SPINOSAD
Technical Bulletin

Dow AgroSciences™

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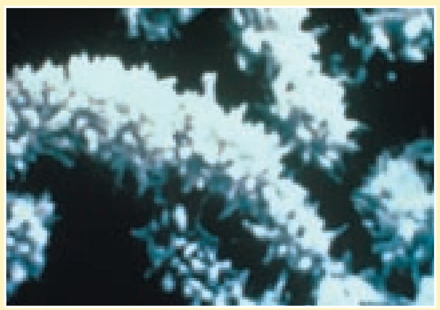
Y45-000-001 (01/01) CBK

Overview

Saccharopolyspora spinosa

Spinosad is the first active ingredient proposed for a new class of insect control products, the Naturalytes. Spinosad is derived from the metabolites of the naturally occurring bacteria, *Saccharopolyspora spinosa*. Spinosad has been shown to be highly active on insects including species from the orders Lepidoptera, Diptera, Hymenoptera, Thysanoptera, and a few Coleoptera. Spinosad may be used to control pests in both agricultural and horticultural environments, and also in greenhouses, golf courses, gardens, and around homes.

Spinosad has been developed to provide rapid control of Lepidoptera and other pests with minimum disruption of beneficial insects and other non-target organisms. Because it is highly effective, only very low use rates are required to achieve efficacy. These attributes permit many users the opportunity to implement integrated pest management tools for the first time.



S. spinosa Colony

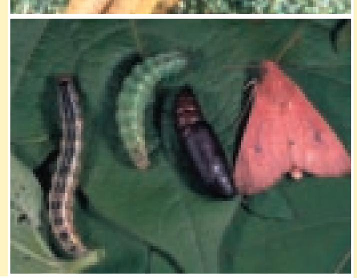
Due to its low effective use rate, safety to the environment, safety to mammals, and safety to beneficial insects, spinosad was registered under the US EPA's reduced risk program. Spinosad was also awarded the *Presidential Green Chemistry Challenge Award* during 1999. This award recognizes the unique contribution of spinosad and also highlights Dow AgroSciences' commitment to producing safer and more effective products for insect control.

Noteworthy Features

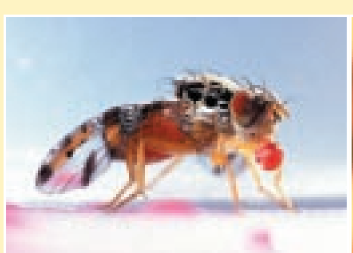
Spinosad provides users with a unique package of very desirable features:

- Highly effective on many pest species
- Low application rates resulting in low environmental load
- Safe for use with most beneficial insects
- Unique mode of action with no known cross-resistance
- Low mammalian toxicity
- Low avian and fish toxicity

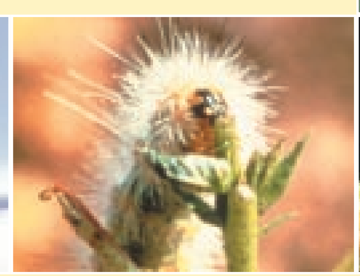
Frankliniella occidentalis
Photo By: Raymond Cloyd, University of Illinois



Alabama argillacea
Photo By: Winfield Sterling, Retired Texas A&M



Ceratitis capitata
Photo By: USDA-ARS

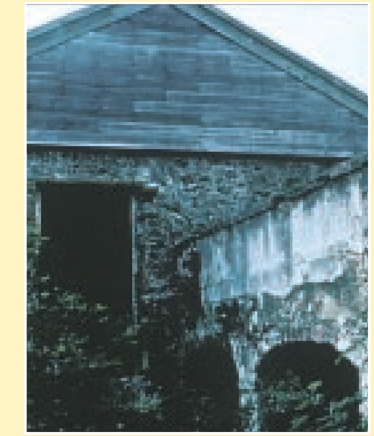


Estigmene acrea

Ostrinia nubilalis

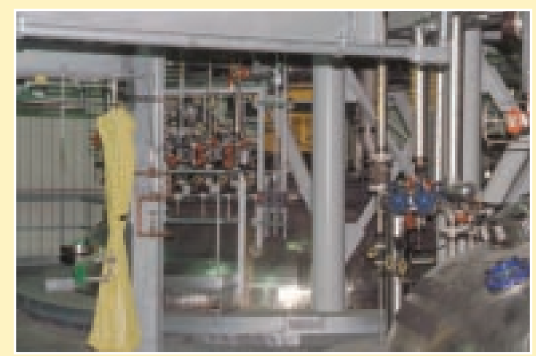
The Spinosad Story

During the late 1950's, companies including The Dow Chemical Company and Eli Lilly and Company began to actively look for naturally occurring pest control products. As a result of these efforts, a scientist from the Natural Products division of Eli Lilly while vacationing in the Caribbean in 1982 visited an abandoned rum still and collected several soil samples. These samples were returned to the laboratory to determine the presence of biological activity. Three years later the fermentation products from these samples were shown to have insecticidal activity. By 1986 Eli Lilly's scientists identified the organism producing the biologically active substances. They determined that this was a new species of actinomycete bacteria and named it *Saccharopolyspora spinosa*. Within one year, scientists had identified the most highly active metabolites of *S. spinosa*. In 1989, the Ag Products division of Eli Lilly, Elanco, was merged with The Dow Chemical Company to form DowElanco, now Dow AgroSciences.



