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Research paper

Therapeutic use of *Bacillus thuringiensis* in the treatment of psoroptic mange in naturally infested New Zealand rabbits

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ABSTRACT

Bacillus thuringiensis is a bacteria known for its bioinsecticidal toxins and it has been proposed as an alternative in the treatment of several parasites that infect domestic animals (helminths, ticks, mites). In this work, we evaluated the clinical efficiency of the *Bacillus thuringiensis* GP532 strain in the treatment of six rabbits naturally infested with the *P. cuniculi* mite. GP532 extract (10 mg/ml) was applied by aspersion in both pinna, with a second application after seven days, and the therapeutic effect was measured in both qualitative and quantitative manner. GP532 application resulted in a decreased infestation rate, which was observed as early as 3 days post-treatment. At day 14, a decrease from 4.66 ± 0.61 to 0.50 ± 0.10 in the left pinna and from 1.66 ± 0.21 to 0.66 ± 0.16 ($P < 0.05$) in the right pinna was observed. This response was comparable to the commercial drug Ivermectin, which induced a decreased infestation rate from 4.00 ± 0.51 to 0.16 ± 0.10 in the left pinna and from 4.66 ± 0.80 to 0.25 ± 0.11 in the right pinna ($P < 0.05$). At day 30 post-treatment, GP532 decreased the total infested area by $76.80 \pm 16.06\%$, whereas Ivermectin resulted in a $97.41 \pm 0.99\%$ decrease. Neither treatment produced irritation or macroscopic lesions. Our results show that the *B. thuringiensis* GP532 strain has a therapeutic potential in the treatment of psoroptic mange in rabbits.

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1. Introduction

Psoroptic mange is a disease produced by mites of the genus *Psoroptes* that infest domestic animals such as goats, sheep, horses, and rabbits, as well as wild animals. The mite *Psoroptes cuniculi* is the causal agent of psoroptic mange in rabbits; such pathology is characterized by the presence of scabs covering the pinna and alopecic zones around the neck (Sweatman, 1958). It is highly contagious and present on farms worldwide, and therefore is of utmost concern in veterinary medicine (Sweatman, 1958; Shang et al., 2013). Moreover, this disease can result in severe complications due to secondary infections such as bacterial meningitis, and in some instances result in vestibular disorders (Arslan et al.,

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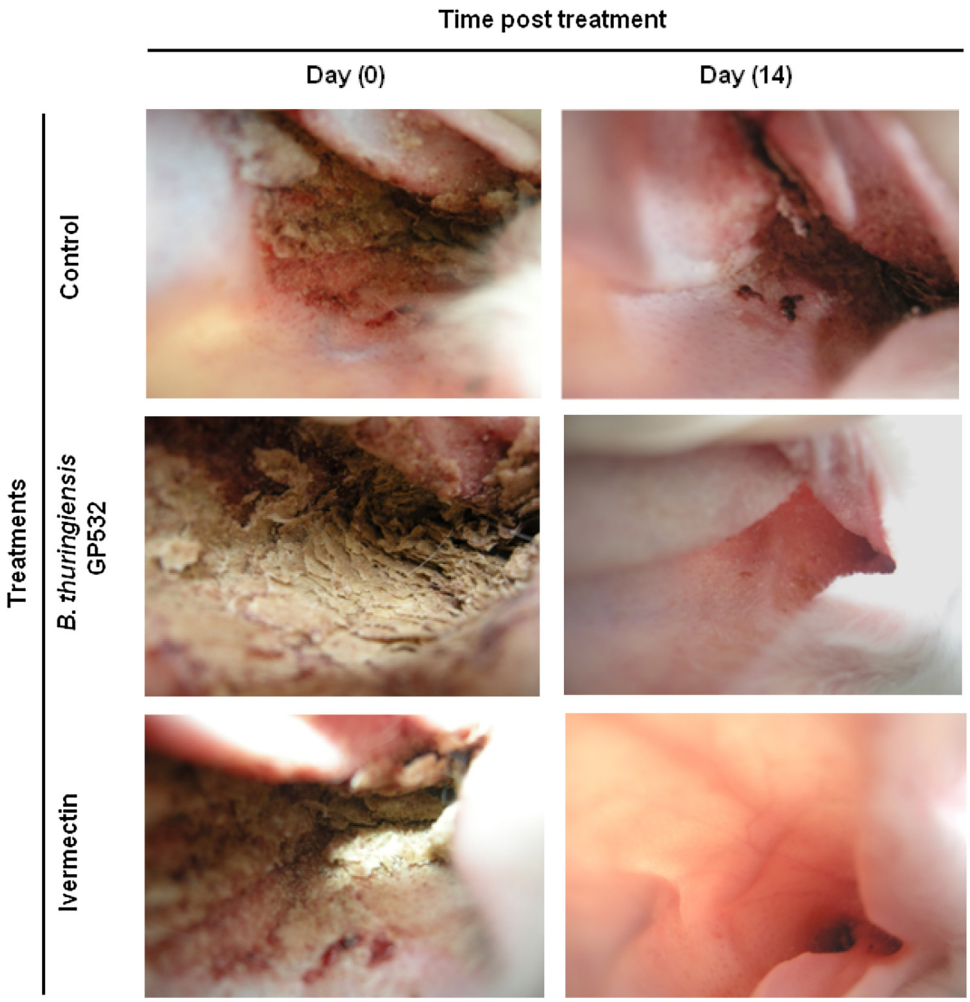

