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Australian Government
Department of the Environment, Water, Heritage and the Arts

Invasive Animals CRC

SODIUM NITRITE SYNERGISTS (Summary report)[1]

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Report for the Australian Government
Department of The Environment, Water, Heritage And The Arts (Extract)

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EXECUTIVE SUMMARY

There is Australian and worldwide demand for improvements in vertebrate pesticides. 1080 use has been curtailed internationally and remains under pressure as it is considered inhumane by the RSPCA. There is an opportunity, and a challenge, to develop new vertebrate pesticides which are a quantum leap ahead in terms of humaneness and improved target specificity. A new class of compounds could emerge targeting red blood cells in mammalian pests, effectively building on the platform created by para-aminopropriophenone (PAPP). Sodium nitrite is a second vertebrate pesticide candidate in this group and is being developed by the IA-CRC for control of feral pigs. Sodium nitrite is less toxic than conventional vertebrate pesticides such as 1080 and brodifacoum on an mg/kg basis. Larger doses are needed to kill large target species, hence the focus on enhancing its acute toxicity. The following approaches should be considered:- i) optimizing particle size, formulation and vehicle effects on bioavailability ii) modification of stomach acidity to increase the rate of sodium nitrite absorption iii) exploiting the toxicity of methaemoglobin (MtHb) inducers with different modes of action, including direct and indirect (MtHb) inducers used in combination, to produce a more profound and rapid onset of acute toxicity or exploring the potential of other red blood cell toxicants that could exacerbate the effects of sodium nitrite iv) co-administration of compounds that cause respiratory depression through mechanisms other than anoxia.

Non-technical impediments are equally challenging. There have been no registrations of new active ingredients in this field since the development of brodifacoum and cholecalciferol in the 1970/80s. Major multinational pharmaceutical and agrochemical companies have very substantial resources and cohesive high caliber research teams. They could develop new vertebrate pesticides but are focused on more lucrative markets. Effective public-private sector collaborations remains essential if smaller research agencies in Australia and NZ are to achieve major advances and deliver new product registrations. This has been proven to be important for the development of PAPP and will apply to the development of any novel vertebrate pesticides including sodium nitrite and synergists to enhance its toxicity. This report provides some ideas for enhancing the toxicity of sodium nitrite. It also outlines some key areas of collaborative research, which could be undertaken immediately to help optimize the potential of sodium nitrite as a vertebrate pesticide.

DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

There have been no registrations of new active ingredients in this field since the development of brodifacoum and cholecalciferol in the 1970/80s. However, a new class of compounds could emerge targeting red blood cells and sodium nitrite is a vertebrate pesticide candidate in this group and is being developed by the IA-CRC for control of feral pigs. Sodium nitrite is less toxic than conventional vertebrate pesticides such as 1080 and brodifacoum on an mg/kg basis and as larger doses are needed to kill large target species, it is important that there is a focus on enhancing its acute toxicity.

Species differences in the metabolism and pharmacokinetics of xenobiotic compounds are linked to differences in susceptibility and to the different effects of target organ toxicants in different species can be used to enhance toxicity. Various studies have reported profound species differences in both the response to xenobiotics, including barbiturates. (Williams 1973; Walker 1978; Gaunt *et al.* 1981; Eason *et al.* 1982; Eason *et al.* 1988). At this stage we do not recommend further work in this direction as there are more immediate and simple avenues to pursue, linked to formulation variables, the acidity of the stomach and exploiting the potential of chemical synergists.

The following approaches are recommeded-in the following order:-

1. optimizing particle size, formulation and vehicle effects on bioavailability.
2. modification of stomach acidity to increase the rate of sodium nitrite absorption.
3. exploiting the toxicity of methaemoglobin (MtHb) inducers with different modes of action, including direct and indirect (MtHb) inducers used in combination to produce a more profound and rapid onset of acute toxicity or exploring the potential of other red blood cell toxicants that could exacerbate the effects of sodium nitrite.
4. co-administration of compounds that cause respiratory depression through mechanism other than anoxia.

This report provides some ideas for enhancing the toxicity of sodium nitrite to help optimize the potential of sodium nitrite as a vertebrate pesticide. It also outlines some key areas of collaborative research, which could be undertaken immediately to help optimize the potential of sodium nitrite as a vertebrate pesticide. We have AEC approval now and resources to test up to 50 pigs with sodium nitrite and could address many of the research questions raised in this report. It is recommended that research questions related to bioavailability be prioritized by Lapidge/Eason and addressed in a scheduled series of experimental pig studies in NZ November 08 to February 09.