

A step closer to treating nagana



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Animal African Trypanosomiasis (AAT), or *nagana* as it is widely known in Africa, is a disease of vertebrate animals that is endemic in 40 African countries. Trypanosome parasites that affect cattle account for up to a 50 percent loss in milk and meat production across the continent. In infected animals, the mortality rate can reach 50-100% within months after exposure, particularly when poor nutrition or other factors contribute to debilitation. Trypanosomiasis is also a major cause of reduced draught power for agricultural production. With all these factors taken into consideration, the total annual cost resulting from the disease is estimated to be US \$628 million.

AAT is transmitted by tsetse flies, which can be controlled by traps and insecticides. Infected cattle can also be treated with drugs but increasing drug resistance is becoming a concern. Developing drugs for neglected tropical diseases is a complex and risky process due to high failure rates and excessive costs associated with research, development and clinical studies. However, a potential new trypanocide (a drug used to kill or control a single-celled parasite) to treat cattle is undergoing early development by a major biopharmaceutical company. The identification and commercial development of a trypanocidal agent is a huge step forward in the progress towards controlling this deadly disease, which would prove highly significant for millions of smallholder farmers and for Africa's economy.

Overcoming the obstacles

Throughout Africa, with few exceptions, governments lack the necessary resources to provide effective veterinary services to control nagana. The present priority in Africa is to promote agricultural production by applying knowledge and methods that are already available. Drugs to treat livestock infected with AAT do exist, but introduced over 40 years ago, these treatments are now outdated with understrength compounds to which the disease is resistant. "An effective treatment for AAT would be fantastic for farmers. It would mean with just one injection, animals could be free from infection for years or for a lifetime," says Dr Rosemary Peter, Programme Manager for AAT at the Global Alliance for Livestock Veterinary Medicines (GALVmed).

A significant hurdle to AAT treatment development is the lack of incentive for pharmaceutical companies, who may not receive a sufficient return on their investment. "Trypanosomiasis is not a blockbuster disease from which large companies can achieve a significant profit - as a purely African disease, the ability to achieve sales worldwide is limited," states Peter. To counter the growing problem of substandard drugs and garner interest in trypanocide development, GALVmed, a not-for-profit company that makes livestock vaccines accessible to smallholder farmers, issued a competitive call to their network of partners with pharmaceutical development experience and those with an interest in developing products for Africa. Novel drugs were tested for their efficacy against the two predominant parasite species that cause AAT – *Trypanosoma congolense* and *T. vivax*.

One major challenge to identifying a potential trypanocidal candidate was finding an effective drug. "It is difficult to find compounds that will work as very little is understood about the trypanosome parasite and the cell biology of each stage differentiation," says Peter. However, a potential trypanocidal drug that closely fits the requirements of the Target Product Profile (the 'wants' and 'musts' of an intended commercial therapeutic, i.e. the ability to treat the target species) has been identified. The potential candidate is about to enter the final stages of testing by GALVmed's pharmaceutical partner, Anacor.

Diagnostic project partnerships

The difficulty in diagnosing trypanosomiasis is another hindrance to its management. Not only are there no specific clinical signs but when looking to diagnose the disease, it is difficult to find parasites in infected animals' blood (as there are generally not a lot). The only way to confirm a diagnosis in affected animals is to demonstrate and identify the parasites in body fluids. To develop a simple and effective trypanosomiasis field diagnostic test GALVmed has worked in partnership with the University of Dundee. Taking a hi-tech approach, the university research team identified the components of *T. vivax*, a strain which stimulates antibody production in cattle. One of these components was then used to develop into a prototype diagnostic device. This was achieved in collaboration with BBI Solutions OEM Limited, who specialise in immunoassay development which detects and measures specific proteins or other substances through their properties as antigens or antibodies. As a result of this collaboration, a simple AAT test has successfully been developed that can be used in the remote settings of rural Africa, without the need for electricity or any additional equipment.

From a single drop of blood, farmers will be able to use the AAT test to detect, within 30 minutes, whether the animal is infected with the parasite *T. vivax*. A positive result indicates the presence of the disease aiding smallholders in the timely treatment of their livestock. The diagnostic is currently being tested in African labs to see how it performs.

Dr Jeremy Salt, Senior Director of Research and Development at GALVmed said, "Such a test could allow millions of smallholder farmers an efficient way to test their cattle for this debilitating disease and give peace of mind that any subsequent treatment for *T. vivax* infection will be done with the certainty that the animal is infected, which saves the farmer money. This will give more control to the smallholder farmers whose quality of life has been affected by this disease that covers over 10 million square kilometres of Africa. To ensure that the final test is widely used throughout the regions where it's endemic, GALVmed will be working with scientists, manufacturers and distributors in the 40 countries where AAT is rife to create a sustainable supply chain for the final product."



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