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Review

Review

The Impact of Artificial Sweeteners on Insects

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Abstract

Artificial sweeteners are sweet-tasting additives found in consumable products as substitutes for naturally occurring sugars. They are derived from plant extracts or manufactured by chemical synthesis. Ingestion of sweeteners by insects can lead to significant physiological effects, such as mortality, decreased fecundity, and behavioral change. Due to their low toxicity toward humans and the issues associated with conventional insecticide usage, artificial sweeteners have recently gained attention for their potential use as biorational insecticides. Here, we review their impact on insects and potential as novel insecticides.

Key words: sugar substitutes, mortality, physiological effects, polyol, additives

Synthetic organic insecticide use has been the primary method of insect pest control for most of the past century (Yu 2014). However, persistent environmental and health concerns such as nontarget effects and bioaccumulation, as well as management concerns such as insecticide resistance have motivated efforts to find alternative treatment strategies (Perveen 2011). Recently, there has been a broad interest in investigating generally recognized-as-safe (GRAS) compounds such as essential oils (Klein et al. 2019) and artificial sweeteners (Burgess et al. 2018, Barrett et al. 2020, Caponera et al. 2020, Wentz et al. 2020) as insecticides for pest management. Due to their low cost, accessibility, and minimal toxicity toward humans, artificial sweeteners are an appealing group of compounds to consider when researching alternative treatment options.

Artificial sweeteners, also known as sugar substitutes, nonnutritive sweeteners, zero-calorie sweeteners, or low-calorie sweeteners, are sweet-tasting additives found in beverages, food, drugs, and other products. These include the sugar alcohols (polyols) and artificially derived compounds such as aspartame, saccharin, sodium cyclamate, acesulfame potassium, and sucralose (Kroger et al. 2006, Chattopadhyay et al. 2014; Table 1). Sweeteners are often marketed as healthy alternatives to naturally occurring sugars due to their lower caloric values and dental health benefits (Kawanabe et al. 1992, Shankar et al. 2013). The projected size of the artificial sweetener market is expected to exceed $20 billion by 2026 (Watson 2019).

Early studies involving insects and sweeteners primarily focused on the caloric differences between sweetener types, phagostimulation, and the ability of insects to digest or utilize different carbohydrates (Vogel 1931, von Frisch 1934, Haslinger 1935). Many low-calorie sweeteners caused premature death in these feeding assays. However, mortality did not attract attention from an insecticidal standpoint until a brief mention in 1968 discussing a sweetener-induced starvation method to control flies (Dethier 1968). More recent work on the toxicity of sweeteners revealed a concentration-dependent mortality response to several polyols across multiple insect orders and other physiological detriments such as hindered development and fecundity (Özalp and Emre 2001, Baudier et al. 2014, Caponera et al. 2020).

Baudier et al. (2014) were the first to study the toxicity of erythritol on *Drosophila melanogaster* Meigen (Diptera: Drosophilidae) with explicit consideration of its insecticide potential. More than a dozen similar studies have followed to evaluate this concept across Diptera, Hymenoptera, Blattodea, and Hemiptera (O'Donnell et al. 2016, 2017; Sampson et al. 2016, 2017, 2019; Zheng et al. 2016; Burgess and King 2017; Choi et al. 2017, 2018; Fisher et al. 2017; Goffin et al. 2017; Tang et al. 2017; Zhang et al. 2017; Burgess et al. 2018; Burgess and Geden 2019; Díaz-Fleischer et al. 2019; Fiocca et al. 2019; Barrett et al. 2020; Caponera et al. 2020; Wentz et al. 2020). At the time of the preparation of this review, the effects of sweeteners have been studied across at least six orders and 30 species of insects. This is the first review to consolidate the known impacts of artificial sweeteners on insects to provide a clearer idea of the current progress and gaps for their utilization as insecticides.

The Impact of Artificial Sweeteners on Insects

Mortality and Survivorship

Mortality after consuming sweeteners has been observed across a number of taxa, with dipterans receiving the most attention (Table 2). Many polyols diluted in water or media offered to *D. melanogaster* significantly reduce survivorship. Media made with erythritol, mannitol, sorbitol, and glycerol were observed to

Table 1. The artificial sweeteners investigated on insects

Name	IUPAC name	Common trade names
Polyols		
Erythritol[a]	(2*R*,3*S*)-Butane-1,2,3,4-tetrol	Truvia
Pentaerythritol	2,2-*bis*(hydroxymethyl)propane-1,3-diol	
Mannitol	(2*R*,3*R*,4*R*,5*R*)-hexane-1,2,3,4,5,6-hexol	
Sorbitol	(2*R*,3*R*,4*R*,5*S*)-hexane-1,2,3,4,5,6-hexol	
Xylitol	(2*R*,3*R*,4*S*)-pentane-1,2,3,4,5-pentol	
Glycerol	Propane-1,2,3-triol	
Saccharin	1,1-Dioxo-1,2-benzothiazol-3-one	Sweet'N Low
Sodium cyclamate	Sodium; *N*-cyclohexylsulfamate	
Aspartame	(3*S*)-3-amino-4-[[(2*S*)-1-methoxy-1-oxo-3-phenylpropan-2-yl]amino]-4-oxobutanoic acid	NutraSweet, Equal
Sucralose	(2R,3R,4R,5R,6R)-2-[(2R,3S,4S,5S)-2,5-*bis*(chloromethyl)-3,4-dihydroxyoxolan-2-yl]oxy-5-chloro-6-(hydroxymethyl)oxane-3,4-diol	Splenda
Acesulfame potassium (Ace K)	Potassium; 6-methyl-2,2-dioxo-1-oxa-2lambda6-thia-3-azanidacyclohex-5-en-4-one	Sweet One

[a] Refers to *meso*-erythritol unless specified otherwise.

Table 2. Mortality and survivorship of insects after artificial sweetener treatments

