

Group	Mode of Action	Examples Multi-site/Unknown	Hyperlinked References
1	Acetylcholinesterase (AChE) inhibitors		Fukuto TR. Mechanism of action of organophosphorus and carbamate insecticides. <i>Environmental Health Perspectives</i> 87:245-254 (1990). Salgado VL, Schnatterer S and Holmes KA. Ligand-gated chloride channel antagonists (fibroles), in <i>Modern Crop Protection Compounds</i> 2nd edition, ed. by Kramer W, Schirmer U, Jeschke P and Witschel M, Wiley-VCH Verlag, Weinheim, pp. 1283-1305 (2012). Chen L, Durkin KA and Casida JE. Structural model for γ-aminobutyric acid receptor noncompetitive antagonism: widely diverse structures fit the same site. <i>Proc Natl Acad Sci</i> 103:5185-5190 (2006). Zhao X, Salgado VL, Yeh JZ and Narahashi T. Differential Actions of Fipronil and Dieldrin Insecticides on GABA-Gated Chloride Channels in Cockroach Neurons. <i>J Pharm Exp Ther</i> 306:914-924 (2003).
2	GABA-gated chloride channel blockers		Grolleau F and Sattelle DB. Single channel analysis of the blocking actions of BIDN and fipronil on a <i>Drosophila melanogaster</i> GABA receptor (RDL) stably expressed in a <i>Drosophila</i> cell line. <i>Br J Pharm</i> 130:1833-1842 (2000). Hainzl D and Casida JE. Fipronil insecticide: Novel photochemical desulfinylation with retention of neurotoxicity. <i>Proc Natl Acad Sci</i> 93:12764-12767 (1996). Hosie AM, Bavlis HA, Buckingham SD and Sattelle DB. Actions of the insecticide fipronil, on dieldrin-sensitive and -resistant GABA receptors of <i>Drosophila melanogaster</i>. <i>Br J Pharm</i> 115:909-912 (1995). Cole LM, Nicholson RA and Casida JE. Action of Phenylpyrazole Insecticides at the GABA-Gated Chloride Channel. <i>Pest Biochem Physiol</i> 46:47-54. Irench-Constant RH, Steichen JC, Rocheleau TA, Aronstein K and Roush RT. A single-amino acid substitution in a γ-aminobutyric acid subtype A receptor locus is associated with cyclodiene insecticide resistance in <i>Drosophila</i> populations. <i>Proc Natl Acad Sci</i> 90:1957-1961 (1993). Davies TGE, Field LM, Usherwood PNR and Williamson MS, DDT, Pyrethrin, Pyrethroids and Insect Sodium Channels. <i>IUBMB Life</i> 59:151-162 (2007). Soderlund DM. Pyrethroids, knockdown resistance and sodium channels. <i>Pest Manag Sci</i> 64:610-616 (2008). Jeschke P, Nauen R and Beck ME. Nicotinic acetylcholine receptor agonists: a milestone for modern crop protection. <i>Angewandte Chemie International Edition</i> 38:103-110 (1999). Uvany I. Nicotine and other insecticidal alkaloids, in <i>Neonicotinoid Insecticides and the Nicotinic Acetylcholine Receptor</i>, ed. by Yamamoto I, Casida JE, Springer Press, Berlin Heidelberg New York, pp. 29-69 (1999). Sparks TC, Watson GB, Loso MR, Geng C, Babcock JM and Thomas JD. Sulfoxafior and the sulfoximine insecticides: chemistry, mode of action and basis for efficacy on resistant insects. <i>Pestic Biochem Physiol</i> 107:1-7 (2013). Nauen R, Jeschke P, Velten R, Beck ME, Ebbinghaus-Kintscher U, Thielert W, Wölfel K, Haas M, Kunz K, Raupach G. Flupyradifurone: a brief profile of a new butenolide insecticide. <i>Pest Manag Sci</i> 71:850-862 (2015). Genn C, Watson GB, Sparks TC. Nicotinic acetylcholine receptors as spirovyn targets for insect pest management, in <i>Advances in Insect Physiology: Target Receptors in the Control of Insect Pests: Part I</i>, Vol. 44, ed. by Cohen E, Academic Press, New York, pp. 103-210 (2014). Watson GB, Chouinard SW, Cook KR, Genn C, Gifford JM, Gustafson GD, Hasler JM, Laminua IM, Letherer TJ, Mitchell JC, Pak WL, Salgado VL, Sparks TC and Stilwell GE. Heterologous expression of a spirovyn-sensitive <i>Drosophila melanogaster</i> nicotinic acetylcholine receptor identifies through chemically induced target site resistance and resistance gene identification. <i>Insect Biochem Mol Biol</i> 40:376-384 (2010).
