Unconventional Approaches to Mosquito Control: Interference with Male Mosquito Fertility

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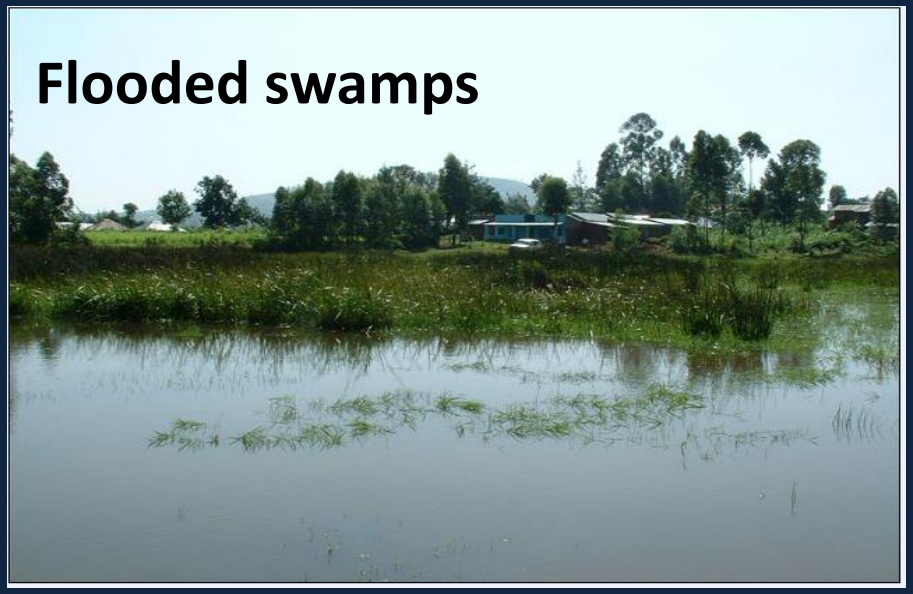
BACKGROUND

- Malaria is a serious public health concern especially in the tropics
- Caused by *Plasmodium* parasites, transmitted by *Anopheles* mosquitoes
- In 2013 alone (World Malaria Report 2015)
  - Estimated 198 million cases worldwide
  - 584,000 death; 90% in Africa

MOSQUITO BREEDING SITES



MALARIA ON THE GLOBAL AGENDA

- **Millennium Development Goals, MDGs (2000-2015)**

  *Target 6C: Have halted by 2015 and begun to reverse the incidence of **malaria** and other major diseases*

- **Sustainable Development Goals, SDGs (2015-2030)**

  *Target 3.3: By 2030, end the epidemics of AIDS, tuberculosis, **malaria** and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases*

➡ Vector control a key component in achieving targets

VECTOR CONTROL

Insecticide Treated Nets, ITNs

Indoor Residual Spraying, IRS

- Challenge of insecticide resistance
- Compounded by resistance to anti-malarial drugs

INTERFERING WITH MALE FERTILITY

- “Contraceptive” for male mosquitoes
- Relies on distinctive behaviour of female mosquitoes following mating
  - Generally mate only once in their lifetime
  - Post-copulatory refractoriness
- “Contraceptive” would have an exponential effect on mosquito densities

THE QUESTION

Proof of Principle:

Can male mosquitoes be rendered sterile through feeding on compounds that have been found to have antifertility effects in other organisms?

METHODS

Three compounds were tested:

- **Nifedipine** – calcium blocker used to treat hypertension & migraines
- **Ornidazole** - antiprotozoal agent, for treatment of genital tract infections
- **Gossypol** – natural phenol from cotton plant

METHODS continued

- Mosquitoes – *Anopheles gambiae* Kisumu stain, colonized
- Starting concentration (x1): concentrations found to have antifertility effects in other organisms
- Test compounds introduced in:
  - Larval water, 1st instar larvae
  - Glucose meals for adults, from emergence

