دراسة مقارنة على تأثير مركبات انستاتين على الفطريات المختلفة

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الملخص العربى

تم فى هذا البحث دراسة تأثير مرهم النستاتين العادى والمرب . وكذلك عجينة النستاتين – العادية والمركبة ٠

كما تم دراسة تأثير خليط من النستاتين والتولنفتات على أنواع متعددة من الفطريات ٠

وقد وجد نتيجة لهذه الدراسة أن جميع مركبات النستاتين لها تأثير واسع الناطق على أنواع كثيرة جدا من الفطريات – كما وجد أن للتولنفتات تأثير على الفطريات السطحية (التى تصيب الجلد) وأن خليطا من الاثنين – النستاتين والتولنفتات – يمكن أن يكون له تأثيرا كبيرا على العدوى نتيجة الاصابة المشتركة من الخمائر والفطريات التى تصيب الجلد ٠

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COMPARATIVE STUDIES ON THE ANTIFUNGAL EFFECT OF DIFFERENT "NYSTATIN" PREPARATIONS

(With one table and 3 figures.)

By

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(Received 7/7/1976)

SUMMARY

The effect of nystatin ointment, nystatin E. comp. ointment. nystatin paste, nystatin E. comp. paste and a mixture of tolnaftate and nystatin on different types of fungi was studied.

It was found that nystatin preparatios was effective against a wide range of fungi. Tolnaftate was effective against dermatophytes and the combination of both would be useful in the treatment of mixed infection due to yeast and dermatophytes.

INTRODUCTION

The importance of treatment of mycotic infection due to yeast has recently increased in Egypt. This may be due to the recognitinon of the role of yeast as causitive organisms of different diseases in man and animals all over the world (AJELLO , 1953 ; GORDON, 1953 ; LA TOUCHE ; 1960 ; PROCHAKI, and BIELUNSKA, 1962 ; REFAI and RIETH, 1964 ; STOCKDAIE, 1968 and REFAI and ABDULLA 1971).

Mycotic mastitis is a known infection among animals. Although general types of yeasts were isolated from such cases, yet *Candida* Species were the most common aetiology of this disease. *Candida tropicalis, candida pelliculosa* (REDAELLI, 1957), *Condida krusei, Candida parapsiolosis* and *Candida pseudotropicalis* (MEHNERT, 1962; BISPING et al. 1964). *Candida albicans* (BISPING, 1961, REFAI 1966) proved to be the cause of mastitis.

Long adminstration of broad spectrum antibiotics as predisposing to yeast infection among man and animals was proved by many workers.

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HULSE (1952) and REDAELLI (1957) proved that antibiotic admin stration is an importent factor in yeast infection of the udder.

Nystatin, which is a tetraene polyne antibiotic was discovered by HAZEN and BROWN in 1950 and has a wide spectrum including all pathogenic and nonpathogenic yeast, and also filamentous fungi. (NEWCOMER, et al. ; 1956).

The numerous studies on different animals show a definite activity and low toxicity of nystatin by oral route and very favourable activity in systemic mycosis by paretral route, but not by the oral route due to poor absorption. It is considered to be the first antifungal antibiotic widely used in human infection and as a counter - acting control for *Candida* infection due to long antibiotic therapy Oral adminstration is not always satisfactory due to poor absorption as STEWART (1956) demonstrated that local application is effective.

It was our aim - in relation to the above mentioned series - to study various preparations of nystatin suitable for application on the skin and mucous membranes infection on different types of fungi. Also a combination of nystatin with Tolnaftate was tried too.

MATERIALS AND METHODS

a) The following preparations were used :

1. *Nystaytin - oinment* :

(Nystatin 10 Mio . E., Polyethylene - paraffin base ad 100.0 g)

2. *Nystatin E. comp . ointment* :

(Nystatin 10 Mio E. 9-flour - 11 B, 17, 12 trihydroxy - 16 - methylene pregna - 1,4 dien - 3, 20- dien - 21 accetate, 0.05g. 5, 7- dichloro - 8- hydroxy chinoldin, 1.09 , polyethylene - paraffin base ad 100.0 g).