Rum still where soil sample was collected.

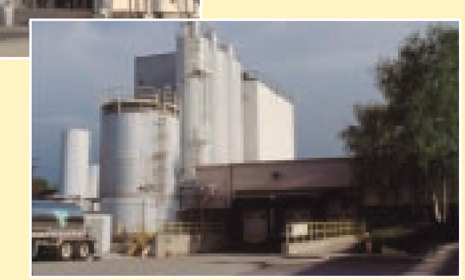
A highly effective formulation was identified and developed through five years of extensive testing around the world. This formulation contained a mixture of two of the most active metabolites, spinosyn A and spinosyn D. The name spinosad is derived by combining the species name, *spinosa*, with the two metabolites, A and D. In 1995, because of its favorable environmental and toxicological profile, spinosad was classified by the U.S. Environmental Protection Agency (EPA) as a reduced risk product and granted an accelerated registration review. Less than two years later during early 1997, the first spinosad products, Tracer® and Conserve® were approved and launched in the U.S. for use on cotton and on turf and ornamentals, respectively.



Spinosad fermentation vessels

Today, spinosad is produced in a state-of-the-art fermentation facility in Harbor Beach, Michigan. *S. spinosa* colonies are grown using natural products such as soybean and cottonseed meal. Computers are used to control temperature, oxygen and nutrient levels to ensure maximum production of spinosyns A and D. Spinosad products are now registered on over 150 crops in more than 30 countries.

Whote broth extraction units



Harbor Beach spinosad fermentation facility

Physical and Chemical Properties

IUPAC NAME:

Spinosyn A - (2R,3aS,5aR,5bS,9S,13S,14R,16aS,16bR)-2-(6-deoxy-2,3,4-tri-O-methyl-∝-L-mannopyranosyloxy)-13-(4-dimethylamino-2,3,4,6-tetradeoxy-β-D-erythropyranosyloxy)-9-ethyl-2,3,3a,5a,6,7,9,10, 11,12,13,14,15,16a,16b-hexadecahydro-14-methyl-1H-8-oxacyclododeca[*b*]*as*-indacene-7,15-dione

Spinosyn D - (2R,3aS,5aR,5bS,9S,13S,14R,16aS,16bR)-2-(6-deoxy-2,3,4-tri-O-methyl-∝-L-mannopyranosyloxy)-13-(4-dimethylamino-2,3,4,6-tetradeoxy-β-D-erythropyranosyloxy)-9-ethyl-2,3,3a,5a,6,7,9,10, 11,12,13,14,15,16a,16b-hexadecahydro-4,14-dimethyl-1H-8-oxacyclododeca[*b*]*as*-indacene-7,15-dione

CAS NAME:

Spinosyn A - 2-((6-Deoxy-2,3,4-tri-O-methyl-∝-L-mannopyranosyl)oxy)-13-((5-(dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl)oxy)-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-14-methyl-1H-as-indaceno(3,2-d)oxacyclododecin-7,15-dione

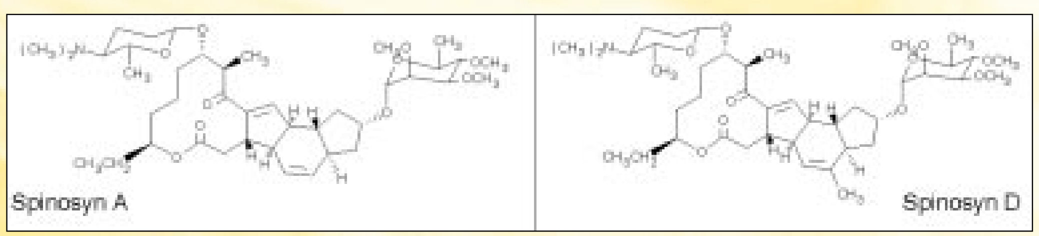
Spinosyn D - 2-((6-Deoxy-2,3,4-tri-O-methyl-∝-L-mannopyranosyl)oxy)-13-((5-(dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl)oxy)-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-1H-as-indaceno(3,2-d)oxacyclododecin-7,15-dione

CAS Registry No. 131929-60-7 (spinosyn A)
131929-63-0 (spinosyn D)

CIPAC No. 636

COMMON NAME: Spinosad (ISO 1750 provisional)

