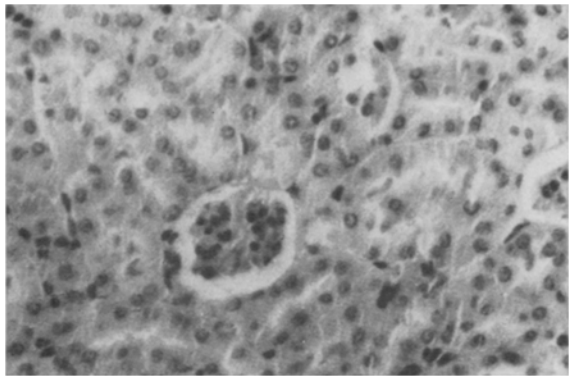

Fig. 3. Section of a normal mouse kidney. ×400.

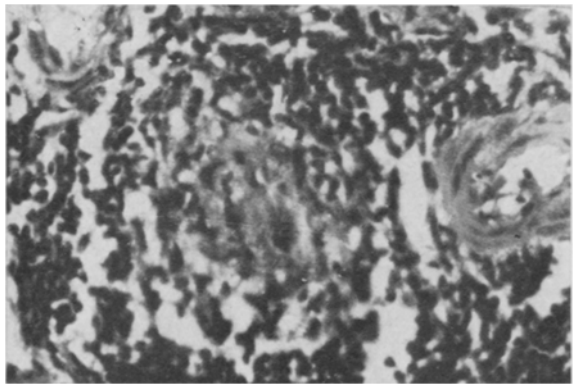

Fig. 4. Sextion of mouse kidney indicating focal accumulation of lymphocytes and focal nephritis. ×400.

citrinin was indicated by the chloroform extraction of the culture filtrate and subsequent co-chromatography with pure citrinin.

The pathological changes observed in our studies on kidney indicate glomerulonephritis, tending towards glomerulosclerosis[9,10]. Glomerulonephritis is understood to arise secondary to specific streptococcus infection of the respiratory tract or the skin[9,11,12]. Probably, our findings may be the first to indicate that the incidence of glomerulonephritis may be due to a primary effect of consuming contaminated toxic food. The isolation and characterization of the toxins are under way.

Zusammenfassung. Diäten, die mit Kulturen oder Kulturfiltraten von *Penicillium piceum* kontaminiert waren, erwiesen sich an Eintagsküken als strak toxisch und verursachten bei Mäusen ausgeprägte Nieren- und Leberschädigungen. Um eventuell vorhandene Oxalsäure und Citrinin, die nephrotoxisch wirken, zu eliminieren, wurde das Kulturfiltrat mit Äther bzw. Chloroform extrahiert. Die wässrigen Lösungen des Ätherextrakts waren bei Küken stark allgemein-toxisch, während bei Mäusen nur die wässrige Lösung des Chloroformextrakts diffuse Leberzellnekrose sowie Nierenveränderungen im Sinne einer Nephritis verursachte.

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Effect of Sulpiride on Oxygen Uptake by Rat's Brain Tissue in vitro

Sulpiride, a psychoactive drug, is a heterocyclic derivate (N(1-ethyl-2-pyrrolidinil-methyl)2-methoxy-5-sulfamoil benzamide) and was introduced by JUSTIN-BEÇANSON et al.[1]. Its pharmacological properties were studied by LAVILLE[2], ERNST and CHOTEAU[3] and LELIÉVRE[4].

It is known that some psychoactive drugs inhibit the oxygen uptake by the brain tissue in vitro and such effect is more evident when the tissue respiration has been stimulated by high potassium concentrations[5,6] or by deficit of calcium in the medium[7].

The purpose of this paper is to study the influence of sulpiride in the oxygen uptake in vitro by brain homogenates and by brain slices with low and high potassium concentrations and in absence of calcium in the medium.

Material and methods. Adult male albino rats were used to prepare brain slices, as described by MCILWAIN and BUDDLE[8], and brain homogenates. The slices were incubated in Krebs-Ringer phosphate medium (pH 7.4) which contained 10 m*M* glucose and 5 m*M* or 100 m*M* potassium or using the same Krebs-Ringer containing 5 m*M* potassium but without calcium. Whole brain homogenates were prepared at 2–4 °C in a Potter-Elvehjen homogenizer mixing 1 g of tissue with 9 ml of a solution containing 0.25 *M* sucrose and 0.1 *M* phosphate buffer (pH 7.4).

Oxygen consumption was determined by direct manometric technique[9] using a conventional Warburg apparatus with air as gas phase. Student's *t*-test was applied for statistical analysis[10].

