March 1992

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ABSTRACT: Aversive agents are proposed as potential additives to rodenticides to increase selectivity to the target species. Examples of various aversive agent categories are given, including odorants, tastants, and emetics, with examples of evaluations. Tastant additives have been found that do not interfere with rodenticidal efficacy. Denatonium benzoate (commercially available as Bitrex®) is an intensely bitter but non-toxic substance, being increasingly used to adulterate common household materials to reduce the potential risks involved with accidental exposures. No known prior research results have been published concerning the incorporation of Bitrex in rodenticides. Rate determination studies utilizing different rodenticidal formulations were conducted. A Bitrex level of 10 ppm was well accepted by wild commensal rats and mice in laboratory tests of brodifacoum pellet and wax block formulations (TALON®, KLERAT® Rodenticides). Bait samples with this level of Bitrex (without anticoagulant) were evaluated in a human taste panel study. Samples with Bitrex were found to show significantly greater average rejection by the panel than similar samples without Bitrex. Field trial results are reviewed, which verified the efficacy of Bitrex-containing commensal rodenticides. The potential role of Bitrex or similar taste deterrents as rodenticide additives is considered opposite accidental toxicant exposure statistics, and perceptions relating to rodenticides and other pesticides.

Proc. 15th Vertebrate Pest Conf. (J. E. Borrecco & R. E. Marsh, Editors) Published at University of Calif., Davis. 1992

INTRODUCTION

Vertebrate control agents of a chemical nature may be potentially hazardous to a variety of nontarget animals, including people, whose biological systems may respond similarly to those of the pest species. Body weight differences between target and nontarget animals may provide some intrinsic protection to the latter against potentially harmful effects from accidental exposure. Some vertebrate toxicants, such as anticoagulant rodenticides, have a ready antidote in the form of vitamin K_1, which is widely available to physicians (and veterinarians) for treatment of suspected accidental poisonings. Further, professional pest management involving toxic chemicals has normally included in-use components that increase selectivity to the pest and decrease hazard to other life through specific and specialized application techniques.

Commensal rodenticide baits, for example, are typically placed in areas judged to be inaccessible to children, pets, domestic animals, and wildlife; or in tamper-resistant bait stations (as is, in fact, mandated by standard US EPA labeling requirements). Yet careful placements may be vandalized or disturbed by natural events such as wind or rain. Further, home owners and farmers, in particular, have access to many retail toxic control materials but may lack the required specialized knowledge of pest behavior and of chemical agents in many situations to ensure efficacy while minimizing hazard.

There are a number of ways that efforts have been made by users, researchers, regulators and manufacturers to try to reduce hazard in both professional and nonprofessional use areas (see Table 1). Education and instruction, including labels, material safety data sheets and product literature, seek to influence and direct literate adult users in the proper storage, use and disposal of toxicants. Such efforts may not reach the young, the illiterate, the foreign speaker, or the careless; nor those who encounter the toxicant apart from such information. Although many nontarget mammal species are color-blind, studies have shown colored rodent baits may reduce bird hazard (Kalmbach and Welch 1946). With people, warning colors or symbols may help in general, but may provide nonspecific or conflicting cues to some cultural or age groups. Brightly-colored foods are often typical of holiday fare in some Latin and other cultures, and candies can be found in a variety of shapes and colors. A skull-and-crossbones may connote pirates, not poison. A symbol such as 'Mr. Yuk' (a grimacing cartoon face) may attract some children, rather

Table 1. Techniques to reduce nontarget hazard of Vertebrate pesticides (particularly commensal rodenticides).

EDUCATIONAL/INFORMATIVE MATERIALS
Product labels
Material safety data sheets
Commercial product literature
Training booklets or programs
VISUAL WARNING CUES
Warning colors
Warning symbols
PROTECTIVE PACKAGING
Child-resistant closures
SELECTIVE/PROTECTIVE PLACEMENTS
Inaccessible baiting (e.g., burrows)
Tamper-resistant bait stations
Pulsed baiting; lower toxicant loading in targets
SELECTIVELY ACCEPTABLE FORMULATIONS
Intrinsic rodent acceptability/nontarget rejection
Adulterants
Emetics
Odorants
Tastants

than repel or warn, unless accompanied by a strong educational component (Fergusson et al. 1982).

With medications and some household products, accidental exposure while such products are being stored are often greater than in-use hazards. For these products (such as aspirin), the adoption of protective packaging (such as child-resistant closures), and increased labeling precautions and restrictions have reduced accidental poisonings, especially of children, by nearly 40% in the USA since the late 1970s (Anon. 1985).

