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ContraPest®, a New Tool for Rodent Control

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ABSTRACT: Lethal rodenticides and other lethal tools of managing commensal rodent populations long-term are not sustainable due to population rebounds and increasing resistance to rodenticides. The use of integrated pest management (IPM) programs are more prevalent due to consumer desire to decrease rodenticide use and utilize environmentally friendly, humane methods. IPM plans often require multiple tools to control an infestation, such as physical, biological and chemical measures. Here, we propose that rodent population management would benefit from a new tool aimed at targeting the biological source of overabundance: reproduction. SenesTech, Inc. (Flagstaff, AZ USA) has developed ContraPest®, a liquid bait that limits the reproductive capacity of both male and female wild Norway and Roof rats. The two active ingredients, 4-vinylcyclohexene diepoxide (VCD) and triptolide, deplete all stages of follicles in the female and disrupt spermatogenesis in the male. Laboratory and field studies reveal that ContraPest® is palatable and repeatedly consumed by rats even when provided with *ad libitum* food and water. Studies involving laboratory and wild caught rats have demonstrated a 93 - 100% reduction in litter sizes of rats treated with ContraPest® compared to control rats. ContraPest® was tested on free ranging rat populations in agricultural and urban settings. Rat populations on protein production farms decreased by an average of 46% following 100 days of treatment with ContraPest®. In a complex urban environment, where property boundaries limit access to populations and foraging areas, ContraPest® reduced the seasonal population peak by 67% after 133 days of baiting. These studies, combined with all of our field studies and population reduction models, demonstrate that ContraPest® is a highly effective rodent contraceptive bait in a variety of environments. We strongly believe that adding/implementing fertility management via ContraPest® to an IPM program would enhance long-term rodent population control in rural, urban, and agricultural environments.

KEY WORDS: ContraPest®, fertility control, integrated pest management, Norway rat, *Rattus norvegicus*, *Rattus rattus,* roof rat, triptolide, vinylcyclohexene diepoxide

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INTRODUCTION

Commensal rodents are a pervasive menace toward human health, food security, and infrastructure. Rats and mice are reservoirs of disease that spread to humans, wildlife, and livestock (Gao and Short 1993). The total cost of destruction by introduced rats in the US is more than $27 billion per year (Pimental 2007). The estimated loss of post harvest grain stores to rodents is 5-10%. Thirty four percent (34%) of the world's undernourished population could be fed across the world if the loss of stored grain to rodents could be reduced by 5% (Singleton 2003, Meerburg et al. 2009). Despite extensive investments in rodent control, traditional pest management techniques are typically inadequate to sustainably control rodents due to rapid reproduction putting upward press on population growth (Stenseth et al. 2003, Witmer 2007). Effective rodent population management requires a new approach that targets the biological source of overabundance: reproduction.

Rodent populations are rarely controlled by the application of lethal rodenticides alone. Even when rodent infestations are reduced through poisoning campaigns, rapid reproduction and immigration enables rodent populations to quickly rebound (Emlen et al. 1948, Witmer 2007). Rodent populations will increase in size as long as adequate resources are available and reproductive rates may be abnormally high following a population suppression, due to lack of competition (Emlen et al. 1948, Gao and Short 1993, Singla and Babbar 2012). To compound the problem, the effectiveness of lethal rodenticides declines with use due to bait shyness (Rzóska 1953, Buckle 1999, Buckle 2002, Keiner 2005) and increased genetic resistance within rat populations to both first- and second-generation anticoagulant compounds (Gao and Short 1993, Buckle and Prescott 2012).

Effective population control requires additional measures to depress the reproductive rates of commensal rodents. The use of fertility management bait, both in conjunction with integrated pest management (IPM) techniques or as the sole means of population management, is a promising tool for depressing rodent populations and decreasing the damage caused by rodent infestations (Knipling and McGuire 1972, Gao and Short 1993, Tobin and Fall 2004, Jacob et al. 2008). Reducing reproduction through fertility management suppresses population growth by retaining reproductively compromised individuals within the population to compete with fertile animals for food, water, shelter, and mates (Knipling and McGuire 1972, Gao and Short 1993). Delivering fertility management to wild rodents requires a palatable, oral bait (taken by choice and in the presence of familiar foods) that does not alter mating behavior and delivers compounds capable of rapidly inhibiting reproduction in both sexes without toxic side effects (Knipling and McGuire 1972, Gao and Short 1993).