CHEMICAL STRUCTURE: Spinosad is a mixture of spinosyn A and spinosyn D



EMPIRICAL FORMULA: spinosyn A: $C_{41}H_{65}NO_{10}$
spinosyn D: $C_{42}H_{67}NO_{10}$

MOLECULAR WEIGHT: spinosyn A: 731.976
spinosyn D: 745.988

ODOR: slightly stale water or earthy

RELATIVE DENSITY: 0.512 @ 20°C

MELTING POINT: spinosyn A: 84-99.5 °C
spinosyn D: 161.5-170 °C

VAPOR PRESSURE: (25°C)

spinosyn A: 2.4 x 10^{-10} mmHg (3.0 x 10^{-11} kPa)
spinosyn D: 1.6 x 10^{-10} mmHg (2.0 x 10^{-11} kPa)

OCTANOL/WATER PARTITION COEFFICIENT (log K_{ow}):

pH	spinosyn A	spinosyn D
5.0	2.78	3.23
7.0	4.01	4.53
9.0	5.16	5.21
Dist. H_2O	3.91	4.38

DISSOCIATION CONSTANT (pK_a):

spinosyn A	spinosyn D
8.10 at 20°C	7.87 at 20°C

SOLUBILITY IN WATER (20°C):

	spinosyn A	spinosyn D
pH 5	290 mg/L	28.7 mg/L
pH 7	235 mg/L	0.332 mg/L
pH 9	16 mg/L	0.053 mg/L
Dist. H_2O	89.4 mg/L	0.495 mg/L

SOLVENT SOLUBILITY (20°C)

Solvent	g/100mL	
	spinosyn A	spinosyn D
Acetone	16.80	1.01
Acetonitrile	13.40	0.26
Amyl Acetate	3.69	2.30
Dichloromethane	52.50	44.80
Ethyl Acetate	19.40	1.90
N-Hexane	0.45	0.07
N-Heptane	1.24	0.03
Methanol	19.00	0.25
1-Octanol	0.93	0.13
2-Propanol	3.98	0.13
Toluene	45.7	15.2
Xylene	>25.00	6.40

Biological Activity

Spectrum of Activity

The spectrum of activity seen in the laboratory includes exceptional activity on Lepidoptera, Diptera, and Thysanoptera. Some species of Coleoptera that consume large amounts of foliage, such as Colorado potato beetle (*Leptinotarsa decemlineata*), are also sensitive. Spinosad has been found to be highly active on almost all Lepidoptera tested. However, western yellowstriped armyworm (*Spodoptera praefica*) and some cutworms such as large mature black cutworm larvae (*Agrotis ipsilon*) are less sensitive, and thus require higher use rates. Spinosad has contact activity on all life stages of a pest including egg, larva, and adult. Eggs must be sprayed directly but larvae and adults can be effectively dosed through contact with treated surfaces. Spinosad is most effective when ingested.

Spinosad demonstrates large margins of safety to predaceous insects such as lady beetles (Coccinellidae), lace wings (Neuroptera), bigeyed bugs (*Geocoris* spp.), and minute pirate bugs (*Orius* spp.). Hymenoptera parasitoids and pollinators are sensitive if treated directly but are able to tolerate dried residues on foliage. Spinosad is generally not active on sucking insects such as aphids. There are no phytotoxicity issues with spinosad.