3. *Nystatin paste* :

(Nystatin 10 Mio . E modified starch titandioxyde, triglyceride, Isopropyle mynistinet, Sarbitonseoquioloeat, hard paraffin, white vaseline ad 100.0 g)

4. *Nystatin E. comp. paste* :

As preparation No . 3 + Fluprednyliden - 21 - accetate 0.05 g and 5, 7 - dichlor - 8 hydroxy - chinoldin 3.08 .

Kimming agar plates were inoculated densely with different types of yeasts (*Candida albicans, C. parapsilosis, C. krasei, C: guilliermondii, C. tropicalis, C. pseudotropicalis, Torulopsis formate* and *T. glabratd.* Four pores of 10 mm. in diameter were made in every plate and filled with the ointment or paste.

The inhibition Zones were measured after one week. In order to study the relationship between the rate of release of nystatin and the inhibition of yeast, the pores in the 4 plates were filled with nystatin ointment and inoculated with *C. albicans* simultaneously, after 2, 4, and 24 hours respectively

Moreover, the relationship between the amount of inoculated yeast and inhibition zones was studied by inoculating 1, 2, 3 and 5 loopfuls of the yeast culture respectively on plates within pores filled by the nystatin ointment.

b) Mixture of tolnaftate and nystatin :

A mixed suspention of *Candida albicans* and *Trichophyton mentagrophytes* was inoculated In the surface of kimming agar plate, Three pores were made; the frist one was filled with 5 drops of nystatin - suspention, the second with 5 drops of nystatin suspention and 5 drops of tolnaftate solution. The third was filled with solution of sodium chloride as control The inhibition zones were measured after 2 weeks.

RESULTS AND DISCUSSION

A) 1. / Nystatin preparations :

All types of yeasts tested showed inhibition zones around the nystatin paste or ointment. however the different types presented variable sensitivities against the preparation. *Candida albicans*, *C. tropicalis* and *T. glabrata* were sensitive to nystatin paste and ointment and more sensitive to the E. comp. preparations. On the contrary. *Tarulopsis famata* was resistant against the ointment or paste, but it was inhibited by E. the comp. preparations. *C. parapsiolosis* was less sensitive (see table 1).

2/ The measurement of the inhibition zone gives an idea about the potancy of the drug against the yeast; however this may be missleading as it was found that the diameter of the inhibition zone depends on the rate of diffusion of the drug. As shown in Fig. 1. the inhibition zone vary in diameter although the same preparation was used. The difference was only in the time elapsing between the filling of the pores with nustatin preparations and inuculation of the plates with the yeast. In Fig. 1. a the icoculation was performed simultaneously while this was made after 24 hours in (in Fig. 1. d)

3/ Relation between the amount of yeast inoculated and the inhibition zone: As shown in (Fig. 2) it is clear that the larger the amount of yeast icoculated the smaller is the inhibition zone. In (Fig. 2, a) where the plate was inoculated with one loopful, the inhibition was 42 mm. in diameter, while in (Fig. 2. d) the inhibition was about 21 mm. only where the plate was inoculated with 5 loopful.

B) Mixture of Nystatin and Tolnaftate :

The nystatin alone could inhibit the *C. albicans* and to a less extent *T. mentagrophytes* as seen in pore No. 1 in (Fig. 3). However, the *T.*

mentagrophytes grow at the border of the pore. On the other hand, the growth of both yeast and dermatophytes was markidly inhibited as shown in pore No. 2 Fig. 3. It is clear that the inhibition zone caused by tolnaftate was a big one reaching 5 mm. in diameter. The pore No. 3 in (Fig. 3) is a control one and shows no inhibition.

TABLE 1.—Inhibition zones in mm. (Average of 3 trials).

