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An Alternative Approach to Rodent Control

Anticoagulants and the rise of the resistant rodent.

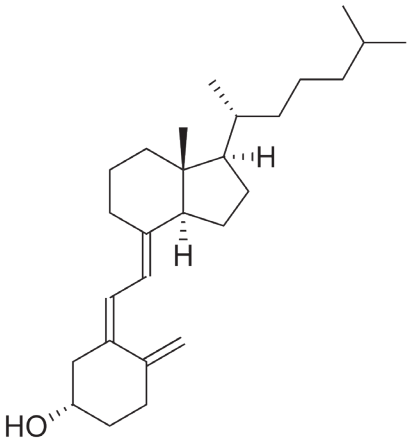
Throughout the years, there have been many innovations focused on making anticoagulant rodent baits work faster and more efficiently. Anticoagulant rodent baits cause disruption of clotting activity three to four days after ingestion; this leads to internal bleeding, a coma, and the subsequent death of the rodent. Anticoagulants have been used for many years due to their effectiveness. They also have the ability to circumvent the taste-aversion phenomenon (due to the delayed action) present in many rodents.

After heavy use of first-generation anticoagulants (warfarin, coumatetralyl, chlorophacinone, diphacinone), resistance cases were described for the first time in Scotland in 1958 (Lund, 1972). The anticoagulants stopped working in practical conditions when bait was applied correctly. A genetic phenomenon linked to mutations of the *VKORC1* gene in rodents allowed them to remain unaffected by these anticoagulants. The rodents were no longer susceptible to these compounds (Greaves, 1994). The genetic basis of resistance was described years later (Rost et al., 2004). The development of second-generation anticoagulants (bromadiolone, difenacoum, flocoumafen, difethialone, brodifacoum) made it possible to overcome this resistance. However, these second-generation anticoagulants all act according to the same mechanism and many of these molecules can lead to genetic resistance in rodents. Resistance to bromadiolone and difenacoum has already appeared in brown rats, black rats and mice. The good news is that resistance to second-generation molecules is far more geographically limited than resistance to first-generation anticoagulants.

above:
If rodents are seen during the day the colony may be so well established that they no longer feel threatened foraging in the daylight.

Recent trends

The use of second-generation molecules, especially the newest molecules of the second generation anticoagulants, (brodifacoum, flocoumafen, and difethialone), has increased and they still work well. Nevertheless, it is crucial to continuously introduce molecules with different modes of action to prevent new resistances from developing in these mammals. Rodent control professionals need alternatives to anticoagulants to complement the current control solutions available for a long term solution.



above:
Chemical structure of cholecalciferol

Possible solutions

There are currently four globally available alternatives to the anticoagulant resistance problem that are considered credible. One is alphachloralose, which acts on rodents' nervous systems and becomes toxic between seven and 12 hours after the bait is consumed. It is extremly effective on mice, but due to poor efficacy against rats alphacholoralose is not registered for use against this pest. It is also restricted to indoor use in Europe. Another is cholecalciferol. It can be used as a rodenticide and is effective on both rats and mice. This molecule acts on calcium homeostatis, and initially causes the animal to stop consuming the bait quickly ("stop-feeding" effect). The toxic symptoms and death occur two to five days after consuming a lethal amount of the bait, which is enough time to prevent the rat or mouse from becoming distrustful. And cholecalciferol is widely accepted by rodents because it is not easy to detect and generates no resistance phenomenon known to date. Zinc phosphide is an acute toxicant and has been widely used in managing mouse populations. It causes cardiac and pulmonary dysfunction after only 15 minutes, but is ineffective with rats who are suspicious of rapid poisons. Also, zinc phosphide is not an approved PT 14 biocide in Europe (only aluminum phosphide). Zinc phosphide is a plant protection active for use against voles (*Microtus arvalis* and *Clethrionomys glareolus*). Finally, bromethalin is a neurotoxic agent that has never been used in Europe but is widely used in the United States against rats and mice. Its action is time-delayed like cholecalciferol, but the symptoms suggest significant suffering in animals.

These alternative active ingredients, in particular cholecalciferol (in rats and mice) and alphachloralose (in mice), slow the development of resistance to anticoagulants and create a unique set of tools to manage rodent populations.

Summary

Humans have always struggled to keep rodents out of our homes and businesses. Sanitation is the primary reason for rodent control. In fact, brown rats, black rats and mice are capable of transmitting hundreds of infectious diseases to humans, including leptospirosis, hantaviruses, and numerous pathogenic bacteria (Lasseur et al., 2007). With the risk of resistance to second-generation anticoagulants, it is critical that we develop alternatives now to increase the modes of action available in our rodent control toolbox.

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