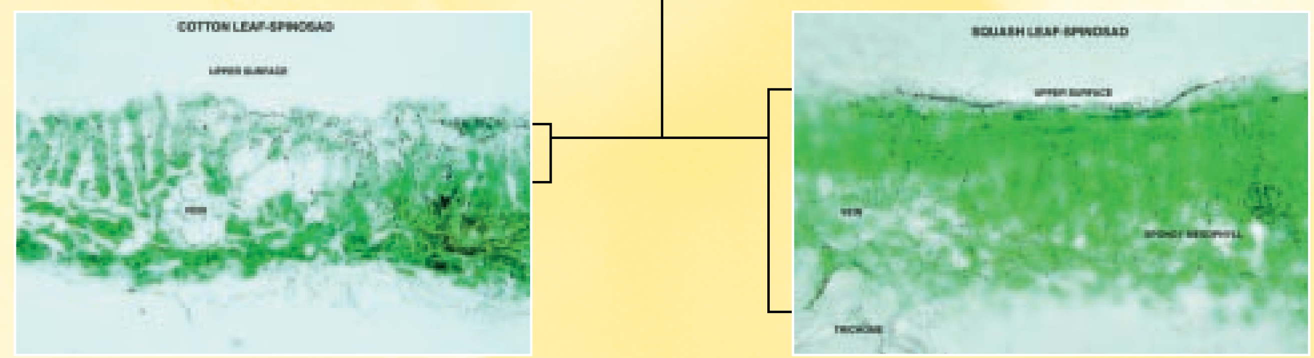
CROPS	PRIMARY TARGETS
Cotton	Lepidoptera and Thysanoptera
Crucifers	All Lepidoptera including Diamondback Moth (*Plutella xylostella*)
Leafy Vegetables	Leafminers and Lepidoptera
Citrus	Thysanoptera, Lepidoptera, and Medfly (*Ceratitis capitata*)
Apples and Pears	Leafrollers, Leafminers, Codling Moth (*Cydia pomonella*), and Apple Maggot (*Rhagoletis pomonella*)
Stone Fruit	Peach Twig Borer (*Anarsia lineatella*) and Navel Orangeworm (*Amyelois transitella*)
Tobacco	Tobacco Budworm (*Heliothis virescens*) and Tobacco Hornworm (*Manduca sexta*)
Almonds	Peach Twig borer (*Anarsia lineatella*) and Navel Orangeworm (*Amyelois transitella*)
Corn	European Corn Borer (*Ostrinia nubilalis*), Corn Earworm (*Helicoverpa zea*), and Fall Armyworm (*Spodoptera frugiperda*)
Wheat and Cereals	Armyworms and Cereal Leaf Beetle (*Oulema melanopus*)
Potatoes	Colorado Potato Beetle (*Leptinotarsa decemlineata*), Armyworms, and Leafminers
Tomatoes	Lepidoptera, Thysanoptera, and Diptera
Peppers	Lepidoptera, Thysanoptera, and Diptera
Tropical Tree Fruits	Thysanoptera and Fruit Flies
Turf and Ornamentals	Lepidoptera, Thysanoptera, and Leafminers
Legume Vegetables	Lepidoptera, Thysanoptera, and Leafminers
Grapes	Lepidoptera
Soybean	Lepidoptera
Rice	Lepidoptera
Cucurbits	Lepidoptera, Thysanoptera, and Diptera
Home and Garden	Fire Ants (mound treatment)

The rapid activity of spinosad facilitates a scout-and-treat-only-as-needed approach. The best activity is obtained when treatments target small larvae. Higher rates are required to be effective on large older larvae. Although spinosad is highly effective on targeted pests, it is difficult to reach cryptic or fruit feeding insects and the majority of damage will already have occurred if insects are allowed to reach later instars prior to treating. Efficacy of spinosad compares favorably with the best synthetic standards such as pyrethroids.

Systemic Activity

Foliar applications are not highly systemic. However, translaminar activity is evident in applications on certain vegetable and ornamental crops. Differences in translaminar movement are demonstrated in the following microautoradiographs of cotton and squash leaf tissue. Spinosad, seen here as black dots, when applied to squash moves through the leaf tissue reaching into the spongy mesophyll layer. On cotton leaf tissue, spinosad still shows translaminar movement, but it is restricted to the first few tissue layers. This differential movement may be explained by leaf type and age. In general, more penetration is seen with younger and rapidly growing leaves. Translaminar activity in some crops may be enhanced through the addition of a penetrating surfactant. Limited root uptake may also occur.

Spinosad penetration into leaf tissue.



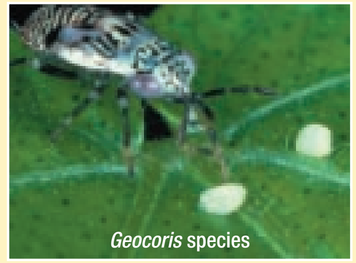
Use Rates

Spinosad, in general, is a gram per hectare or ounces per acre compound when compared to older products that were generally measured in kilograms per hectare or pounds per acre. The recommended use rates vary widely and are highly impacted by the target pest, target pest size and number, host crop and crop age, climate and economic threshold or acceptable damage. For actual use directions, request product labels for the geography and crop of interest. The majority of crop labels are between 25 and 200 grams per hectare (0.023 and 0.184 lbs per acre) of active ingredient. Turf rates are 88-450 g ai/ha (0.078-0.4 lb ai/acre). Ornamental rates are 0.046-0.17 lb ai/100 gallons or 55-204 ppm. Regional labels compensate for a positive temperature correlation that results in better activity with higher temperatures. Performance against some pests such as leafminers and thrips are positively impacted by the addition of nominal rates of penetrating surfactants such as crop oils.

Safety to Beneficials

Spinosad displays a high level of selectivity toward most beneficial insects, and use of spinosad is compatible with integrated pest management (IPM) programs. Although pollinators such as honeybees and bumble bees are highly sensitive to spinosad administered via oral and contact routes of exposure in the laboratory, exposure to dried residues under field conditions are considered harmless to foraging bees.

Predators and Parasitoids



Geocoris species

Photo By: Winfield Sterling, Retired Texas A&M

Spinosad has relatively low impact on many predaceous beetles, sucking insects, lacewings, and mites. Large margins of safety have been demonstrated in laboratory studies on such species as *Phytoseiulus persimilis* (predatory mite), *Hippodamia convergens* (lady beetle), *Chrysoperla rufilabris* (lacewing), *Encarsia formosa* (whitefly parasitoid), *Orius insidiosus* (minute pirate bug), and *Geocoris punctipes* (bigeyed bug).