Types of yeast	Nystatin paste	Nystatin E. comp. paste	Nystatin ointment	Nystatin E. comp. oint.
Candida				
Parapsiolosis . . .	24	32	20	32
albicans	21	27	20	26
krusei	20	22	20	22
guilliermondii . .	20	34	24	30
tropicalis	22	30	22	30
pseudotropiecalis .	20	31	20	30
Torulupsis				
famata	—	33	—	31
globrata	22	32	22	28

The results obtained in this work indicated the wide range of effeciency of nystatin preparation on diffrent fungi. This support the work of HAZEN and BROWN (1950), NEWCOMER *et al.* (1956) and GOBBA *et al.* (1970). Also the combination of nystatin and tolnaftate found to be useful in the treatment of mixed infection due to yeast and dermatophytes.

ACKNOWLEDGMENT

Our sincerest thanks are due to Dr. M. K. REFAI Assistant professor of Microbiology, Faculty of Veterinary Medicine, Cairo Univeristy for identification and confirmation of the fungi in this work.

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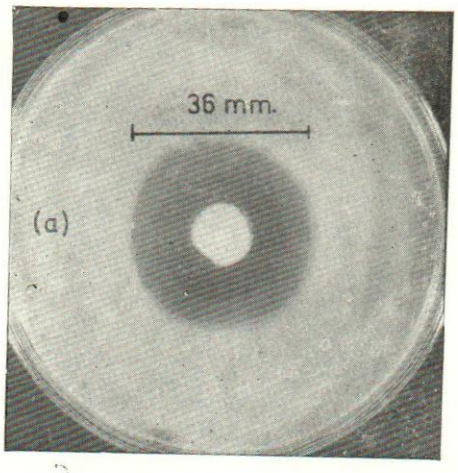

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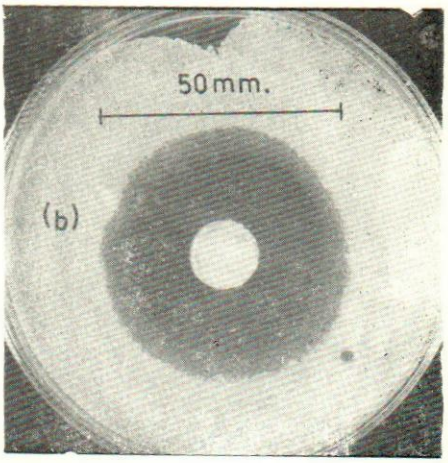

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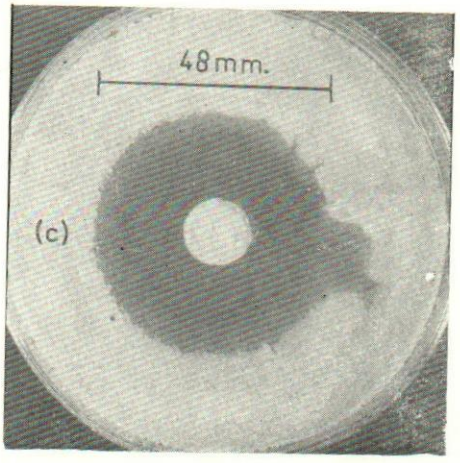

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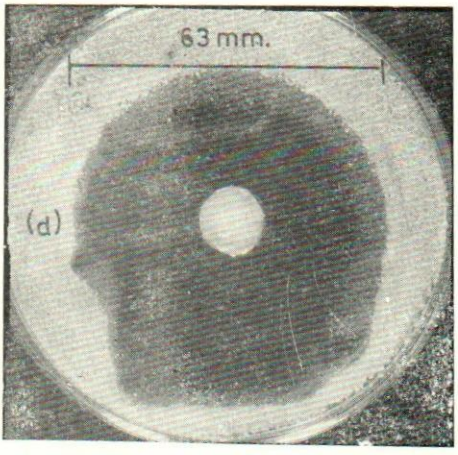

