the excitomotory picture induced by amphetamine, cocaine and caffeine, potentiates the hexobarbital induced sleep, and shows an anticonvulsant action against electroshock seizures, whereas it is ineffective against experimental seizures by pentylenetetrazol and strychnine. In the voluntary muscular activity of mice, DA 1128 orally displays an action rather similar to mephenesin in rota rod test, 50% in traction and in inclined screen tests, 25% in paralysing test. Like mephenesin, the new drug does not modify the corneal reflex, whereas it exhibits on pinna reflex an activity equivalent to one-half. It is interesting to note that ED_{50} calculated for traction test, anticonvulsant action and spontaneous activity in mice, both normal and pretreated with amphetamine, cocaine and caffeine, have been found to be, respectively, 20%, 41%, 33%, 25%, 28% and 27% of the paralysing ED_{50}.

DA 1128 is less toxic than mephenesin and mostly does not exhibit any haemolytic activity, either *in vivo* or *in vitro*. The LD_{50}, in mg/kg, have been recorded as follows: 458 intravenously, 674 intraperitoneally and 1056 orally in mice; 1637 orally in rats. Three months of oral treatment with 280 mg/kg daily of DA 1128 did not affect the blood picture and the body growth, and did not cause any pathological change in the chief organs.

Blood levels in rats and rabbits administered orally and intramuscularly with DA 1128 have shown the new drug to be quickly absorbed. DA 1128 displays in such animals a disappearance rate from blood circulation quite similar to mephenesin. It is excreted unchanged in small amounts; large amounts are found in urine of a metabolite which proved to be α-hydroxy-β-(4-propionyl-2-methoxyphenoxy)-propionic acid.

Zusammenfassung. Die hauptsächlichsten pharmakologischen Eigenschaften von 3-(*p*-Propionyl-*o*-methoxyphenoxy)-1, 2-propandiol (DA 1128) werden beschrieben. Wie Mephenesin zeigt DA 1128 eine beträchtliche depressorische Wirkung auf das Z.N.S. Das neue Arzneimittel jedoch zeigt – in Abweichung von Mephenesin – nur eine schwache paralytische Wirkung und eine geringe muskelrelaxierende Wirkung, ist weniger toxisch und besitzt keine hämolytische Wirkung. DA 1128 wird bei Versuchstieren rasch resorbiert.

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Incorporation of H^3-Progesterone Activity into 18-OH-Corticosterone and 18-OH-11-Desoxycorticosterone, Aldosterone and Corticosterone Following Treatment of Formaldehyde and Hydrocortisone, in Pregnant and New-Born Rats and Immediately *post partum*

It has been proved by several authors (PÉRON[1-3], WARD and BIRMINGHAM[4], ULICK[5], SÁNDOR et al.[6,7], KAHNT and NEHER[8]) that a significant quantity of 18-OH-corticosterone and 18-OH-11-deoxycorticosterone is produced by the adrenal of various species. The biological role of these steroids has not been clarified. It was, therefore, decided to study, under different physiological and pathological conditions, the incorporation of the radioactivity of H^3-progesterone into 18-OH-corticosterone and 18-OH-11-deoxycorticosterone. The investigations were carried out on the surviving adrenal slices of rats. An opportunity of examining the incorporated activity into aldosterone and corticosterone was also provided.

The present experiments were carried out on female rats of identical breed, as follows: 0.5 ml/100 g 2% formaldehyde was administered daily intramuscularly for 5 days; 5 mg hydrocortisone was given subcutaneously twice daily for 12 to 14 days. The investigations were carried out 24 h after the last treatment. The pregnant animals were in the last third of pregnancy; the new-born rats were 1 to 5 days old. Mother animals, deprived of their offspring, were used for the examination of the *post partum* condition.

The rats were killed by decapitation. The adrenals were removed, cleaned and cut in four, incubated in 10 ml/100 mg Krebs-Ringer-bicarbonate solution containing 200 mg % glycose, perfused with a mixture of 95% O_2 + 5% CO_2 at 38°C temperature. After a preliminary incubation of $^1/_2$ h, the medium was changed. The object of the examination consisted of a 4-h incubation. When changing the medium, 1 μg/mg H^3-progesterone dissolved in $^1/_{100}$ Vol ethanol and $^1/_{100}$ Vol propylene-glycol was added to the incubation mixture. (H^3-progesterone of random labelling according to Wilzbach's procedure, of 73 μC/mg spec. activity and 97% radiochemical purity was put at our disposal by the Isotope Institute of the National Atomic Energy Committee, Budapest.) 100 to 300 mg adrenal, taken from 4 to 10 rats, were incubated in each tube. The number of new-born animals was naturally much higher, that of pregnant rats was less; the adrenals of 2 to 3 rats were incubated together.

The incubation fluid was extracted with dichlormethane and chromatographed on Whatman No. 4 filter paper in a propylene-glycol-toluene system for 10 to 16 h. The steroids were localized by means of a UV lamp at 254 mμ and a fluorescence screen. Identification was done with aldosterone and corticosterone running simultaneously, i.e. by estimating the Rf. For the estimation of Rf, data of investigations carried out under similar conditions by WARD and BIRMINGHAM[4] and SHEPPARD et al.[9], were taken into consideration.