3	Sodium channel modulators		Rugg D, Buckingham SD, Sattelle DB and Jansson RK. The insecticidal macrocyclic lactones, in <i>Insect Pharmacology: Channels, Receptors, Toxins and Enzymes</i>, Gilbert LI, Gill SS eds, Academic Press, Cambridge, MA, pp.69-99 (2010). Palmer T. Chloride channel activators / new natural products: Avermectins and milbemycins, in <i>Modern Crop Protection Compounds</i> 2nd Ed, Vol. 3, Kramer W, Schirmer U, Jeschke P, Witschel M, eds, Wiley-VCH, pp.1305-1326 (2012).
4	Nicotinic acetylcholine receptor (nAChR) competitive modulators		Dubrovsky EB and Bernardo TJ. The juvenile hormone receptor and molecular mechanisms of juvenile hormone action, in <i>Advances in Insect Physiology: Target receptors in the control of insect pests Part II</i>, Vol. 46, E. Cohen, ed. Academic Press, Cambridge, MA, pp.305-388 (2015). Hatakoshi M, Pyrioxifen: A new juvenoid, in <i>Modern Crop Protection Compounds</i> 2nd Ed, Vol. 3, Kramer W, Schirmer U, Jeschke P, Witschel M, eds, Dhadialla TS, Retnakaran A and Smaghe G, Insect growth- and development-disrupting insecticides, in <i>Insect Control: Biological and Synthetic Agents</i>, Gilbert LI, Gill SS, eds, Academic Press, pp. 121-184 (2010).
5	Nicotinic acetylcholine receptor (nAChR) allosteric modulators – Site I		Price NR. The mode of action of fumigants. <i>J Stored Prod Res</i> 21:157-164 (1985). Sparks SF, Quistad GB and Casida JE. Chloropirrin: Reactions with biological thiols and metabolism in mice. <i>Chem Res Toxicol</i> 10:1001-1007 (1997). Barbier O, Arepola-Mendoza L, Del-Razo LM. Molecular mechanisms of fluoride toxicity. <i>Chemico-Biological Interactions</i> 188:319-333 (2010). Cryolite Summary Document Registration Review: Initial Docket EPA-HQ-OPP-2011-0173 March 2011 Cochran DG. Toxic effects of boric acid on the German cockroach. <i>Experientia</i> 51:561-563 (1995).
6	Glutamate-gated chloride channel (GluCl) allosteric modulators		Currently no known publications
7	Juvenile hormone mimics		Nesterov A, Spalthoff C, Kandasamy R, Katana R, Ranki NB, Andres M, Jaehde P, Dorsch J, Stam LF, Braun F-J, Warren B, Salgado VL and Goepfert MC. TRP Channels in Insect Stretch Receptors as Insecticide Targets. <i>Neuron</i> 86:665-671 (2015). Auborn J, Wolf H, Mader W and Kayser H. The insecticide pymetrozine selectively affects chordotonal mechanoreceptors. <i>J Exp Biol</i> 208:4451-4466. Harewin P. Pymetrozine, a Fast-Acting and Selective Inhibitor of Aphid Feeding. In-situ Studies with Electronic Monitoring of Feeding Behaviour. <i>Bretschneider T and Nauen R. Mite growth inhibitors (dofentazine, hexylthiazox, etoxazole). In <i>Modern Crop Protection Compounds</i> 2nd Edition (Eds. W. Kraemer, U Schirmer), Volume 3, Wiley-VCH, Weinheim, pp.1012-1027 (2012).</i> Demaeght P, et al. (2014). "High resolution genetic mapping uncovers chitin synthase-1 as the target-site of the structurally diverse mite growth inhibitors dofentazine, hexylthiazox and etoxazole in <i>Tetranychus urticae</i>." <i>Insect Biochemistry and Molecular Biology</i> 51: 52-61.