Order	Species	Artificial sweetener	Testing method	Observations	References
Diptera	*Drosophila melanogaster*	Erythritol	Solution; 0.1–0.5 M	Adult mortality; 50% at 2–3 d	Hassett (1948)
			Food; 0.0952-g/ml Truvia (99% erythritol, 1% rubiana)	Adult mortality; 100% at 5.8 d	Baudier et al. (2014)
			Food; 0.1–2 M	Adult mortality; 50% at <5 to <30 d	Baudier et al. (2014)
			Food; 1–2 M erythritol plus 1 M sucrose	Adult mortality; 50% at <5 to <15 d	Baudier et al. (2014)
			Food; 1 M	Adult mortality; 100% at 6 d	O'Donnell et al. (2016)
			Food; 20-ml 0–2 M Truvia in 3.75 g diet	Adult mortality; LC_{50} = 930 mM 4-h exposure	Sampson et al. (2016)
			Food; 0–2 M	Adult mortality; LC_{50} = 1.56 M at 24 h	O'Donnell et al. (2017)
			Food; 0–2 M	Larval mortality; LC_{50} = 0.59 M at 24 h	O'Donnell et al. (2017)
			Treated substrate	No contact toxicity on eggs	O'Donnell et al. (2017)
			Food; 20-ml 0–2 M Truvia in 3.75-g diet	Decreased pupal counts; 0 at > 500 mM	Sampson et al. (2016)
		Mannitol	Solution; 0.1 M	Adult mortality; 50% at 6 d	Hassett (1948)
			Food; 1 M	Adult mortality; ~50% at 17 d	O'Donnell et al. (2016)
			Food; 1 M	Sex dependent differential mortality	O'Donnell et al. (2016)
			Media; 0.25–2 M	Sex dependent differential mortality; up to and beyond 50% mortality at 21 d	Fiocca et al. (2019)
			Solution; 0.1 M	Adult mortality; 50% at 17 d	Hassett (1948)
		Sorbitol	Solution; 0.1 M	Adult mortality; 50% at 5 d	Hassett (1948)
		Glycerol	Solution; 0.1 M	Adult mortality; 50% at 14 d	Hassett (1948)
		Xylitol	Food; 1 M	Survivorship	O'Donnell et al. (2016)
	Drosophila suzukii	Erythritol	Food; 20-ml 0–2 M Truvia (99% erythritol, 1% rubiana) in 3.75 g diet	Adult mortality; LC_{50} = 1150 mM 4-h exposure	Sampson et al. (2016)
			Solution; 0.05–1 M	Adult mortality; 100% at 7 d	Choi et al. (2017)
			Solution; 0.5–2 M erythritol and 0.5–1 M sucrose separate	Survivorship with sucrose choice	Choi et al. (2017)
			Solution; 0.5–2 M erythritol and 0.5–1 M sucrose	Adult mortality; up to 100% at 7 d	Choi et al. (2017)

Table 2. Continued

Order	Species	Artificial sweetener	Testing method	Observations	References
			Solution; 0.5–1 M sucrose and 0.5–2 M erythritol	Adult mortality; up to 100% at 7 d	Tang et al. (2017)
			Media; 55-g/liter erythritol and/or 55-g/liter sugar	Adult mortality; up to 100% at 7 d	Goffin et al. (2017)
			Solution; 0.5–2 M erythritol and/or 0.5 M sucrose plus wounded/unwounded blueberries	Decreased mortality in presence of wounded blueberries; erythritol and sucrose treatment from 100% at day 7 to 85% or 87%	Choi et al. (2018)
			Treated blackberries; 2 M Truvia (99% erythritol, 1% rubiana)	Larval mortality; 88.9 ± 11.1%	Sampson et al. (2016)
			Media; 0 g/100 ml–2,750 g/100 ml sugar and/or 0 g/100 ml–2,750 g/100 ml erythritol	Larval mortality, reduced pupae and adult development	Goffin et al. (2017)
			Food; 20-ml 0–2 M Truvia (99% erythritol, 1% rubiana) in 3.75-g diet	Decreased pupal counts; 0 at > 500mM	Sampson et al. (2016)
			Media; 0.25–1 M	*Meso*-erythritol caused net population decline	Sampson et al. (2019)
			Spray; 0.5 M *meso*-erythritol, 0.5 M pentaerythritol, or 0.25 M *meso*-erythritol and 0.25 M pentaerythritol	Egg and larvae numbers reduced by pentaerythritol treatment (64 and 93%), *meso*-erythritol treatment (64 and 93%), and combined treatment (82 and 93%) on blackberry and blueberry bushes	Sampson et al. (2019)
			Spray; 0.5 M erythritol (Truvia Baking Blend) and/or 10 ppm lufenuron	Erythritol alone or paired with lufenuron reduced larvae number on *Vaccinium virgatum* and *Rubus* sp., ~75%	Sampson et al. (2017)
		Xylitol	Solution; 0.05–1 M	Adult mortality; 0.05 M, 30% at 7 d	Choi et al. (2017)
		Mannitol	Solution; 0.05–1 M	Adult mortality; 0.05 M, 68% at 7 d	Choi et al. (2017)
		Sorbitol	Solution; 0.05–1 M	Adult mortality; 0.05 M, 50% at 7 d	Choi et al. (2017)
		Glycerol	Solution; 4.18 M glycerol and 50% sucrose	Low mortality; <20% at 72 h	Díaz-Fleischer et al. (2019)
	Drosophila wheeleri	Xylitol	Solution; 5%	Adult mortality	Kircher and Al-Azawi (1985)
		Mannitol	Solution; 5%	Adult mortality	Kircher and Al-Azawi (1985)
	Drosophila arizonensis	Xylitol	Solution; 5%	Adult mortality	Kircher and Al-Azawi (1985)
	Phormia regina	Erythritol	Solution; 0.1 M	Adult mortality; 50% at 3 d	Hassett et al. (1950)
		Glycerol	Solution; 0.1 M	Adult mortality; 50% at 4.5 d	Hassett et al. (1950)
		Sorbitol	Solution; 0–1 M	No impact on mortality	Gelperin and Dethier (1967)
	Calliphora erythrocephala	Erythritol	Solid	No survivorship; 100% dead at 3.5 d	Fraenkel (1940)
			Solution	No survivorship; 100% dead at 3.5 d	Fraenkel (1940)
		Sorbitol	Solid	Survivorship; 100% dead at 80 d	Fraenkel (1940)
		Mannitol	Solid	Survivorship; 100% dead at 41 d	Fraenkel (1940)
	Ceratitis capitata	Mannitol	Solution; 5–9.1%	Adult mortality; 57–100% at 4 d	Gothilf et al. (1971)
	Aedes aegypti	Erythritol	Solution; 0.5–2.0 M	Adult female mortality; LC_{50} at 3 d was 1.60 M and at 6 d was 0.63 M	Gilkey et al. (2018)
			Solution; 0.1–0.4 M	Larval mortality; 48-h LC_{50} = 0.11 M for 3-d-old larvae and 0.42 M for 5-d-old larvae	Gilkey et al. (2018)
		Sorbitol	Solution; 5%	Increased survivorship versus water only; 100% mortality at 63 vs ~9 d	Galun and Fraenkel (1957)
		Mannitol	Solution; 5%	Adult mortality; 100% at 6 d	Galun and Fraenkel (1957)
		Glycerol	Solution; 5%	Adult mortality; 100% at 7 d	Galun and Fraenkel (1957)

