AGENCY FOR INTERNATIONAL DEVELOPMENT
WASHINGTON, D. C. 20523

BIBLIOGRAPHIC INPUT SHEET

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1. SUBJECT CLASSIFICATION	A. PRIMARY: Agriculture	AH10-0000-0000
	B. SECONDARY: Pests of plants	

2. TITLE AND SUBTITLE
UK 786 possible species-specific toxicant for Norway rats

3. AUTHOR(S)
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4. DOCUMENT DATE	5. NUMBER OF PAGES	6. ARC NUMBER
1973	4p.	ARC

7. REFERENCE ORGANIZATION NAME AND ADDRESS
Interior

8. SUPPLEMENTARY NOTES *(Sponsoring Organization, Publishers, Availability)*
(In Nature,v.241,no.5391,p.551-552)

9. ABSTRACT

10. CONTROL NUMBER PN-RAA- 594	11. PRICE OF DOCUMENT
12. DESCRIPTORS Rats Rodenticides Species-specific? Toxic tolerances	13. PROJECT NUMBER 14. CONTRACT NUMBER PASA RA(ID)1-67 Res. 15. TYPE OF DOCUMENT

AID 590-1 (4-74)

(Reprinted from Nature, Vol. 241, No. 5391, pp. 551–552, February 23, 1973)

UK 786 Possible Species-Specific Toxicant for Norway Rats

UK 786[1] (5-(N-piperidino)-10,11-dihydro-5H-dibenzo (a.d.)-cycloheptene (Dr J. Morrison, Pfizer Ltd.)) is a compound whose acute oral LD_{50} has been reported to be 6.6 mg kg^{-1} in male albino rats and 1,160 mg kg^{-1} in male albino mice[2]. These data suggested that UK 786 might be a highly specific toxicant for rats, and we conducted the following series of tests with thirteen species of birds and mammals to investigate this.

In acute oral toxicity tests, single doses of UK 786 were administered by stomach tube. Propylene glycol solutions were used for red-winged blackbirds, and the animals observed for seven days post treatment, but for all other animals, the chemical was prepared in 0.5% gum tragacanth and the observation period was 14 days. LD_{50}'s with 95% confidence limits were calculated by the methods of Litchfield and Wilcoxon[3] (for wild and albino Norway rats and albino mice) or Thompson[4] and Thompson and Weil[5] (for Polynesian rats and house sparrows). Sprague-Dawley albino rats, Swiss-Webster albino mice, and domestic rabbits were purchased from commercial suppliers, gerbils and bob-white quail were from our laboratory colonies, and all other animals were wild-trapped. All animals were adults and were individually caged, except the pigeons, which were caged together.

The acute oral toxicity tests indicated that of the thirteen species tested, only wild and albino Norway rats were highly susceptible to the lethal action of UK 786 (Table 1). Symptoms of poisoning in Norway rats included laboured breathing and cyanosis of the extremities, and death usually

Table 1 Acute Oral Toxicity of UK 786 in Animals

Common name and species	No. and sex tested	Dose (mg kg^{-1})	No. died	LD_{50} and 95% confidence limits
Bobwhite quail (*Colinus virginianus*)	2M, 2F	100	0	
Pigeon (*Columba livia*)	4*	500	0†	
Starling (*Sturnus vulgaris*)	2M, 2F	500	0	
Red-winged blackbird (*Agelaius phoeniceus*)	2M	100	0	
House sparrow (*Passer domesticus*)	6M	—	—	354 (——)
	2F	500	0	
Rabbit, domestic (*Oryctolagus cuniculus*)	3M	500	1	
	2M	100	0	
Deer mouse (*Peromyscus maniculatus*)	4M	1,600	1	
	4F	1,600	1	
Gerbil (*Meriones unguiculatus*)	2M, 2F	500	0	
Rat, ricefield (*Rattus r. mindanensis*)	8F	7.5, 15, 30, 120	0	
Rat, wild Norway (*R. norvegicus*)	12M	—	—	8.4 (5.3–13.4)
	12F	—	—	8.9 (4.4–18.2)
Rat, albino (*R. norvegicus*)	16M	—	—	11.9 (5.7–24.5)
Rat, Polynesian (*R. exulans*)	6M	—	—	354 (——)
Mouse, albino (*Mus musculus*)	40M	—		205 (85.4–492)

* Sex not determined.
† Three of the four birds regurgitated after dosing.

occurred in 1 to 4 h. Gross pathological examination revealed massive haemorrhaging within the lungs. In other animals that succumbed to UK 786, death occurred two to six days after dosing and no typical symptoms could be identified.