8	Miscellaneous non-specific (multi-site) inhibitors	Alkyl halides Chloropirrin Sulfonyl fluoride and cryolite Borax Tartar emetic	Bravo A, Gill SS and Soberon M. Mode of action of <i>Bacillus thuringiensis</i> Cry and Cyt toxins and their potential for insect control. <i>Toxicol</i> 49:423-445 (2007). Peper GR and Casida JE. Housefly adenosinetriphosphatases and their inhibition by insecticidal organotin compounds. <i>J Econ Entomol</i> 58:392-400. Ruder FJ, Guyer W, Benson JA and Kayser H. The thiourea insecticide/acaricide diafenthiuron has a novel mode of action: inhibition of mitochondrial respiration by its carbodiimide product. <i>Pest Biochem Physiol</i> 41:207-219 (1991). Petroske E and Casida JE. Diafenthiuron action: carbodiimide formation and ATPase inhibition. <i>Pest Biochem Physiol</i> 53:60-74 (1995). Black BC, Hollingworth RM, Ahnmadrasah KI, Kukul CD and Donovan S. Insecticidal action and mitochondrial uncoupling activity of AC-303, 630 and related halogenated pyroles. <i>Pest Biochem Physiol</i> 50:115-128 (1994). Schnellmann RG and Manning RO. Perfluorooctane sulfonamide: A structurally novel uncoupler of oxidative phosphorylation. <i>Biochimica et Biophysica Acta</i> 1050:1-12 (1988). Miyoshi H and Fujita T. Quantitative analyses of the uncoupling activity of substituted phenols with mitochondria from flight muscles of house flies. <i>Biochim et Biophysica Acta</i> 935:312-321 (1988).
9	Chordotonal organ TRPV channel modulators		Sattelle DB, Harrow ID, David JA, Pelhate M, Calle J, Gerner JI and Hall LM. Nereistoxin: Actions on a CNS acetylcholine receptor/ion channel in the cockroach <i>periplaneta americana</i>. <i>J Exp Biol</i> 118:37-52 (1995). Delpech VR, Ihara M, Coddou C, Matsuda K and Sattelle DB. Action of nereistoxin on recombinant neuronal nicotinic acetylcholine receptors expressed in <i>Xenopus laevis</i> oocytes. <i>Invert Neurosci</i> 1:29-35 (2003). Nagata K, Iwanaga Y, Shono T and Narahashi T. Modulation of the neuronal nicotinic acetylcholine receptor channel by imidacloprid and cartap. <i>Pest Biochem Physiol</i> 59:119-128 (1997).
10	Mite growth inhibitors affecting CHS1		Lee S-J, Tomizawa M and Casida JE. Nereistoxin and cartap neurotoxicity attributable to direct block of the insect nicotinic receptor/channel. <i>J Agric and Food Chem</i> 52:95-98 (2004). Douris V, Steinbach D, Pantelen R, Livadara L, Pickett JA, Van Leeuwen T, Nauen R and Vontas J. Resistance mutation conserved between insects and mites unravels the benzoylurea insecticide mode of action on chitin biosynthesis. <i>PNAS</i> 113:14692-14697 (2016). Sun R, Liu C, Zhang H, Wang Q. Benzoylurea Chitin Synthesis Inhibitors. <i>J Agric Food Chemistry</i> 63:6847-6865 (2015). Douris V, et al. (2016). "Resistance mutation conserved between insects and mites unravels the benzoylurea insecticide mode of action on chitin biosynthesis." <i>Proc Natl Acad Sci U S A</i> 113(51): 14692-14697.
