STUDIES ON THE GENERAL METABOLISM AS AFFECTED BY THE HORMONE HEXOESTROL

A Thesis

Presented for

the Degree of Ph. D.

By

ABO BAKR EL SEDDIK OTHMAN

B. Sc., M. Sc.

Department of Biochemistry

Faculty of Science

Ain Shams University

1968

ACKNOWLEDGMENT

The author wishes to express his deep gratitude to Professor Dr. S. A. Eisa, Head of Biochemistry Department, Faculty of Science, Ain Shams University, for his general supervision and guidance, and for his constructive criticism and suggestions in preparing the manuscript.

The author is also greatly indebted to Dr. F. E. A. Zaki, Assistant Professor of Animal Physiology, Faculty of Science, Ain Shams University, for suggesting the problem, his direct supervision and valuable advice.

Thanks are also due to the members of the Zoology Department, Faculty of Science, Ain Shams University, for various facilities offered.

THIS THESIS HAS NOT BEEN
SUBMITTED FOR A DEGREE AT THIS
OR ANY OTHER UNIVERSITY.

C O N T E N T S

	Page
Aim of the work...	1
Introduction	2
Natural and synthetic sex hormones	5
Literature	24
Experiments and results	31
Discussion	124
Summary	128
References	134
Arabic summary	

******

AIM OF THE WORK

In a previous study the effect of the intraperitoneal injections of 1 μ gm./kg. body weight, of the synthetic female sex hormone hexoestrol on the white mouse and the desert mammal Gerbillus gerbillus daily for two months showed :

An increase in the total nitrogen content of the gastrocnemius muscles of the animals experimented on. The increase varied from 1 - 4 gm.% of lipid free-dry tissue as compared with the control animals.

With the exception of the male white mice, the animals showed an increase in the total body lipids.

The injected mice showed a decreased liver glycogen opposing to the increased effect manifested by the female Gerbillus gerbillus.

It became of value to extend the work with different doses of the hormone (0.05 μ gm. and 10 μ gm./kg. body weight) and with more animals in order to follow its action on the metabolic pathways of proteins, fats

and carbohydrates. The work includes a trial to give the possible chemical explanation and the applied economical utilisation of the results.

INTRODUCTION

The present study concerns the effect of the intraperitoneal injection of the synthetic female sex hormone hexoestrol on the general metabolism of some animals represented by the adult white rat Rattus rattus and the adult desert mammal Gerbillus gerbillus. The white rat was preferred to the white mouse because of its greater blood yield that facilitates the blood analysis carried out in this study. Two different doses of the hormone hexoestrol were applied: a low dose which was 0.5 µ gm./kg. body weight and a high dose which was 10 µ gm./kg. body weight. These doses were daily intraperitoneally injected to the animals. The injection continued for two months to study their effect on the water content and weight gain of the body. The effect of the hormone on the protein metabolism was studied by following the total nitrogen and total protein contents of the plasma and gastrocnemius muscle. The metabolism of carbohydrates was also investigated through the estimation of the glucose content of the plasma besides the glycogen content

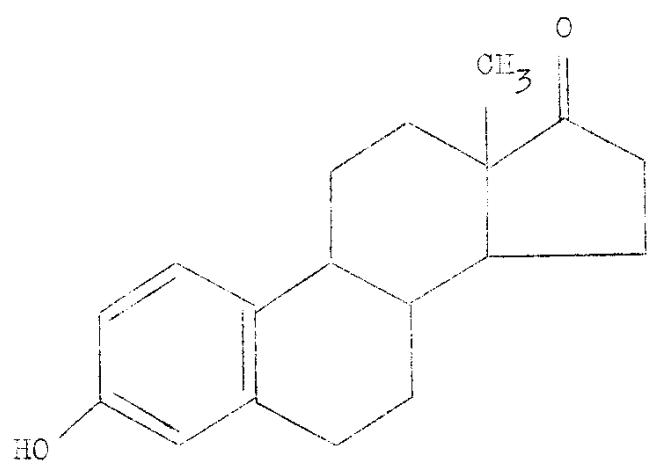
of both the liver and the gastrocnemius muscle. The biochemical study was also extended to include the total cholesterol content of the plasma and the lipid content of the whole body as well as that of some selected organs represented by the brain, lung, liver, kidney, cardiac muscle and skeletal muscle (gastrocnemius). In addition to this chemical study, morphological examination of the genital organs and histological study of the testes and the ovaries were carried out to study the effect of the hormone on the size of the genital organs and on the process of spermatogenesis and ovogenesis.

