stimulation of contralateral and ipsilateral forepaws, were recorded. Paraoxon dissolved in CSF was applied to the pial surface through especially designed cortical cups. In most experiments the drug was applied to only one cortex while the other cortex was bathed with normal CSF and served as control throughout the experimental period.

A continuous record of spontaneous electrocortical (EEG) activity and cortical and rectal temperatures was obtained on the different channels of the polygraph (Devices).

Paraoxon was applied in different concentrations (10^{-5} M ; 3×10^{-5} M ; 10^{-4} M and 10^{-3} M) to the cortex for a period of 30 minutes, and its effect on the somatosensory evoked potentials was observed. With each concentration at least 4 to 6 experiments were performed.

In most of the experiments paraoxon produced an increase in the amplitude of the repetitive after-discharges of the cortical evoked potentials. The short latency positive-negative complex was not affected after cortical application of paraoxon. This effect was more marked with less concentrations of paraoxon (up to 10^{-4} M); higher concentration had little effect and even caused the death of some of the animals. The best effect was however obtained with 3×10^{-5} M of paraoxon. The effect on the repetitive after-discharges usually started within 15–20 minutes of the application of the drug, and lasted for more than 6–8 hours after washing off the drug.

In the control cortex the evoked potentials following contralateral or ipsilateral stimulation were unchanged.

The present study shows that paraoxon only produces its effect on the long latency (repetitive after-dicharge) component of the cortical evoked potentials, whereas the primary complex remains unaffected. This effect of paraoxon is due to preservation of acetylcholine because of inhibition of the enzyme acetylcholinesterase. The result thus provides an electrophysiological evidence that the afferent pathways responsible for the repetitive after-discharges are cholinergic in nature while those for the primary complex probably do not involve cholinoceptive synapses. A more detailed study has to be done for further confirmation of this intra-cortical cholinergic mechanism.

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BIOSYNTHESIS OF PLANT STEROLS THE MECHANISM OF THE ALKYLATION OF α-SPINASTEROL AT C-24

IN the mechanism postulated for the alkylation of phytosterols, the hydrogen atom at C-24 migrates to C-25.[1,2] We reported earlier[3] that the incorporation of (3RS)-[2-^{14}C(4R)-4-^{3}H$_1$]-mevalonic acid into *Camellia sinensis* yielded α-spinasterol which had ^{3}H/^{14}C atomic ratio of 2·44 : 5 instead of 3 : 5. It was pointed out that the process of alkylation in this phytosterol may proceed simultaneously by two routes; one route involving the intermediate in which ^{3}H at C-24 is lost, possibly during the formation of 24-methylene intermediate and the other route in which ^{3}H is transferred to C-24 through the carbonium ion mechanism. In the present communication we report experimental evidence supporting the above possibility.