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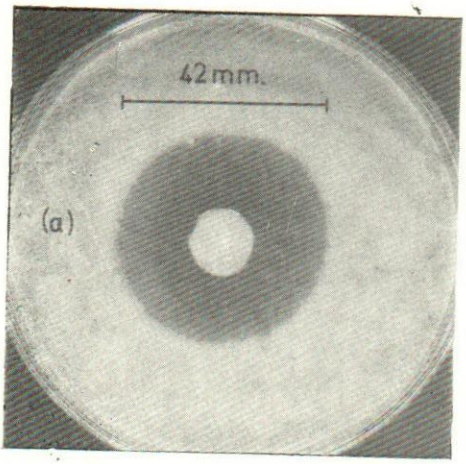
Fig. 1 : Relationship between the rate of nystatin diffusion and the inhibition zones.



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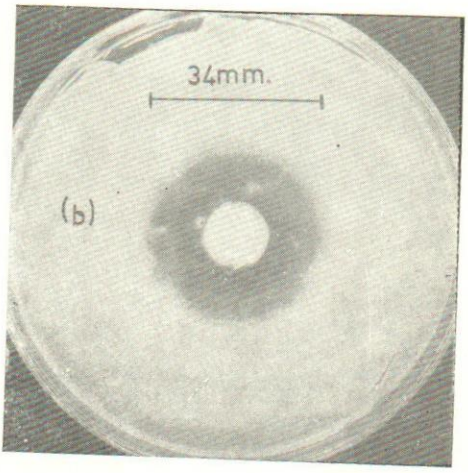

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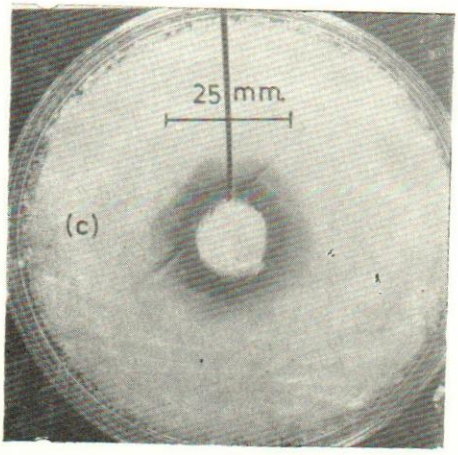

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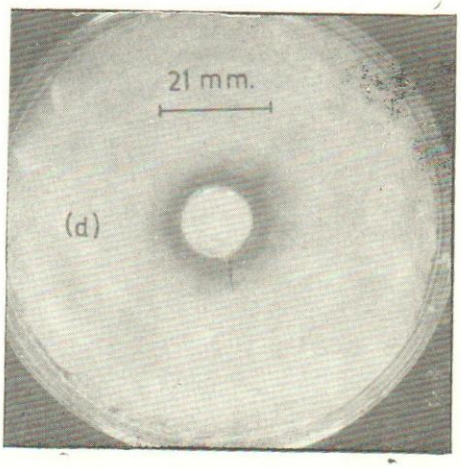

(d)

Fig. 2 : Relationship between the amount of yeast inoculated and the inhibition zones.

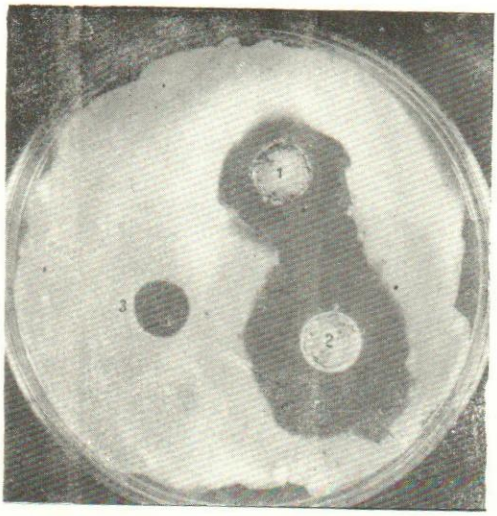

Fig. 3 : Effect of nystatin tolnaftate mixture on *C. albicans* and *T. mentagrophyte*.