterium spp.</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>spp. (10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micrococcus spp. (11)</td>
<td>0.5</td>
<td>6</td>
</tr>
<tr>
<td>CNS (60)</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>E.coli (113)</td>
<td>0.25</td>
<td>0.25</td>
</tr>
<tr>
<td>K.pneumoniae (14)</td>
<td>0.25</td>
<td>0.25</td>
</tr>
<tr>
<td>S.marcescens (11)</td>
<td>0.25</td>
<td>0.25</td>
</tr>
<tr>
<td>S.aureus (163)</td>
<td>0.5</td>
<td>2</td>
</tr>
</tbody>
</table>

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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


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


Presence or absence of MRSA after 14 days

<table>
<thead>
<tr>
<th>Treatment</th>
<th>MRSA negative</th>
<th>MRSA positive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>56</td>
<td>58</td>
<td>114</td>
</tr>
<tr>
<td>Tea tree</td>
<td>46</td>
<td>64</td>
<td>110</td>
</tr>
<tr>
<td>Total</td>
<td>102</td>
<td>122</td>
<td>224</td>
</tr>
</tbody>
</table>
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MRSA carriage and clearance at different sites

<table>
<thead>
<tr>
<th></th>
<th>Std total</th>
<th>Std cl (%)</th>
<th>TT total</th>
<th>TT cl (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nose</td>
<td>74</td>
<td>58 (78)</td>
<td>76</td>
<td>36 (47)</td>
</tr>
<tr>
<td>Throat</td>
<td>34</td>
<td>16 (47)</td>
<td>36</td>
<td>10 (28)</td>
</tr>
<tr>
<td>Axilla</td>
<td>4</td>
<td>2 (50)</td>
<td>14</td>
<td>8 (57)</td>
</tr>
<tr>
<td>Groin</td>
<td>14</td>
<td>4 (29)</td>
<td>10</td>
<td>8 (80)</td>
</tr>
<tr>
<td>Wound</td>
<td>26</td>
<td>8 (31)</td>
<td>34</td>
<td>16 (47)</td>
</tr>
</tbody>
</table>

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 Touwsranden & 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

- 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
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