Beyond labeling, packaging and placement, what can be done to rodenticide products to increase selectivity? In addition to warning colors or symbols, intentional adulteration of product by emetic, or addition of a taste or odor is possible. Yet rodenticidal toxic baits must remain sufficiently palatable to the target species to be effective, and conventional wisdom has eschewed adulterants that might well decrease bait acceptability to rodents. Rodenticides typically contain grain components highly preferred by most pest rodent species, bolstered with sweeteners in order to better compete with existing pest food sources and to pass government registration standards that help ensure adequate product performance. Commercially-prepared baits are normally highly processed and usually bear little resemblance to grain-based products consumed as human foodstuffs. The most popular commercial rodenticides today are pelletized or are wax impregnated blocks. These are typically hard and dry, and too bland or otherwise too unlike normal foodstuffs to appeal to the average human palate. However, some younger children may have less 'food experience' and may possess different taste preferences as compared with adults (Engen 1974, Engen and Gasparian 1974). One also must recognize, among nontarget animals potentially exposed to rodenticides, that many domestic animals, such as dogs and cats, have been conditioned to eat a variety of 'pet foods' quite dissimilar in appearance (if not also in taste) from naturally-occurring foodstuffs.

POTENTIAL ADULTERANTS

Potential types of adulterants to increase selectivity or reduce hazard to nontarget animals such as humans, pets, domestic animals or wildlife include emetics and aversive odors and tastes. The use of several of these approaches to reduce nontarget wildlife hazard from rodent control has been discussed by Marsh (1985). The term 'adulterant', 'denaturant', or simply, 'additive' is perhaps preferred to 'protectant', which implies (perhaps incorrectly), that the additive does universally provide differential selectivity. Likewise, although the term 'saftener' has been used with reference to vertebrate pest research, this term more commonly refers to a herbicide additive which protects plants from phytotoxicity.

Emetics

Few emetics have been widely proposed as protectants for inclusion in rodenticides, despite the fact that rodents cannot vomit. Most commonly, tartar emetic (potassium ammonium sulfate), which was once combined with the more hazardous older acute materials, is suggested for reconsideration (Muktha Bai and Majumdar 1984). Yet most authors concede that the addition of tartar emetic will very much lower the acceptability of the poison baits containing it (Marsh 1985). Experience gained in ICI trials with tartar emetic and proprietary ICI pyrimidine emetic compounds resulted in unacceptably reduced efficacy at emetic levels required for nontarget protection (see Table 2).

Table 2. Results of testing of potential emetics (tarter emetic and ICI emetic) in pelletized rodenticidal formulations (10 animal groups, 8 day choice tests).

Species	Rate	Treated (g)	Total eaten (g)	% Accept.
TARTAR EMETIC (antimony potassium tartrate)				
Microtus pennsylvanicus	0.02%	65.6	409.2	16
ICI EMETIC (PP796)				
Microtus pennsylvanicus	0.005%	9.7	241.6	4
(ICI Unpublished)				

If emetics produce a vigorous emesis action, they may themselves be hazardous for the nontarget animals they are to protect, from potential aspiration of vomitus and resultant complications, including potential respiratory failure.

Odorants

Repellent odors have not been studied to any extent as additives to increase rodenticide selectivity. Carbon disulfide, a natural component of commensal rodent saliva, has previously been suggested as a possible bait additive to increase its attractiveness to rodents (Mason et al. 1988). This compound has, to most human noses, a highly objectionable odor. Tests by ICI to evaluate this material's utility as a commercial rodenticide bait attractant found that rodents rejected treated bait (Table 3), and were hampered by the volatility of the material. Palatability problems were also observed with butyric acid, a component of rodent urine that had been implicated as a potential rodent attractant following work such as Stoddart and Smith (1984) (see Table 3). Even if particular odorants were found acceptable or attractive to rodents and aversive to nontargets, the incorporation of such volatile and transient constituent into a bait would present considerable formulation and production difficulties, and might well be objectionable to applicators and persons living or working in baited areas.

