Potential new insecticide candidate classes & lessons learnt from agricultural practices

Dr. Gerhard Hesse
8th February 2010
5th RBM Vector Control Working Group
IRM IS AN INTEGRATED APPROACH

Means:
- We have to have the knowledge about the situation (M&E)
- the adequate insecticide active ingredient
- the right formulation
- and the adequate strategy
  - to fight the existing resistance with existing proper tools
  - to prevent selection for new resistance development
  - we have to search for new modes of action
Actual situation is not bright for adult mosquitoes

- four chemical classes act on only three different target sites
- and address only two different modes of action
- only pyrethroids remain uncontroversial with regard to human & environmental toxicity.

### Major biochemical mechanisms conferring resistance to important classes of insecticides in mosquitoes

<table>
<thead>
<tr>
<th>Biochemical mechanism of resistance</th>
<th>Metabolic</th>
<th>Target-site</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Esterases</td>
<td>Monooxygenases</td>
</tr>
<tr>
<td>Pyrethroids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DDT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organophosphates</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
…we have to search for “new” modes of action

1. Really new chemical classes
2. Convert agricultural compounds into public health ones
3. Convert public health compounds into adult mosquito control ones
4. Classical synthetic chemistry
5. Biologicals
6. Strong synergists
7. Strong repellents
8. Combination of existing tools with new tools
... and there are some very promising candidates

- new chemistry is in the mandate of IVCC (no mention here)
- Nicotinyl’s can be synergised with pyrethroids
- delayed action compounds:
  - some agro chemicals kills only older, infective mosquitoes
  - classical mosquito larvicides like IGR’s sterilize the females
    - population control versus individual pest control
- some IGR’s prevent even blood feeding (!!!!!)
- biological products like fungi and plant extracts + classical chemistry
- check negative cross-resistance occurring when an allele confers (i) resistance to one toxic chemical and (ii) susceptibility to another
- some agro chemicals disrupt blood feeding w/o KD or killing
- toxic sugar baits with classical stomach poisons
Conclusions and recommendations for our discussion

- New chemical classes might be found, but: don’t rely on the fact

- Use existing vector control tools in the right manner

- There is new, non vector control, chemistry with potential but we need to be creative
  - in testing guidelines
  - in application
  - in program planning
  - in changing perception by the people protected
  - etc

➢ Think out of the box!
….can we learn from agriculture?

Bayer IRM workshop (MIM, Nairobi, Nov 2009): quote Greg Devine

- Vector control tends to be a heavily centralized operation.
- Because of the limited markets available for intervention products, public institutions / academia play a major role in R & D.
- Given these conditions, current political will, healthy funding levels, and the absence of a wholly market-driven environment, might make it possible to develop cleverer and more sustainable strategies for control than those that have been developed in agriculture.

- IRM for vector control needs to define its own paradigms
- new tools are urgently needed, but don’t use the new tools like the old ones