Evaluation of mosquito (*Aedes aegypti*) organic anion transporters through microinjection of sulfonate group dyes.

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Abstract

The Gates Foundation estimates that every year, 750,000 people die from mosquito-borne diseases. During a blood meal, mosquitoes voluntarily ingest a large variety of foreign substances, some are essential to metabolic function (metabolites) and others are potentially harmful and need to be excreted through the urine (xenobiotics). Their effective xenobiotic transport system has made the development of mosquitoicides challenging. The relationship between mosquito excretory transporters (specifically organic anion transporters) and the structures they preference could yield valuable insight into pesticide development. Previous work has shown that charge plays a significant role in xenobiotic transport. In our study we injected mosquitoes with a variety of compounds that differ in their number of sulfonate groups (R-SO3-). We found that the addition of a sulfonate group significantly decreased the toxicity of the compound to the mosquitoes. While it is unclear if this decrease in mortality is due to preferential excretion, this work does yield promising results for the development of adjuvants to current mosquitocides.

Background

A study on the grasshopper *Schistocerca gregaria* observed a collection of sulfonate chlorophenol red (CPR) in malpighian tubes, indicating the presence of organic anion transporters (OAT's). Competitive inhibition of the OAT has been observed through the inhibition of fluorine by the sulfonate indigo carmine in the cockroach *Blaberus giganteus*. In *Aedes aegypti*, competitive inhibition of other excretory transporters has been linked to an increase in toxicity of the pesticides.

Dyes

- **Indigo Carmine**
- **Sulforhodamine B**
- **Rhodamine B**
- **Hydroxynapthol Blue**
- **Acid Fuchsin**
- **Basic Fuchsin**
- **Methyl Orange**
- **Methyl Red**
- **Dimethylsulfoxide (DMSO)**

Methods

- Mosquitoes were injected with a 345 nl bolus (a conservative estimation for the volume of a blood meal) of dye at various concentrations using a micro-injector. Mosquitoes were then monitored for 24 hours and a dose-response curve was generated.
- Controls were a Phosphate buffer solution (1X) with 5% Dimethylsulfoxide (DMSO)

Results

- Pilot studies on saturated dye solutions indicate the addition of a sulfonate group significantly decreased the compounds mortality in a variety of parent compounds.
- The dose-response curves for rhodamine B and sulforhodamine B suggest that the substitution of the carboxyl group for a sulfonate group significantly decreased xanthene toxicity.
- More cases are required to determine whether this finding is a blanket trend for all dyes.
- Injection of parent xanthene is required to quantify the effect of sulfonate groups on toxicity.
- Excretion trials are needed to identify if the decrease in excretion preference.
- It is our expectation that the anions with a greater amount of sulfonate groups will be transported with greater efficiency by the OATs and therefore enter into the mosquito's Malpighian tubules more readily.

Conclusions and Future Aims

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References


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