Ricefield, Polynesian, and wild Norway rats were used in voluntary feeding tests with treated bait, made by mixing UK 786 and ground commercial rat chow, and forming the mixture into 105–110 mg tablets. Ricefield and Polynesian rats were each offered one cup containing 10 g of treated tablets for one night. Norway rats were first offered two cups each containing about 20 g of untreated tablets for two consecutive nights; consumption from each cup was recorded daily, and on the third night 20 g of treated tablets were placed in the "preferred" cup and 20 g of untreated tablets in the second cup. Treated tablets were offered for two to four consecutive nights; on subsequent test nights, positions of the treated and untreated cups were alternated.

Table 2 Consumption and Mortality when Food Tablets Containing UK 786 were Offered to Individually Caged Rats for One Night

Rat species	Concentration of UK 786 (%, w/w)	No. and sex tested	Amount eaten: Treated food (g) Mean	Treated food (g) Range	UK 786 (mg kg^{-1}) Mean	UK 786 (mg kg^{-1}) Range	Mortality No.
Ricefield *	0.125	4 F	9.9	9.5 –10.0	61.6	52.4– 69.8	0
		5 M	10.0 †		56.5	47.3– 69.6	0
	0.25	5 F	4.9	1.9 – 7.4	75.2	30.0–122	0
	2.0	5 F	3.5	2.1 – 6.0	320	189 –468	0
Polynesian *	0.25	5 F	1.7	1.2 – 2.9	103	55.7–156	0
	2.0	5 F	0.8	0.1 – 2.1	273	12.9–848	0
Wild Norway ‡	0.25	5 F	3.1	0.41– 8.5	36.9	4.6–118	1
		5 M	1.9	0.64– 4.1	21.3	6.8– 45.3	0
	0.5	5 F	2.1	0.67– 3.9	45.1	18.2– 90.0	3
		5 M	2.1	0.33– 3.3	46.8	5.7– 81.8	2
	1.0	5 F	0.8	0.20– 1.4	50.7	12.1– 97.1	2
	2.0	10 F	0.7	0.14– 1.0	56.2	18.3–121	9
		10 M	0.6	0.03– 1.9	34.5	1.5–112	7

* Ricefield and Polynesian rats were offered 10 g of treated tablets only.
† Rats consumed all the bait.
‡ Norway rats were offered 20 g each of treated and untreated tablets.

The results of the feeding tests are summarized in Table 2. There was no mortality in ricefield and Polynesian rats offered bait for one night, but acceptance was poor at the higher concentrations. Although Norway rats were offered treated tablets for two to four nights, mortality occurred only the first night; acceptance was also poor at the higher concentrations, but they ate enough 2% bait to cause 80% mortality. After the first night, consumption of treated tablets was highly variable; some animals completely rejected the bait, others ate less than, as much as, or more than the first night.

Public health and agricultural workers have been searching for many years for chemicals for use in Norway rat control programmes that are relatively nontoxic to man, domestic animals and nontarget wildlife. 'Warfarin' has been in the forefront as a rat toxicant, but after the detection of 'Warfarin'-resistant Norway rats in Great Britain[6], and recently in the United States[7], the search for new chemicals to replace it has become more important. Norbormide is selectively toxic to rats[8] but causes "bait shyness". Our primary target species are ricefield and Polynesian rats, but the preliminary data reported here indicate that UK 786 may be a useful rodenticide for Norway rats.

We thank Pfizer Ltd for providing UK 786. This work was conducted in part with funds provided by the US Agency for International Development.

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Received October 13, 1972.

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Printed in Great Britain by Flarepath Printers Ltd., St. Albans, Herts.