In response to the need for reproductive control of pest rodent populations, SenesTech Inc. (Flagstaff, AZ USA) developed ContraPest® (EPA Reg. No. 91601-1) a highly palatable fertility management bait capable of suppressing the reproductive capacities in both female and male Norway and roof rats. The bait contains two active compounds that target ovarian function in female rats, 4-

vinylcyclohexene diepoxide (VCD, 0.09604%), which depletes primordial follicles (Mayer et al. 2002, Mayer et al. 2004, Kanter et al. 2006), and triptolide (0.00118%), a plant-based compound extracted from the thunder god vine (*Tripterygium wilfordii* Hook f) that disrupts estrous cycling and promotes apoptosis in secondary follicles (Xu and Zhao 2010). Triptolide also leads to infertility in male rats by disrupting spermatogenesis (Hikim et al. 2000, Huynh et al. 2000). The reproductive effects of these compounds are reversible, however when consumed by rodents there are two dramatic impacts to fecundity: 1) onset of compromised fertility is immediate and 2) continued consumption can lead to long term fertility management.

We conducted a series of trials to determine the efficacy and utility of ContraPest® for controlling Norway (*Rattus norvegicus*) and black (*R. rattus*) rats in both captive and free ranging populations. A brief summary of our findings are highlighted below.

TRIALS

Laboratory Trials

ContraPest® has been investigated in controlled laboratory settings on both inbred and wild caught rats. During these free choice studies, rats were provided ContraPest® in addition to unlimited food and water. In summary, ContraPest® was 93-100% effective at reducing pup numbers in treatment animals compared to matched control groups. Greater details regarding these studies can be found in Dyer et al. 2013, Dyer and Mayer 2014, and Witmer et al. 2017.

Field Trials

Given the effectiveness of laboratory trials in suppressing fertility, field studies were conducted to determine the effect of ContraPest® would be in realistic, uncontrolled settings when made available to wild pest rat populations.

Agriculture Trial

One trial performed on six protein production farms in the southeastern US, had three farms per control and treatment group. The control group was baited with rodenticide only, while the treatment group was baited with both bromethalin-based rodenticide (Cykill, Neogen) and ContraPest®. Bait stations were placed along the perimeter of the barns following the company's standard operating procedure of one bait station every 25-50 feet. Prior to deploying active baits, initial rat activity scores were established utilizing tracking plate procedures detailed in Quy et al. (1993). The final rat activity measurement occurred immediately following the end of the baiting period.

Through the use of tracking plates it was observed that sites treated with a combination of ContraPest® and rodenticides displayed 46% lower rodent populations than sites treated with rodenticides alone (SenesTech unpubl.). Over the course of the study, rats consumed an average of 15.2 ±4.0 L of ContraPest® on the three treatment farms. Consumption of ContraPest® was seen while in the presence of rodenticides, animal feed, other food options, and abundant water sources. When consumption data was analyzed, it was observed that 90% of ContraPest® consumption came from 50% of the bait stations. This observation led to altered baiting strategies in future studies, as standard spacing may not be the most effective in every situation.

Urban Trials

A palatability trial was conducted in subway refuse rooms in New York City. This trial confirmed that urban wild Norway rats would consume ContraPest® while in the presence of abundant alternative food sources (Pyzyna et al. 2014). Following this trial, two additional trials utilizing ContraPest® in complex urban environments have been conducted in mid-western US and northeastern US.

In both follow-up trials, tracking plates were used to monitor rodent activity. Bait stations, in both studies, were placed through the use of chew cards instead of standard spacing. Chew cards were constructed as outlined in Sweetapple and Nugent (2010). Baited chew cards were deployed throughout sites and monitored for 48 hours. After 48 hours, cards were checked for distinctive signs of rat gnawing (paired incisor markings of appropriate size). Cards were assigned a binary score: 0 = card not chewed by rats; 1 = card chewed by rats. Cards scored as '1' indicated a location where rats were potentially comfortable foraging. Chew cards were deployed periodically throughout the trials to compare foraging activity to bait station placement.

