which are arranged according to the increasing strength of the female expression in the partners.

A 5th kind of cross ♂♂×(♂♀), has been carried out between males and oocyte carrying individuals which have been taken from mass cultures, and must therefore be regarded either as stable females or as inducible hermaphrodites.

Results of crosses 1, 4 and 5 only are available at the present stage of the research and sex ratios of the IU progenies (therefore male-female ratios only) obtained from the 3 different crosses in both the Venezia and Napoli IV strains are given in table 2.

Statistically highly significant differences are demonstrated between the varying strengths of the male and female sex expressions of the parental phenotypes and the sex ratios of their offspring. In fact type 1 crosses, where the male expression of the parents is the highest, give also the highest proportion of males in the progeny of both the Venezia and the Napoli IV strain. Type 4 cross, with the highest expression of the female factors in the pairs, produces the highest proportion of female progeny and the mixed crosses of type 5, where pure females or female phase hermaphrodites have been introduced as egg bearing partners, give in both strains a number of female progeny which is consistently higher than in cross 1 where only hermaphrodites are present.

The following general conclusions can be drawn from the present experiments: 1. a new kind of hermaphroditism, the inducible hermaphroditism, is found among otherwise gonochoristic populations, which 2. is obtained through interactions between adult females - or female phase hermaphrodites - and juveniles. 3. The different crosses between inducible hermaphrodites, male and female individuals produce progenies whose sex ratios are correlated with the sex phenotypes of the parents. 4. Multiple sex genotypes, with different balances between male and female sex factors, are present in the populations, as well as in the mass cultures. 5. The variety of the sex phenotypes can be regarded as the result of the environmental interactions taking place between the different sex genotypes[7] available in the sexual gene pools.

It is suggested that the existence of multiple sex genotypes capable of interacting with one another at the level of the sex expression enhances the probabilities of forming fertile pairs, especially in small, isolated populations.

Table 2

Strains	Crosses	Progenies Males	Females
Venezia	1 ♂♂×♂♀	60 (57.14%)	45 (42.86%)
	5 ♂♂×(♂♀)	32 (45.71%)	38 (54.29%)
	4 ♂♀×♀♀	7 (22.58%)	24 (77.42%)
Napoli IV	1 ♂♂×♂♀	62 (67.39%)	30 (32.61%)
	5 ♂♂×(♂♀)	59 (57.84%)	43 (42.16%)

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Ketoconazole - a new broad spectrum orally active antimycotic[1]

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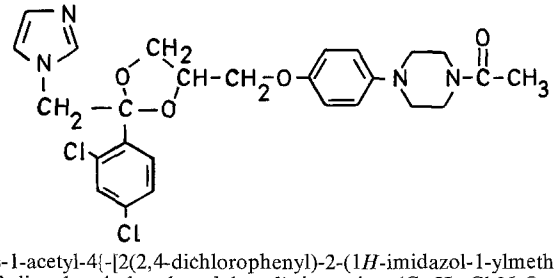
Summary. Oral treatment with ketoconazole prevented and cured artificial crop candidosis of the turkey, vaginal candidosis of the rat and skin candidosis of the guinea-pig. It was also highly effective against artificial systemic candidosis of the guinea-pig and chicken as well as against dermatophytoses of the guinea-pig.

We wish to report the discovery of a new orally active antimycotic agent with broad spectrum activity (table) against a wide variety of yeasts, dermatophytes and dimorphic fungi: ketoconazole (R 41400; figure) an imidazole derivative chemically related to miconazole[2-4].

When administered for 10-14 days at dietary levels of 16-63 ppm corresponding to oral doses of 2.5-10 mg per kg b.wt, ketoconazole is effective against crop candidosis of young turkeys, the disease being induced by gavage into the crop of $4 \cdot 10^6$ cells of *Candida albicans* (strain B 12377 isolated from crop candidosis of a partridge) with final assessments made 14 days later. This prophylactic and therapeutic effectiveness is almost 100% from doses of 5 mg/kg onwards.

At oral doses of 2.5-10 mg/kg b.wt, ketoconazole is also capable of preventing and curing vaginal candidosis in ovarectomized and hysterectomized Wistar rats, kept in pseudopregnancy by weekly injections of 0.1 mg of oestradiol undecylate and infected intravaginally with $8 \cdot 10^5$ cells of *C. albicans* (strain B 2630 isolated from trush of a parrot). High prophylactic activity was also found against artificially induced skin candidosis in guinea-pigs[5] at doses of 10 mg/kg b.wt, given orally for 14 days.



cis-1-acetyl-4{-[2(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-ylmethyl)-1,3-dioxolan-4-ylmethoxy]phenyl}piperazine. ($C_{26}H_{28}Cl_2N_4O_4$; mol.wt 531.4). Serial number R 41400. Generic name ketoconazole.