PARAMETERS

- **Antifertility effects**
  - Sperm production (6day old, male testes dissection, Giemsa stain, relative sperm densities; Ponlawat and Harrington 2007)
  - Egg laying by females mated with the males; mating 6 days post-emergence, females fed on standard glucose
  - Adult emergence rates
- **Preference / Avoidance** of glucose containing compounds when presented with a choice; Standard Food Blue No.1 dye (Schlein nd Muller, 2008)
- **Mating Competitiveness**; Food Blue labeling, mating observe under low-watt light and mating pairs removed

Mosquito insectary

Mosquito larvae rearing pans

Adult mosquitoes in cage

Mosquito larvae

RESULTS

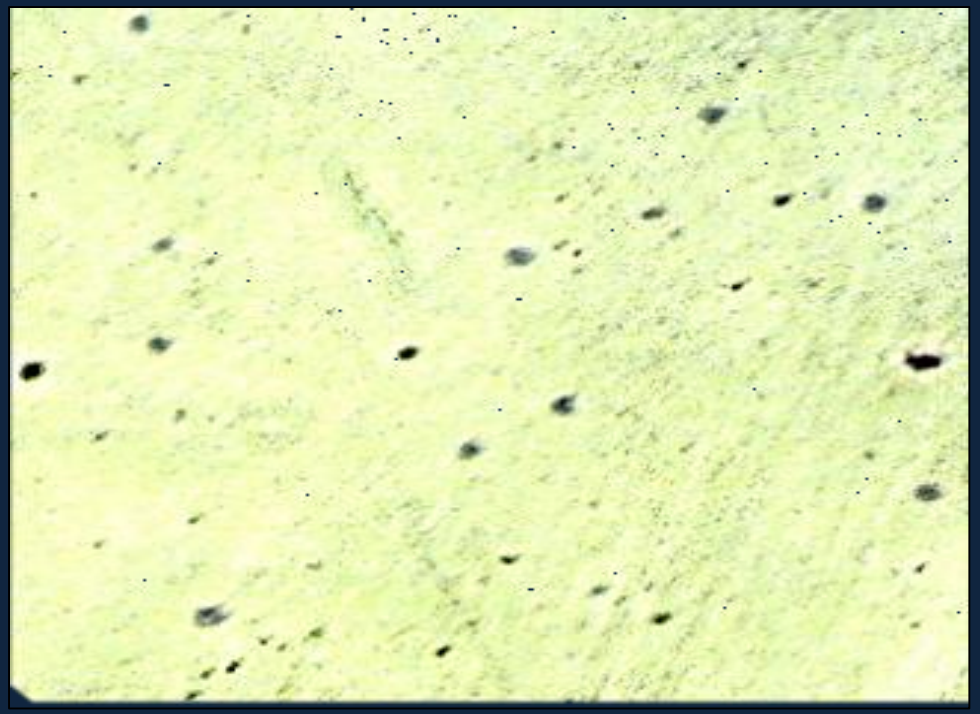
- Mosquito feeding at larval stage
  - Total mortality within 3 days
  - Even at extremely low concentrations e.g. $5x10^{-5}$