Table 2. Continued

Order	Species	Artificial sweetener	Testing method	Observations	References
	Sarcophaga bullata	Sorbitol	Solution; 5%	Increased survivorship versus water only; 100% mortality at 32 vs 5 d	Galun and Fraenkel (1957)
		Mannitol	Solution; 5%	Increased survivorship versus water only; 100% mortality at 33 vs 5 d	Galun and Fraenkel (1957)
		Glycerol	Solution; 5%	Intermediate survivorship between sucrose and water only; 100% mortality at 10 vs 34 and 5 d	Galun and Fraenkel (1957)
	Anastrepha ludens	Erythritol	Unspecified	Adult mortality; 3-d survivorship	Baker et al. (1944)
			Solution; 1–2.78 M erythritol and 50% sucrose	Adult mortality; 76% at 72 h with 2.78 M treatment	Díaz-Fleischer et al. (2019)
		Mannitol	Unspecified	Adult mortality; 15-d survivorship	Baker et al. (1944)
		Glycerol	Solution; 1.67–4.18 M glycerol and 50% sucrose	Adult mortality; 22–50% at 72 h	Díaz-Fleischer et al. (2019)
	Anastrepha obliqua	Glycerol	Solution; 4.18 M glycerol and 50% sucrose	Adult mortality; ~70%	Díaz-Fleischer et al. (2019)
	Bactrocera dorsalis	Erythritol	Solution; 0.082 M	Adult mortality; 96.6 ± 2.28% at 60 h	Zheng et al. (2016)
		Aspartame	Solution; 0.034M	Adult mortality; 80.0 ± 4.87% at 60 h	Zheng et al. (2016)
		Saccharin	Solution; 0.005 M	Adult mortality; 62.22 ± 8.01% at 60 h	Zheng et al. (2016)
	Musca domestica	Erythritol	Solution; 0.5–2 M	Adult mortality; ~100% at 10 d	Burgess and King (2017)
			Dried mixture; 10:90, 50:50, 90:10 sucrose–Truvia (99% erythritol, 1% rubiana)	Adult mortality; ~20 to 70% by day 14	Fisher et al. (2017)
			Solid; 100% Truvia	Adult mortality; ~90% by day 14	Fisher et al. (2017)
			Food; 1-g erythritol and 1–10 g *Beauveria bassiana* conidia	Adult mortality when paired with *Beauveria bassiana*; ~100% by day 8	Burgess et al. (2018)
			Media; 6.0–64.0 mg/g	Larval mortality; LC_{50} 34.94 mg/g	Burgess and Geden (2019)
			Media; 34.94 mg/g	Decreased successful development; 0.7% to pupa, 0% to adult	Burgess and Geden (2019)
		Xylitol	Solution; 0.5–2 M	Adult mortality; > 75% at 10 d	Burgess and King (2017)
			Solid; 100%	Adult mortality; ~70% by day 14	Fisher et al. (2017)
			Food; 1-g erythritol and 1–10 g *Beauveria bassiana* conidia	Adult mortality when paired with *Beauveria bassiana*; ~100% by day 8	Burgess et al. (2018)
			Media; 48.8–97.6 mg/g	Larval mortality; $LC_{50\,=}$ 74.91 mg/g	Burgess and Geden (2019)
			Media; 74.91 mg/g	Decreased successful development; 26.0% to pupa, 23.3% to adult	Burgess and Geden (2019)
		Sorbitol	Solid; 100%	No effect on survivorship versus sucrose by day 14	Fisher et al. (2017)
			Solution; 5%	Intermediate survivorship between sucrose and water only; 100% mortality at 15 vs 31 and 2.5 d	Galun and Fraenkel (1957)
		Mannitol	Solid; 100%	Adult mortality; ~75% by day 14	Fisher et al. (2017)
			Solution; 5%	Intermediate survivorship between sucrose and water only; 100% mortality at 22 vs 31 and 2.5 d	Galun and Fraenkel (1957)
		Glycerol	Solution; 5%	Intermediate survivorship between sucrose and water only; 100% mortality at 7 vs 31 and 2.5 d	Galun and Fraenkel (1957)
	Stomoxys calcitrans	Erythritol	Media; 10.97–37.03 mg/g	Larval mortality; LC_{50} = 22.10 mg/g	Burgess and Geden (2019)
			Media: 22.10 mg/g	Decreased successful development; 33.2% to pupa, 3.2% to adult	Burgess and Geden (2019)
		Xylitol	Media; 16.46–55.56 mg/g	Larval mortality; LC_{50} = 41.58 mg/g	Burgess and Geden (2019)
			Media; 41.58 mg/g	Decreased successful development; 40.4% to pupa, 9.6% to adult	Burgess and Geden (2019)

Table 2. Continued

Order	Species	Artificial sweetener	Testing method	Observations	References
Hymenoptera	*Tetramorium immigrans*	Erythritol	Food; 0.5–2.0 M	Concentration dependent worker mortality; up to 100% at 15 d	Barrett et al. (2020)
			Food; 0.5–2.0 M erythritol and ad lib water separate	Worker mortality; up to ~50% at 15 d	Barrett et al. (2020)
			Food; 0 M or 1.5 M	Horizontal transfer of lethal dose; ~75% mortality in secondarily exposed workers at 15 d	Barrett et al. (2020)
	Formica glacialis	Erythritol	Food; 1.5 M	Worker mortality; 100% at 15 d	Barrett et al. (2020)
			Food; 1.5 M and ad lib water separate	Worker mortality; ~75% at 15 d	Barrett et al. (2020)
	Camponotus chromaiodes	Erythritol	Food; 1.5 M and ad lib water separate	Worker mortality; <50% at 15 d	Barrett et al. (2020)
	Camponotus subarbatus	Erythritol	Food; 1.5 M	Worker mortality; >50% at 15 d	Barrett et al. (2020)
	Solenopsis invicta	Erythritol	Solution; 0.2 g/ml	Worker mortality; >90% at 72 h	Zhang et al. (2017)
			Solution; 0.001–0.2 g/ml	Caste dependent differential mortality; ~20 to 100% at 72 h	Zhang et al. (2017)
			Solution; 0.1-g/ml erythritol and blue dye	Horizontal transfer to all castes	Zhang et al. (2017)
		Aspartame	Solution; 0.01 g/ml	Worker mortality; >80% at 72 h	Zhang et al. (2017)
		Saccharin	Solution; 0.2 g/ml	Worker mortality; >90% at 72 h	Zhang et al. (2017)
	Apis mellifera	Erythritol	Solution; sucrose and erythritol	Worker mortality	Vogel (1931)
			Solution	Worker mortality	von Frisch (1934)
			Solution; 0.5–2.0 M erythritol and/or 0.5 M sucrose	Similar survivorship among treatments	Choi et al. (2018)
	Pimpla turionellae	Sorbitol	Food; 14%	Adult mortality; 38.58 ± 1.42 d survival	Özalp and Emre (2001)
		Mannitol	Food; 14%	Adult mortality; 15.83 ± 3.79 d survival	Özalp and Emre (2001)
Blattodea	*Blattella germanica*	Erythritol	Food; 0.003 moles/g erythritol and 30% casein	Reduced survival versus casein and glucose	Gordon (1959)
		Sorbitol	Food; 0.001–0.002 moles/g sorbitol and 30% casein	No effect on survival versus casein and glucose	Gordon (1959)
		Mannitol	Food; 0.002-moles/g mannitol and 30% casein	No effect on survival versus casein and glucose	Gordon (1959)
		Glycerol	Food; 0.002-moles/g glycerol and 30% casein	No effect on survival versus casein and glucose	Gordon (1959)
	Reticulitermes flavipes	Erythritol	Paper towel; 0.25–1.25 M	Concentration dependent mortality; 100% by day 8	Caponera et al. (2020)
Hemiptera	*Bemisia tabaci*	Mannitol	Diet; 10% mannitol, 15% sucrose, 10% FreAmine III	Adult mortality; ~1-d survival	Hu et al. (2010)
			Diet; 10% mannitol, 15% sucrose, 5% Difco yeast extract	No nymph mortality	Hu et al. (2010)
		Sorbitol	Diet; 10% sorbitol, 15% sucrose, 10% FreAmine III	Adult mortality; ~2-d survival	Hu et al. (2010)
			Diet; 10% sorbitol, 15% sucrose, 5% Difco yeast extract	No nymph mortality	Hu et al. (2010)
	Cacopsylla pyricola	Erythritol	Solution; 1–30%	Adult mortality; ~10 to ~100% at 3 d	Wentz et al. (2020)
			Treated leaves; dipped in 30% erythritol	Adult and nymph mortality on treated leaves; ~70% at 3 d	Wentz et al. (2020)
			Spray; 20% erythritol or 20% erythritol + Regulaid (surfactant)	Variable nymph reduction in pear orchards; approx.. 20–60%	Wentz et al. (2020)
			Treated leaves; heated or unheated erythritol solution	Heating solution to 31°C during preparation required for reduction; ~70% mortality with heated vs <10% for unheated	Wentz et al. (2020)
Coleoptera	*Tribolium castaneum*	Mannitol	Gypsum diet; 0.2 M	No impact on mortality	Kikuta (2018)

