the important question of their possible participation in pathophysiological conditions which affect the middle ear compartment. In recent experimental studies it has been shown that the initial effusion material in otitis media with effusion (OME) originates from the attic space - the compartment which is laterally bordered by pars flaccida[12]. Moreover the induction of effusion e.g. by a blocked tympanic isthmus or mechanical stimulation of the external auditory canal is accompanied by a degranulation of the pars flaccida mast cells and a subsequent release of histamine into the middle ear cavity[6,13]. It has also been found that onset of effusion may be brought about by instilling the potent mast cell degranulating drug, compound 48/80, into the external auditory canal[4]. The mechanisms involved in this pathological entity are at present being further explored.

1 Acknowledgments. The study was supported by grants from the Swedish Medical Research Council (B83-17X-06578-01), the Magnus Bergvall Foundation and the Medical Faculty, University of Umeå.

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0014-4754/83/030287-03$1.50+0.20/0

Diethylpropion decreases food intake in fish[1]

W. Mrowka

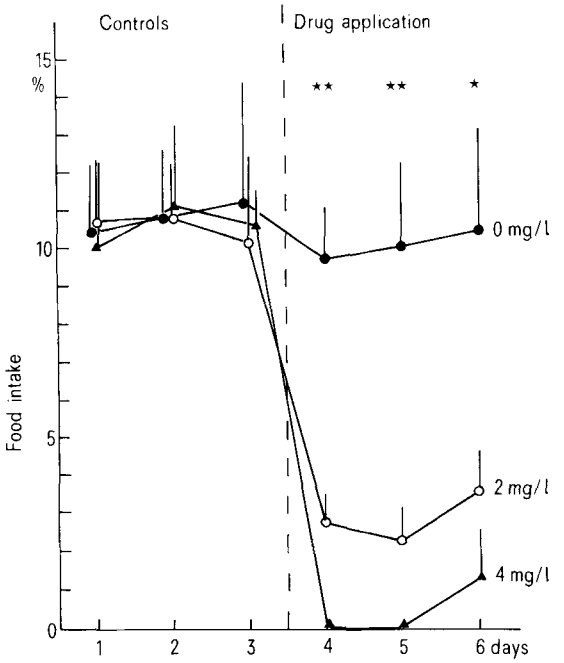
Zoologisches Institut, Technische Universität Braunschweig, Pockelsstrasse 10a, D-3300 Braunschweig (Federal Republic of Germany), June 18, 1982

Summary. Daily food intake of 5 specimens of *Haplochromis burtoni,* measured in a 30-min feeding session, was reduced by the application of water solutions of 2 and 4 mg/l diethylpropion (2-diethylamino-propiophenon).

Diethylpropion (2-diethylamino-propiophenon) is known for its anorectic effects in rats and dogs[2-7]and is used therapeutically in man[8,9]. The purpose of this study was to investigate how this anorectic drug influences feeding in fish.

Material and methods. 5 nonbreeding female *Haplochromis burtoni (Cichlidae)* served as test animals. Their weight ranged from 4.8 to 7.7 g. They were housed individually at 27 °C in optically isolated tanks containing 5-6 l water and fine gravel. A daily 30-min feeding session was held between 14.00 and 15.00 h. In preparation for this feeding session, 1-1.5 g Tubifex worms per fish were washed, dried for 5 min on blotting paper, weighed (with an accuracy of 10 mg) and then placed in special feeding containers, each consisting of a small pot (2 cm diameter) with a perforated plastic cover. The Tubifex worms could not leave the container on their own, but the fish could pull them out. At the end of the feeding session the remaining Tubifex worms were washed, dried and weighed again as described above. The differences between the initial weights and the end weights were expressed as a percentage of the body weight of the individual fish. The same 5 fish were used in 3 consecutive experimental series with an interval of at least 1 week between each series. One week proved ample time for complete recovery from previous experimental effects on daily food intake. Each series began with 3 days of normal feeding according to the schedule described above. On day 4 at 9.00 h diethylpropion was added to the tanks so that the concentrations were 0 mg/l (controls), 2 mg/l and 4 mg/l respectively. Water conditions remained unchanged for the next 3 days. Then the solutions were replaced by fresh water.

Results. As can be seen from the figure, diethylpropion decreases dose-dependently the daily food intake of the fish. Application of 4 mg/l results in a complete inhibition of feeding. Intermittent observation of the feeding behavior of the fish during the feeding session did not reveal any



Effects of different concentrations of diethylpropion on daily food intake (in percent b.wt) of 5 *Haplochromis burtoni.* Means and SD. Differences were tested using Friedman's 1-way analysis of variance; * $p < 0.05$; ** $p < 0.001$.

pathological behavioral changes. There was, however, a slight decrease in general swimming activity.

