sense that a definitely increased utilization occurs over that found at the start of the experiment.

One cannot conclude from these results that the same holds true for the digestive enzyme production by the mid-gut gland. This is an entirely different process. We can only say that the *resorption* of digested material is apparently decreased in the snails (particularly in the starch snails). It may be possible that the initial rate of resorption may be reached again, provided a long period (more than 7 weeks) of adaptation is allowed. The slow rise of both curves at the end of the experimental period indicates such a possibility. The low metabolism of these sluggish animals may also support this.

What causes this decrease in utilization of the food, when put on a special diet, must be left undecided for the time being. It is quite possible that certain important substances, present in the natural food (these snails are notorious scavangers and their natural diet therefore consists of many different materials), are missing. This lack may affect the rate of resorption, but nothing definite is known of this in snails. In any case the results of this investigation do not support the hypothesis of a true adaptation (in 7 weeks) by the individual snail to a special diet. On the contrary, if there is a correlation between utilization and diet, this seems to be a negative one.

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Zusammenfassung

Eine spezielle Diät (Stärke oder Fleisch) induziert keine Adaptation in *Achatina fulica* in dem Sinn, dass mehr Kohlehydrate, bzw. Proteine resorbiert werden als mit normalem Futter.

Metabolites of LSD and Ergometrine[1]

Chemical and pharmacological studies of metabolites of lysergic acid derivatives produced in the animal body have been carried out by two main groups[2,3]. AXELROD, BRADY, WITKOP, and EVARTS[2], in particular, have shown that with guinea pig liver homogenates only one metabolite was produced from lysergic acid diethylamide (LSD). This metabolite had no LSD-like action in the central nervous system, gave negative Ehrlich tests and was shown[4] to be 2-oxy LSD by methods including spectrophotometry, paper chromatography, and synthesis. However, STOLL, ROTHLIN, RUTSCHMANN, and SCHALCH[3] with C-14 side chain labelled LSD isolated three radio-active metabolites from rats, two of which fluoresced in ultraviolet light and gave a positive Ehrlich colour reaction. Repetition of the work of STOLL *et al.*[3] in this laboratory substantiated their results. Two metabolites were shown to be present in extracts of bile collected from male rats after an intravenous dose of 3 mg/kg of LSD when run on downward paper chromatograms using butanol:acetic acid:water (4:1:5)[5]. The more polar metabolite (metabolite A, *Rf* 0·10) was produced in much larger quantities than the less polar substance (metabolite B, R_f 0·14) whereas LSD had an R_f value of 0·77.

Similarly, two metabolites were produced from ergometrine, a predominant one with an R_f of 0·07 and a second with an R_f of 0·10 on the same paper chromatographic system. Both metabolites gave a positive Ehrlich reaction and a blue fluorescence in ultra-violet light characteristic of lysergic acid derivatives. On this chromatography system ergometrine has an R_f of 0·6. The mixture of these two metabolites contracted isolated guinea pig uterus in the same manner as ergometrine.

Metabolites A and B produced from LSD have been shown to inhibit 5-hydroxy-tryptamine (5-HT) using the isolated rat uterus preparation. The inhibitory effect of each metabolite was expressed in terms of a dose ratio[6], which ranged from 5 to 7 at a concentration of $2:10^{-8}$ for each metabolite after a period of 10 min contact with the muscle. The small amount of metabolite B available precluded determination of the effect of further increasing the exposure time on the dose ratio. However, this was possible with metabolite A, and after 20 min exposure the dose ratio exceeded 50. The inhibitory action of this metabolite developed slowly after its addition and disappeared slowly after its removal. From preliminary experiments metabolite A has approximately 5% of the inhibitory potency of LSD, though the accuracy of this figure is limited by the purity of the metabolite at present available and by its stability in aqueous solution.

The blue fluorescence exhibited by all these metabolites is characteristic of the lysergic acid nucleus. STOLL *et al.*[3] showed that the side chain of LSD is retained in the metabolite and the positive Ehrlich reaction indicates the presence of an indole nucleus with unsubstituted α-position. Hydrolysis of metabolite A by boiling with N-hydrochloric acid for 1 h gives a compound exhibiting the blue fluorescence and Ehrlich reaction and having an R_f of 0·50 on the butanol:acetic acid:water system. This could indicate the presence of a conjugated hydroxyl group in the metabolite. That the LSD metabolites act as 5HT antagonists precludes the possibility that hydroxylation of the 9:10 double bond has occurred to give a lumialkaloid derivative which would be inactive[7]. From known biological examples position 5 and possibly position 7 of the indole ring are most likely to be hydroxylated. Further evidence of the extreme polarity of metabolite A was indicated by its low R_f value (0·34) on the basic system used by FRETER *et al.*[4] (2:4-lutidine:tert-amyl alcohol:water). On this system 2-oxy LSD had an R_f of 0·85.

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Zusammenfassung

Vorläufige Untersuchungen über die Verwandlung von LSD und Ergometrin bei der Ratte zeigen, dass von beiden Substanzen zwei Hauptprodukte gewonnen werden. Beide Metaboliten von LSD antagonisieren 5-HT am isolierten Rattenuruspräparat; es scheint sich um hydroxilierte und konjugierte Derivate des LSD zu handeln.

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