

### Synthetic Oestrogenic Agents without the Phenanthrene Nucleus

THE preparation and physiological properties of synthetic oestrogenic agents were first described in these columns and elsewhere<sup>1,2,3</sup>. The active compounds described in these publications were derivatives of phenanthrene or 1:2:5:6-dibenzanthracene, and it was noted that at the time of writing no active substances had been discovered which did not contain the phenanthrene nucleus.

Subsequent work has been directed towards an attempt to discover which portions of the molecule were responsible for the oestrogenic activity. It has been found that the phenanthrene condensed-ring structure is not necessary for this activity, and the accompanying table gives a number of these substances together with a measure of their activity.

Substance	Dose in mgm.	Percentage positive
1:2-Dihydroxy-1:2-di- $\alpha$ -naphthyl-acenaphthene	100	100*
" " "	10	100
1:1-Di- $\alpha$ -naphthyl acenaphthene	100	100
$\alpha$ -Naphthyl benzoïn	100	40
Diphenyl- $\alpha$ -naphthyl glycol	100	60
Diphenyl- $\alpha$ -naphthyl carbinol	100	100
4-4-Dihydroxydiphenyl methane	100	100
Di-(p-Hydroxyphenyl) dimethyl methane	100	100
Di-(p-Hydroxyphenyl) methyl ethyl methane	100	100
Di-(p-Hydroxyphenyl) methyl propyl methane	100	100
Di-(4-Hydroxy-3-methyl phenyl) di methyl methane	100	100
Di-(4-Hydroxy-3-methyl phenyl)-1:1-cyclohexane	100	100
2:4-Dihydroxy-triphenyl methane carboxylic acid lactone	100	100
4:4'-Dihydroxy benzophenone	100	60
4:4'-Dihydroxy diphenyl	100	100

\* Rats remained in œstrus 40 days.

The technique of testing the activity of these substances is that described in previous communications<sup>4</sup>. In every test, five ovariectomised rats were used. The weighed dose was dissolved or suspended in 3 c.c. of sesame oil and given in six separate injections of 0.5 c.c., morning and evening on three successive days. Vaginal smears were examined twice daily until the œstrus change disappeared. Only full cornification and complete absence of leucocytes was regarded as a positive œstrus response.

Other derivatives of diphenyl and diphenyl methane have been tested, but up to the present only those containing two hydroxyl groups in the para positions have been found to be active. It is premature to discuss the significance of these experiments, and further work on these lines is proceeding.

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E. C. DODDS.  
WILFRID LAWSON.

Courtauld Institute of Biochemistry,  
Middlesex Hospital,  
London, W.1.

<sup>1</sup> Cook, Dodds and Hewett, *NATURE*, **131**, 56 (1933).

<sup>2</sup> Cook and Dodds, *NATURE*, **131**, 205 (1933).

<sup>3</sup> Cook, Dodds, Hewett and Lawson, *Proc. Roy. Soc., B*, **114**, 272 (1934).

<sup>4</sup> Allan, Dickens and Dodds, *J. Physiol.*, **68**, 348 (1930).

### Echinenone as a Provitamin A

THE pigment echinenone was recently isolated by one of us from the sexual glands of the sea urchin *Echinus esculentus*<sup>1</sup>. The glands from 400 urchins were first extracted with acetone. The extracted pigments were then separated into hydrocarbon and xanthophyll fractions by partition between petroleum ether and 90 per cent methyl alcohol. The echinenone was contained in the former solvent both before and after saponification, and was separated from  $\beta$ -carotene by the chromatogram method. The new pigment was absorbed as a dark violet layer in the upper part of the column of slaked lime. After extraction, 4 mgm. of dark violet needles with a metallic lustre (m.p. 192°-193°) were obtained. In carbon disulphide solution a broad band with three ill-defined maxima at 520, 488 and 450 m $\mu$  was shown; in alcohol these bands were even less pronounced. From the spectroscopic properties and elementary analysis (C<sub>40</sub>H<sub>58</sub>O) ( $\pm$  H<sub>2</sub>) it would appear probable that echinenone is a mono-ketone occupying an intermediate position between  $\beta$ -carotene and semi- $\beta$ -carotene.

A specimen of the pigment, after a preliminary separation from carotene by adsorption on aluminium oxide, was purified by two further adsorptions on the same adsorbent, two adsorptions on slaked lime, two recrystallisations from benzene and ethyl alcohol mixture, one from petrol ether and alcohol, and finally once more from benzene and alcohol. This specimen was sent to Cambridge, and was examined for biological activity as a provitamin A. Rapid restoration in growth was observed in rats restricted to a diet deficient in vitamin A when daily doses of 5  $\gamma$  or 10  $\gamma$  of the pigment were given; a temporary slow resumption of growth was observed with 2.5  $\gamma$ . The administration of about 4 mgm. of the pigment, spread over several days, to a rat already cured by small doses, resulted in the appearance in the liver of an amount of vitamin A equivalent to 400 blue units (roughly 0.1 mgm. of the 'pure' vitamin). Only traces (30 y.u.) of yellow pigment were present. The band at 630 m $\mu$  characteristic of the blue colour given by vitamin A with antimony trichloride was clearly observed.

From this evidence it is clear that echinenone may function as a provitamin A. The degree of activity is apparently of the same order as that of the carotene isomers, although the tests carried out were insufficiently extensive to decide whether the activity approximated more closely to that of  $\beta$ -carotene, or, as might be expected from the presence of only one  $\beta$ -ionone ring system, to that of the presumably somewhat less active  $\alpha$ -form. It may be worthy of note that echinenone, apart from  $\beta$ -carotene which is found in both plants and animals, is the first animal carotenoid found to possess vitamin A activity.

E. LEDERER.

Institut de Biologie Physico-Chimique,  
Paris.

T. MOORE.

Nutritional Laboratory, Cambridge.

<sup>1</sup> Lederer, *C.R. Acad. Sci.*, **201**, 300 (1935).

### Production of Attached X-Chromosomes in *Drosophila melanogaster* Males

KAUFMANN<sup>1</sup> and Neuhaus<sup>2,3</sup> indicated the likelihood of crossing-over between X- and Y-chromosomes in females of *Drosophila melanogaster*. They explained the frequent attachment of the long arm of the Y-chromosome to the proximal end of the X-chromo-