demonstrate antiarrhythmic properties. Most studies demonstrating antiarrhythmic properties of PGs have used relatively high concentrations. However, endogenous myocardial PG production which would be expected to be at a low level may actually contribute to dysrhythmogenesis under various situations such as hypoxia or ischemia.

The mechanism for the dysrhythmogenic actions of PGs as well as the reason for the resistance observed with guinea-pig and rabbit hearts is difficult to suggest at this time. The rat heart is resistant to dysrhythmias[13] and therefore the increased sensitivity observed in this investigation is surprising. It would be unwise to extrapolate these results to the human situation although the possibility that locally synthesized PGs may be contributing arrhythmogenic factors in ischemic heart disease should be considered. Recent reports have in fact strenghtened such a possibility. Thus Moschos et al.[14] reported an antiarrhythmic property of aspirin, a PG synthesis inhibitor after coronary artery occlusion in the dog which would perhaps suggest an involvement of endogenous PGs in the generation of cardiac arrhythmias. Furthermore, Dix et al.[12] demonstrated an arrhythmogenic and cardio-deleterious influence of prostacyclin, the main cardiac PG after infusion into cats subjected to coronary artery ligation.

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Insect antifeedant properties of withanolides and related steroids from Solanaceae

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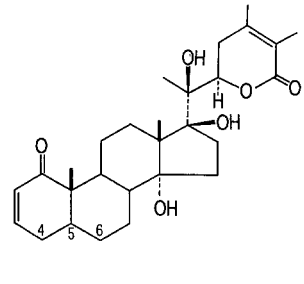
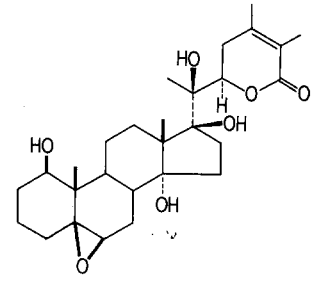
Summary. Physalis peruviana shrubs were not attacked by larvae of *Spodoptera littoralis.* It was demonstrated that withanolide E, a steroid isolated from *P. peruviana,* as well as several related steroids, have insect antifeedant properties.

For our studies on the steroidal constituents of solanaceous plants[1], we have maintained for several years small field plots of various *Physalis* and *Nicandra* spp. During an infestation by larvae of the Egyptian cotton leafworm, *Spodoptera littoralis* (Boisd.), in the summer of 1978, it was noted that *Physalis peruviana* L. (cape gooseberry) shrubs were not attacked, whereas other *Physalis* and *Nicandra* spp. suffered heavy damage. Laboratory experiments conducted at 27 °C were therefore initiated with *S. littoralis* larvae obtained from a culture on alfalfa. At first, 80–100 and 170–190 mg larvae kept singly in large petri dishes were allowed to feed on leaves of either *P. peruviana* or *P. ixocarpa* Brot. (tomatillo) and on alfalfa. The results (table 1) indicated that P. peruviana deterred the larvae from feeding to such an extent that their weight loss was nearly the same as that of starved larvae.

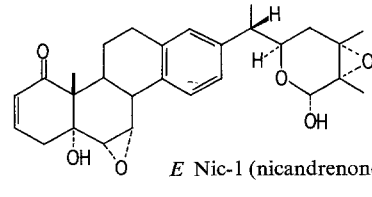
In subsequent experiments (table 2) an attempt was made to grow larvae of 3 weight ranges on leaves of *P. peruviana* in mass cultures in large enamel basins. No feeding and no mortality occurred after 1 day; heavy mortality began after 3 days and was practically complete after 7 days. In order to detect the antifeedant[2] principle(s), methanolic *P. peruviana* leaf extracts, and aqueous-methanolic (2:1) solutions obtained from them after removal of pigments, were prepared, and the latter diluted stepwise with the same solvent mixture; 5% sucrose was dissolved in each test concentration. To assess antifeeding activity, the 'Styropor method'[3] was employed: lamellae (6×4 cm) of 'Styropor' (foamed polystyrene) of density 0.016 (P_{16}) were dipped into the solutions, left to dry for 24 h, then weighed individually. They were then offered singly, in large petri dishes, to *S. littoralis* larvae weighing 170–190 mg, together with



A 5β,6β-epoxy (withanolide E)[4,5]
B 4β-hydroxy-5β,6β-epoxy (4β-hydroxywithanolide E)[5]
C 5α,6β-dihydroxy (withanolide S)[4]



D 5β,6β-epoxy-1β,14α,17β,20-tetrahydroxywith-24-enolide[4]



E Nic-1 (nicandrenone)[6]

water absorbed in cotton wads in small plastic covers. The weight of 'Styropor' consumed per larva and the weight of fecal pellets voided were recorded after 24 and 48 h and served as criteria of antifeedant activity. For the sake of brevity, only the 48 h 'Styropor' consumption will be reported in this communication.