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Table I. Effect of Sulpiride on oxygen uptake by brain slices in vitro

Drug concentration	Potassium concentration (mM)	Calcium concentration (mM)	Oxygen uptake (μl/100 mg wet tissue/h)
Control	5	2.5	64.56 ± 3.61 (10)
	100	2.5	78.21 ± 2.76 (12) [c]
	5	0	69.50 ± 4.68 (9)
1×10^{-2} M	5	2.5	53.62 ± 4.41 (10) [a]
	100	2.5	47.10 ± 3.19 (12) [b]
	5	0	52.49 ± 3.13 (9) [c]
1×10^{-3} M	5	2.5	69.40 ± 7.17 (11)
	100	2.5	69.95 ± 3.11 (12)
	5	0	70.08 ± 4.68 (9)
1×10^{-4} M	5	2.5	61.40 ± 6.53 (8)
	100	2.5	78.65 ± 3.76 (10)
	5	0	68.09 ± 6.83 (9)

[a] $P < 0.02$; [b] $P < 0.001$; [c] $P < 0.01$. The figures are means ± SEM. In brackets the number of slices.

Table II. Effect of Sulpiride on oxygen utilization by brain homogenates

Drug concentration	No. of experiments	Oxygen uptake (μl/100 mg wet tissue/h)
Control	12	54.77 ± 3.14
1×10^{-2} M	8	43.91 ± 1.99 [a]
1×10^{-3} M	7	52.77 ± 4.49
1×10^{-4} M	8	53.61 ± 4.81

[a] $P < 0.025$. The figures are means ± SEM.

Results. The data on the oxygen uptake by brain slices are shown in Table I and shows that, under control conditions, in Krebs-Ringer phosphate medium with high concentration of potassium (100 mM), the oxygen uptake is increased up to 21.1%. The absence of calcium in the medium does not change significantly the oxygen consumption.

Sulpiride, at high concentrations (10^{-2}), inhibits significantly the oxygen uptake at 60 min of incubation; this inhibition appears greater when the medium contained high potassium concentrations.

The data on the oxygen uptake by brain homogenates are shown in Table II; the results show that Sulpiride at highest concentration (10^{-2}) significantly inhibits the oxygen utilization. Lower doses of sulpiride (10^{-3} and 10^{-4}) do not have any significant inhibitory action on the oxygen uptake, either by brain slices or by brain homogenates.

Discussion. The excess of potassium in the incubation medium increases the oxygen uptake in rat's brain slices. These data agree with those of ASHFORD and DIXON[11] and DICKENS and GREVILLE[12]. According to our data, the absence of calcium in the medium, using air as gas phase, did not enhance the oxygen utilization. These results are in disagreement with BUCHEL's data[2], but this author used O_2 as gas phase.

Sulpiride appears to have a depressor effect on the oxygen uptake in vitro only at very much higher concentrations than those which might be considered pharmacologically active. For that reason, we cannot suppose that the inhibition of oxygen uptake induced by Sulpiride will be the mechanism of its action on the central nervous system. This inhibiting effect appears more evident when the oxygen uptake was previously stimulated by higher potassium concentrations in the medium, in such manner as occurs with several central nervous system depressors in the same experimental conditions[5,6]. However, the presence or the absence of calcium in the medium did not influence the depressor effect of Sulpiride on the oxygen uptake in vitro.

Resumen. El Sulpiride in vitro a la concentración de 1×10^{-2} M disminuye el consumo de Oxígeno en cortes de cerebro de rata. El exceso de potasio o ausencia de calcio en el medio de incubación, no modifican este efecto. En homogeneizado de cerebro total, unicamente a la concentración de 1×10^{-2} M deprime el consumo de oxígeno. A las concentraciones 1×10^{-3} y 1×10^{-4} M no modifica el consumo de oxígeno en cortes ni homogeneizados de cerebro.

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Ultrastructure of Renal Collecting Tubules Following Ingestion of a Bipyridinium Herbicide (Morfamquat)

Morfamquat dichloride (MFQ), 1, 1′-*bis*(3,5-dimethylmorpholinocarbamylmethyl) 4,4′ bipyridylium dichloride dihydrate, is a herbicide for farm and garden[1]. Similar to other bipyridinium compounds it reacts with the atmospheric O_2 to form labile hydroperoxides, which in turn give off activated oxygen.

High toxic doses of MFQ produce degenerative changes and necrosis of the proximal convoluted tubules in the kidneys of rats and dogs, whereas a low dietary concentration (0.015%) has been reported by FERGUSON et al.[2] to cause a marked increase in the number of mitochondria in the epithelial cells of the collecting ducts of Alderley Park strain rats.

A phenomenal increase in mitochondria is the hallmark of the oncocyte, a peculiar epithelial cell type seen in various human organs[3]. Since the factors leading to the development of oncocytes are not known and animal models for them have not yet been found, the experimental production of oncocyte-like cells appeared to possibly offer insight into the ultrastructural changes preceding or accompanying their development. The present communication reports the results of an attempt to induce mitochondrial proliferation in collecting duct cells by feeding low dietary concentrations of MFQ.

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