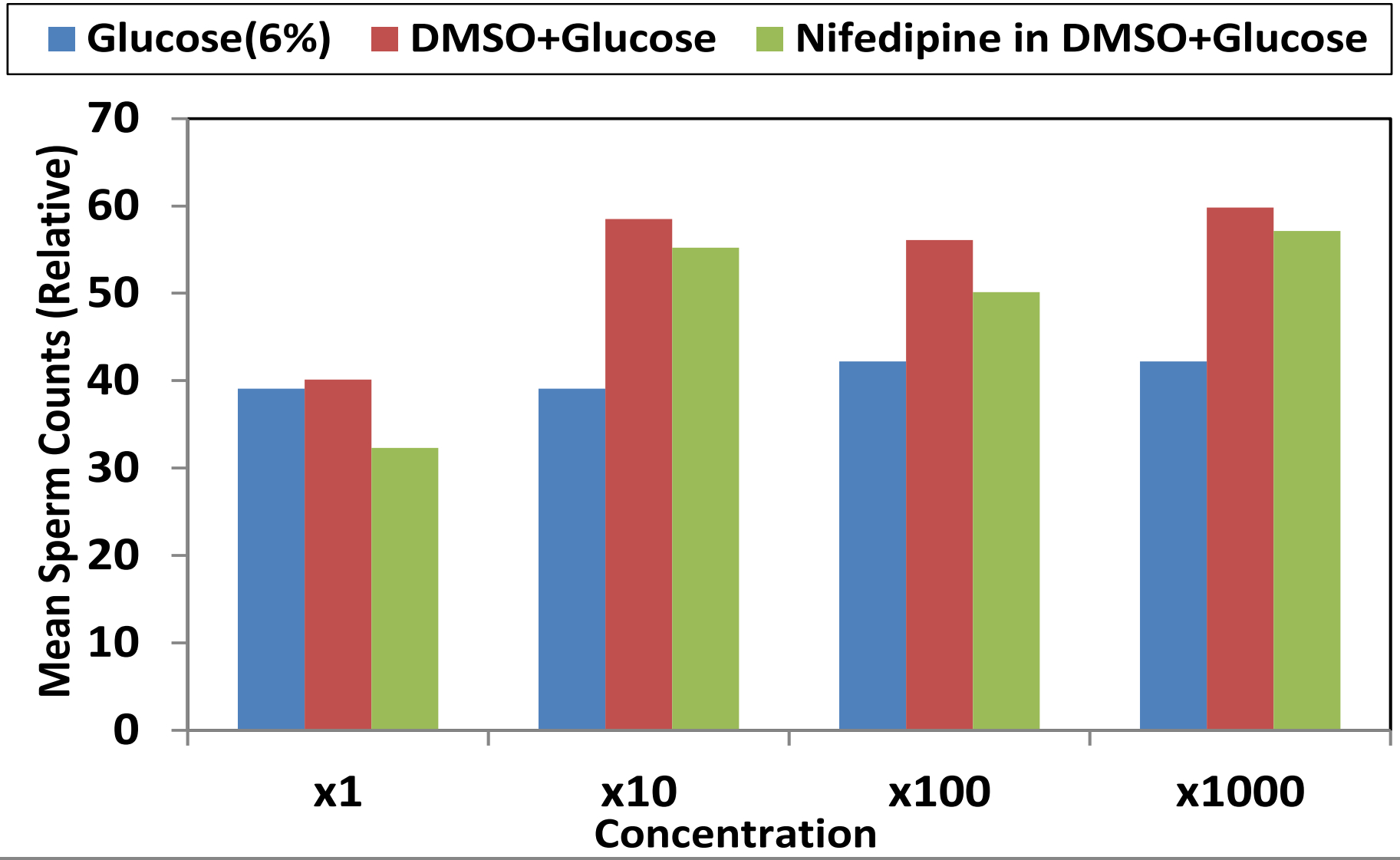
- Mosquito feeding at adults stage
  - High mortality of males; up to 67.5% compared to maximum 15% in controls

