Retrieving and retaining older and advancing novel rodenticides-as alternatives to anticoagulants

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Abstract

Anticoagulant compounds are likely to play an important role in the control of commensal rodents for crop protection and conservation for the foreseeable future. However there are concerns regarding their persistence and the development of more widespread resistance. We are seeking to retrieve and retain older alternatives and develop novel rodenticides. Our three pronged approach is firstly to improve the performance of older non-anticoagulant rodenticides such as zinc phosphide, secondly to optimise the performance of 1st generation anticoagulants and thirdly to identify alternatives to anticoagulant rodenticides with the same mode of action as paraminopropiophenone (PAPP), which was registered in New Zealand as a predacide in April 2011.

Keywords: anticoagulants, paraminopropiophenone, synergists, zinc phosphide

Introduction

The most prolific period of rodenticide development occurred between the 1940s and the 1980s. First generation anticoagulant rodenticides and zinc phosphide were developed in the 1940s, 50s and 60s, with cholecalciferol, bromethalin and second generation anticoagulant rodenticides developed in the 1970's and 80's, partly to overcome resistance to the less potent anticoagulants (Buckle and Smith, 1994). During this period it was recognised that it was important to have two classes of rodenticides, both anticoagulants and alternatives to anticoagulants. In recent times the need for toxicants for field use that are effective but less persistent than second-generation anticoagulants, and therefore likely to be less hazardous to non-target bird species and other non-target species has been highlighted. Ironically registration requirements in Europe and around the world have reduced the number of options available for rodent management. We believe it is important to retain and refine the use of rodent control tools for conservation, disease control and agricultural protection and develop new alternatives to anticoagulants. Ideally alternatives to existing anticoagulants would combine limited persistence and humaneness, however this is a significant challenge. A microencapsulated form of zinc phosphide has been developed and a low dose of cholecalciferol combined with diphacinone or coumatetralyl is being re-evaluated (Eason et al., 2010a) to provide three low residue alternatives. In April 2011 para aminopropiophenone (PAPP), a methaemoglobinaemia inducer was registered for the control of predators in New Zealand. PAPP is humane in its mode of action and does not bioaccummulate. It has an antidote and is highly toxic to species like stoats (Eason et al., 2010b) but unfortunately not toxic to rodents. Approximately 50 compounds with the same mode of action including analogues of PAPP have recently been screened to assess their potency as rodenticides.

Methods

Groups of caged rats have been presented with a microencapsulated form of zinc phosphide containing 1.5% in a palatable paste bait. Coumatetralyl (0.03%) combined with cholecalciferol (0.015%) and diphacinone (0.05%) also combined with cholecalciferol (0.015% and 0.03%) have been tested on caged rats in the same bait matrix. Analogues of PAPP have been screened for their potency as rodenticides. *In vitro* work was carried out using a methaemoglobin assay involving hepatic microsomes and rat erythrocytes. The toxicity of the most promising candidates from the *in-vitro* screening has recently been assessed *in vivo* in laboratory rats by oral gavage.

Results

A microencapsulated form of zinc phosphide containing 1.5% has been shown to be 100% effective in caged rats. A combination of coumatetralyl (0.03%) and cholecalciferol (0.015%) has also been confirmed as having high potency in rats and similar to that achieved by diphacinone (0.05%) and cholecalciferol (0.15%). Diphacinone (0.05%) was partially effective as a single dose rodenticide when combined with cholecalciferol (0.015%) and more effective when combined with a higher dose of cholecalciferol (0.03%). PAPP and sodium nitrite have been developed as vertebrate pesticides in New Zealand and Australia (Eason et al., 2010b). In laboratory rats neither compound is sufficiently potent to be an effective rodenticide. Approximately 50 compounds with the same mode of action including analogues of PAPP have been screened for their potency as rodenticides. This screening has identified a compound with an LD50 of approximately 40-50mg/kg. Further derivatives of this more potent analogue are being synthesized and screened.

Conclusion

It has been suggested that product innovation needs to be stimulated to encourage alternatives to the current suite of rodenticides, as a number of these are associated with secondary poisoning or bioaccumulation or they are viewed as inhumane (Mason and Littin, 2003). We have advanced an improved formulation of zinc phosphide and are confirming the synergistic effects of cholecalciferol when co-administered with first generation anticoagulants. These developments may provide partial solutions and help provide products that break the cycle of rodenticide resistance. However to produce completely new rodenticides a new level of innovation is needed. Our current approach is to attempt to build on the platform created by PAPP. We are part way through a programme of research, development and registration activity and further in vitro and in-vivo testing is scheduled over the next 3 years on novel candidates as well as field trials. Any new tools that emerge would most likely need to be integrated with anticoagulant rodenticides which are likely to play an important role in the control of rodents for the foreseeable future.

References

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