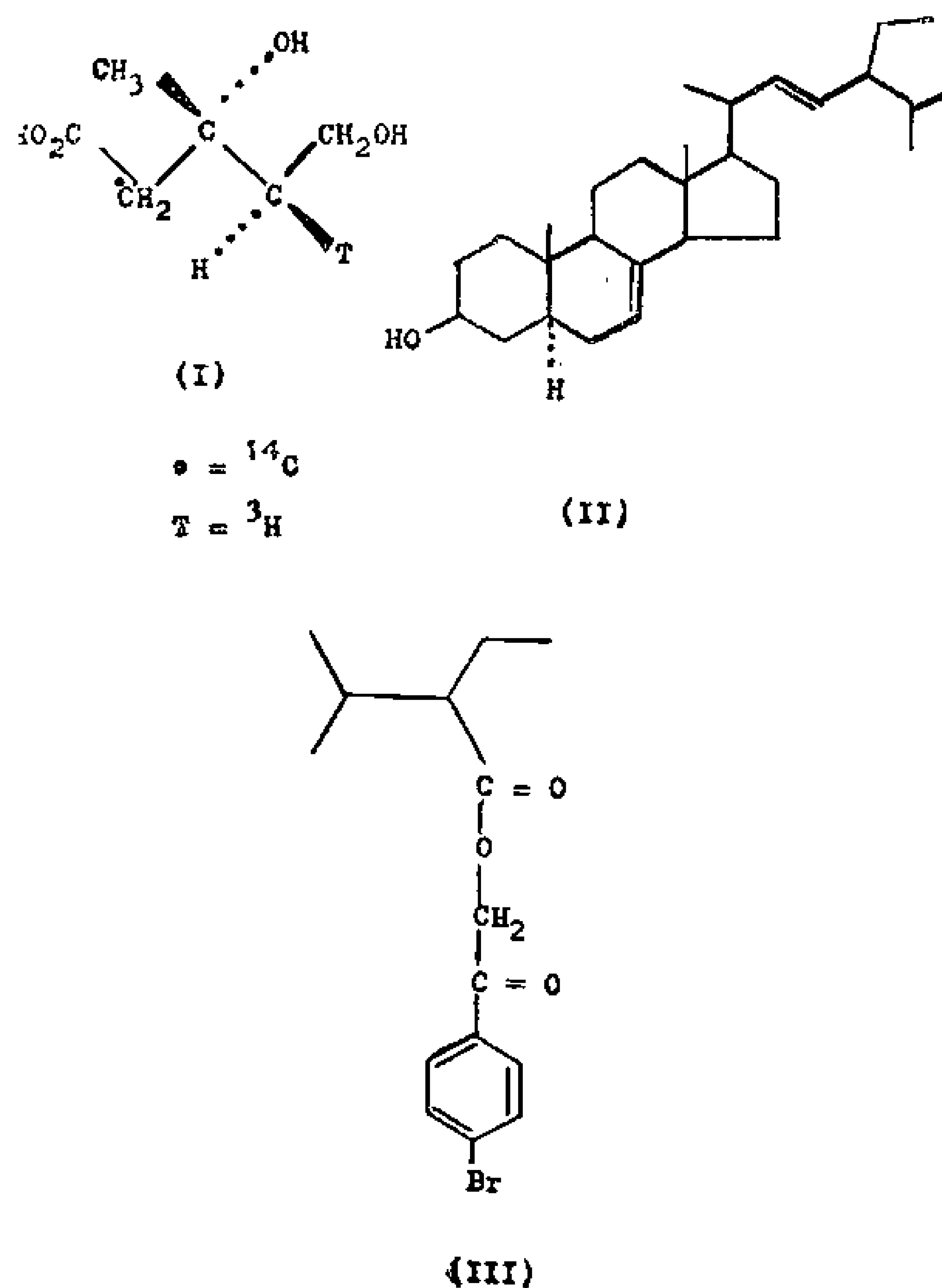

FIG. 1

(3RS)-[2-^{14}C-(4R)-4-^{3}H$_1$]-mevalonic acid (I) (^{3}H/^{14}C ratio 5·37 ; 50 μc of ^{14}C) was

administered to the *Camellia sinensis* plant as previously described.[3] The plant was harvested after five weeks and α-spinasterol (II) was isolated from the non-saponifiable lipid in the usual manner.[3] The carrier α-spinasterol was added and the sterol crystallized to constant specific activity and $^{3}H/^{14}C$ ratio 2·67, atomic ratio (a.r.) 2·44 : 5. Oxidation[4] of the biosynthetic α-spinasterol yielded 2-ethyl-3-methylbutanoic acid which was isolated as the *p*-bromophenacylester derivative (III) and purified by *tlc* on silica gel. The $^{3}H/^{14}C$ ratio obtained was 2·74 (a.r. 0·51 : 1).

These results indicate that only 50% of the expected tritium migrates to the C-25 position and the other 50% is eliminated, probably during the formation of the intermediate C-24-methylene derivative.

The author wishes to thank Dr. K. R. Varma, Department of Chemistry, Harvard University, Cambridge, Massachusetts, for sending the sample of authentic *p*-bromophenacylester derivative of 2-ethyl-3-methylbutanoic acid. He also wishes to thank Professor W. R. Nes, Drexel University, Philadelphia, Pennsylvania, for his stimulating discussion during this study.

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ANTIESTROGENICITY OF NORGESTREL

NORGESTREL (*dl*-17 α-ethinyl-13 β-ethyl-17 β-hydroxygon-4-en-3-one), a synthetic progestogen has been reported to be a highly potent estrogen antagonist at the same time being completely free from estrogenicity.[1] Continuous daily oral administration of this steroid in micro doses prevents pregnancy in women and rats.[2,3] The antiestrogenic property has been considered to be a crucial factor in contraceptive *modus operandi* of the progestogen.[3]

The present communication is concerned with the assessment of antiestrogenic potency of norgestrel in terms of its effect on vascular permeability of the rat uterus.

Colony-bread albino rats (150–200 gm.) of the Institute with regular estrus cycle (4–5 days) were used. Norgestrel (0·3 μg./rat, oral), estrone (1 μg./rat, i.m.) and progesterone (0·25, 0·50, 1·00 and 2·00 mg./rat, i.m.) were given in olive oil. The vascular permeability of the uterus was determined by the method of Cecil *et al.*[4] with the modification that intact diestrus animals were used instead of ovariectomized ones.

After a single dose of norgestrel the vascular permeability of the uterus registered a marked fall between 3 and 9 hr. (*vs.* control $P < 0·01$, Table I), but returned to normal at 12 hr.

TABLE I
Effect of norgestrel on vascular permeability of the rat uterus

Control	Hours after norgestrel administration			
	3	6	9	12
6·41 ±0·65 (*9*)*	1·00 ±0·26 (*6*)	3·02 ±0·41 (*9*)	2·13 ±0·2) (*9*)	7 60 ±1·06 (*9*)

* Mean ± S E. with number of animals in parentheses; vascular permeability expressed as μg. trypan blue/100 mg. uterine tissue.

Assessment of graded doses of progesterone (3 hr. after injection) showed that the inhibition of uterine permeability caused by 0·5 mg. dose was equivalent to the effect seen after administration of 0·3 μg. norgestrel (Table II).

TABLE II
Effect of graded doses of progesterone on vascular permeability of the rat uterus

Treatment		μg. trypan blue/100 mg. uterine tissue
Control	..	6·41 ±0·65 (*9*)*
Progesterone—		
0·25 mg.	..	3·25 ±0·23 (*4*)
0·50 mg.	..	2·11 ±0·22 (*5*)
1·00 mg.	..	1·35 ±0·39 (*5*)
2·00 mg.	..	0·51 ±0·03 (*4*)

* Mean ± S.E. with number of animals in parentheses.

In other words, the antipermeability effect of the latter was about 1666 times as high as that of progesterone. Further, it was evident that 2 mg. progesterone reduced the permeability to about 1/15th of the normal value within 3 hr. When assayed by the mouse vaginal cornification method norgestrel was found to be about 730 times more active than progesterone.[1]

Administration of norgestrel to rats either concurrently or 3 hr. after estrone (*i.e.*, 3 hr. prior to sacrifice) not only prevented the