Effectiveness of oral treatment with ketoconazole in artificial mycoses.

Animal species	Infection site	Treatment mode*	Number of animals with complete cure versus total number of infected animals at stated doses (mg/kg)					
			0	2.5	5	10	20	40
Candida albicans								
Turkey	Crop	prop.	0/18	16/22	13/14	-	-	-
Turkey	Crop	ther. 10**	0/28	10/19	18/19	10/10	-	-
Rat	Vagina	prop.	0/106	21/26	22/22	-	-	-
Rat	Vagina	ther. 5**	0/17	1/5	27/30	18/18	-	-
Rat	Vagina	ther. 3**	0/62	-	3/6	83/85	6/6	-
Guinea-pig	Skin	prop. a)	0/22	10/17	-	20/22	-	-
Guinea-pig	i.v.	prop. a)	0/15	4/6	6/11	15/15	-	-
Chicken	i.v.	prop.	0/18	3/6	6/6	12/12	-	-
Trichophyton mentagrophytes								
Guinea-pig	Skin	prop. a)	0/12	-	1/12	5/11	10/10	-
Guinea-pig	Skin	ther. b)	0/10	-	-	5/11	12/12	-
Microsporum canis								
Guinea-pig	Skin	prop. a)	0/20	-	-	3/22	24/24	-
Guinea-pig	Skin	ther. b)	0/10	-	-	6/12	6/12	11/12

* prop.: prophylactic treatment: starts either day of infection or 24 h prior to infection a); ther.: therapeutic treatment: starts 72 h after infection or 48 h after infection b). ** The duration of treatment was 14 days except when indicated.

Oral doses of 5 or 10 mg/kg b.wt and given for 14 days are 100% effective against systemic candidosis in chickens and guinea-pigs, respectively. The disease, induced in adult male guinea-pigs by injecting $8 \cdot 10^6$ cells of *C. albicans* (strain B 2630) in a lateral vein of the penis, resulted in the death of at least 50% of the control animals during the 2nd week after infection, with all survivors showing generalized deep candidosis and pronounced mucocutaneous candidosis. Systemic candidosis in young Hysex chickens was induced by i.v. administration of 10^8 cells of the same *C. albicans* strain.

The oral activity of ketoconazole against dermatophytoses was evaluated in guinea-pigs artificially infected on the back with either *Microsporum canis* or with *Trichophyton mentagrophytes*[3], it was found to be excellent both prophylactically and therapeutically at dose levels of 10–40 mg/kg b.wt given for 14 days.

The details of these and other investigations to delineate the compound's in vivo and in vitro chemotherapeutic spectrum of activity, its safety, mechanism of action, metabolism, etc. will be published in subsequent papers. Clinical studies are underway.

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Tsetse fly feeding sites (Diptera: Glossinidae)

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Summary. Tsetse flies are attracted to radiant heat, but do not use mammalian skin energy flux differentials to find sites from which blood is obtainable. Tsetse flies only feed where the pelt is less than 5 mm thick.

Tsetse flies are attracted to hosts from a distance by visual and olfactory cues[2–8]. But at short range it would be interesting to know if tsetse flies are attracted by radiant heat and use mammalian skin energy flux differentials to find sites which could provide a blood meal.

Materials and methods. All experiments were performed at 25 °C, 80% relative humidity and under an illumination of 120±20 lux. Live pupae of *Glossina morsitans* Westwood and *G. austeni* Newstead were obtained from the Tsetse Research Laboratories, Langford, Bristol. Pilot experiments and stereo electron micrographs of tsetse fly mouthparts failed to reveal any sex feeding habit differences and both sexes have been used in all experiments. Radiant energy flux of mammalian skin was measured with a Moll thermopile held 2.5 cm from the skin and the output recorded on a Solatron Digital Voltmeter. The thermopile gave 40±5% mV/W/cm^2, with a response time of 2 sec. A mean of 10 readings taken as the final result. A linear response with the amount of energy flux radiated was obtained[9]. Measurements were made on guinea-pig and rabbit, and the results given in table 2. The reactions of flies to radiant heat was tested using an 800 ml conical flask painted matt black, placed against either end of a cage 76×48×48 cm formed from a metal frame covered with black nylon netting. The flask was filled with hot water at 30–50 °C and the control flask at 25 °C. Tests showed the nylon netting prevented convection currents forming within the cage. In each experiment 10 unfed teneral flies were introduced into the cage and subjected to 12 h light and 12 h darkness for 2 days. At the start of the 3rd day, the hot flask was placed