Aversive Tastant Agents

Aversive (or 'adversive') tastant agents cause nontarget animal rejection of a material by presenting unpleasant gustatory cues such as flavors, textures, or other taste (and sometimes associative odor) characteristics. Aversive tastants may generally be viewed with caution because of concerns of reducing product palatability to the target species. Use of 'hot-pepper' extracts (capsicum) have been informally proposed in the past for inclusion in potentially hazardous materials (Jones-Smith 1990), but ICI tests found capsicum-treated pellets were significantly less acceptable than untreated pellets (ICI, unpublished). Mason et al. (1985) proposed using a grape flavoring, dimethyl anthranilate (DMA), to provide a bird-aversive agent in cattle feed under feedlot conditions. The idea that this might also protect commensal rodenticides from bird ingestion was discouraged by ICI tests which found DMA significantly decreased rodent acceptability of baits

Table 3. Results of testing of potential odorants (carbon disulfide and butyric acid) in *Microtus* challenge diet (50% ground rodent chow, 50% ground oats) versus untreated diet (10 animal groups).

Species	Rate	Treated (g)	Untreated (g)	% Accept.	S.D.
CARBON DISULFIDE					
M. pennsylvanicus	0.5%	2.4	138.0	2%	1.5
M. pennsylvanicus	1.0%	7.4	92.1	6%	2.0
Rattus norvegicus	0.5%	68.2	767.8	9%	10.0
BUTYRIC ACID					
M. pennsylvanicus	2.5%	4.5	146.7	3%	0.5
M. pinetorum	0.25%	55.9	92.8	39%	22.0
(ICI, unpublished)					

Table 4. Results of testing of potential tastant DMA (dimethyl anthranilate) in EPA challenge diet (60% ground com, 25% ground oats, 5% corn oil, 5% sugar) versus untreated EPA meal (2 voles and 4 pheasants per group, 3 day choice tests).

Species	Rate	Treated (g)	Untreated (g)	% Accept.	S.D.
VOLES					
M. pennsylvanicus	2.0%	2.5	67.8	4%	3
M. pennsylvanicus	1.0%	4.0	25.4	14%	6
M. pennsylvanicus	0.5%	4.5	40.2	10%	12
RING-NECKED PHEASANTS					
Phasianus colchicus	1.0%	49.1	637.0	7%	NA
Phasianus colchicus	0.5%	157.9	903.1	15%	NA
(ICI Unpublished)					

Table 5. Toxicity of denatonium benzoate.

Acute Oral LD_{50} Values (mg/kg)	
Rat	612
Mouse	>1000
Rabbit	583
Guinea Pig	805
96-Hr LC_{50} Values (mg/l)	
Shrimp	400
Rainbow Trout	>1000
Results of Hazard Studies	
Non-mutagenic	
Non-irritating	
No inhalation hazard	
(after Anon. 1989)	

(see Table 4).

Bittering Agents

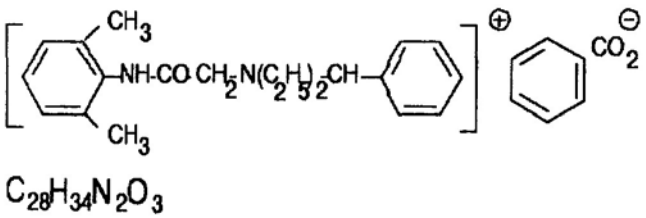
Denatonium benzoate was discovered some 30 years ago (Payne 1988). A related form, denatonium saccharide, was described some 8 years ago (Davis et al. 1987). These are bittering agents used to denature various household products. Denatinoum benzoate is commercially available as Bitrex, Bitrexene®, and other tradenames. Denatonium benzoate is listed in the Guiness Book of Records and the Merck Index as "the bitterest substance known to man". The full chemical name is N-[2-[(2,6-dimethylphenyl) amino]-2-oxoethyl)-N,N-diethyl-benzenemethan aminium benzoate, and the structure is given in Figure 1. Denatonium benzoate can be detected by the average person at 10 ppb, and has a generally recognized bitter taste at 50 ppb (Anon.1989). The normal application range is 6-50 ppm, depending on the nature of the product to which it is added. Bitrex chemically resembles natural bitter substances such as quinine in having a molecular structure with separately charged elements that act on taste receptors.

Denatonium benzoate was first used in rubbing alcohol as a denaturant in the 1970s, at a level of 6 ppm in the USA, and 10 ppm in the UK (Klein-Schwartz 1991). Discovered by J. E. Hay in the 1950s (Payne 1988), the efficacy and safety of denatonium benzoate as a general product additive has been most recently reviewed by Klein-Schwartz (1991).

