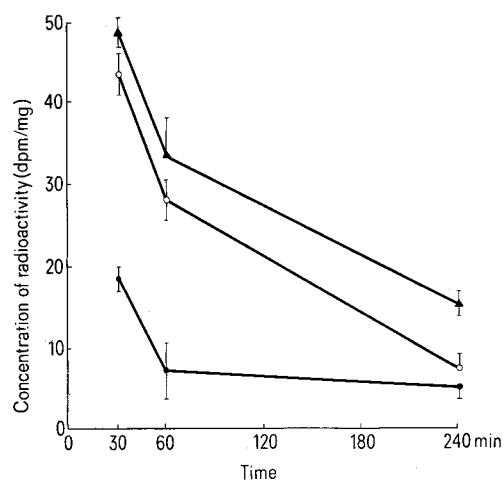


Epididymal fluid was collected as previously described<sup>7</sup>, and separated into epididymal plasma and spermatozoa by centrifugation at  $12,000 \times g$  for 45 min in a micro-haematocrit centrifuge (Hawksley Ltd). At autopsy, the following organs were removed and weighed: seminal vesicles, coagulating gland, prostate gland, epididymides, testes and ductus deferentes. The epididymides were divided into caput, corpus and caudae epididymides. A known weight of each organ was taken, solubilized with NCS tissue solubilizer (Amersham/Searle: 0.5 ml) for

Distribution of radioactivity (dpm/g) in the reproductive system of the male rat at various times after i. v. administration of [<sup>3</sup>H]LSD (24  $\mu$ Ci/kg b. wt)

Tissue	Time (min)		
	30 (n = 3)	60 (n = 4)	180 (n = 3)
Blood plasma	42440 $\pm$ 1370	35480 $\pm$ 1850	27200 $\pm$ 3370
Epididymal plasma	8340 $\pm$ 2440	9000 $\pm$ 2450	18500 $\pm$ 3580
Spermatozoa	10520 $\pm$ 590	13750 $\pm$ 1600	14870 $\pm$ 2440
Seminal fluid	13420 $\pm$ 1300	16250 $\pm$ 960	13060 $\pm$ 1370
Seminal vesicle	31200 $\pm$ 2090	31670 $\pm$ 1030	23940 $\pm$ 3100
Coagulating gland	27930 $\pm$ 1300	39750 $\pm$ 2040	26120 $\pm$ 4930
Prostate gland	51510 $\pm$ 4800	49500 $\pm$ 4530	21230 $\pm$ 1580
Caput epididymides	42640 $\pm$ 5090	47000 $\pm$ 5690	30470 $\pm$ 3390
Corpus epididymides	74360 $\pm$ 27650	54670 $\pm$ 2490	31190 $\pm$ 4453
Cauda epididymides	33360 $\pm$ 7230	21330 $\pm$ 1030	19560 $\pm$ 1860
Seminiferous tubules	23580 $\pm$ 1960	27000 $\pm$ 1120	14510 $\pm$ 1660
Vas deferens	50650 $\pm$ 17940	30670 $\pm$ 1030	21400 $\pm$ 1080

Each value represents the mean  $\pm$  SEM; n = number of animals.



Distribution of radioactivity in the placenta (▲-▲) foetus (●-●) and maternal blood plasma (○-○) after i.v. administration of [<sup>3</sup>H]LSD (24  $\mu$ Ci/kg b. wt) to 18 day pregnant rats. Each point represents the mean  $\pm$  SEM of 3 experiments.

12 h and the radioactive content determined by liquid scintillation spectrometry<sup>8</sup>.

Experiment 2. 18 day pregnant Wistar rats were anaesthetized as previously described and catheters inserted into a femoral vein and carotid artery. [<sup>3</sup>H]LSD (24  $\mu$ Ci/kg) was administered i.v. and blood samples obtained prior to autopsy at 30, 60 or 240 min. At autopsy, both uterine horns were removed, and each foetus weighed and homogenized. A known weight of each placenta and foetal homogenate was solubilized and the radioactive content determined.

**Results and discussion.** The distribution of radioactivity in the male reproductive system after i.v. administration of [<sup>3</sup>H]LSD is shown in the table. All tissues contained LSD and/or metabolites. The concentration of radioactivity in epididymal plasma and spermatozoa was greater at 180 min than at 60 min. In contrast, in all other tissues the concentration at 180 min was less than at 60 min. In most tissues the concentration of radioactivity approximated to that in blood plasma.

These experiments clearly show that LSD and/or metabolites is distributed in the male accessory sex organs. Moreover, the presence of radioactivity has been shown both in the seminiferous tubules, where spermatozoa are being formed, and associated with spermatozoa undergoing maturation in the epididymis. These findings raise the interesting question as to whether or not LSD and/or metabolites is actually present within the sperm nucleus, and if so whether the presence of the drug could adversely influence spermatozoa development and maturation.

Radioactivity present in maternal blood plasma, placental tissue and the foetus at different time intervals is shown in the figure. The concentration, highest in the placenta, declined between 30 and 240 min. The percentage of administered radioactivity recovered per foetus was as follows: 0.11  $\pm$  0.01% (mean  $\pm$  SEM) at 30 min; 0.04  $\pm$  0.02% at 60 min; 0.03  $\pm$  0.01% at 240 min. Autoradiographic studies on the placental transfer of LSD in mice<sup>9</sup> have indicated that in late pregnancy 0.5% of the radioactive dose passed the placental barrier into the foetus in 5 min. The teratogenic effects observed in rats when LSD was injected in early pregnancy<sup>9,10</sup> indicate placental transfer in this species. The present experiments have confirmed this and demonstrated the appearance of a significant fraction of the dose in the near-term foetus.

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### Anti-arthritis activity of bredinin, an immunosuppressive agent

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**Summary.** Bredinin has been found to have an inhibitory effect upon the secondary lesions occurring from adjuvant injection in rats.

Bredinin, a nucleoside antibiotic isolated from *Eupenicillium brefeldianum*, was found to have potent immunosuppressive effects, causing suppression of both primary and secondary immune responses in mice<sup>3</sup>. With respect to the mechanism of the immunosuppressive action of

bredinin, Sakaguchi et al.<sup>4,5</sup> reported a growth inhibitory action of bredinin on mammalian cells due to blockade of the pathway from inosine 5'-monophosphate to xanthosine 5'-monophosphate or from xanthosine 5'-monophosphate to guanosine 5'-monophosphate. Recently,