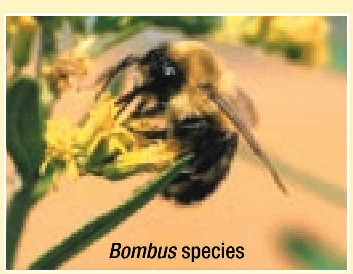
Field studies have also confirmed the generally low activity of spinosad for many beneficial insect species. Against the sensitive indicator species, *Typhlodromus pyri*, spinosad was harmful in the laboratory but safe under field conditions at rates up to 48 g ai/ha approximately one week after application. Against another sensitive indicator species, *Aphidius rhopalosiphi*, spinosad was toxic to the adult wasps, but a level of safety was confirmed to wasps developing within mummified aphids. Spinosad was harmless to *Poecilus cupreus* (ground dwelling predator) and had limited adverse effects on *Episyrphus balteatus* and *Coccinella septempunctata* (foliage dwelling predators). Against another foliage dwelling predator, *Chrysoperla carnea*, spinosad was harmless at 36 g ai/hL in an extended laboratory study involving realistic application methods.

Greenhouse applications are typically made at much higher rates than those commonly used in agricultural situations. Under greenhouse conditions, studies have shown that *Encarsia formosa* populations may be reduced when exposed to spinosad residues shortly after application. However, the wasp population was not seriously impacted when exposed to residues that had aged at least one week. Studies have indicated that at one week post-application, spinosad, depending on formulation, would be classified as either slightly harmful or harmless (WHO). Additional greenhouse studies have shown that *Amblyseius cucumeris*, a predatory mite, is not affected by spinosad applications. Any adverse affect on greenhouse parasitoid populations may be mitigated by ensuring that adequate refugia is available and by making augmentive releases at least one week post-application.

Pollinators

Under laboratory conditions, honeybees (*Apis mellifera*) and other pollinators (e.g., bumble bees) are highly sensitive to spinosad via both oral and contact routes of exposure. The acute oral LD_{50} value is 0.060 µg/bee, and the acute contact LD_{50} between 0.0025 and 0.045 µg/bee. However, dry residues of spinosad on plant foliage appear to be harmless to foraging bees. For example, no significant mortality of honeybees resulted following laboratory exposure to alfalfa which had been sprayed with formulated spinosad product at 18 g/m^2 and allowed to dry for 3, 8, or 24 hours.

The lack of toxicity of dry residues of spinosad indicates that the risk to bees will be negligible if applications of spinosad are made when bee activity is low or if bees are allowed to reenter treated areas only after spray deposits have dried. Studies conducted in citrus and almond orchards in which night applications of spinosad were made have confirmed the lack of mortality to foraging adults or brood development. In addition, field studies in which bees have been introduced the day following applications to orchards have also demonstrated the lack of spinosad impacts. Applications of spinosad to alfalfa fields, in which honeybee hives were covered for the first 3 hours post-application, also demonstrated no adverse effects to honeybees or leafcutter bees.