decrease survivorship of adult *D. melanogaster* compared with sucrose (or other nontoxic material)-only media (Hassett 1948, Baudier et al. 2014, O'Donnell et al. 2016, Sampson et al. 2016, Fiocca et al. 2019). O'Donnell et al. (2017) also confirmed larval toxicity of erythritol but recorded no contact toxicity toward eggs. *Drosophila suzukii* (Matsumura) (Diptera: Drosophilidae) that fed on media (Sampson et al. 2016, 2019; Goffin et al. 2017) and solutions (Choi et al. 2017, Tang et al. 2017, Choi et al. 2018, Díaz-Fleischer et al. 2019) treated with erythritol, xylitol, mannitol, or sorbitol also showed increased adult mortality. This effect was reduced for erythritol solutions in the presence of competing food sources (e.g., blueberries; ~14% decrease), but combining erythritol with sucrose increased mortality across all concentrations compared with erythritol alone (Choi et al. 2017, Tang et al. 2017, Choi et al. 2018). The larval impact has also been studied in fruit flies, with erythritol exposure and treatments reducing the overall number of immatures in laboratory and field settings (Goffin et al. 2017; Sampson et al. 2017, 2019).

Erythritol is the most promising polyol for *D. suzukii* control, with a few preliminary tests demonstrating the efficacy and viability of erythritol spray in the field. Several erythritol derivatives were screened by Sampson et al. (2019) to find potential lower-cost alternatives to *meso*-erythritol (the 'common' erythritol) as potential insecticides. Pentaerythritol was discovered to be an effective adulticide, but only *meso*-erythritol caused a net population decline in laboratory settings. Several field treatments were conducted to test *meso*-erythritol and pentaerythritol efficacy on blackberry and blueberry bushes. Both compounds reduced egg and larval numbers by 64 and 93%, respectively, and a combined treatment achieved a greater egg reduction of 82% (Sampson et al. 2019). This corroborated the earlier findings of Sampson et al. (2017) that demonstrated that *D. suzukii* larvae decline on *Vaccinium virgatum* (Aiton) (Ericales: Ericaceae) and *Rubus* sp. (Rosales: Rosaceae) after spray treatment with erythritol.

The toxicity of erythritol and other sweeteners has been observed across other fly groups with diverse feeding strategies. *Phormia regina* (Meigen) (Diptera: Calliphoridae) and *Calliphora erythrocephala* (Macquart) (Diptera: Calliphoridae) reached up to 100% mortality within several days when fed erythritol solutions (Fraenkel 1940, Hassett et al. 1950). *Aedes aegypti* (L.) (Diptera: Culicidae) adult females and larvae were killed when exposed to 0.1–2.0 M erythritol food sources (Gilkey et al. 2018); 5% mannitol and glycerol solutions reduced survival time of adults compared with sucrose solutions and water only (Galun and Fraenkel 1957). The fruit flies *Anastrepha ludens* (Loew) (Diptera: Tephritidae) and *Bactrocera dorsalis* Hendel (Diptera: Tephritidae) succumbed to erythritol solutions, with *An. ludens* also showing a comparable response to glycerol and *B. dorsalis* to aspartame and saccharin solutions as well (Baker et al. 1944, Zheng et al. 2016, Díaz-Fleischer et al. 2019). Multiple authors reported mortality of *Musca domestica* L. (Diptera: Muscidae) after the ingestion of erythritol and xylitol presented as solutions or solids (Burgess and King 2017, Fisher et al. 2017, Burgess et al. 2018). Both sweeteners are toxic to filth fly larvae and reduced the number of successful adult emergences in *M. domestica* and *Stomoxys calictrans* (L.) (Diptera: Muscidae) by up to 100% when raised in media treated with 22.10–74 mg/g of sweetener (Burgess and Geden 2019).

Despite most assays repeatedly demonstrating the insecticidal effects of erythritol and other polyols toward studied fly species, several compounds consistently have a negligible or opposite effect. In survivorship assays on the ability of flies to use sweeteners as food sources, *Cal. erythrocephala* survived on sorbitol and mannitol, as did *P. regina* on sorbitol (Fraenkel 1940, Hassett et al. 1950, Gelperin and Dethier 1967). Similarly, *Sarcophaga bullata* Parker (Diptera: Sarcophagidae) and *Ae. aegypti* had increased survivorship in the presence of 5% sorbitol solutions versus water only (Galun and Fraenkel 1957). Likewise, no difference in survivorship was observed when *M. domestica* was presented with solid sorbitol compared with sucrose over a 14-d period (Fisher et al. 2017).

Most evaluations of sweetener-induced mortality in Hymenoptera focused on pest ant species. Unlike flies, investigation of toxicants on ants warrants the consideration of horizontal transfer in addition to direct mortality. Barrett et al. (2020) assessed these properties of erythritol on *Tetramorium immigrans* Santschi, *Formica glacialis* Wheeler, *Camponotus chromaiodes* Bolton, and *C. subbarbatus* Emery (Hymenoptera: Formicidae). Workers of all species except *C. chromaiodes* experienced up to 100% mortality when fed 0.5–2.0 M erythritol in nonchoice feeding studies. The addition of a water source reduced mortality by approximately 25–50%. In addition, there was a differential mortality response in *T. immigrans* depending on caste, and workers that had fed on treated solutions were shown to transfer lethal doses to other individuals in the colony (Barrett et al. 2020). Similar effects of erythritol were previously reported by Zhang et al. (2017) who showed worker mortality in *Solenopsis invicta* Buren (Hymenoptera: Formicidae) after feeding on 0.1–20% erythritol, aspartame, or saccharin solutions. Erythritol was potentially transferred throughout the colony, and its toxicity was observed to be concentration and caste-dependent (Zhang et al. 2017).

The European honey bee, *Apis mellifera* L. (Hymenoptera: Apidae), was a frequent subject of early researchers studying survivorship of insects on carbohydrates, in which erythritol was repeatedly shown to be lethal (Vogel 1931, von Frisch 1934). Choi et al. (2018) revisited the impact of erythritol on *Ap. mellifera* survivorship in the context of off-target insecticidal effects of field treatments. The authors concluded that honey bee mortality may occur from prolonged exposure, but this is unlikely in situations where erythritol is purposed for the control of other insects.