Such an intensely bitter substance as denatonium benzoate offered considerable promise as an adulterant for a variety of applications, particularly when studies showed it had low mammalian toxicity (Table 5), and in toxicological testing was found to be not mutagenic, non-irritating, and to pose no inhalation hazard (Anon. 1989). Its bitter properties and proposals for use as an adulterant to reduce potential hazard in various products was set forth in various patents, such as the US patent 3,080,327 granted in 1963.

Early work indicated a universal dislike of Bitrex by children in the age range 14 months to 8 years (Payne 1988). An example of research leading to the inclusion of denatonium benzoate in liquid laundry detergents in the USA is given in Berning, Griffith and Wild (1982).

Denatonium benzoate is available from several sources, such as Macfarlan Smith Ltd. of Edinburgh, Scotland. Sources in the USA include Henley Chemicals, Inc., and Atomergic Chemetals, both of New Jersey. Denatonium benzoate is an EPA approved inert additive, and is present as an additive in a variety of products in the USA and elsewhere, including denatured alcohols, cleaners, disinfectants, laundry detergents, nail-biting and thumb-sucking deterrents, and other products



$C_{28}H_{34}N_2O_3$

Figure 1. Denatonium benzoate.

(Anon. 1989).

A number of bills have been introduced in the U.S. Congress and in states such as the California Assembly dealing with recommendations that denatonium benzoate be added to such materials (Jones-Smith 1990). The American Association of Poison Control Center's Executive Committee in 1989 circulated a resolution encouraging individual manufacturers to add bittering agents to potentially toxic liquid formulations of household and commercial production. Various consumer advocates have also championed Bitrex (Hinds 1989).

Bitrex has been developed as various animal repellents, such as cat, dog and bird repellents, for prevention of cannibalism in pigs, to keep horses from chewing their stalls, deer from nibbling tree shoots, and to keep hedgehogs from eating slug pellets (Payne 1988). The related agent, denatonium saccharide, is sold as an animal repellent spray under the name ROPEL® (Burlington Scientific Corp., Farmingdale, NY), and has general claims of efficacy against dogs, cats, raccoons, gulls, rats, squirrels, and other animals. It is proposed for spraying of garbage and garbage containers to prevent such animals from garbage depredations.

With these animal repellent applications, it is somewhat counter-intuitive to consider adding such bittering agents to a product that must be eaten to be effective, such as a rodenticide. Langley (1987) found denatonium benzoate caused aversion in the grasshopper mouse (*Onychomys leucogaster*). One clue that a bittering agent might hold promise for rodenticide inclusion lay in the paper by Davis, et al. (1987), which concluded, for denatonium saccharide, that although human subjects rated denatonium saccharide as significantly more unpleasant than quinine, rat subjects did not. These authors expressed caution with regard to the use of this material as a rodent repellent. Similarly, unpublished results by researchers at the Denver Wildlife Research Center and the Monell Chemical Senses Center showed poor repellency of these materials to deer mice (when tested as a seed repellent) and to various other species tested (Mason, 1992). Johnson (1988) described the inclusion, without rodent aversion, of an unidentified bittering agent in rodenticidal baits utilizing the anticoagulant flocoumafen, but did not give research results.

METHODS

In ICI research, after trying various levels of denatonium benzoate in several bait formulations, an optimum formulation with Bitrex was found that did not significantly affect rodent palatability. Both Norway rat and house mice were tested. In direct comparisons involving singly caged groups of 10 animals, palatability of brodifacoum formulations (TALON; KLERAT, etc.) containing 10 ppm Bitrex were not significantly different from formulations that were identical except that they did not contain the Bitrex. (see Table 6).

REGISTRATION STUDIES

Efficacy tests were required for USEPA registration of TALON Rodenticide containing denatonium benzoate, because the product is for public health use. These tests were in the form of acceptance tests against an unpoisoned standard diet known as EPA meal, which is composed of corn-

Table 6. ICI test results with 10 ppm denatonium benzoate (Bitrex) bittering agent in brodifacoum rodenticidal formulations (10 animal groups, 4 day choice tests).

