been found which incorporates thymidine-^{3}H during G_2 phase and which hybridizes with RNA[14]. Replication beyond the level of duplication(= amplification[15]) of nucleolar DNA cistrons coding for ribosomal RNA[13] has been found in oocytes[16]. It will be of interest to study nucleolar DNA replication in nuclei which were prevented from dividing by similar methods, but for longer periods of time than it was possible in the present experiments. Such an investigation is now in progress.

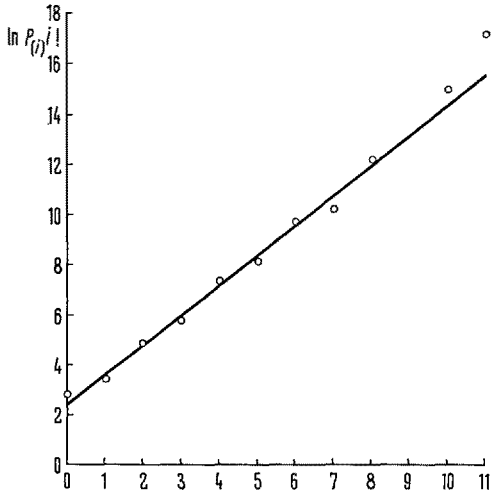

Fig. 3. Poisson distribution of grain counts over premitotic nuclei in postmitotic plasmodia (same preparation as in Figure 2). The following formula was used, $P = N A^i \cdot e^{-A}/i!$. A, mean value of grain counts (= 3.35); i, number of grains found (0, 1, 2, 3, etc.); P, probability of finding i grains over nuclei; N, actual number of nuclei counted (316).

Zusammenfassung. Wird bei einem künstlich synchronen Plasmodium des Myxomyceten *Physarum polycephalum* die Mitose promitotischer Kerne durch deren Verlagerung in postmitotische (=S phase) Zonen des gleichen Plasmodiums verhindert, so behält die nucleoläre DNS, im Gegensatz zur extranukleolären DNS, weiterhin die Fähigkeit, ^{3}H-Thymidin einzubauen. Es wird die Hypothese vorgeschlagen, dass die Synthese der nukleolären DNS einem anderen Kontrollmechanismus unterliegt als die der extranukleolären DNS.

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Inhibition of Monoamine Oxidase by 3-Amino-2-Oxazolidinone and 2-Hydroxy-Ethylhydrazine

3-Amino-2-oxazolidinone was recognized in a mouse behavior screen in these laboratories as a compound having activity like that of known inhibitors of monoamine oxidase (MAO), and further study showed that it had dopa-potentiating activity typical of MAO inhibitors in mice. We found that the compound did not inhibit MAO in vitro but that brain homogenates from treated mice showed nearly complete inhibition of MAO. 3-Amino-2-oxazolidinone is a known metabolite of furazolidone[1]; neither agent inhibits MAO in vitro, but both cause in vivo inhibition[1,2] suggested to be due to their conversion to 2-hydroxy-ethylhydrazine (HEH)[1]. We describe here some comparisons of 3-amino-2-oxazolidinone and HEH as inhibitors of MAO.

MAO activity was assayed by the method of WURTMAN and AXELROD[3] except that C^{14}-phenethylamine ($8 \times 10^{-5} M$) was used as substrate in place of tryptamine. Male albino mice (16–20 g) obtained from a local supplier were given i.p. injections of the drugs. The mice were then killed by decapitation, and the organs were rapidly removed and frozen on dry ice. Whole homogenates were used for the assay of MAO activity. Homogenates of tissues from untreated mice were used for in vitro studies with the inhibitors.

The Table shows that 3-amino-2-oxazolidinone did not inhibit MAO activity in vitro, whereas HEH inhibited in a manner typical of irreversible inhibitors, that is it required preincubation with enzyme prior to substrate addition for maximum inhibition.

Figure 1 shows the in vivo inhibition of MAO by these compounds. Maximum inhibition occurred rapidly, within 60 min or less, after the compounds were injected into mice. The onset of inhibition by 3-amino-2-oxazolidinone, which apparently acts indirectly, was as rapid as the onset of action of HEH, which can act directly. Both compounds caused greater inhibition of MAO in liver than in brain, but this difference was more pronounced with HEH.

In vitro inhibition of MAO

Inhibitor	Concentration (M)	Inhibition (%)	
		No preincubation	30 min preincubation
Brain			
3-Amino-2-oxazolidinone	10^{-3}	4	0
2-Hydroxyethylhydrazine	10^{-3}	96	99
	10^{-4}	61	99
	10^{-5}	22	98
	10^{-6}	3	47
	10^{-7}	0	2
Liver			
3-Amino-2-oxazolidinone	10^{-3}	9	8
2-Hydroxyethylhydrazine	10^{-3}	99	100
	10^{-4}	60	99
	10^{-5}	14	96
	10^{-6}	4	68
	10^{-7}	0	9

Where indicated, enzyme and inhibitor were preincubated in buffer at 37 °C prior to addition of substrate. Control values, in nanomoles of substrate oxidized/min/g tissue were 34 and 32 for brain, respectively, without and with the 30 min preincubation and 609 and 600 for liver, respectively, without and with the 30 min preincubation.