Discussion. This is the 1st demonstration of the efficacy of an anorectic drug to reduce food intake in fish. From experiments on rats it is known that diethylpropion decreases dose-dependently the excitability of the hunger area in the lateral hypothalamus[10]. It may also be possible that it acts upon the satiation center of the ventromedial hypothalamus[11]. In fish, as in mammals, there is evidence for a hypothalamic feeding area (HFA)[12,13]. This HFA is situated near the lateral recess of the 3rd ventricle in the inferior lobe of the hypothalamus. It represents the general region from which low-threshold feeding responses can be evoked by electrical stimulation and the area in which bilateral lesions cause drastic reductions in feeding[14–16]. It may be possible that diethylpropion acts in fish in a way analogous to that in mammals by reducing the excitability of the HFA.

1 This work was carried out at the Institut für Biologie III der Universität Tübingen. Abt. physiologische Verhaltensforschung, Tübingen (FRG). I want to thank Prof. Dr H.M. Peters for suggesting this study, the Temmler-Werke, Marburg for providing the substance and Dr B. Schulz for improving the English.

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0014-4754/83/030289-02$1.50 + 0.20/0

Effect of ketoconazole and miconazole on skeletal muscle mitochondrial calcium transport system

K.S. Cheah and A.M. Cheah

Muscle Biology Division, Agricultural Research Council, Meat Research Institute, Langford, Bristol BS18 7DY (Great Britain), June 28, 1982

Summary. Both ketoconazole and miconazole inhibit the state 3 respiration induced by Ca^{2+}, stimulate the state 4 respiration during succinate oxidation, inhibit the uptake of Ca^{2+} and also induce Ca^{2+} release in the aerobic steady state of skeletal muscle mitochondria. Miconazole is twice as effective as ketoconazole.

Ketoconazole, cis-1-acetyl-4-(4-((2,4-dichlorophenyl)-2-(1H-imidazole-1-ylmethyl)-1,3-dioxalan-4-yl)methoxy)-phenyl)piperazine, and miconazole nitrate, 1-(2-(2,4-dichlorophenyl)2-((2,4-dichlorophenyl)methoxy ethyl)-1H-imidazole nitrate, are chemically related imidazole antimycotic agents reported to interfere with the biosynthesis of ergosterol in fungal[1,2] and yeast[3] cells. Several observations have indicated that these imidazole compounds interfere with the cellular permeability of yeast[4–6] by binding to the cell membranes and selectively inhibiting[6] the uptake of precursors of RNA and DNA and mucopolysaccharide. It is suggested that miconazole competes with divalent cations for the membrane binding sites, which results in alteration in cell membrane permeability and ultimately leads to leakage of amino acids, protein and cations[5]. Miconazole, at high concentrations, also affects the exchange of intracellular K^+ for extracellular H^+ in yeast[7] and competitively inhibits both the yeast plasma membrane-bound and lipid-reconstituted purified plasma membrane ATPase activity[8]. Yeast mitochondrial ATPase activity is inhibited 50% at pH 6.0 with 40 μM miconazole[9].

Ketoconazole, at high concentrations, has recently been shown[10] to inhibit calcium binding and accumulation, and to induce calcium release in sarcoplasmic reticulum. The Mg^{2+}-ATPase and the $(Ca^{2+} + Mg^{2+})$-ATPase activities are stimulated at low but inhibited at high concentrations of ketoconazole. This paper reports studies of the imidazole antimycotic agents specifically showing the effect of both ketoconazole and miconazole on the Ca^{2+} transport system of isolated skeletal muscle mitochondria.

Materials and methods. ATP, antimycin A, bovine serum albumin, murexide, oligomycin, rotenone and sodium succinate were purchased from Sigma Chemical Corp.; carbonyl cyanide *p*-trifluoromethoxy-phenylhydrazone (FCCP) from Boehringer Mannheim; crystalline *Bacillus subtilis* (Nagarse) proteinase from Teikoku Chemical Co.; ketoconazole and miconazole were kindly supplied by Janssen Pharmaceutica, Beerse; all other reagents were of analytical grade.

Mitochondria were isolated from porcine longissimus dorsi muscle immediately post-mortem with *B. subtilis* proteinase[11]. Oxygen uptake was determined with a Clark oxygen electrode (Yellow Spring Oxygen Monitor (Model 53)) in a total volume of 2.60 ml at 25 °C. The Ca^{2+}-stimulated respiration for succinate oxidation was carried out in a reaction medium (pH 7.20) containing 225 mM mannitol, 75 mM sucrose and 15 mM Tris-HCl in the presence of 5 mM P_i. The rates of Ca^{2+} uptake and efflux of skeletal muscle mitochondria were monitored in a magnetically-stirred cuvette (10 mm light-path) with murexide (92 μM) at 21 °C with an Aminco-Chance (DW 2A) dual-wavelength/split-beam spectrophotometer operating in the dual-wavelength mode at 540–507 nm. The reaction medium was identical to that used for measuring oxygen