There has been limited testing of artificial sweeteners on orders Blattodea and Hemiptera, with only a few studies and species being represented. Recently, Caponera et al. (2020) conducted preliminary laboratory assessments of erythritol as an insecticide for *Reticulitermes flavipes* (Kollar) (Blattodea: Rhinotermitidae). They observed a concentration-dependent worker mortality response between 0.25 and 1.25 M and no preference between treated or untreated paper media (Caponera et al. 2020). An early nutritional study revealed that *Blattella germanica* (Linnaeus) (Blattodea: Ectobiidae) nymphs could not survive on a casein and erythritol diet, although other sweeteners did not affect the tested insects (Gordon 1959).

Hu et al. (2010) reported the insecticidal effects of mannitol and sorbitol on *Bemisia tabaci* (Gennadius) (Hemiptera: Aleyrodidae). Both sweeteners reduced the survival of adults but failed to affect nymphs, although this disparity was not explored further (Hu et al. 2010). By providing solutions and leaves dipped in the solution, Wentz et al. (2020) demonstrated toxicity of erythritol on adult and nymph *Cacopsylla pyricola* (Förster) (Hemiptera: Psyllidae). Spray treatments using 20% erythritol were effective in reducing nymph numbers in the field by up to ~60%, but only when the erythritol solution was heated during preparation (Wentz et al. 2020).

Impact on Reproduction and Development

In addition to causing mortality, some evidence suggests that certain artificial sweeteners impact the life cycle parameters of insects after sublethal exposure (Table 3). Mannitol-treated media significantly increased the development time of male and female *D. melanogaster* (Fiocca et al. 2019), and exposure of females to 1 M erythritol decreased the overall number of eggs laid (O'Donnell et al. 2017). *Blattella germanica* nymphs were able to develop normally on sorbitol, mannitol, or glycerol mixed with casein, whereas erythritol severely impacted their growth (Gordon 1959).

Table 3. Impact of artificial sweeteners on reproduction and development of insects

Order	Species	Artificial sweeteners	Testing method	Observations	References
Diptera	*Drosophila melanogaster*	Erythritol	Food; 1 M	No oviposition preference	O'Donnell et al. (2017)
			Food; 1 M	Decreasing egg laying with increasing exposure time day 1: ~8 eggs/female-day day 2: ~6 eggs/female-day day 2–7: ~0 eggs/female-day	O'Donnell et al. (2017)
		Mannitol	Media; 0.4–0.8 M	Eclosion day delayed for both sexes (approx.. 12–15 d) vs 0 M control (~11 d)	Fiocca et al. (2019)
	Drosophila suzukii	Erythritol	Media; 0 g/100 ml–2,750 g/100 ml sugar and/or 0 g/100 ml–2,750 g/100 ml erythritol	Decreased egg laying	Goffin et al. (2017)
			Solution; 0.5–1 M sucrose and 0.5–2 M erythritol	Decreased eggs laying at all concentrations of erythritol (<2 to ~6 eggs) vs sucrose control (~22 eggs)	Tang et al. (2017)
			Solution; 0.5–2 M erythritol and/or 0.5 M sucrose plus wounded/unwounded blueberries	Decreased egg laying; ~43% reduction from erythritol treatments	Choi et al. (2018)
			Solution; 0.5–2 M erythritol and/or 0.5 M sucrose	Decreased eggs laid (~7.5/female) vs sucrose only (~15/female)	Choi et al. (2018)
			Solution; 0.5–2 M erythritol and/or 0.5 M sucrose	Greater ovarial eggs in erythritol + sucrose treatment (~8/female) vs erythritol or sucrose alone (~5/female)	Choi et al. (2018)
	Musca domestica	Erythritol	Media; 34.94–69.88 mg/g	No effect on oviposition preference	Burgess and Geden (2019)
		Xylitol	Media; 74.91–149.82 mg/g	Oviposition preference for low versus high concentration	Burgess and Geden (2019)
	Stomoxys calcitrans	Erythritol	Media: 22.10–44.20 mg/g	No effect on oviposition preference	Burgess and Geden (2019)
		Xylitol	Media; 41.58–83.16 mg/g	No effect on oviposition preference	Burgess and Geden (2019)
Hymenoptera	*Pimpla turionellae*	Mannitol	Food; 14%	Complete reduction in fertility and fecundity	Özalp and Emre (2001)
Blattodea	*Blattella germanica*	Erythritol	Food; 0.003 moles/g erythritol and 30% casein	Reduced growth versus casein and glucose	Gordon (1959)
		Sorbitol	Food; 0.001–0.002 moles/g sorbitol and 30% casein	No effect on growth versus casein and glucose	Gordon (1959)
		Mannitol	Food; 0.002 moles/g mannitol and 30% casein	No effect on growth versus casein and glucose	Gordon (1959)
		Glycerol	Food; 0.002 moles/g glycerol and 30% casein	No effect on growth versus casein and glucose	Gordon (1959)

Reduction in *D. suzukii* egg numbers after erythritol exposure has been demonstrated on multiple occasions (Goffin et al. 2017, Tang et al. 2017, Choi et al. 2018). Choi et al. (2018) suggest that erythritol affects the fecundity of *D. suzukii* by decreasing egg production and interfering with ovipositional behavior. Flies on a sucrose-only diet laid twice the number of eggs than flies on an erythritol-only or mixed (erythritol and sucrose) diet. Dissections of flies revealed that an erythritol-only diet led to similar amounts of ovarial eggs as a sucrose diet. However, flies on a mixed diet had ~60% more ovarial eggs than flies on the sucrose diet despite laying fewer eggs, suggesting an impact on the oviposition activity itself (Choi et al. 2018).

Some evidence suggests that sweeteners may act as ovipositional deterrents, but current research is minimal. When offered choices between 74.91 and 149.82 mg/g xylitol treated media, *M. domestica* laid more eggs on the low-concentration media than on the high-concentration media and water-only controls (Burgess and Geden 2019). However, unlike xylitol, erythritol had no effect on egg-laying preference for *M. domestica*, and neither erythritol nor xylitol treated media affected *S. calcitrans* preference (Burgess and Geden 2019). *Drosophila melanogaster* oviposition choice was also shown to be unaffected by THE presence of erythritol in treated and untreated food choices (O'Donnell et al. 2017). Wentz et al. (2020) reported that adult *Cac. pyricola* showed a clear preference for untreated versus erythritol-treated leaves for resting, which may reflect oviposition preference behavior.