	Formulation with Bitrex		Formulation without Bitrex		
	eaten (g)	% Accept.	eaten (g)	% Accept.	% S.D.
PELLETS					
Norway Rat					
albino	466.1	58%	337.5	42%	15
wild	386.6	59%	255.3	41%	17
House Mouse					
albino	78.5	48%	88.5	52%	17
wild	56.2	58%	41.8	42%	20
BLOCKS					
Norway rat					
albino	527.1	57%	403.9	43%	11
wild	431.3	49%	410.8	51%	10
House Mouse					
albino	75.3	50%	79.6	50%	19
wild	51.0	54%	64.7	46%	32
Roof rats (wild)	165.9	67%	322.7	37%	11

meal, oatmeal, corn oil, and sugar. At least one-third (33%) of the total average consumption by animals in these tests had to be of the TALON with Bitrex in order to pass the EPA criteria for registration. In addition, at least 90% kill of the test group of 20 albino rats or mice had to be achieved. One replication (two tests total) was required, plus concurrent control groups (fed EPA Meal only). Results with denatonium benzoate in brodifacoum formulations (TALON; KLERAT) are given in Table 7. Control group data is not given; no control animals died.

These TALON formulations with denatonium benzoate all passed the minimum EPA test criteria, and led to EPA's statement in their letter to ICI of March 29, 1990, that "The efficacy tests submitted for [Bitrex-containing brodifacoum products] are acceptable."

FIELD EFFICACY STUDIES

Various field trials have been conducted in the UK and USA to evaluate the efficacy of ICI brodifacoum formulations containing 10 ppm Bitrex. In the UK, trials of the wax block (e.g., KLERAT or TALON WEATHERBLOK) at two farms against warfarin-resistant Norway rats were conducted according to standard methods involving indirect census methods of food consumption and tracking counts (Kaukeinen, 1979). Results are given in Figure 2, a and b. Results obtained indicated over 95% reduction in rat activity at these farms. These results meet or surpass all efficacy criteria and compare favorably with other trials of similar blocks but without denatonium benzoate.

Trials against house mice on a pig farm in North Carolina compared brodifacoum (TALON; KLERAT) pellets with 10 ppm Bitrex against brodifacoum pellets without Bitrex, a further experimental formulation, and vs. the resident pig ration (unpoisoned pelletized diet) according to the method of Buckle and Kaukeinen (1988). The pellets containing Bitrex were preferred equally to those without Bitrex, see Figure 3.

EFFICACY OF BITREX TO HUMAN SUBJECTS

A 10 ppm Bitrex level was tested in orange juice in Britain with young children (Sibert and Frude 1988). It was found that only 2 or 3 of 30 children drank more than their first sip of the Bitrex-laced juice. A further study on 10 youngsters who had previously poisoned themselves showed these accident-prone children reacted as strongly to Bitrex as the majority of children not previously poisoned.

But what about denatonium benzoate in solid materials like rat baits? ICI commissioned a study with humans given specially formulated blank (no active ingredient) TALON blocks and pellets containing Bitrex. Volunteers were asked to taste wax blocks containing 0, 1 ppm and 10 ppm Bitrex and rate their response on a hedonistic scale from 1 to 7, ranging from 'like extremely' to 'dislike extremely'. The response of subjects to blocks containing 10 ppm Bitrex was dramatic. The test was repeated the following day with pellets containing similar Bitrex loadings, with similar results (see Figure 4, a and b). The same 10 ppm level was found to significantly discourage human consumption (ICI, unpublished).

Although only much higher levels of denatonium benzoate than 10 ppm in solid baits would universally discourage nontarget animals such as dogs, such levels would also prevent rodent consumption (ICI, unpublished). Even so, these

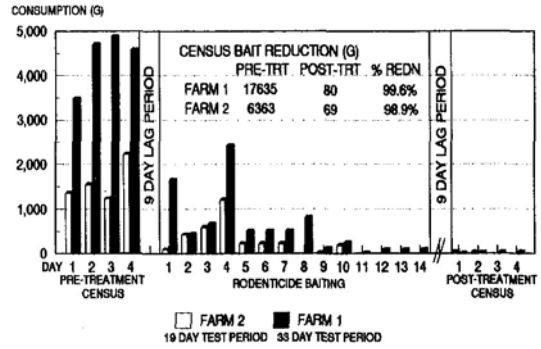


Figure 2a. Daily consumption. UK field trials of 50 ppm brodifacoum blocks with Bitrex versus warfarin-resistant Norway rats.