11	Microbial disruptors of insect midgut membranes		Uchida M, Asah T and Sugimoto T. Inhibition of cuticle deposition and chitin biosynthesis by a new insect growth regulator, buprofezin, in <i>Nilaparvata lugens</i>. <i>Agr and Biol Chem</i> 49:1233-1234 (1985). Asai T, Fukuda M, Maekawa S, Ikeda K and Kanno H. Studies on the mode of action of buprofezin I. Nymphoidal and ovidicial activities on the brown rice planthopper, <i>Nilaparvata lugens</i> STAL. (Homoptera: Delphacidae). <i>Applied Ento and Zoology</i> 18:550-552 (1983). Bei Y, Wiesner P and Kayser H. Candidate target mechanisms of the growth inhibitor cyromazine: studies of phenylalanine hydroxylase, puparial amino acids, and dihydrofolate reductase in dipteran insects. <i>Arch Insect Biochem and Physiol</i> 45:69-78 (2000).
12	Inhibitors of mitochondrial ATP synthase		Wing KD, RH 5849, a nonsteroidal ecdysone agonist: effects on a <i>Drosophila</i> cell line. <i>Science</i> 241:467-469 (1988). Retnakaran A, Hiruma K, Pali SR and Riddford LM. Molecular analysis of the mode of action of RH-5992, a Lepidopteran-specific, non-steroidal ecdysteroid agonist. <i>Insect Biochem and Mol Biol</i> 25:109-117 (1995). Carlson GR, Dhadialla TS, Hunter R, Jansson RK, Janz GS, Lidert Z and Slawicki RA. The chemical and biological properties of methoxyfenozide, a new insecticidal ecdysteroid agonist. <i>Pest Manag Sci</i> 57:115-119 (2001). Tova T, Fukasawa H, Masui A and Endo Y. <i>Biochem Biophys Res Comm</i> 292:1087-1091 (2002). Or GL, Orr N, Comfield L, Cole JWD and Downer RGH. Interaction of formamidin pesticides with insect neural octopamine receptors: Effects on radioligand binding and cyclic AMP production. <i>Pesticide Science</i> 30:285-294 (1990).
13	Uncouplers of oxidative phosphorylation via disruption of the proton gradient		Davenport AP, Morton DB and Evans PD. The action of formamidines on octopamine receptors in the locust. <i>Pest Biochem Physiol</i> 24:45-52 (1985). Evans PD and Gee JD. Action of formamidin pesticides on octopamine receptors. <i>Nature</i> 287:60-62 (1980). Hüllingshaus JG. Inhibition of mitochondrial electron transport by hydramethylnon: A new amidinohydrazone insecticide. <i>Pestic Biochem Physiol</i> 27:61-70. Kinoshita S, Koura Y, Kariya H, Ohsaki N and Watanabe T. AKD-2023, a novel miticide. <i>Biological activity and mode of action. Pestic Sci</i> 55: 659-660. Dekeyser MA. Acaricide mode of action. <i>Pest Manag Sci</i> 61:103-110 (2005). Lümmen P. Mitochondrial Electron Transport Complexes as Biochemical Target Sites for Insecticides and Acaricides, in: Ishaaya, I., et al. (ed.) <i>Insecticides: Design Using Advanced Technologies</i>. Springer-Verlag, Berlin, (2007).
14	Nicotinic acetylcholine receptor (nAChR) channel blockers		Van Nieuwenhuyse P, van Leeuwen T, Khaehjal J, Vanholme B and Tirry L. Mutations in the mitochondrial cytochrome b of <i>Tetranychus urticae</i> Koch. (Acari: Tetranychidae) confer cross-resistance between bifentazate and acequinocyl. <i>Pest Manag Sci</i> 65:404-412 (2009). Van Nieuwenhuyse P, Demaeght P, Khalighi M, Stevens CV, Vanholme B, Tirry L, Luemmen P and Van Leeuwen T. On the mode of action of bifentazate: New evidence for a mitochondrial target site. <i>Pest Biochem Phys</i> 104:88-95 (2012).