Table 4. Impact of artificial sweeteners on phagostimulation and consumption in insects

Order	Species	Artificial sweeteners	Testing method	Observations	References
Diptera	*Drosophila melanogaster*	Erythritol	CAFE[b]; 5% solutions, erythritol and sucrose separate	Greater erythritol consumption in females, ~0.015 vs ~0 µl; no difference in males, ~0.0075 µl both	Baudier et al. (2014)
			CAFE[b]; 5% solutions, erythritol and sucrose paired choice	Greater erythritol consumption in both sexes; ~0.015 vs ~0 µl female, ~0.01 vs 0 µl male	Baudier et al. (2014)
		Sorbitol	Varied	Pairing sorbitol with sweet taste creates preference	Burke and Waddell (2011), Fujita and Tanimura (2011)
			PER[a]; 0.1 M	11–16% response	Gordesky-Gold et al. (2008)
			Agar with dye in microplate; 0.2 M	79–88% response	Gordesky-Gold et al. (2008)
		Glycerol	PER[a]; 0.1 M	25–43% response	Gordesky-Gold et al. (2008)
			Agar with dye in microplate; 0.002 M	69–78% ingestion	Gordesky-Gold et al. (2008)
		Aspartame	PER[a]; 0.002 M	11–16% response	Gordesky-Gold et al. (2008)
			Agar with dye in microplate; 0.002 M	69–78% ingestion	Gordesky-Gold et al. (2008)
		Sucralose	PER[a]; 0.002 M	11–16% response	Gordesky-Gold et al. (2008)
			Agar with dye in microplate; 0.002 M	89–100% ingestion	Gordesky-Gold et al. (2008)
		Saccharin	PER[a]; 0.002 M	11–16% response	Gordesky-Gold et al. (2008)
			Agar with dye in microplate; 0.002 M	69–78% ingestion	Gordesky-Gold et al. (2008)
		Mannitol	CAFE[b]; 5% solutions	Sex-dependent feeding; female consumption greater than male; ~0.4 vs ~0 µl/fly/h	Fiocca et al. (2019)
			CAFE[b]; 5% solutions	No difference in feeding versus sucrose	Fiocca et al. (2019)
	Drosophila suzukii	Glycerol	PER[a]; 4.18 M and 100%	Extensions to 100% glycerol (~4) similar to 50% sucrose (~5)	Díaz-Fleischer et al. (2019)
		Erythritol	Solution; 0.5 M, erythritol, sucrose, and/or water no choice	Greater consumption of erythritol (0.12 µl/fly) than sucrose (0.01 µl/fly) and water (–0.02 µl/fly)	Choi et al. (2017)
			Solution; 0.5 M erythritol, sucrose, and/or water choice	Greater consumption of sucrose (0.50 µl/fly) and water (0.50 µl/fly) than erythritol (~0.25 to ~0.37 µl/fly) at 72 h	Choi et al. (2017)
	Phormia regina	Erythritol	Solution; tarsi contact	Nonstimulating at all concentrations	Hassett et al. (1950)
		Glycerol	Solution; tarsi contact	Nonstimulating at all concentrations	Hassett et al. (1950)
		Mannitol	Solution; tarsi contact	No effect on stimulation threshold when mixed with fructose	Dethier et al. (1956)
			Solution; tarsi contact	Nonstimulating at all concentrations	Hassett et al. (1950)
		Sorbitol	Solution	Nonstimulating to papillae	Dethier and Hanson (1965)
			Solution; tarsi contact	Nonstimulating at all concentrations	Hassett et al. (1950)
	Calliphora erythrocephala	Sorbitol	Solution; tarsi and mouthparts	Stimulation; 0.03 M starvation threshold	Haslinger (1935)
		Mannitol	Solution; tarsi and mouthparts	Stimulation; 0.1 M starvation threshold	Haslinger (1935)
	Ceratitis capitata	Mannitol	Solution; 0.5 M	No response in taste receptors	Gothilf et al. (1971)
	Anastrepha ludens	Glycerol	PER[a]; 4.18 M and 100%	Decreased proboscis extensions (~1 to ~4) vs 50% sucrose (~8)	Díaz-Fleischer et al. (2019)
	Anastrepha obliqua	Glycerol	PER[a]; 4.18 M and 100%	Decreased proboscis extensions (~3) vs 50% sucrose (~14)	Díaz-Fleischer et al. (2019)

Table 4. Continued

Order	Species	Artificial sweeteners	Testing method	Observations	References
	Musca domestica	Erythritol	PER[a]; 20% solutions	Equal proboscis extensions versus sucrose at same concentrations	Burgess and King (2017)
			PER[a]; solid	Similar response (12% female, 34% male) vs sucrose (26% female, 43% male)	King et al. (2019)
			PER[a]; 20% solutions	Decreased response (17% male, 18% female) vs sucrose (77% both sexes)	King et al. (2019)
			Solid	Less consumption versus sucrose	King et al. (2019)
			Solution	Less consumption versus sucrose	King et al. (2019)
			Solid; 100%	Less consumption by adult females versus 100% sucrose; 0.35 mg versus 2.33 mg	Burgess et al. (2018)
		Xylitol	PER[a]; 20% solutions	Equal proboscis extensions versus sucrose at same concentrations	Burgess and King (2017)
			PER[a]; solid	Greater response (50% female, 80% male) vs sucrose (26% female, 43% male)	King et al. (2019)
			PER[a]; 20% solutions	Decreased response (41% male, 37% female) vs sucrose (77% both sexes)	King et al. (2019)
			Solid	Similar consumption by females, decreased consumption by males	King et al. (2019)
			Solution	Less consumption versus sucrose	King et al. (2019)
			Solid; 100%	Comparable consumption by adult females versus 100% sucrose	Burgess et al. (2019)
		Acesulfame potassium	PER[a]; solid	Decreased response (2% female, 11% male) vs sucrose (26% female, 43% male)	King et al. (2019)
			PER[a]; 20% solutions	Decreased response (7% male, 0% female) vs sucrose (77% both sexes)	King et al. (2019)
		Sucralose	PER[a]; solid	Decreased response (7% female, 14% male) vs sucrose (24–26% female, 43% male)	King et al. (2019)
			PER[a]; 20% solutions	Decreased response (28% male, 25% female) vs sucrose (86% female, 88% male)	King et al. (2019)
		Sodium cyclamate	PER[a]; solid	Similar response (2% female, 5% male) vs sucrose (26% female, 43% male)	King et al. (2019)
			PER[a]; 20% solutions	Decreased response (7% male, 0% female) vs sucrose (77% both sexes)	King et al. (2019)
Hymenoptera	*Atta capiguara*	Saccharin	Treated cellulose rectangles	Not attractive to workers	Boaretto et al. (2003)
		Sodium cyclamate	Treated cellulose rectangles	Not attractive to workers	Boaretto et al. (2003)
	Solenopsis invicta	Erythritol	Solution; 1%	No more attractive to workers versus water	Vander Meer et al. (1995)
		Sorbitol	Solution; 1%	No more attractive to workers versus water	Vander Meer et al. (1995)
		Mannitol	Solution; 1%	No more attractive to workers versus water	Vander Meer et al. (1995)
		Xylitol	Solution; 1%	No more attractive to workers versus water	Vander Meer et al. (1995)
	Lasius niger	Erythritol	Solution; mouthparts	No stimulation of mouthparts	Schmidt (1938)
		Mannitol	Solution; mouthparts	No stimulation of mouthparts	Schmidt (1938)
		Sorbitol	Solution; mouthparts	Reduced stimulation of mouthparts; 0.25 M minimum threshold	Schmidt (1938)
	Myrmica rubra	Erythritol	Solution; mouthparts	No stimulation of mouthparts	Schmidt (1938)
		Mannitol	Solution; mouthparts	Reduced stimulation of mouthparts; 1.0 M minimum threshold	Schmidt (1938)
		Sorbitol	Solution; mouthparts	Reduced stimulation of mouthparts; 0.0625 M minimum threshold	Schmidt (1938)
	Manica rubida	Erythritol	Solution; mouthparts	No stimulation	Schmidt (1938)
		Mannitol	Solution; mouthparts	No stimulation	Schmidt (1938)
		Sorbitol	Solution; mouthparts	No stimulation	Schmidt (1938)