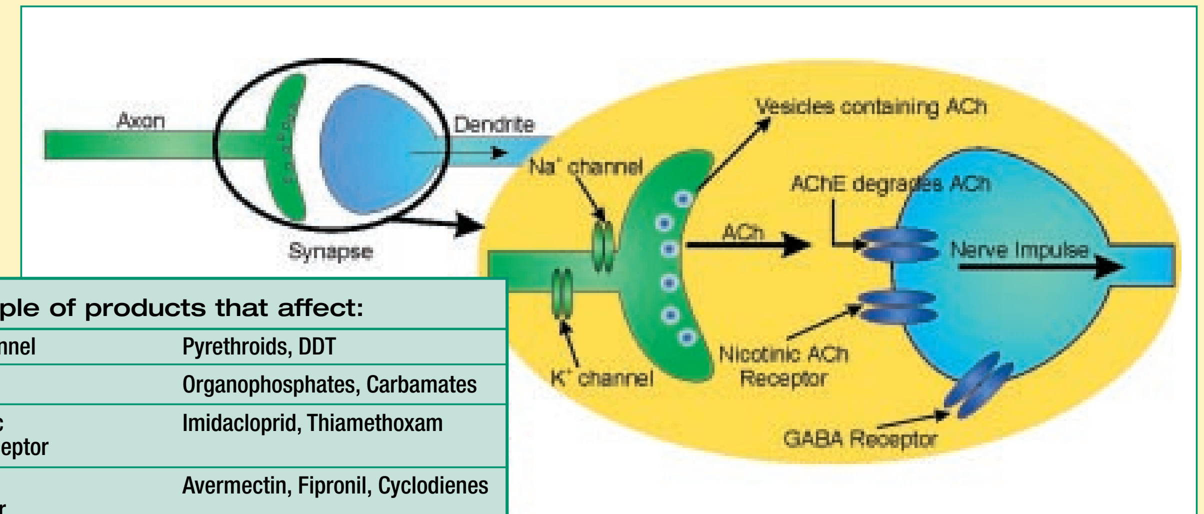


Bombus species

Biochemistry & Resistance Management

Symptomology

Sensitive insects exposed to spinosad exhibit unique symptomology that is typified by a general paralysis accompanied by loss of body fluids resulting in flaccid paralysis. Under close examination, minute tremors of the mandibles and crochets can be seen. The onset of paralysis is quite rapid for a biological material. The length of time required was 81 minutes before 50 percent of third instar *Heliothis virescens* larvae treated topically with 10 mg of technical material failed to respond to a hot needle probe. That can be compared to 25 minutes for cypermethrin treated larvae. However, intoxicated insects remain on the plant for one to two days without feeding; whereas, insects treated by excitatory compounds, such as pyrethroids or organophosphates, tend to fall off the plants more rapidly.



Example of products that affect:	
Na* channel	Pyrethroids, DDT
AChE	Organophosphates, Carbamates
Nicotinic ACh Receptor	Imidacloprid, Thiamethoxam
GABA Receptor	Avermectin, Fipronil, Cyclodienes
Unique Target Site	Spinosad

Mode of Action

In insects, the mode of action of spinosad is associated with excitation of the insect nervous system (Salgado 1998). Spinosad uniquely alters the function of nicotinic and GABA-gated ion channels (Salgado 1998, Watson unpublished data), in a manner consistent with the observed neuronal excitation. However, spinosad does not interact with known binding sites for other nicotinic or GABAergic insecticides such as neonicotinoids, fiproles, avermectins and cyclodienes (Orr unpublished data). These data indicate that spinosad acts through a unique insecticidal mechanism.

Resistance

Spinosad has a novel mode of action that makes it ideal for resistance management programs. It has shown no cross-resistance with existing chemistries and can be rotated with all other classes of existing and experimental products. Spinosad has excellent activity on many insects with historic resistance problems. Therefore, Dow AgroSciences (DAS) is taking a proactive stance in regard to resistance management. Specific resistance management strategies have been identified for key pests. These strategies may vary depending on crop, pest, and geography. Specific resistance management strategy recommendations for key pests may be found on labels of products targeted at that pest and crop. For additional information regarding specific resistance management strategies, contact your local DAS representative.

Regulatory Information

Registrations

Spinosad has been approved for use by registration authorities in more than 30 countries and the first registrations were granted during late 1996 and early 1997 for cotton, almonds, vegetables, and turf and ornamentals. Since that time, many additional crop and non-crop uses have been approved worldwide, ranging from Australian cotton to Japanese crucifers to Mexican tomatoes to Chilean stone fruit to Israeli melons. Spinosad products have found utility for pest management for a wide variety of crops, and in the U.S. alone use has been approved on more than 150 crops. In addition to crop uses, spinosad is also approved for non-crop uses on turfgrass and ornamental plants, for livestock pest control, and fire ant control.

Reduced Risk Classification

Spinosad has been classified by the U.S. Environmental Protection Agency (EPA) as a reduced risk pesticide product. This classification affords preferential registration and expedited label expansions to select products that meet the Agency's stringent criteria and pose less risk to public health and the environment than available alternatives. Spinosad has been classified by EPA as a reduced risk insecticide product because of its:

- Low acute mammalian toxicity
- Low toxicity to fish and wildlife
- Safety to beneficials and compatibility with integrated pest management

Green Chemistry Award

Spinosad has also been awarded one of the U.S. government's top environmental honors, the *Presidential Green Chemistry Challenge Award* in 1999. The award recognizes technologies and products that incorporate the principals of green or sustainable chemistry into chemical design, manufacture, and use. The recognition of "Spinosad - A New Natural Product for Insect Control" with this prestigious honor was based on its highly selective insecticidal activity and environmentally compatible characteristics. The category for which spinosad was chosen to receive the award was "Designing Safer Chemicals."

Reduced Risk

The reduced risk registration program was established by U.S. EPA during 1994 to expedite the review and approval of new pesticides with more favorable human safety and environmental impact profiles than currently available alternatives. Since the inception of this program, a total of only 18 new pesticides have met the stringent criteria established by EPA and have been classified as reduced risk products:

- Reduced risks to human health
- Reduced risks to non-target organisms
- Reduced potential for contamination of valued environmental resources (water, air, soil)
- Broadened adoption of integrated pest management programs

Green Chemistry Award

The *Presidential Green Chemistry Challenge Award* was established by the White House during 1995 to recognize outstanding contributions of chemical processes and products that reduce negative impacts on human health and the environment relative to the currently available technology. The award is highly competitive in nature and categories for awards include "designing safer chemicals," "alternate synthetic pathways," and "alternate solvents and reaction conditions." Spinosad is one of only 4 pesticide products to be honored with this award.