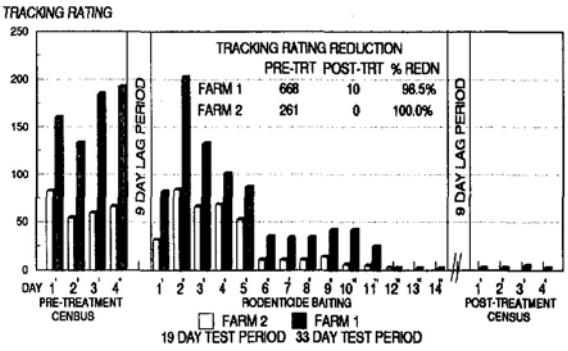


Figure 2b. Daily tracking ratings. UK field trials of 50 ppm brodifacoum blocks with Bitrex versus warfarin-resistant Norway rats.

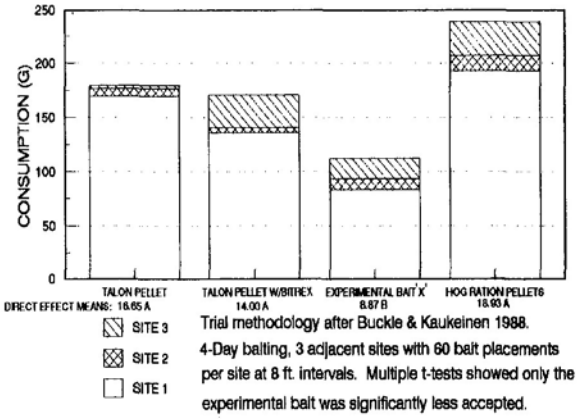


Figure 3. Comparative field trial on house mice on a North Carolina hog farm indicating the consumption (g) of three baits plus control.

lower levels of Bitrex may somewhat reduce the likelihood of accidental poisonings with pets, domestic animals, and wildlife. Other rodenticide manufacturers have also independently registered denatonium benzoate in some of their formulations. J.T. Eaton's in Ohio have 50 ppm denatonium benzoate in their BAIT BLOCKS® for mice. Purina Mills, St Louis, has registered 20 ppm denatonium benzoate in their bromethalin formulation, ASSAULT®. Shell has 10 ppm denatonium benzoate in the STORM® wax briquettes that are sold in several countries. Sorex in the UK also incor-

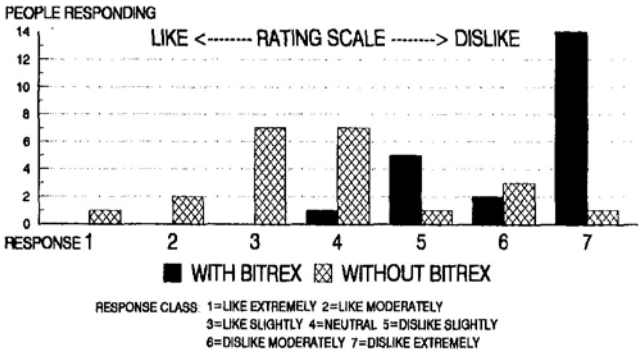


Figure 4a. Human taste test. Blank Talon Weatherbloks with versus without 10 ppm Bitrex.

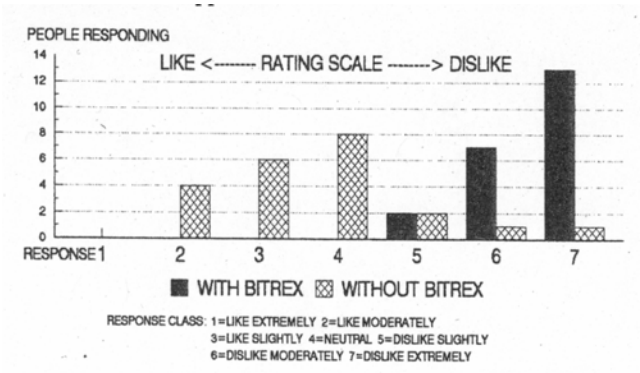


Figure 4b. Human taste test. Blank Talon pellets with versus without 10 ppm Bitrex.

porate 10 ppm denatonium benzoate into their various warfarin, calciferol and other baits (e.g., SOREXA®, NEOSOREXA CR®).

Taste perception of denatonium benzoate is highly dependent upon specific components of the formulation, particularly sweeteners. This may explain why different levels of denatonium benzoate have been adopted. Doubtless further research by other manufacturers will follow, resulting in additional denatonium benzoate-containing rodenticidal products.