Table 4. Continued

Order	Species	Artificial sweeteners	Testing method	Observations	References
	Apis mellifera	Erythritol	Solution; mouthparts	No stimulation	Vogel (1931)
		Mannitol	Solution; mouthparts	No stimulation	von Frisch (1934)
		Sorbitol	Solution; mouthparts	No stimulation	von Frisch (1934)
Lepidoptera	*Vanessa atalanta*	Erythritol	Solution; tarsi	No stimulation of mouthparts	Weis (1930)
		Mannitol	Solution; tarsi	Reduced stimulation of mouthparts; >1.0 M median threshold	Weis (1930)
Coleoptera	*Tribolium castaneum*	Mannitol	Two-electrode voltage clamp, *Xenopus* oocyte expressing *TcGr20*	Response in presence of mannitol	Takada et al. (2017)
			TcGr20 silenced with RNAi	Decreased consumption of mannitol treated gypsum block	Takada et al. (2017)
		Sorbitol	Two-electrode voltage clamp, *Xenopus* oocyte expressing *TcGr20*	Response in presence of sorbitol	Takada et al. (2017)

[a]Proboscis extension reflex.
[b]Capillary feeder.

Phagostimulation and Consumption

The palatability of artificial sweeteners holds important implications for their potential as insecticides, especially for baits. Deterrent properties may reduce insecticidal efficacy by lowering the frequency and duration of exposure. Unlike the universally sweet taste of sugars (monosaccharides and disaccharides), artificial sweeteners could vary in magnitude and nature of their reception by insects (Table 4). In many cases, insects have a reduced sensory response to artificial sweeteners, although this could depend on the sweetener type, sweetener concentration, species, and testing method.

Erythritol, glycerol, mannitol, and sorbitol failed to elicit significant proboscis extensions from *P. regina* after tarsal contact, and papillae electrical activity after contact with sorbitol show minimal stimulation of the sugar receptor (Hassett et al. 1950, Dethier and Hanson 1965). Neither *An. ludens* nor *An. obliqua* had comparable proboscis extension reflex (PER) responses toward 4.18 M or 100% glycerol compared with 50% sucrose (Díaz-Fleischer et al. 2019). Taste receptors of *Ceratitis capitata* (Wiedemann) (Diptera: Tephritidae) did not show any response to 0.5 M mannitol (Gothilf et al. 1971). Erythritol and mannitol caused no stimulation and reduced stimulation of *Vanessa atalanta* (Linnaeus) (Lepidoptera: Nymphalidae) mouthparts, respectively (Weis 1930).

Two studies were conducted to assess sweeteners as phagostimulants and attractants for ant baits, but both were unpromising. Saccharin- and sodium cyclamate-treated cellulose were not attractive to *Atta capiguara* (Goncalves) (Hymenoptera: Formicidae) based on lack of carrying by workers (Boaretto et al. 2003). One-percent erythritol, sorbitol, mannitol, and xylitol droplets were no more attractive to *So. invicta* than water, and much less attractive than sugars such as glucose or fructose (Vander Meer et al. 1995). In one of the earliest sweetener studies, erythritol, mannitol, and sorbitol were shown to cause reduced or no stimulation to *Lasius niger* (L.), *Myrmica rubra* (L.), and *Manica rubida* (Latreille) (Hymenoptera: Formicidae) (Schmidt 1938).

Some exceptions include *Drosophila* spp., which appear to be generally receptive to materials perceived as sweet by humans. Aspartame, sucralose, saccharin, glycerol, and sorbitol elicited some proboscis extensions from *D. melanogaster* through tarsal contact and were preferentially ingested when incorporated in agar (Gordesky-Gold et al. 2008). In *D. suzukii,* a high concentration of glycerol (100%) elicited a similar PER response compared to 50% sucrose when presented in a capillary tube (Díaz-Fleischer et al. 2019). The red flour beetle *Tribolium castaneum* (Herbst) (Coleoptera: Tenebrionidae) was shown to be chemoreceptive of mannitol and sorbitol, and readily consumed mannitol-treated gypsum blocks (Takada et al. 2017).

The gustatory response of *M. domestica* may depend on the physical state of the sweetener and other unknown factors. Twenty percent solutions of erythritol, xylitol, and sucrose were equally stimulatory based on proboscis extensions (Burgess and King 2017). In dry form, xylitol elicited a twofold increase in PER response compared with sucrose, but no significant difference was observed with dry erythritol (King et al. 2019). However, a discrepancy exists between the two studies on the response toward erythritol solution. Unlike the equal response toward erythritol and sucrose reported by Burgess and King (2017), King et al. (2019) found an approximately 77% decrease in PER response toward erythritol compared with sucrose when provided in solutions. Other sweeteners such as acesulfame potassium, sucralose, and sodium cyclamate failed to generate substantial levels of PER response (King et al. 2019).

Despite the marginal response of many insects toward sweeteners, there is no evidence of strong feeding deterrence in any sweetener. Several studies have confirmed consumption of sweeteners by insects through no-choice assays, dyes, or direct measurement, indicating that these compounds are accepted under varying experimental conditions (Baudier et al. 2014, Choi et al. 2017, Fiocca et al. 2019, Caponera et al. 2020). Sweeteners that do not elicit much feeding response from insects may simply be perceived as inert or neutral compounds. In such situations, pairing with a stimulating sugar may cause preferential consumption (Burke and Waddell 2011, Fujita and Tanimura 2011). The success of this method can be seen in assays that showed increased mortality with the addition of sucrose in erythritol treatments compared with the sweetener alone (Choi et al. 2017, 2018, Tang et al. 2017).

Other Impacts

In some cases, the ingestion of artificial sweeteners causes motor, behavioral, or other physical changes in the insect (Table 5). Climbing ability of *D. melanogaster* was reduced after consuming erythritol, with many postfed adults unable to climb up the side of a vial under