SPERM PRODUCTION

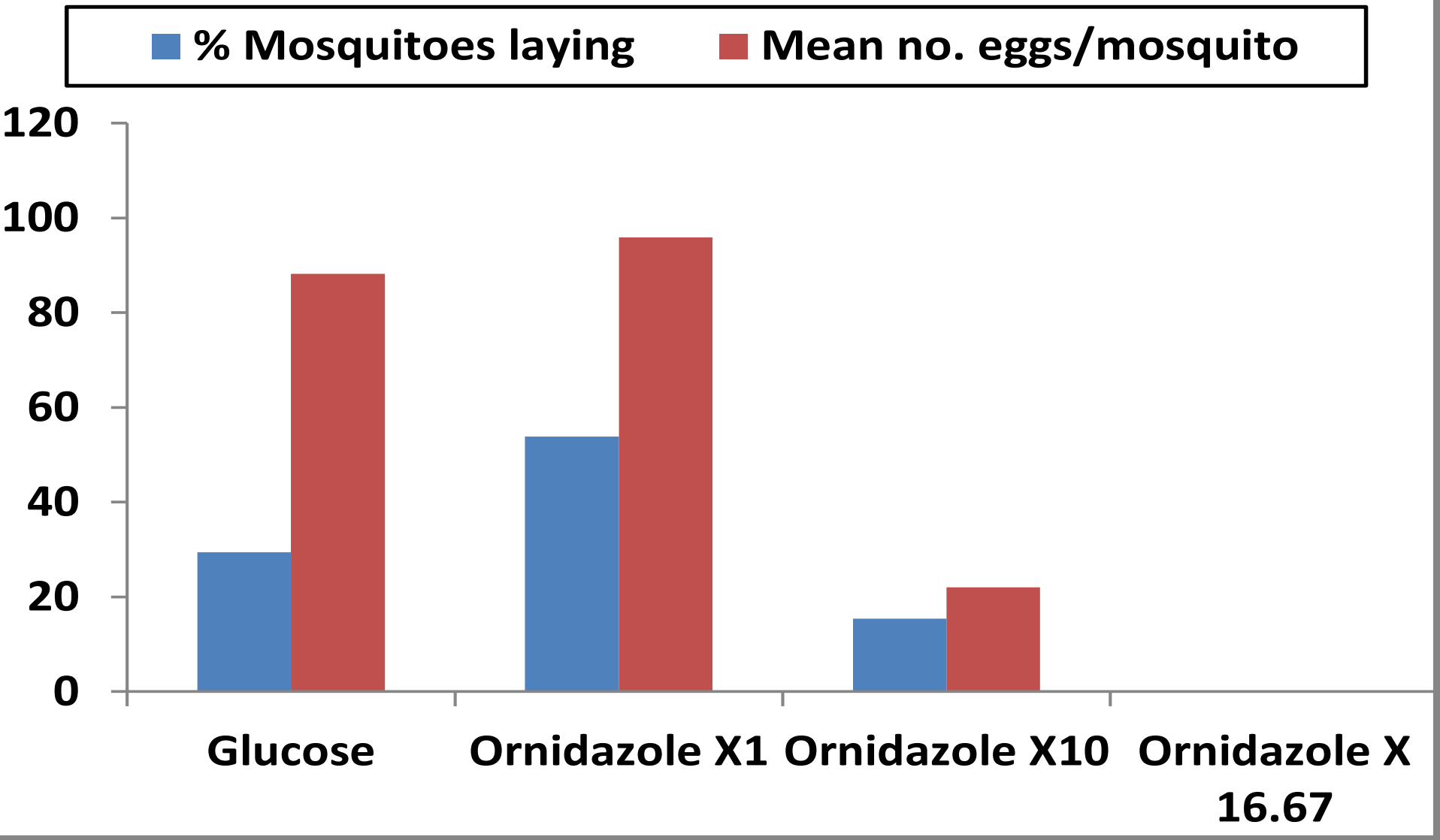
Mosquito testicles

Mosquito sperm heads, Giemsa-stained