PERCEPTIONS OF RODENTICIDE HAZARD

Efforts to increase the selectivity of vertebrate pesticides such as rodenticides through the use of adulterants like denatonium benzoate are deserving of further research and adoption. While thankfully few rodenticide exposures result in medical complications, they still constitute a frequent source of inquiry to poison control centers across the U.S. due to the perception of their hazard, and their frequency in the home. Most calls involve children found playing with product, or with a pellet in the mouth. The American Association of Poison Control Centers Report (Litovitz et al. 1991) states that anticoagulant rodenticides comprised nearly 86% of a total of 13,817 rodenticide calls reported by their network in 1990 (rodenticides comprised only 1% of the total of 1,054,655 calls on nonpharmaceutical substances). This is not surprising considering that anticoagulants form the principal rodent control materials currently used by professionals and home owners alike in the USA.

Of all American anticoagulant rodenticide calls, including both first-generation (e.g., warfarin) and second-generation (brodifacoum and bromadiolone) products, the AAPCC reports that nearly 91 % of calls, where age of the person was determined, involved children under 6 years of age, compared with 2% between 6-17 years old, and 6% for persons over 17. Of 5,798 cases where outcome was determined following exposure to anticoagulant rodenticides, nearly 92% showed no observed effect, 7% showed a minor effect, 0.5% a moderate effect, and 13 cases (less than 0.2%) had a major medical effect. There were no deaths from anticoagulant ingestions. Nearly 70% of all anticoagulant calls involved "long-acting" anticoagulants like TALON, but comparisons with first generation materials showed no greater observed effects than seen with first-generation materials like war-

Table 7. USA registration studies (EPA protocols). Laboratory efficacy tests involving Bitrex in ICI rodenticidal formulations with albino rats and mice (20 animal groups, 3 day choice tests).

		EPA Meal (g)	Formulation (g)	% Accept.	S.D.	Kill
STANDARD PELLETS WITH BITREX						
Norway rats	Test 1	716.6	747.3	51%	12	20/20
	Test 2	585.4	737.3	55%	20	19/20
House mice	Test 1	127.2	143.4	54%	20	20/20
	Test 2	90.8	193.4	69%	17	20/20
MINIPELLETS WITH BITREX						
Norway rats	Test 1	805.0	761.4	44%	21	18/20
House mice	Test 1	72.9	233.4	77%	16	20/20
WEATHERBLOK WITH BITREX						
Norway rats	Test 1	861.1	524.5	38%	15	20/20
	Test 2	750.8	583.4	43%	11	20/20
House mice	Test 1	135.3	155.2	51%	30	18/20
	Test 2	141.2	97.6	40%	14	20/20

farin. (Insufficient data is available for most non-anticoagulant rodenticides to allow for useful relative comparisons).

However, this more benign outcome does little to lessen parental or medical concern (and the child's trauma) at the time of exposure, when the likelihood, quantity and time of ingestion, or even the identity of the ingested material itself, may not be well established. Knowledge by the medical community that Bitrex is present in some products may provide some additional basis impacting diagnosis and treatment.

Stewardship issues are of critical importance today for all involved in efforts to provide for pest animal management and control. Public perception of rodents as noxious and feared animals provide continued sympathy supporting the careful use of rodenticides in most countries and use areas. Yet frequently, the perception remains that any pesticide is necessarily very hazardous to humans, pets and wildlife, whether or not exposure statistics support such a view. This perception, as well as legitimate exposure cases, can be modified, though not eliminated by toxicant additives such as denatonium benzoate.

However, rodenticides (or any pesticide or potential toxicant) containing Bitrex retain the same toxicity to nontarget species, and must be used in the same careful way, according to good practices and label directions. The public and safety advocacy groups must be educated that such additives are not 'pesticide panaceas,' or simple and quick product modifications. Additive inclusion can require extensive research by manufacturers and others (including testing required for modified product registrations) encompassing, but not limited to, determinations ensuring additives do not interfere with product efficacy and stability, and that they do offer some increased product aversion in nontarget animals.

With the many threats to the continued availability and use of remaining vertebrate pesticides, and the significant development costs of creating new chemical tools, such adulterants provide a useful adjunct to other efforts to reduce potential nontarget hazard. Continued research to identify and refine aversive agents as additives to increase the selectivity of rodenticides is strongly recommended.

LITERATURE CITED

ANONYMOUS. 1985. A prime case for bitterness. New Scientist, 9 May, p 40.

ANONYMOUS. 1989. Bitter taste as a deterrent to accidental product ingestion, Macfarlan Smith, Edinburgh, Scotland, unpub doc., 8pp, Revised.

BAGLEY, J.L. 1989. New developments in poison prevention. Creative innovations reduce the number of tragedies. Am. Drug. 199:35-36.