The evident antifeedant activity of the pigment-free extracts (table 3) encouraged us to investigate the feeding inhibition of withanolide E (compound A)[4,5] and 4β-hydroxywithanolide E (compound B)[5], the main steroidal components of *P. peruviana,* as well as of several related steroids isolated from other solanaceous plants.

Assays were done with the 'Styropor' method; the compounds were dissolved in ethanol:water (7:3) and 5% sucrose was again added to each test solution. According to the results (table 4), the most potent antifeedant of this group is withanolide E (A), followed closely by compound D, obtained by reduction of A with sodium borohydride. Comparison of the results obtained with compounds A–D leads to the conclusion that the substitution pattern of carbons 4, 5 and 6 is critical for the antifeeding activity. Addition of a β-oriented hydroxy-group at position 4 (compound B) reduced the activity by a factor of 10, whereas hydrolysis of the 5,6-epoxide to the 5,6-diol system present in withanolide S (compound C) led to nearly total inactivation.

Nic-1[6] (nicandrenone, E), which was isolated[7] from *Nicandra physaloides,* a plant which does not encourage feeding or support growth when offered to *Manduca sexta* (L.) larvae[8], was the only compound of this series ever tested before. It was found to be a feeding deterrent for larvae of *M. sexta*[7] and (according to a personal communication of C.A. Elliger to E.G.) *Pectinophora gossypiella* (Saund.), but not for *Heliothis virescens* (F.) or *H. zea* (Boddie). When tested on *S. littoralis* (table 4), it was found to be inactive at a concentration of 0.01% and had only poor activity at 0.1%. The compounds withaferin A[9], withanolide D[10], 4β,7β,20-trihydroxy-1-oxowitha-2,5,24-trienolide[11], and physalin B[12], all of which are structurally related to compound A, were inactive at the 0.01% screening concentration.

Table 1. Weight gain of *Spodoptera littoralis* larvae feeding on leaves of *Physalis peruviana* and on alfalfa, compared with that of starved larvae

Plant	Average initial weight (mg)	Average weight after 24 h	Δw (mg)	Average weight after 48 h	Δw (mg)
80–100 mg larvae					
Starved larvae	91	80	−11	62	−29*
P. peruviana	88	82	−6	68	−20
Alfalfa	90	189	+99	234	+144
170–190 mg larvae					
Starved larvae	177	152	−25	117	−60*
P. peruviana	178	164	−14	142	−36*
Alfalfa	180	451	+271	854	+674

* 10% mortality. Experiments were conducted in 15 cm diameter petri dishes, with 80 1-larva-per-dish replicates. Under similar conditions, *P. ixocarpa* leaves were eaten strongly by 170–190 mg larvae. After 48 h, Δw was 325 mg.

Table 2. The mortality of *Spodoptera littoralis* larvae of 3 weight ranges kept in mass cultures on leaves of *Physalis peruviana*

Range of larval weight (mg)	Mortality (%) after days 3	4	5	7
90–140	79	87.5	95	99.5
180–200	94	97	98	100
350–400	86	96	98.5	99.5

Experiments were carried out in large enamel basins containing a layer of sawdust, with 200 larvae per basin.

Table 3. Feeding of 170–190 mg *Spodoptera littoralis* larvae on 'Styropor' lamellae treated with different concentrations of aqueous-methanolic (2:1) solutions (containing 5% sucrose) of *Physalis peruviana* leaf extracts

	Concentration of extract (%) 1.0	0.5	0.25	0.1	0.05
	48 h 'Styropor' consumption (mg/larva)				
P. peruviana extract + 5% sucrose	1.8	1.4	1.3	1.9	3.6
5% sucrose (control)	26.9	21.6	21.1	23.1	24.6

Experiments were carried out in 40 1-larva-per-dish replicates.

Table 4. Antifeedant properties of several withanolides against *Spodoptera littoralis* larvae

Compound	Concentration of compound in dipping liquid (%) 0.1	0.01	0.005	0.0025	0.001	0.0005
	48-h 'Styropor' consumption (mg/larva)					
A + 5% sucrose	0 (27.5)*	0.8 (29.3)	0.9 (22.1)	2.2 (20.6)	7.5 (23.6)	27.9 (32.6)
B + 5% sucrose	0.5 (30.0)	8.3 (30.4)	20.3 (36.9)			
C + 5% sucrose	15.7 (26.7)	16.0 (28.7)				
D + 5% sucrose	0.4 (26.7)	2.2 (24.6)	3.5 (25.6)	9.8 (21.6)	12.8 (21.6)	
E + 5% sucrose	11.8 (21.2)	28.6 (34.2)				

*Numbers in parentheses denote feeding on lamellae treated with 5% sucrose only (controls).
Experiments were carried out in 15-cm petri dishes, with 40–80 1-larva-per-dish replicates; 170–190 mg larvae were employed. The compounds were fed as dry residues obtained from the corresponding methanolic-aqueous (7:3) solutions, containing also 5% sucrose, on 'Styropor' lamellae.

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