Fig. 1. Qualitative therapeutic effect of the treatment of psoroptic mange in rabbits with B. thuringiensis GP532 strain. Representative image taken from rabbits that were treated during 14 days with B. thuringiensis GP532 strain or with ivermectin.

2014). As well as its impact on animal health and welfare, this parasite can inflict economic losses as well, including those due to poor skin quality, low reproduction rate, impaired growth, weight loss, and even death of the afflicted animals (Kirkwood, 1980).

Acariasis in animals, including rabbits, is commonly treated using drugs derived from active agents that may be of organophosphate, organochloride, pyrethroid, or macrolide origin, among others (Cetin et al., 2010). Due to its clinical effectiveness, ivermectin is one of the most widely used drugs in the treatment of psoroptic mange in rabbits, closely followed by doramectin and selamectin (Wilkins et al., 1980; Kurtdede et al., 2007; Narayanan et al., 2004; Alawa et al., 2003).

The use of chemical therapeutic agents contributes to a great degree to environmental pollution, as well as necessitate the implementation of long delay periods before the animal can be used for human consumption (Alawa et al., 2003), and increase the incidence of resistance in the targeted organism (Currie et al., 2004; Reck et al., 2014). Therefore, there is an impending need to find alternative therapies with a lower negative impact on the environment and animal health, and that also minimize or eliminate the possibility of human ingestion of chemical residues contained in animals that are destined for human consumption (Lans and Turner, 2011)

The use of essential oils and plant-derived extracts with therapeutic potential has been documented in the treatment of psoroptic mange in rabbits (Hu et al., 2014a; Hu et al., 2014b), however, no information has been generated regarding the use, *in vivo,* of *B. thuringiensis* in naturally infested rabbits.

B. thuringiensis is characterized by the synthesis of crystalline inclusions of protein origin that are highly toxic to arthropods of the orders Lepidoptera, Diptera and Coleoptera (Bradley et al.1995; Armengol et al., 2007). Within the derived protein families of *B. thuringiensis*, the Cry endotoxins are of particular interest for bioinsecticide development due to their selective toxicity, low residual presence in the environment, and innocuity to mammals, including humans. Moreover, these proteins have been shown to possess toxicity against a wide spectrum of parasites, including nematodes, flatworms, and ticks, as well as showing pro-apoptotic activity in human tumor cells (Hall et al., 1971; Wei et al., 2003; Peña et al., 2013).

It must be highlighted that *B. thuringiensis* could contribute towards the control of some mites of veterinary relevance, such as ticks that affect cattle: specifically, experimental treatment with four isolated *B. thuringiensis* strains (GP129, GP138, GP139 and GP140) induced a mortality rate of 79.15-95.8% of the cattle tick (*Rhipicephalus microplus*), which are known for their resilience against organophosphates, pyrethroids and amidines (Brasseur et al., 2015). A fifth strain of *B. thuringiensis (*GP543) was tested in steers experimentally infested with *R. microplus*, and obtained a higher clinical effectiveness compared with the entomopathogen fungi *Metarhizium anisopliae* (MA379 strain), and the *Solanum*

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