BERNING, C.K., J.F. GRIFFITH, and J.E. WILD. 1982. Research on the effectiveness of denatonium benzoate as a deterrent to liquid detergent ingestion by children. Fundam. Appl. Toxicology 2:44-48.

BUCKLE, A.P., and D.E. KAUKEINEN 1988. A field method for assessing the palatability of rodenticidal baits. In: (A.C. Crabb and R.E. Marsh, Eds.), Proc. Vertebr. Pest Conf. 13:156-159.

DAVIS, S.F. et al. 1987. Analyzing aversiveness of denatonium saccharide and quinine in rats. Perceptual and Motor Skills, 64:1215-1222.

ENGEN, T. 1974. The potential usefulness of sensations of odor and taste in keeping children away from harmful substances. Ann. N.Y. Acad. Science 237:224-228.

ENGEN, T., and F.E. GASPARIAN. 1974. A study of taste preference in young children. J. Safety Res. 6(3): 114-117.

FERGUSSON, D.M., L.J. H0RW00D, A.L. BEAUTRAIS and F.T. SHANNON 1982. A controlled field trial of a poisoning prevention method [Mr. Yuk]. Pediatrics 69(5): 515-520.

HINDS, M. D. 1989. Mother fights to ruin the taste of poison. New York Times, May 20.

JONES-SMITH, J. 1990. Status report. Study of aversive agents. Report to the Honorable Dan Quayle, President of the Senate, Washington, D.C., Consumer Product Safety Commission response to the Consumer Product Safety Improvement Act of 1990 (Pub. L.101-608, 104 Stat.3110, 3pp.

JOHNSON, R.A. 1988. Performance studies with the new anticoagulant rodenticide flocoumafen against *Mus musculus andRattus norvegicus.* EPPO Bulletin 18:481-488.

KALMBACH, E.R., and J.F. WELCH 1946. Colored rodent baits and their value in safeguarding birds. J. Wildlife Manage. 10(4):353-360.

KAUKEINEN, D. E. 1979. Field methods for census taking of commensal rodents in rodenticide evaluations. Vertebrate Pest Control and Management Materials, ASTM STP 680:68-83.

KLEIN-SCHWARTZ, W. 1991. Denatonium benzoate: review of efficacy and safety. Vet. Human Toxicol. 33(6): 545-548.

LANGLEY, W.M., et al. 1987. Effects of denatonium saccharide on the drinking behavior of the grasshopper mouse (*Onychomys leucogaster*). Bulletin of the Psychonomic Society 25:17-19.

LITOVITZ, T.L., et al. 1991. 1990 Annual report of the American Association of Poison Control Centers National Data Collection System. Amer. J. Emergency Medicine 9(5): 461-509.

MARSH, R.E. 1985. Techniques used in rodent control to safeguard nontarget wildlife. In: Laudenslayer, W.F., Ed., Cal-Neva Wildlife Transactions, pp. 47-55.

MASON, J.R., N.J. BEAN, and B.G. GALEF, JR. 1988. Attractiveness of carbon disulfide to wild Norway rats. In: A.C. Crabb and R.E. Marsh, Eds.) Proc. Vertebr. Pest Conf., UC-Davis, 13:95-97.

MASON, J.R., et al. 1985. Field evaluation of dimethyl anthranilate as a bird repellent livestock feed additive. J. Wildl. Manage. 49(3): 636-642.

MASON, J.R., 1992. USDA/APHIS, DWRC, Monell Chemical Senses Center, Personal Communication.

MUKTHA BAI, K., and S.K. MAJUMDAR. 1984. Enhancement of mammalian safety by incorporation of antimony potassium tartrate in zinc phosphide baits. Pesticides 18: 34-37.

PAYNE, H.A. 1988. Bitrex - a bitter solution to safety. Chemistry and Industry, 21 Nov., pp. 721-723.

SIBERT, J., and N. FRUDE 1988. Poison prevention is more than child-resistant closures: bittering agents in the prevention of accidental poisoning; reaction of children to denatonium benzoate (Bitrex). Pres. Nat. Safety Council Cong., Orlando, FL, Oct. 19, 1988. (Cited in Klein-Schwartz 1991, above).

STODDART, D.M., and P.A. SMITH 1984. Woodmice (*Apodemus sylvaticus*) can distinguish conspecific from heterospecific odors in the field, J. Chem. Ecol. 19(6): 923.