15	Inhibitors of chitin biosynthesis affecting CHS1		
16	Inhibitors of chitin biosynthesis, type 1		
17	Moulting disruptors, Dipteran		
18	Ecdysone receptor agonists		
19	Octopamine receptor agonists		
20	Mitochondrial complex III electron transport inhibitors		

		<p>Van Leeuwen T, Tirry L and Nauen R. Complete maternal inheritance of bifentazate resistance in <i>Tetranychus urticae</i> Koch (Acari: Tetranychidae) and its implications in mode of action considerations. <i>Insect Biochem Mol Biol</i> 36:869-877 (2006).</p> <p>Molpa K, Suzuki T and Uchida M. Effect of a new acaricide, fenpyroximate, on energy metabolism and mitochondrial morphology in adult female <i>Tetranychus urticae</i> (two-spotted spider mite). <i>Pestic Biochem Physiol</i> 43:37-43 (1992).</p> <p>Friedrich T, Ohnishi T, Forche E, Kunze B, Jansen R, Trowitzsch W, Höfle G, Reichenbach H and Weiss H. Two binding sites for naturally occurring inhibitors in mitochondrial and bacterial NADH:ubiquinone oxidoreductase (complex I). <i>Biochem Soc Trans</i> 22:226-230 (1994).</p> <p>Hollingsworth RM, Ahammadsahib KI, Gadelhak G and McLoughlin JL. 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Spider-venom peptides as bioinsecticides. <i>Toxins</i> 4:191-227 (2012).</p> <p>Tedford HW, Gilles N, Menez A, Doering CJ, Zamponi GW and King GF. Scanning Mutagenesis of α-Baculovirus-Hv1a Reveals a Spatially Restricted Epitope That Confers Selective Activity against Insect Calcium Channels. <i>J Biol Chem</i> 279:44133-44140 (2004).</p> <p>Gunning SJ, Maggio F, Wendley MJ, Valenzuela SM, King GF and Nicholson GM. The Janus-faced atracotoxins are specific blockers of invertebrate K_{Ca} channels. <i>FEBS</i> 275:4045-4059 (2008).</p>
21	Mitochondrial complex I electron transport inhibitors	
22	Voltage-dependent sodium channel blockers	
23	Inhibitors of acetyl CoA carboxylase	
24	Mitochondrial complex IV electron transport inhibitors	
25	Mitochondrial complex II electron transport inhibitors	
28	Ryanodine receptor modulators	
29	Chordotonal organ Modulators - undefined target site	
30	GABA-gated chloride channel allosteric modulators	
31	Baculoviruses	
32	Nicotinic Acetylcholine Receptor (nAChR) Allosteric Modulators - Site II	
UN	Compounds of unknown or uncertain MoA	<p>Azadirachtin Mordue AJ, Morgan ED and Nisbet AJ. Azadirachtin, a Natural Product in Insect Control. In Insect Control, L.I. Gilbert and S.S. Gill, eds., Academic Press, 2013.</p> <p>Benzoximate Currently no known publications</p> <p>Bromopropylate Soderlund DM and Adams PM. Inhibition of Octopamine-Stimulated Adenylate Cyclase Activity in Two-Spotted Mites by Dicofof and Related Diphenylcarbinol Acaricides. <i>Pest Biochem Physiol</i> 46:228-235 (1993).</p> <p>Chinomethionat Carlson GP and DuBois KP. Studies on the toxicity and biochemical mechanism of action of 6-methyl-2,3-quinoline-dithiol cyclic carbonate (Morestan). <i>J Pharmacol Exp Ther</i> 173:60-70 (1970).</p> <p>Dicofof Soderlund DM and Adams MA. Inhibition of octopamine-stimulated adenylate cyclase activity in two-spotted mites by dicofof and related diphenylcarbinol acaricides. <i>Pest Biochem Physiol</i> 46:228-235 (1993).