Ecotoxicology

Spinosad is not acutely toxic to terrestrial birds and wildlife or to fish and most aquatic invertebrates. Laboratory studies indicate that some free-swimming and sediment-dwelling aquatic invertebrates may be sensitive to long-term exposure to spinosad. Under field conditions, this sensitivity may be mitigated by the rapid dissipation of spinosad which occurs from the water column as well as sorption and binding of that small portion of residues which becomes associated with the sediment. Molluscs exhibit greater sensitivity to spinosad on an acute basis than most other aquatic organisms. Results of key ecotoxicity studies with technical product for terrestrial and aquatic non-target organisms are summarized below:

Common Name	Scientific Name	Effect Level(s)
Bobwhite Quail	*Colinus virginianius*	Acute LD_{50} > 2000 mg/kg 5-d Dietary LC_{50} > 5253 ppm in feed
Mallard Duck	*Anas platyrhynchos*	Acute LD_{50} > 2000 mg/kg 5-d Dietary LC_{50} > 5156 ppm in feed
Rainbow Trout	*Oncorhynchus mykiss*	96-hr Acute LC_{50} 30 mg/L
Bluegill Sunfish	*Lepomis macrochirus*	96-hr Acute LC_{50} 5.9 mg/L
Sheepshead Minnow	*Cyprinodon variegatus*	96-hr Acute LC_{50} 7.9 mg/L
Common Carp	*Cyprinus carpio*	96-hr Acute LC_{50} 5.0 mg/L
Water Flea	*Daphnia magna*	48-hr Acute EC_{50} 1.5-14.0 mg/L 21-d NOEC 0.001-0.007 mg/L
Midge	*Chironomus riparius*	25-d NOEC 0.002 mg/L
Grass Shrimp	*Palaemonetes pugio*	48-hr LC_{50} > 9.7 mg/L
Mysid Shrimp	*Americamysis bahia*	48-hr LC_{50} > 7.9 mg/L
Eastern Oyster	*Crassostrea virginica*	96-hr EC_{50} 0.3 mg/L
Honeybee	*Apis mellifera*	48-hr Acute oral LD_{50} 0.06 µg/bee 48-hr Acute contact LD_{50} 0.003-0.045 µg/bee
Earthworm	*Eisenia foetida*	14 d LC_{50} > 970 mg/kg
Microorganisms	Soil Sewage	No effect at 7 mg/L No effect at 100 mg/L
Green Algae	*Selenastrum capricornutum*	7-d EC_{50} > 105.5 mg/L
Blue Green Algae	*Anabaena flos-aquae*	5-d EC_{50} 8.1 mg/L
Freshwater Diatom	*Navicula pelliculosa*	5-d EC_{50} 0.14 mg/L
Marine Diatom	*Skeletonema costatum*	5-d EC_{50} 0.23 mg/L
Duckweed	*Lemna gibba*	14-d EC_{50} 10.6 mg/L

Environmental Fate

Fate in Soil

Spinosad degrades readily in the soil environment and is non-persistent. Primary mechanisms of degradation are sunlight photolysis and microbial breakdown. Under field conditions, spinosad dissipates rapidly from soil surfaces with observed half-lives of less than 1 day. Photolysis studies in the laboratory under artificial sunlight have revealed photodegradation half-lives of 9 to 10 days. Spinosad present in deeper soil layers or shaded soil also degrades rapidly. Under laboratory conditions of darkness, spinosad degradation half-lives of 9 to 17 days (25°C) and 5 to 68 days (20°C) were observed. Initial degradation products of spinosad in soil are formed by removal of one or more of the sugar groups and also by oxidation reactions, and these degradates are further transformed to carbon dioxide and water by the soil microbial community.

Spinosad and its degradates are not of concern from a groundwater quality standpoint. Spinosad is moderately to strongly sorbed by soil particles (K_d sorption coefficients of 4 to 337 mL/g), and is considered to be "relatively immobile to immobile" to leaching. Laboratory soil column and field studies have confirmed the lack of leaching mobility for spinosad.

Fate in Water

In natural water systems spinosad rapidly dissipates, with the primary route of degradation involving sunlight photolysis. A water column half-life of less than 1 day has been observed in artificial pond systems under outdoor conditions. This matches well with laboratory studies conducted under simulated sunlight which have confirmed photolysis half-lives of < 1 day. Spinosad residues are stable to hydrolysis at a variety of pH conditions, and exhibit slow-to-moderate degradation rates in sediment under anaerobic conditions.

Fate in Plants

Residues of spinosad present on plant surfaces dissipate at a moderate-to-rapid rate, primarily due to sunlight photolysis. Dissipation half-lives of 2 to 16 days have been observed for residues on leaf and fruit surfaces, with the rate dependent on the amount of sunlight received and degree of shading. For trace residues absorbed by plant tissues, the major route of metabolic degradation involves oxidation and demethylation. Due to the minor quantities of degradates formed within or on plants, the residue definition for spinosad only includes the active ingredient, spinosyns A and D. Degradates have been excluded from the residue definition based on structure-activity conclusions of toxicological significance.