L I T E R A T U R E

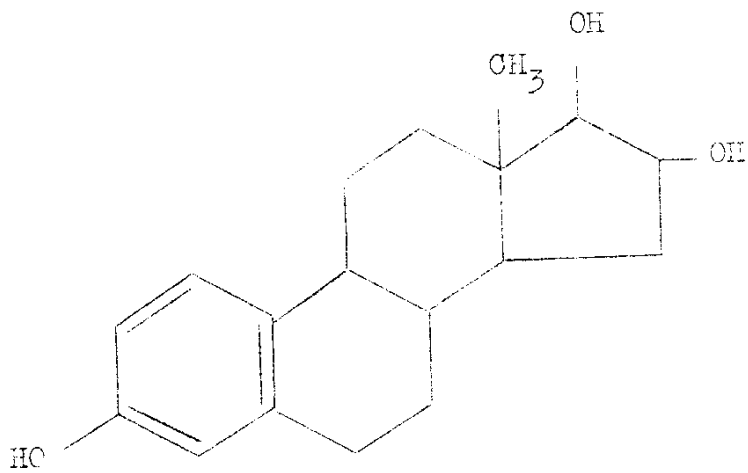
Natural and synthetic female sex hormones

Hormones are chemical substances carried by the blood to the organs of the body. These chemical substances are secreted by the endocrine glands.

Concerning the natural oestrogens, they are chemical compounds which if injected into oophorectomized animals they bring on the state of oestrus. These substances can be extracted from the ovaries, the placenta and from the urine of both men and women. In the latter condition the amount increases at about the time of ovulation, and during pregnancy. Examples of these oestrogens are:
Oestrone and oestriol.