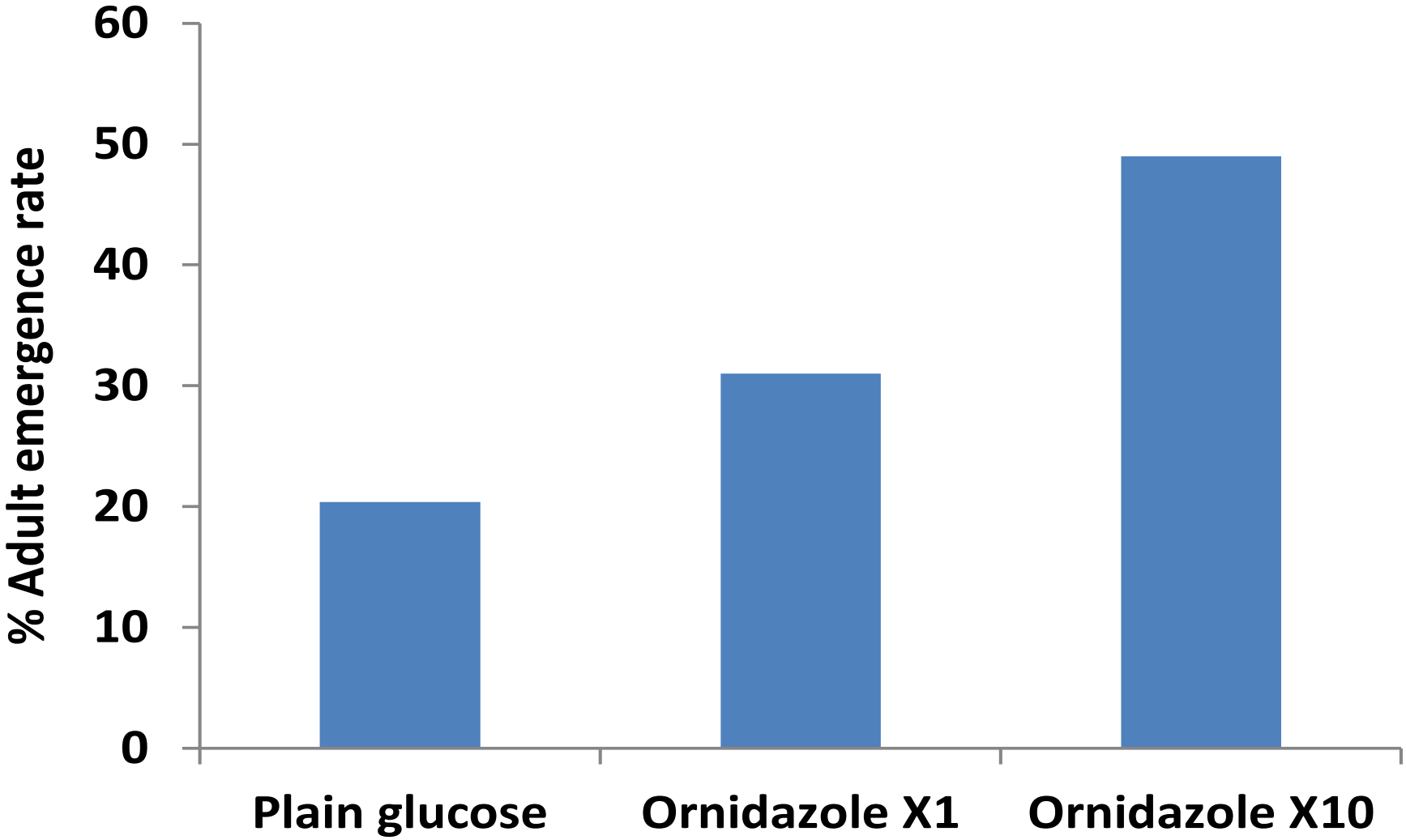




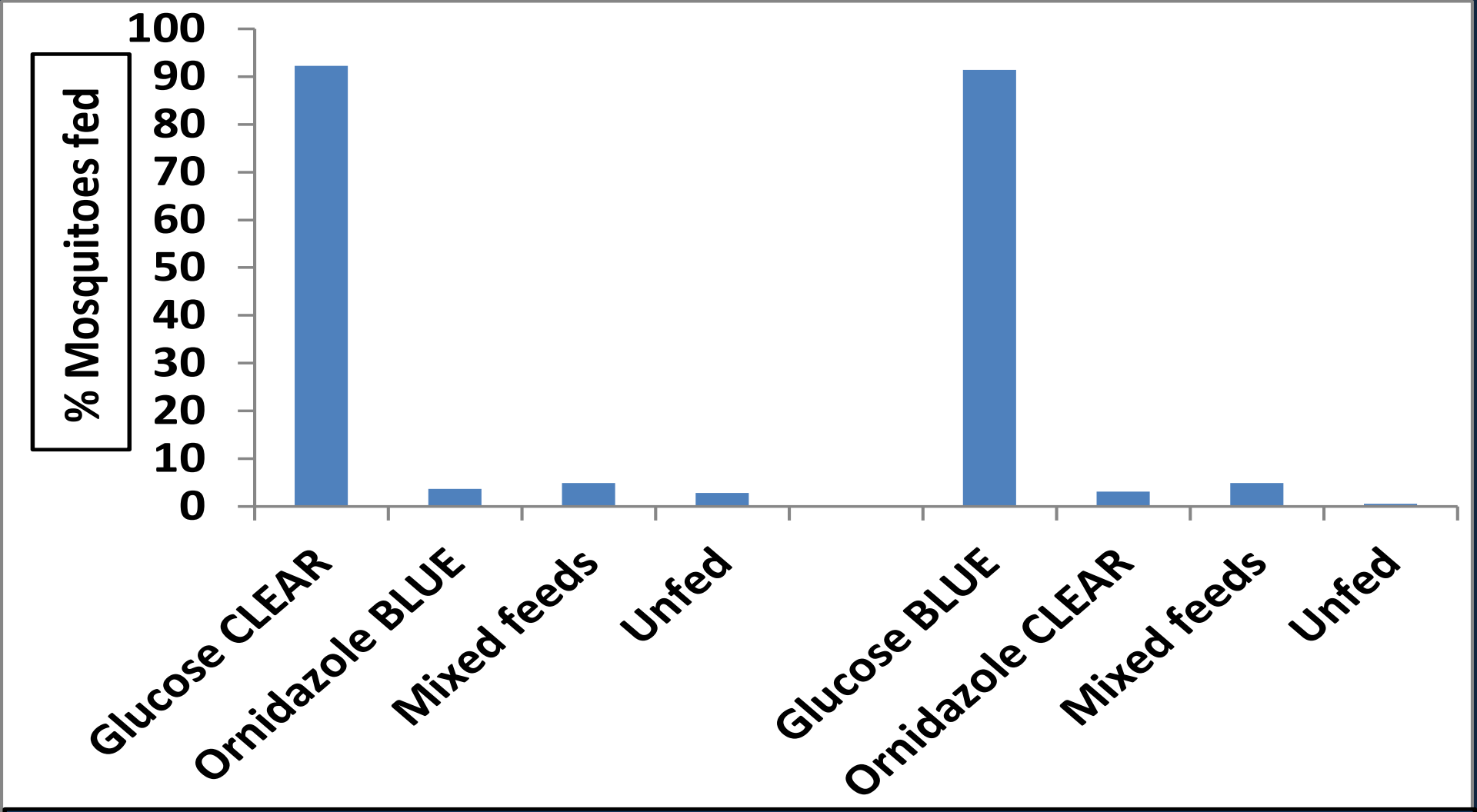
SPERM PPRODUCTION: No effect for Nifedipine (the only compounds tested) for concentrations x1, x10, $x10^2$ and $x10^3$ (*n=40, t-test, p<0.05*)