Fate in Animals

Trace residues of spinosad that may be absorbed from food or water by terrestrial and aquatic organisms have been found to be readily metabolized and excreted, and as a result, spinosad and its metabolites do not accumulate in living tissues. Spinosad residues present in water may be slowly absorbed by fish, but observed bioconcentration factors (19 to 33 mL/g) for spinosyn A and D in whole fish do not predict accumulation of spinosad in the aquatic food chain. This is because fish are able to rapidly metabolize and excrete any absorbed spinosad residues. Spinosad elimination half-lives of around 4 days are observed in fish.

Mammalian Toxicology

Spinosad is a highly selective insect control product with high potency for target insects but low toxicity toward mammals and other non-target organisms.

Short-Term Toxicity

Spinosad is not acutely toxic to mammals and is essentially non-hazardous by the oral, dermal, ocular, and inhalation routes. The oral LD_{50} is > 3738 mg/kg bw for male rats and > 5000 mg/kg bw for female rats and male and female mice. The dermal LD_{50} is > 5000 mg/kg bw for male and female rabbits and the inhalation LC_{50} is > 5.18 mg/L/4 hours for male and female rats. In addition, spinosad does not cause skin sensitization and only very slight dermal or ocular irritation.

Long-Term Toxicity

Spinosad has been tested in intermediate-term (90-day) and lifetime (1-2 years) feeding studies involving rats, mice, and dogs. Spinosad has not been found to cause tumors in laboratory animals or to have any potential to cause neurotoxicity. In addition, spinosad did not cause embryotoxicity, fetotoxicity, or teratogenicity in either rats or rabbits at dose levels that affected maternal animals. The primary effects of spinosad observed at high dosages include vacuolation, inflammation, and degeneration of selected tissues. These effects are similar to those caused by other cationic amphiphilic compounds including several pharmaceuticals. Based on no-observable effect levels (NOEL's) of 2.4 mg/kg/day (rats), 11.4 mg/kg/day (mice), and 2.68 mg/kg/day (dogs), the acceptable daily intake (ADI) for spinosad has been established as 0.02 mg/kg/day by U.S. EPA and other regulatory authorities. This ADI is based on application of standard safety factors to the observed NOEL's. U.S. EPA has determined no need for the use of additional uncertainty factors to account for special sensitivities of the young or unborn.

Mutagenicity

Spinosad has been investigated in a battery of genotoxicity studies, and has been found to posses no mutagenic potential.

Pharmacokinetics and Metabolism

Spinosad is slowly and poorly absorbed through the skin. Dermal exposures in the rat for 24 and 120 hours resulted in only 1 and 2% absorption, respectively. Spinosad, which is absorbed via the oral or dermal routes of exposure, has been found to be rapidly metabolized and eliminated in mammalian systems. Within 48 hours of dosing, approximately 60-80% of spinosad or its metabolites was eliminated via the urine and feces. Depletion of spinosad residues from tissues occurs rapidly following cessation of exposure.

Worker Safety & Formulations

Worker Safety

Toxicity of Formulated Products

The above information has been generated with spinosad active ingredient, but testing with formulated products has also demonstrated the low toxicity of spinosad toward mammals.

WHO Classification

Spinosad has been classified by the World Health Organization (WHO) as an insect control product "unlikely to present acute hazard," which represents the most favorable of 5 classifications recognized by this advisory body.

Posting Requirements and Worker Protection

In all countries with current registrations no posting or setbacks are required for use of spinosad products. The minimum worker protective equipment is required for mixer/loaders (long-sleeved shirts, long pants, shoes, and socks).

Re-Entry Interval (REI)

In the U.S. where Worker Projection Standards apply, spinosad products have the minimum REI allowable by law of 4 hours. Workers entering treated areas less than 4 hours after application should wear coveralls and shoes plus socks.

Formulations

Suspension Concentrate

An aqueous suspension is the primary formulation for delivering spinosad to the global marketplace. The concentration of spinosad ranges from 25 g ai/L to 480 g ai/L.

Wettable-Granules

A 25% water dispersible granule is available in Japan.

Fire Ant Bait

A fire ant bait containing 0.015% spinosad is currently available for consumer use in the United States to control the Red Imported Fire Ant, *Solenopsis invicta*.

Fruit Fly Bait

A 0.02% spinosad bait concentrate is available to control a variety of fruit flies, including the Mediterranean fruit fly, *Ceratitis capitata*.

Selected Publications

Discovery and Mode of Action

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Saunders, D. G.; Bret, B. L. "Fate of Spinosad in the Environment." *Down to Earth*, 52:14-20 (**1997**).

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