In these studies, the use of chew cards helped maximize ContraPest® uptake. In areas where positive chew card results were seen, ContraPest® was consumed in the presence of rodenticides, trash, other food sources, and water options. Tracking plate surveys revealed between 18% and 67% reduction in rat activity when compared to initial tracking plates scores prior to treatment with ContraPest®. Analysis of tracking plate scores revealed seasonal population peaks in these urban trials. Seasonal population peaks were calculated by comparing ContraPest® treated sites verus control, which had no rodent management.

CONCLUSION

Together, our studies reinforce that ContraPest® is a highly attractive, palatable, liquid contraceptive bait that, with repeated consumption, was effective in reducing rat populations, as determined by activity scores, in a variety of settings. The challenges of rodent pest management professionals vary with individual environmental conditions. What is consistent across all environments is that even a near-complete eradication with lethal tools will result in a rebound of rodent populations. These situations lend themselves to the inclusion of a fertility control tool for balance and better management strategies that block the rebounding populations resulting from the root cause: reproduction.

Given the summary of results presented here, we believe that ContraPest® is an innovative and versatile tool that can be used within current IPM programs to reduce reproduction and magnify success, or as a standalone product to reduce usage of lethal products.

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LITERATURE CITED

Buckle, A. P. 1999. Rodenticides: their role in rodent pest management in tropical agriculture. Ecologically-based management of rodent pests. ACIAR Monograph 59:163-177.

Buckle, A. 2002. Rodenticides and insecticides. Pages 267-286 *in* D. J. Knight, and M. Cooke, editors. The biocides business: regulation safety and applications. Wiley, Weinheim, Germany.

Buckle, A., and C. Prescott. 2012. The current status of anticoagulant resistance in rats and mice in the UK. Report from the Rodenticide Resistance Action Group of the United Kingdom of Health and Safety Executive.

Dyer, C. A., S. Raymond-Whish, S. Schmuki, T. Fisher, B. Pyzyna, A. Bennett, and L. P. Mayer. 2013. Accelerated follicle depletion in vitro and in vivo in Sprague-Dawley rats using the combination of 4-vinylcyclohexene diepoxide and triptolide. Journal of Zoo and Wildlife Medicine 44:S9-S17.

Dyer, C. A., and L. P. Mayer. 2014. Sprague Dawley female rat consumption of a liquid bait containing vinylcyclohexene diepoxide and triptolide leads to subfertility. Proceedings of Vertebrate Pest Conference 26:386-390.

Emlen, J. T. Jr., A. W. Stokes, and C. P Winsor. 1948. The rate of recovery of decimated populations of brown rats in nature. Ecology 29:133-145.

Gao, Y., and S. Roger. 1993. The control of rodent populations. Oxford Reviews of Reproductive Biology 15:265-310.

Hikim A. P. S., Y. H. Lue, C. Wang, V. Reutrakaul, R. Sangsuwan, and R. S. Swerdloff. 2000. Posttesticular antifertility action of triptolide in the male rat: evidence for severe impairment of cauda epidiymal sperm ultrastructure. Journal of Andrology 21:431-437.

Huynh, P. N., A. P. S. Hikim, C. Wang, K. Stefonovic, Y. H. Leu, A. Leung, V. Atienza, S. Baravarian, V. Reutrakaul, and R. S. Swerdloff. 2000. Long-term effects of triptolide on spermatogenesis, epididymal sperm function, and fertility in male rats. Journal of Andrology 21:689-699.

Jacob, J., G. R. Singleton, and L. A. Hinds. 2008. Fertility control of rodent pests. Wildlife Research 35:487-493.

Kanter E. M., R. Walker, S. Marion, M. A. Brewer, P. B. Hoyer, and J. K. Barton. 2006. Dual modality imaging of a novel rat model of ovarian carcinogenesis. Journal of Biomedical Optics 11:041123-041123.