The dose of HEH was less effective in inhibiting the brain enzyme but more effective in inhibiting the liver enzyme than the dose of 3-amino-2-oxazolidinone. One possible explanation, based on the premise that 3-amino-2-oxazolidinone acts only after it is converted to HEH, is as follows. In the first pass through the liver after i.p. injection, HEH enters as an active inhibitor whereas 3-amino-2-oxazolidinone enters as an inactive precursor to an inhibitor. Thus greater inhibition of liver MAO occurs with HEH. By the time these agents reach the brain, much of the HEH has been inactivated by metabolism whereas the 3-amino-2-oxazolidinone has been activated by metabolism, so the latter compound has a greater effect on brain MAO.

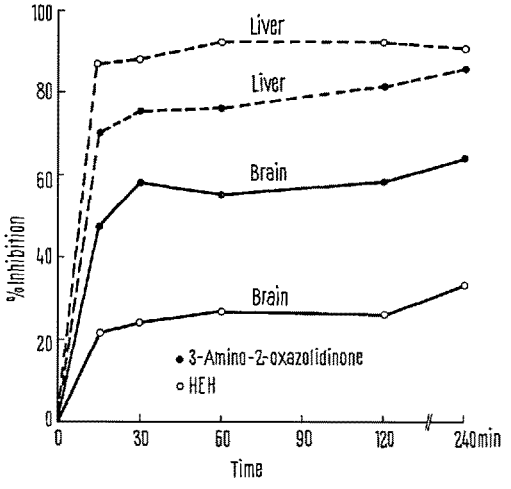

Fig. 1. Time course of in vivo inhibition of MAO. 3-amino-2-oxazolidinone (0.01 mmole/kg) or 2-hydroxy-ethylhydrazine (0.05 mmole/kg) was injected i.p. into mice. MAO activity was determined, and results are expressed as percent inhibition compared to activity in untreated mice. Mean values for 3 mice per group are shown. Activity in untreated mice was 42.5 ± 1.3 nanomoles of substrate oxidized/min/g brain and 577 ± 20 nanomoles/min/g liver.

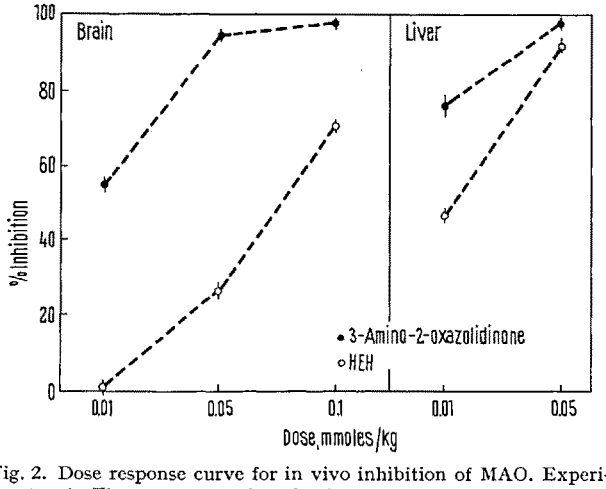

Fig. 2. Dose response curve for in vivo inhibition of MAO. Experiment as in Figure 1 except that the dose was varied and drugs were injected 60 min before the mice were killed. Means and standard errors for 3 mice per group are shown. Activity in untreated mice was 45.1 ± 5.1 nanomoles of substrate oxidized/min/g brain and 615 ± 42 nanomoles/min/g liver.

Since 3-amino-2-oxazolidinone does not inhibit MAO in vitro, its in vivo effects presumably occur after it is converted to some active metabolite. Previously that active metabolite was suggested to be HEH[1]. If that were so, then 3 findings that we report here would not have been expected: 1. there was no lag of in vivo MAO inhibition by 3-amino-2-oxazolidinone behind that of HEH, 2. 3-amino-2-oxazolidinone was actually more potent than HEH in causing in vivo inhibition, and 3. the relative liver/brain effects were different with the 2 agents. If 3-amino-2-oxazolidinone does act through conversion to HEH, then it must be an efficient vehicle for delivering HEH to tissues, especially the brain. Alternatively, 3-amino-2-oxazolidinone may act in vivo by conversion to some metabolite other than HEH, that metabolite being a more powerful inhibitor than HEH and having less selective affinity for liver MAO relative to brain MAO.

Zusammenfassung. Die MAO-hemmende Aktivität von 3-Amino-2-Oxazolidinon und von 2-Hydroxy-Äthylhydrazin wird beschrieben.

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The Lipid Content of Musculature and of Tissue Preparations with Enriched Plasma Membranes in Paramyotonia congenita

Our interest in the lipid content of musculature in cases of various forms of Myotonia congenita has been aroused by 2 findings: first a myotonic syndrome could be produced by the supply of azacholesterol[1,2]. Second KUHN et al.[2] found a change of the fatty acid composition of the lipids in an experimentally induced myotonic syndrome. They discussed the possibility of a membrane lesion as the effect of the enzymatic basic defect of this disease. A changed conductivity of the plasma membrane proved to be the cause of the myotonic syndrome also from electrophysiological view[3].

We had the opportunity to take a larger bioptic sample from a 9-year-old boy suffering from Paramyotonia congenita (P.c.). The patient shows the typical clinical