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# Long-effective and slowly released calcium cyanamide can inhibit mosquito growth and development: Implications for the prevention and control of dengue fever

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Dengue fever is one of the most serious mosquito-borne infectious diseases in the tropical world, causing substantial human morbidity and mortality, yet there is no specific treatment till now, and the main measures preventing dengue fever include applying pesticide to kill adult vector mosquitos and removing standing water to prevent the breeding of mosquitoes *etc.* Appropriate uses of such approaches can reduce dengue epidemic risk via reducing mosquito density. In fact, vector control using insecticides is the most common method to prevent and control mosquito-borne disease transmission. Nevertheless, recent research has shown that *Aedes albopictus* and *Aedes aegypti*, the two key vectors for dengue fever transmission, have rapidly developed high resistance to the most commonly used adult insecticide pyrethroid (deltamethrin and permethrin) and larvicide organophosphate (temephos). Therefore, it is of great significance to obtain a new drug with longer-term efficacy to prevent dengue virus transmission. Pesticides currently used act on adult stage of mosquitoes, typically applying to the environment where mosquito bites (on humans) occur, and very few target on egg or juvenile stages of the mosquitoes in the water environment. Calcium cyanamide (CaCN<sub>2</sub>), widely used as a fertilizer in many different settings, was recently shown to have potential to prevent tropical diseases by eliminating or inhibiting the growth and development of intermediate hosts. The main compounds of calcium cyanamide (CaCN<sub>2</sub>) are CaCN<sub>2</sub> (50%-60%) and calcium oxide (15%). The representative products of calcium cyanamide (CaCN<sub>2</sub>) are PERLKA® from Germany and ROEBON® from China. CaCN<sub>2</sub> has recently been recognized to have the fungicidal effect on the pathogens of the soil borne diseases and addition of CaCN<sub>2</sub> could benefit the thermophilic phase and the composting could quickly reach the sanitary standard and will contribute to solve the feces disposal problems. According to our team's long-term investigation and research, we found that ROEBON® (50% CaCN<sub>2</sub>) can be used to eliminate *Oncomelania* and effectively control the spread of schistosomiasis. In the latest research, we have confirmed that 10 mg/L CaCN<sub>2</sub> (20 mg/L ROEBON®) can completely inhibit the emergence of mosquito larvae and the population growth from the perspective of inhibiting development and the efficacy can lasts for three months. Calcium cyanamide is a good candidate drug to control mosquito-borne infectious diseases transmission, especially for dengue fever prevention. In 2014, Scientific Committee on Health and Environmental Risks in European Commission promoted preliminary opinion on potential risks to human health and the environment from the utilization of calcium cyanamide as fertilizer, but convincing evidences for the causal connections between the exposure to CaCN<sub>2</sub> and human health damages are missed. Given a 96-h acute zebrafish toxicity study, the No Observed Effect Concentration (NOEC) of calcium cyanamide to zebrafish was 100 mg/L CaCN<sub>2</sub>. In summary, most of the data are based on the evaluation of the effect of CaCN<sub>2</sub> as a fertilizer, and the related research as a mosquito inhibitor is still very scarce. The research on toxicity of CaCN<sub>2</sub> in mosquitoes needs to be further strengthened.

**Keywords:** Calcium cyanamide; Dengue fever; Mosquito

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