

Crystal Proteins: a novel alternative to manage gastrointestinal parasites in sheep and goats

AMERICAN CONSORTIUM FOR SMALL RUMINANT PARASITE CONTROL

An urgency for alternative methods

Gastrointestinal nematode (GIN) parasites were once controlled by conventional anti-parasitic dewormers (anthelmintics), however frequent and non-targeted use of these dewormers has resulted in the development of widespread anthelmintic resistance in GIN parasites globally. As dewormer resistance in parasites continues to rise, the need to identify new, safe, efficacious alternative therapies for GIN control is critical for the long-term sustainability of the small ruminant industry.

What are crystal proteins?

The soil bacterium, *Bacillus thuringiensis* (Bt), is one of the most widely utilized bio-insecticides worldwide, making up about 90 percent of the bioinsecticide market. The main insecticidal component of *B. thuringiensis* strains are crystal proteins that have been bio-engineered into a variety of crops (corn, cotton, rice, soybean) and have been approved by FDA and EPA to control specific plant insect pests. The crystal proteins produced by *B. thuringiensis* are non-toxic to humans and the surrounding environment. Dr. Raffi Aroian and Dr. Gary Ostroff and their research group at the University of Massachusetts Chan Medical School have been conducting extensive research over the last decade to identify and develop Bt crystal proteins that have antiparasitic efficacy against GIN in livestock into novel anti-parasitic treatments.

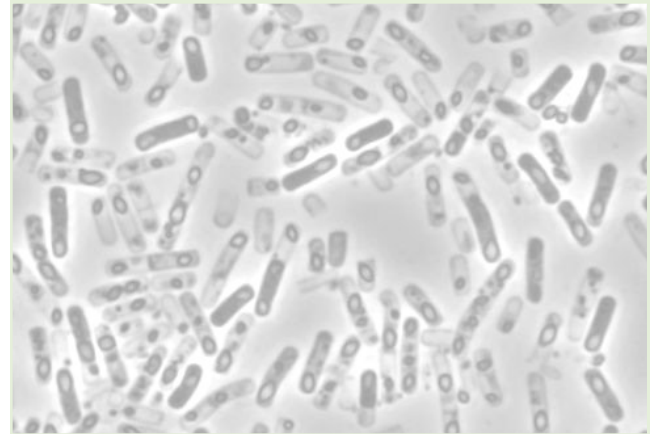


Photo courtesy of Raffi V. Aroian

How do crystal proteins work?

Crystal proteins produced by Bt only target specific invertebrates, animals without a backbone, such as the GIN worms in small ruminants. The crystal proteins bind to specific receptors in the worm's gut creating pores that kill the worm. There are numerous crystal proteins produced by Bt that differ in their spectrum of anti-parasitic activity. Research analyzing crystal protein activity against GIN parasites of sheep and goats initially focused on the anti-parasitic activity of crystal protein 5Ba (Cry5Ba) against *Haemonchus contortus*, more commonly known as the barber's pole worm. As an additional precaution, the Aroian-Ostroff research groups developed an Inactivated Bacterium with Cytosolic Crystals (IBaCC), a form of Bt Cry5Ba whose crystals are biologically active, but the Bt bacterium is dead and unable to reproduce in the environment.

A novel and safe option, *Bacillus thuringiensis* crystal proteins have shown promising anthelmintic properties.



Activity against *Haemonchus contortus*

The anti-parasitic activity of Bt Cry5Ba IBaCC against a *H. contortus* infection in lambs was first demonstrated in research conducted at the Virginia-Maryland College of Veterinary Medicine by John Sanders and Dr. Anne Zajac in collaboration with the Petersson research lab at the University of Rhode Island (URI) and the Aroian and Ostroff groups¹. In more recent collaborative work with the Aroian-Ostroff groups conducted at URI, lambs infected with *H. contortus* were separated into two groups, a treatment group and a control group. Lambs were orally administered 60 mg/kg of Cry5Ba IBaCC (treatment) or water for three days. Rectal fecal samples were collected daily to determine fecal egg counts (FEC). A sharp reduction in fecal egg counts (FEC) was seen two days after administration of Cry5Ba IBaCC, eventually reducing FEC by 96 percent compared to FEC in the control animals (Figure 1.) Additionally, at the end of the study adult *H. contortus* worms were counted and the lambs treated with Cry5Ba IBaCC cleared over 70 percent of adult *H. contortus* worms as compared to the control lambs. These findings demonstrate the potential of Bt crystal proteins as a novel method to treat GIN parasites in small ruminants.

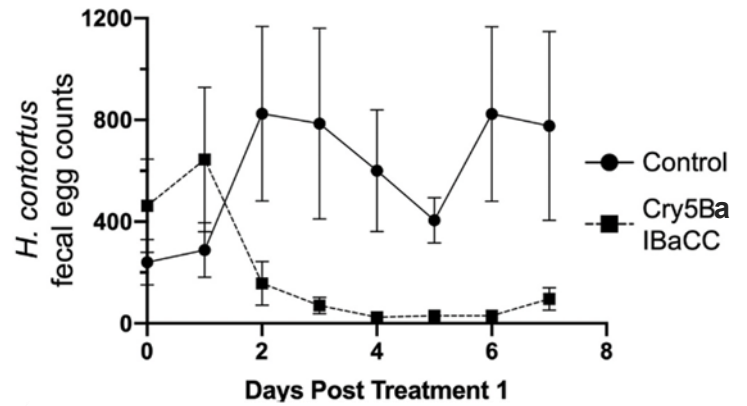


Figure 1
Fecal egg counts of treatment vs control lambs

The future of crystal proteins

Ongoing research between the Aroian-Ostroff groups and the Petersson group conducted at URI by pre-doctoral student Elizabeth Kass, is examining the anti-parasitic efficacy of single doses of Cry5Ba IBaCC as well as other promising crystal proteins on GIN infections in sheep. It is anticipated that as the research continues Bt Cry proteins will have the potential of being established as a new therapeutic treatment against GIN parasites in sheep and goats.

Reference

Sanders J, Xie Y, Gazzola D, Li H, Abraham A, Flanagan K, et al. A new paraprobiotic-based treatment for control of *Haemonchus contortus* in sheep. *Int J Parasitol Drugs Drug Resist.* 2020 Dec;14:230–6.

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