Keiner, C. 2005. Wartime rat control, rodent ecology, and the rise and fall of chemical rodenticides. Endeavour 29:119-125.

Knipling, E. F., and J. U. Mcguire. 1972. Potential role of sterilization for suppressing rat populations: a theoretical appraisal. Technical Bulletin No. 1455, Agricultural Research Service, US Department of Agriculture, Washington, D.C.

Mayer L. P., N. A. Pearsall, P. J. Christian, C. M. Payne, M. K. McCuskey, S. L. Marion, I. G. Sipes, and P. B. Hoyer. 2002. Long term effects of ovarian follicular depletion in rats by 4-vinylcyclohexene diepoxide. Reproductive Toxicology 16:775-781.

Mayer L. P., P. J. Devine, C. A. Dyer, and P. B. Hoyer. 2004. The follicle-depleted mouse ovary produces androgen. Biological Reproduction 71:130-138.

Meerburg, B. G., G. R. Singleton, and H. Leirs. 2009. The year of the rat ends - time to fight hunger! Pest Management Science 65:351-352.

Pimentel, D. 2007. Environmental and economic costs of vertebrate species invasions into the United States. Pages 2-8 *in* G. W. Witmer, W. C. Pitt, and K. A. Fagerstone, editors. Managing Vertebrate Invasive Species. Proceedings of an International Symposium, USDA National Wildlife Research Center, Fort Collins, CO.

Pyzyna, B., L. Cunningham, E. Calloway, C. Dyer and L. Mayer. 2014. Liquid fertility management bait uptake by urban rats within New York City subway refuse rooms. Proceedings of the Vertebrate Pest Conference 26:375-379.

Quy, R. J., D. P. Cowan, and T. Swinney. 1993. Tracking as an activity index to measure gross changes in Norway rat populations. Wildlife Society Bulletin 21:122-127.

Rzóska, J. 1953. Bait shyness, a study in rat behaviour. British Journal of Animal Behaviour 1:128-135.

Singla, N, and B. K. Babbar. 2012. Critical timings of rodenticide bait application for controlling rodents in sugarcane crop grown in situations like Punjab, India. Sugar Tech 14:76-82.

Singleton, G. R. 2003. Impacts of rodents on rice production in Asia. IRRI Discussion Paper Series 45:1-30.

Stenseth, N. C., H. Leirs, A. Skonhoft, S. Davis, R. P. Pech, H. Andreassen, G. R. Singleton, L. Mauricio, R. S. Machang'u, R. H. Makundi, Z. Zhang, P. R. Brown, S. Dazhao, and W. Xinrong. 2003. Mice, rats, and people: the bio-economics of agricultural rodent pests. Frontiers in Ecology and the Environment 1:367-375.

Sweetapple, P. and G. Nugent. 2011. Chew-track-cards: a multiple species small mammal detection device. New Zealand Jounal of Ecology 35:153-162.

Tobin, M. E., and M. W. Fall. 2004. Pest control: rodents. Agricultural Science, Vol. II *in* Encyclopedia of life support systems. Eolss Publishers, Oxford, U.K.

Witmer, G. 2007. The ecology of vertebrate pests and integrated pest management (IPM). Pages 393-401 *in* M. Kogan and P. Jepson, editors. Perspectives in ecological theory and integrated pest mangement. Cambridge University Press, Cambridge, U.K.

Witmer, G., S. Raymond-Whish, R. Moulton, B. Pyzyna, E. Calloway, C. A. Dyer, L. P. Mayer, and P. Hoyer. 2017. Compromised fertility in free feeding of wild-caught Norway rats (*Rattus norvegicus*) with a liquid bait containing 4-vinylcyclohexene diepoxide and triptolide. Journal of Zoo and Wildlife Medicine 48:80-90.

Xu, C. K., and Y. H. Zhao. 2010. Apoptosis of rat's ovarian follicle cells induced by triptolide in vivo. African Journal of Pharmacy and Pharmacology 4:422-430.