Table 5. Other impacts of artificial sweeteners on insects

Order	Species	Artificial sweeteners	Testing method	Observations	References
Diptera	*Drosophila melanogaster*	Erythritol	Food; 0.0952 g/ml Truvia (99% erythritol, 1% rubiana)	Climbing behavior impacted by day 7	Baudier et al. (2014)
		Mannitol	Media; 0.25–2 M	Accumulation of 'white matter' in crop	Fiocca et al. (2019)
	Drosophila suzukii	Erythritol	Solution; 0.5 M	Lower sugar levels in erythritol-fed (~15 µg in males, ~20 µg in females) vs sucrose-fed (~50 µg in males, ~80 µg in females) at 24 h (and 48 h)	Choi et al. (2017)
			Solution; 0.5 M	Lower glycogen levels in erythritol-fed (~50 µg in males, ~150 µg in females) vs sucrose-fed (~200 µg in males, ~350 µg in females) at 24 h (and 48 h)	Choi et al. (2017)
			Solution; 0.5 M erythritol and/or 0.5M sucrose	Elevated sweetener levels in hemolymph (~60 µg) and absence in frass	Tang et al. (2017)
			Solution	Increased excretion	Tang et al. (2017)
			Unspecified	Mummification	Sampson et al. (2016)
		Glycerol	Solution; 4.18 M glycerol and 50% sucrose	Increased regurgitation (~10 droplets) vs sucrose only (~0 droplets)	Díaz-Fleischer et al. (2019)
	Anastrepha ludens	Erythritol	Solution; 2.78 M erythritol and 50% sucrose	Increased regurgitation (~25 droplets) vs sucrose only (~5 droplets)	Díaz-Fleischer et al. (2019)
		Glycerol	Solution; 1.67–4.18 M glycerol and 50% sucrose	Increased regurgitation (~30 – ~70 droplets) vs sucrose only (~20 droplets)	Díaz-Fleischer et al. (2019)
	Anastrepha obliqua	Glycerol	Solution; 4.18 M glycerol and 50% sucrose	Increased regurgitation (~40 droplets) vs sucrose only (~20 droplets)	Díaz-Fleischer et al. (2019)
	Bactrocera dorsalis	Erythritol	Solution; 0.008 M	Decreased climbing ability (~3 climbing flies) vs sucrose (~7.5 climbing flies) at 24 h	Zheng et al. (2016)
			Solution; 0.008 M	Increased inactivity (~1 time in 10 min) vs sucrose (~0 times in 10 min)	Zheng et al. (2016)
		Aspartame	Solution; 0.003 M	Decreased climbing ability (~3.5 climbing flies) vs sucrose (~7.5 climbing flies) at 24 h	Zheng et al. (2016)
		Saccharin	Solution; 0.005 M	Decreased climbing ability (~4 climbing flies) vs sucrose (~7.5 climbing flies) at 24 h	Zheng et al. (2016)
			Solution; 0.005 M	Decreased walking (~3.5 times in 10 min) and grooming (~2.5 times in 10 min) vs sucrose (~5.5 and ~3.5 times in 10 min)	Zheng et al. (2016)

a standard amount of time (Baudier et al. 2014). Similarly, climbing behavior and frequency of inactivity, walking, or grooming of *B. dorsalis* were impacted after consuming erythritol, aspartame, or saccharin (Zheng et al. 2016).

Sweeteners have also been observed to cause irregularities of the alimentary system. A buildup of 'white matter' was found in the alimentary tract of *D. melanogaster* after being killed by mannitol (Fiocca et al. 2019). Erythritol was observed to increase the defecation of *D. suzukii* (Tang et al. 2017). *Drosophila suzukii*, *An. ludens*, and *An. obliqua* experienced significantly increased regurgitation frequency after consuming glycerol (Díaz-Fleischer et al. 2019). These impacts on regurgitation and excretion suggest that sweeteners cause disruption of the alimentary system. Digestion of sweeteners has seldom been studied, but current data show that *D. suzukii* is incapable of digesting erythritol. Analysis of glycogen and sugar levels in the hemolymph of flies that consumed erythritol revealed lower levels than those that consumed sucrose (Choi et al. 2017). Higher levels of erythritol were also detected in the hemolymph of postfed flies compared to feces, indicating that the compound accumulates for extended periods without being metabolized (Tang et al. 2017).

Proposed Mechanisms and Future Research

The mechanism(s) on how artificial sweeteners exert mortality on insects remains largely unknown. Early researchers assumed that sweeteners induced mortality because of lower caloric values that led to starvation, inability of insects to digest certain compounds, or its unpalatability (Vogel 1931, Fraenkel 1940, Hassett 1948, Dethier 1968). Later evidence provides support that erythritol is indigestible in *D. suzukii* (Choi et al. 2017, Tang et al. 2017), and that starvation was the likely cause of mortality in *M. domestica* (Fisher et al. 2017). However, starvation alone does not explain some of the digestive irregularities observed in *D. melanogaster*, *D. suzukii*, *An. obliqua*, and *An. ludens* (Tang et al. 2017, Díaz-Fleischer et al. 2019, Fiocca et al. 2019), and other data demonstrate that the timing of mortality in sweetener treatment assays may be different from that of the starvation treatment assays (O'Donnell et al. 2016, Zheng et al. 2016, Burgess and King 2017, Goffin et al. 2017). The issue is further complicated in studies where the administration of combined treatments (i.e., sweetener and sucrose in the same resource) or assays with alternative food sources do not completely rescue and may even exacerbate the toxic effect (Burgess and King 2017; Choi et al. 2017, 2018; Tang et al. 2017; Gilkey et al. 2018).

Alternatively, the insects may experience dehydration as a consequence of sweetener ingestion. Provision of a water source in treatment assays has been shown to reduce the potency of erythritol for *Ae. aegypti*, *T. immigrans*, and *F. glacialis* (Gilkey et al. 2018, Barrett et al. 2020). Choi et al. (2017) and Tang et al. (2017) suggest that the indigestibility and buildup of erythritol causes an osmotic imbalance between the alimentary tract and hemocoel. In response to restore homeostasis, the insect may attempt to expel the sweetener through regurgitation or defecation, an effect observed in *D. suzukii*, *An. obliqua*, and *An. ludens* after glycerol consumption (Tang et al. 2017, Díaz-Fleischer et al. 2019). Continuous water loss in this manner may be a contributing factor to mortality, which is potentially also the cause of observations by Sampson et al. (2016) of the 'shriveled' remains of erythritol-killed flies.

Given the high variability of impacts across different insects and sweeteners, mechanisms may also be species-dependent. Future projects designed to rule out confounding variables of these two potential mechanisms for each study organism will more accurately assess the effects of sweeteners. Furthermore, because of the high variation in responses already seen, it is unlikely that any specific sweetener (or a group of sweeteners) has a broad effect on most groups of insects. Methods will need to be designed for family, genus, or even species-specific systems and their implications limited as such. It is worth mentioning, however, that highly specific treatment systems also will be relatively free of off-target effects and have greater value as safe alternatives to conventional insecticides.

Nonetheless, current research does not provide optimal support for sweeteners as viable alternatives to conventional chemical treatments. In many laboratory assays, sweeteners have been tested in concentrations that were much higher than active ingredients in most conventional insecticide sprays or baits (upward of 20% sweetener vs <1% conventional). In fact, frequently tested concentrations of polyols (up to and including 2 M) are within an order of magnitude of their maximum solubilities in water (~4 M) (Yalkowsky et al. 2010). This severely limits the potential to control any insecticide-resistant population with sweeteners due to solubility difficulties when increasing beyond these concentrations to overwhelm resistance. The sweeteners also act slower than conventional insecticides, often taking several days of exposure to reach high levels of mortality. Other untested factors such as limited persistence or longevity under field conditions may also hinder already marginal performance of the compounds.

Because of these issues, the utility of artificial sweeteners as insecticide treatments will need to be carefully considered. Only erythritol treatments for *D. suzukii* have been evaluated in the field; other pest species and sweeteners remain untested. One aspect that can be kept in mind for future studies is the apparent lack of contact toxicity of the sweeteners. Delivery systems should be designed to involve some form of oral administration to ensure optimal performance. To address the comparatively low mortality rates, artificial sweetener treatments may be combined with other strategies to act as a supplement or synergist instead of the sole toxicant. The potential synergistic effect of sweeteners, when combined with other insecticides or formulations, has not been explored and warrants further investigations.

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