</p> <p>Pyridalyl Powell GF, Ward DA, Prescott MC, Spiller D.G, White MR H, Turner P.C, Earley FGP, Phillips J and Rees HH. The molecular action of the novel insecticide, Pyridalyl. <i>Insect Biochem Mol Biol</i> 41:459-69 (2011). Saito S. Effects of pyridalyl on ATP concentrations in cultured Sf9 cells. <i>J Pest Sci</i> 30:403-405 (2005). Saito S, Akamoto NS and Meda KU. Effects of pyridalyl, a novel insecticidal agent, on cultured Sf9 cells. <i>J Pest Sci</i> 30:17-21 (2005). Saito S, Yoshioka T and Umeda K. Ultrastructural effects of pyridalyl, an insecticidal agent, on epidermal cells of <i>Spodoptera litura</i> larvae and cultured insect cells Sf9. <i>J Pest Sci</i> 31:335-338 (2006).</p> <p>Mancozeb Quilino, M. L., et al. (2010). <i>Plant Dis</i> 94(9): 1076-1087.</p>
UNB	Bacterial agents (non-B) of unknown or uncertain MoA	<p><i>Burkholderia</i> spp Ruiu, L. (2015). "Insect Pathogenic Bacteria in Integrated Pest Management." <i>Insects</i> 6(2): 352-367.</p> <p><i>Wolbachia pipiensis</i> (Zap) Stouthamer, R., et al. (1999). "Wolbachia pipiensis: microbial manipulator of arthropod reproduction." <i>Annual review of microbiology</i> 53(1): 71-102.</p>
UNE	Botanical essence including synthetic, extracts and unrefined oils with unknown or uncertain MoA	<p><i>Chenopodium ambrosioides</i> near <i>Pennyroyal</i> essential oils with glycerol or emulsifier Chiasson, H., et al. (2004). "Insecticidal properties of a Chenopodium-based botanical." <i>J Econ Entomol</i> 97(4): 1378-1383.</p> <p>Neem oil Currently no known publications</p> <p>Formentini M. A., et al. (2016). <i>Braz J Biol</i> 76(4): 951-954.</p>
UNF	Fungal agents of unknown or uncertain MoA	<p><i>Beauveria bassiana</i> strains Wright, S. P., et al. (2000). "Evaluation of the Entomopathogenic Fungus <i>Beauveria bassiana</i> and <i>Paeclomyces fumosoroseus</i> for Microbial Control of the Silverleaf Whitefly, <i>Bemisia argentifolii</i>." <i>Biological Control</i> 17(3): 203-217.</p> <p><i>Metarhizium anisopliae</i> strain F52 Jackson, M. A. and S. T. Jaronski (2009). "Production of microsclerotia of the fungal entomopathogen <i>Metarhizium anisopliae</i> and their potential for use as a biocontrol agent for soil-inhabiting insects." <i>Mycol Res</i> 113(Pt 8): 842-850.</p> <p><i>Paeclomyces fumosoroseus</i> Apopka strain 97 Jackson, M. A., et al. (1997). "Liquid culture production of desiccation tolerant blastospores of the bioinsecticidal fungus <i>Paeclomyces fumosoroseus</i>." <i>Mycological Research</i> 101(1): 35-41. Vega, F. E., et al. (1999). "Germination of conidia and blastospores of <i>Paeclomyces fumosoroseus</i> on the cuticle of the silverleaf whitefly, <i>Bemisia argentifolii</i>." <i>Mycopathologia</i> 147(1): 33-35.</p>
UNM	Non-specific mechanical disruptors	<p>Diatomaceous earth Athanassiou, C. G., et al. (2004). "Insecticidal Effect of Three Diatomaceous Earth Formulations Against Adults of <i>Sitophilus oryzae</i> (Coleoptera: Curculionidae) and <i>Tribolium confusum</i> (Coleoptera: Tenebrionidae) on Oat, Rye, and Triticale." <i>Journal of Economic Entomology</i> 97(6): 2160-2167.</p>
UNP	Repases of unknown or uncertain MoA	
UNV	Viral agents (non-baculovirus) of unknown or uncertain MoA	