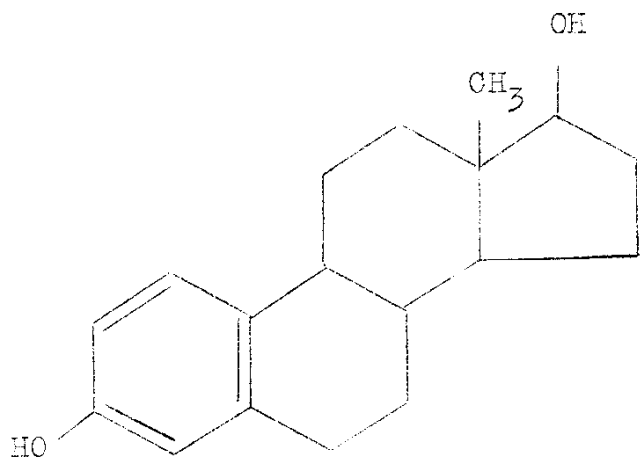
oestrone



oestriol

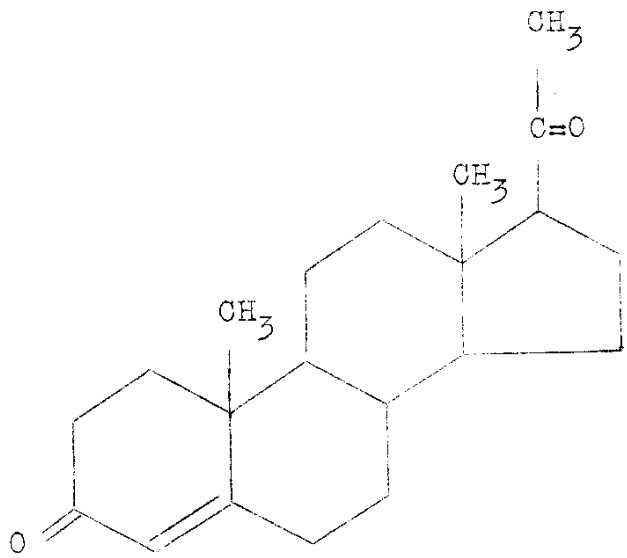
These two compounds are present in the urine of normal women (100 - 600 units daily), and of men (20 - 100 units daily) but present in large amounts in the urine of pregnant women in a combined form as glucuronides of low oestrogenic power. One of the hormones produced by the ovary is oestradiol which induces the growth of endometrium. Oestradiol is conjugated and eliminated as oestrone and oestriol. The liver is the main site of inactivation of oestrogens. Alpha oestradiol is converted into oestrone or oestriol derivatives which are less active. Oestrogens are active when administered subcutaneously in dilute alcohol or in oil, or by implantation

under the skin. They are much less effective when taken by mouth. Injection of oestrogens into castrated females causes the onset of the uterine and vaginal changes characteristic of oestrus and also enlargement of the mammary glands.

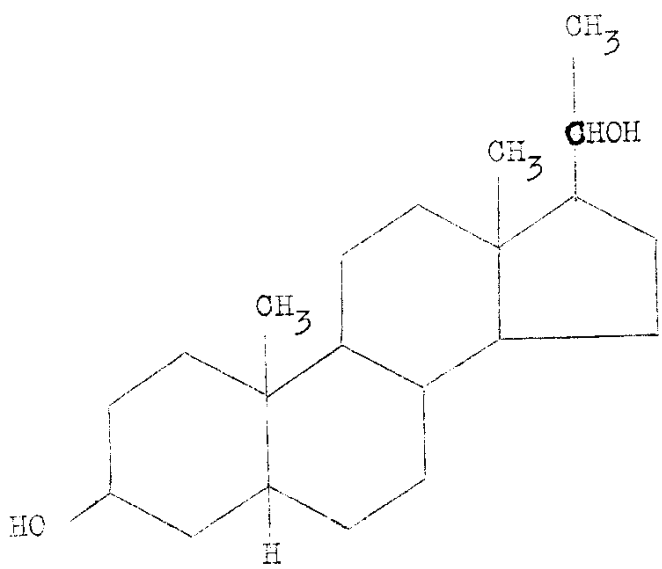


oestradiol

Progesterone is another natural female hormone derived from the corpus luteum which is formed from the mature Graafian follicle after its rupture. The hormone assists in fixing the fertilised ovum in the uterine wall. The hormone is eliminated in the urine as pregnanediol. The presence of pregnanediol in the urine indicates a progestational endometrium and its absence a follicular endometrium.



Progesterone



pregnanediol

All the steroid hormones, oestrogens, androgens and cortical hormones are inactivated or destroyed in the liver. Oestrogens incubated with liver slices are partly destroyed. Castrated female rats with oestrogen pellets implanted in the spleen do not give into heat unless the spleen is transplanted from the portal to the sytemic circulation. The destruction or inactivation in the liver does not occur in animals defficient in thiamine, riboflavine and methionine and thus implantation of oestrogens in the spleen of castrated animals defficient in these vitamins produce oestrus.

A number of synthetic organic compounds have been discovered which induce oestrus in castrated animals and stimulate the actions of the naturally occuring oestrogens. The earliest known of these synthetic organic compounds were phenanthrene and dibenzanthrene derivatives, which are chemically similar or related to the natural steroids. e.g. 3-oxo-testosterone that shows no testicular action but a follicular action.