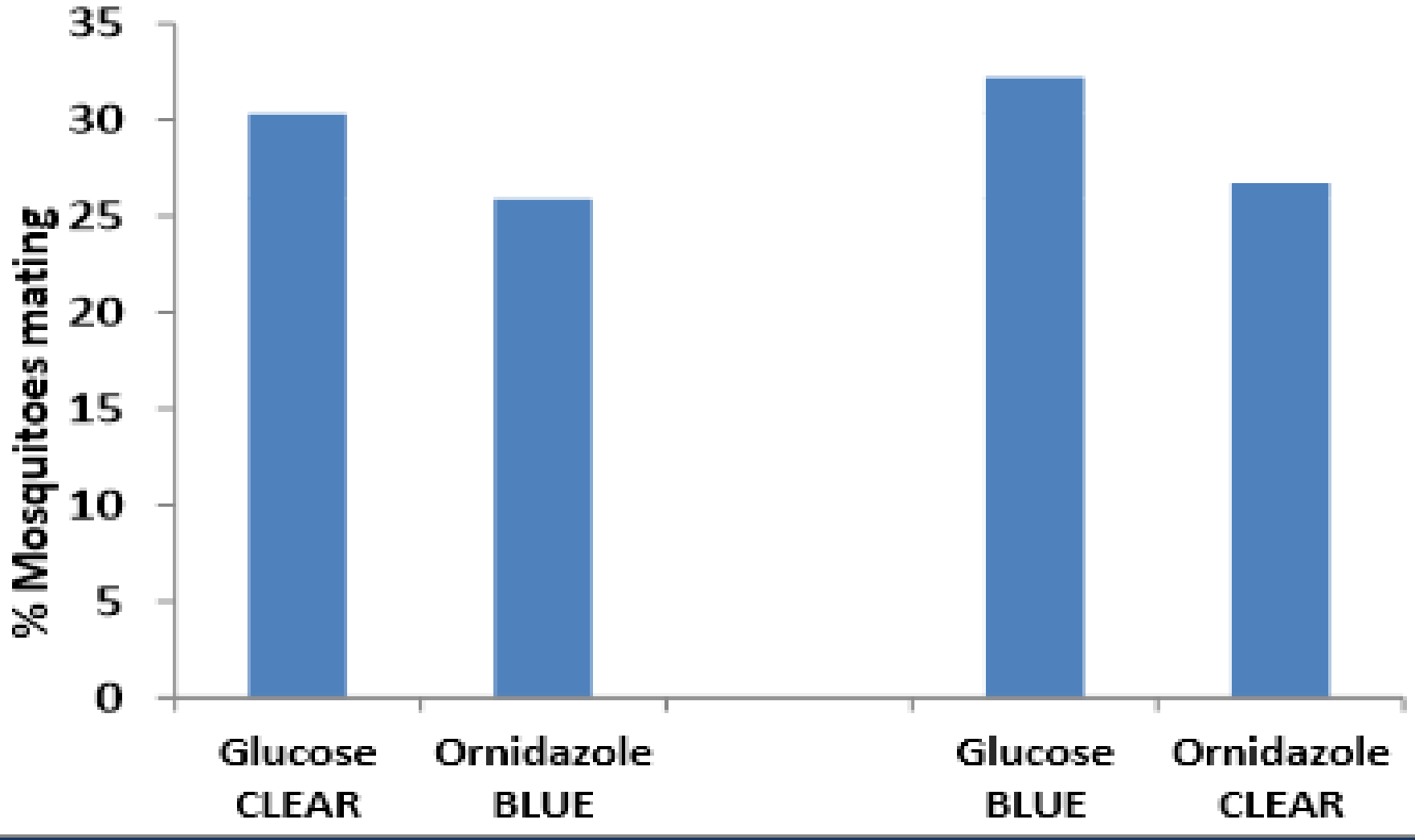
EGG PRODUCTION: Significantly lower % layers and mean no. eggs per laying mosquito for x10 *(n=143; p=0.0140 and p=0.0040 respectively*); no eggs for x16.667



ADULT EMERGENCE RATES: Significantly higher emergence rates with Ornidazole x1 and x10 (n=1416 , 98; p=0.000 in both cases)



FEEDING PREFERANCE/AVOIDANCE: Mosquitoes preferred plain glucose meals over those spiked with Ornidazole irrespective of whether the meal was stained with the blue dye or not (*n=1005, paired t-test, p<0.05*)



MATING COMPETITIVENESS: Neither the dye nor Ornidazole had an effect on mating competitiveness (n=240, Z test, *p>0.05)*

DISCUSSION AND CONCLUSION

- High mortality observed suggests potential use as insecticides
- Lack of effect on sperm production commensurate with effect on sperm function rather than production
- Avoidance of males of glucose containing Ornidazole would pose a challenge in the deployment of the approach tested

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Thank you for your attention