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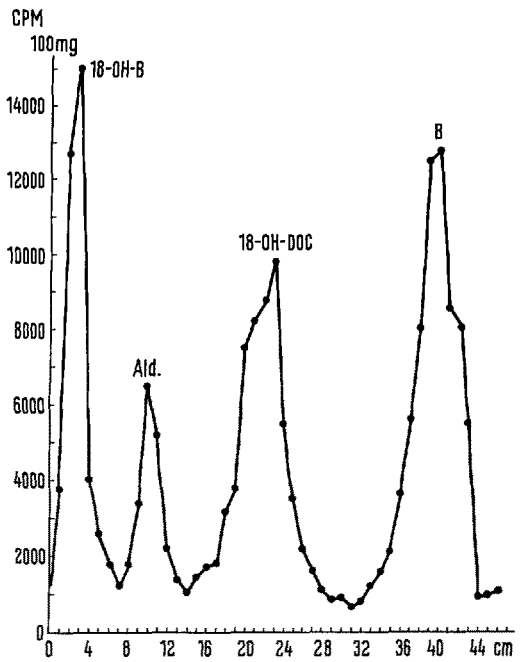
The chromatograms were cut into pieces of 1 cm, eluated and the radioactivity determined by a windowless gas-flow counter. The degree of incorporation is given in the percentage of the activity of H^3-progesterone added to the incubate. The radioactivity curve obtained in this way is illustrated in the Figure. The results are shown in the Table. The formaldehyde treatment was used as 'stress' in producing the state of resistance of the general adaptation syndrome[10]. It can clearly be seen from the Table that following formaldehyde treatment it is the increased 18-OH-B production which is eventually responsible (atrophy of the lymph organs, antiphlogistic effect, etc.).

After hydrocortisone treatment, no assessable change could be obtained in any of the cases; even the decrease of corticosterone activity was of minimum significance. This corroborates our experience that the decreased corticosteroid production of rat adrenals treated with hydrocortisone increased after adding progesterone to the incubation mixture, similarly to that of the controls[11].

In pregnancy, in spite of certain changing tendencies (18-OH-corticosterone, 18-OH-11-deoxycorticosterone) no statistically assessable differences were recorded. It can clearly be seen from the Table that activity determined *post partum* is generally lower. This is especially noticeable if this activity is compared with that in pregnant subjects examined some days earlier rather than with that of the controls. The significance and interpretation of the changes thus obtained are at the moment unknown.

Corticosterone activity in the new-born rats decreases, thus corroborating our results, according to which[12] in new-born rats first of all the immaturity of glycocorticoid production has to be taken into account. Investigations in progress in which, under similar experimental conditions, the quantity of the produced corticosteroid is determined and not the activity, show that, in agreement with literary data[9], quantitative and activity values do not in every instance show parallel changes. For the elucidation of the question thus raised, our investigations continue.



Running in a propylene-glycol-toluene system during 16 h. 18-OH-B = 18-hydroxy-corticosterone, Ald = aldosterone, 18-OH-Doc = 18-hydroxy-11-deoxycorticosterone, B = corticosterone.

Incorporation of H^3-progesterone radioactivity into corticosteroids produced by surviving adrenal slices, expressed in percentage of the added total radioactivity

	18-OH-Corticosterone	Aldosterone	18-OH-11-Desoxycorticosterone	Corticosterone
Control	1.60	0.80	3.40	7.50
Number of incubated group	13	20	13	9
Average deviation	0.75	0.62	1.96	2.18
Formaldehyde treatment	2.60[a]	1.20	3.50	6.40
Number of groups	11	15	11	11
Average deviation	0.91	0.59	0.99	1.41
Hydrocortisone treatment	1.20	0.83	2.70	5.30[c]
Number of groups	8	12	8	6
Average deviation	0.54	0.32	0.75	1.57
Pregnant	2.20	0.70	4.60	8.00
Number of groups	6	6	6	5
Average deviation	0.62	0.54	1.07	1.32
Post partum	0.72[c,d]	0.34[a]	2.90[c]	4.70[b,c]
Number of groups	4	4	4	4
Average deviation	0.58	0.18	1.44	1.16
Newborn	1.50	0.80	2.00[c]	4.00[a]
Number of groups	5	5	5	5
Average deviation	0.32	0.45	0.48	1.87

$$\text{Average deviation} = \sqrt{\frac{\Sigma (x - x_1)^2}{n - 1}} \; 1$$

In the groups of control animals and rats treated with formaldehyde 5 each, following treatment with hydrocortisone, 4 such groups were also included in the aldosterone values in which, instead of the propylene-glycol-toluene isolation, the chromatographic isolation was carried out in Bush B 5 system (benzol:methanol:water – 100:55:45). [a] Deviation from values of the controls is strongly significant ($p < 0.01$). [b] Deviation from values of the controls is slightly significant ($p < 0.05$). [c] Deviation from values of the controls is of minimum significance ($0.1 > p > 0.05$). [d] Deviation from pregnant rats is strongly significant ($p < 0.01$). [e] Deviation from pregnant rats is of minimum significance ($0.1 > p > 0.05$). In the rest of the cases deviation is not significant ($p > 0.1$).

Zusammenfassung. Der Einbau von H^3-Progesteron-Radioaktivität in verschiedenen Corticosteroiden wurde bei mit Formalin und Hydrocortison behandelten, trächtigen und neugeborenen Ratten mit Hilfe von *in vitro* überlebenden Nebennierenschnitten *post partum* untersucht. Die 18-OH-Corticosteronaktivität steigt nach Formalinbehandlung an; die Aktivität *post partum* gebildeter Corticosteroide vermindert sich im allgemeinen; bei neugeborenen Ratten ist die Aktivität des Corticosterons vermindert.

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