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Abortifacient effect of steroids from *Ananas comosus* and their analogues on mice

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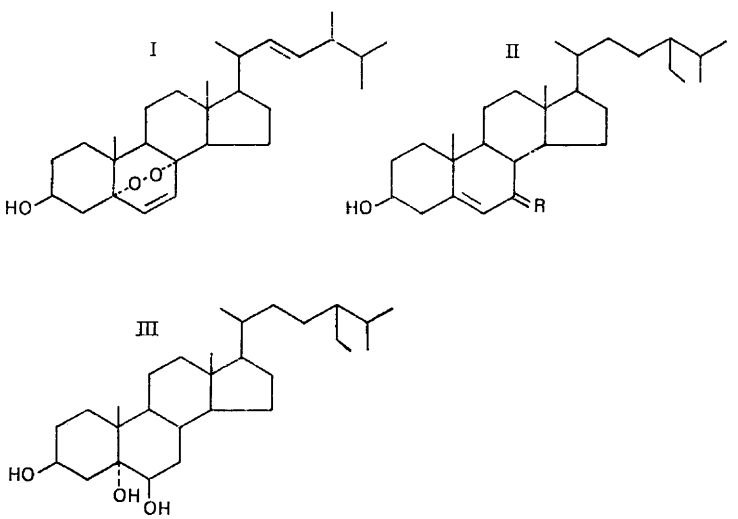
The juices of the unripe fruits and leaves of *Ananas comosus*, the common pineapple plant, have long been claimed to possess abortifacient properties in Indian medicine (Manjunath, 1948). More recently, an antifertility effect of the petroleum ether extract of the rhizome (Bhaduri, Ghosh, Bose, Moza & Basu, 1968) and of the green fruits (Garg, Saksena, Chaudhury, 1970; Näf-Müller & Willhalm, 1971) has been reported.

In a preliminary investigation, we observed an antifertility effect of an extract of the white parts of the leaves of the plant. We therefore undertook a follow-up study of the pure constituents, ergosterol peroxide (Compound I), β-sitosterol (Compound IIa) and 5-stigmastene-3β,7α-diol (Compound IIb) isolated (Pakrashi, Achari & Majumdar, 1975) from the petroleum ether and benzene extracts of the whole leaves, and their synthetic analogues, 5-stigmastene-3β,7β-diol (Compound IIc), 7-oxo-5-stigmasten-3β-ol (Compound IId) and 5α-stigmastane-3β,5,6β-triol (Compound III) (see Text-fig. 1).



Text-fig. 1. The structures of the steroids from *Ananas comosus* and their analogues (see text). For Compounds IIa, R=H_2; IIb, R=H, OH(α); IIc, R=H, OH(β); IId, R=O.

Colony-bred adult mice of proven fertility and weighing 22–25 g were fed a balanced diet and caged in the ratio of one male to two females in a controlled-temperature (24–25°C) room. The day of finding spermatozoa in the vaginal smear was designated Day 1 of pregnancy. The test compounds (IIb and IIc as dibenzoate and IId and III as 3-benzoate) in olive oil were administered orally in a single dose of 30 mg/kg body weight on Day 1 or Days 6–7 of pregnancy. Control animals were treated with olive oil. A preliminary trial with different doses of Compound IIb had shown that 30 mg/kg body weight was the minimum effective dose for this compound, and this dose level was therefore used for the other compounds of which only small amounts were available. Laparotomy

was performed under ether anaesthesia for all animals between Days 6–7 and Days 8–16 of pregnancy, i.e. before and after implantation when changes of vagina and mammary gland indicated that pregnancy had been disrupted.

The results in Table 1 showed that all the compounds exerted some degree of abortifacient activity when administered on Day 1, but β-sitosterol (Compound IIa) and the 7-oxo derivative (Compound IId) were devoid of activity when given on Days 6–7.

Table 1. Abortifacient effect of steroids from *Ananas comosus* and their analogues on mice when administered orally before and after implantation at a dose of 30 mg/kg body weight

Treatment	Preimplantation		Postimplantation	
	No. of mice used	No. with degenerating or no i.s. (%)	No. of mice used	No. with no i.s. (%)
None (controls)	10	0 (0)	10	0 (0)
Ergosterol peroxide (I)	10	10 (100)	8	8 (100)*
β-Sitosterol (IIa)	15	14 (93·3)	11	0 (0)
5-Stigmastene-3β,7α-diol (IIb)	10	9 (90)	13	12 (92)
5-Stigmastene-3β-7β-diol (IIc) dibenzoate	15	14 (93·3)	12	9 (75)
7-Oxo-5-stigmasten-3β-ol (IId) benzoate	15	10 (66·6)	10	0 (0)
5α-Stigmastane-3β,5,6β-triol (III) 3-monobenzoate	25	22 (88)	20	19 (95)

i.s.=implantation site.
* Abortion occurred at a very late stage of pregnancy.

Ergosterol peroxide (Compound I) showed the maximum abortifacient effect at both stages of pregnancy, but the action was delayed (starting from Days 13–16), especially when given after implantation. Loss of weight, lethargy and anaemia of the treated animals were observed. Delayed action (from Days 10–16) and similar side effects were also observed with β-sitosterol (Compound IIa). The most consistent results before and after implantation and without apparent side effects were shown by Compound IIb and Compound III followed by Compound IIc. Laparotomy revealed either the absence of or disruption of implantation sites between Days 6–7 when these compounds were administered on Day 1, and on Days 9–11, 8–10 and 10–11, respectively, when they were given on Days 6–7.

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