

RESPIRATORY RESPONSES OF *CANDIDA ALBICANS* AS INFLUENCED BY NYSTATIN AND HYDROCORTISONE

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Summary

The R. Q. of *Candida albicans* indicates that fermentation goes side by side with respiration. Nystatin inhibited the respiratory rate of the organism, whereas hydrocortisone enhanced it.

The genus *Candida* is widely distributed in nature and *Candida albicans* which has a wide range of synonyms is shown to be the species most pathogenic to man causing candidiasis. There are considerable clinical and experimental evidences¹ to support that nystatin prevents and corticosteroid enhances the development of candidiasis. Topical application^{2,3,4,5}, experimental infection to human skin^{6,7}, experimental infection to animal⁸, growth rate in culture media^{8,9,10} and serum fluorescent antibody^{4,11} were among the evidences of the effect of such medicaments on *Candida albicans*.

In the present investigation, the respiratory quotient of *Candida albicans* and the effect of nystatin and hydrocortisone on the respiratory rate of the fungus were studied. The aim is to find out if these medicaments influence the intact cultured cells of the organism in their oxygen uptake.

Material and Method

Determination of respiratory quotient. Manometric technique¹² was

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used for this study. Warburg respirometer vessels (Fig. 1 page No. 65) were divided into two groups. The first group was used for oxygen uptake determination. Each vessel contained 62 ml. of fungal cell suspension. This suspension was prepared by suspending the fungal cells in equal volumes of Sabouraud broth and 0.1 M potassium phosphate buffer at pH 6.0. In the central well of the vessel, 0.2 ml. of 10% KOH solution was placed. The second group of the vessels resembles the first one but without KOH solution and serve for determination of CO₂ evolved. The respiratory quotient (R.Q.) values were determined every hour till a period of 5 hours from the following equation:

$$R.Q. = -CO_2/O_2$$

Effect of nystatin and hydrocortisone on the respiratory rate of Candida albicans. Nystatin (Mycostatin, E. R. Squib & Sons Ltd.) was used in the following concentrations: 2,500, 5,000, 7,500, 10,000 and 12,500 units/ml., whereas hydrocortisone sodium succinate (Efcortelan, Glaxo Laboratories Ltd.) concentrations used were: 20, 40, 60, 80, and 100 mg./100 ml. The medicament was placed in the side arm of the vessel. The vessels contained the fungal cell suspension,

and KOH solution was placed in the central as previously described. Control treatment was made similar to these treatments but without the medicaments. Warburg water-bath was set at 30°C. The oxygen uptake by the fungal cells was recorded every half hour till a period of 2½ hours after which the medicament, in the side arm, was added to the cell suspension, and the recording of oxygen uptake continued to another 2½ hours.

The cell number in the suspension at the beginning of the experiment was determined by using a haemocytometer. The amount of oxygen respired by 10 million cells was calculated and represented graphically.

Results

Respiratory quotient of Candida albicans. (Fig. 2 page No. 65) shows that the R.Q. values of *Candida albicans* were above 2 throughout the experiment, except at the second hour of inoculation, when the values recorded above 3.5. The high amount of CO₂ evolved indicates that fermentation goes side by side with respiration.

Effect of nystatin and hydrocortisone on the respiratory rate of Candida albicans. (Fig. 3 page No. 65) shows that the respiratory rate of the organism increases linearly with the increase in time to a period of three hours after which the organism shows a constant rate. Nystatin inhibited the respiratory rate of the organism and the inhibition increases with the increase in nystatin concentration. The high concentrations of the medicament cause a sudden drop in the respiratory rate after its addition by one hour. Also after this period of time the rate became low and constant in all concentrations.

Fig. 4 page No. 66 shows that hydrocortisone increases the respiratory

rate of *Candida albicans* as against the control. At high concentrations, 80 and 100 mg./100 ml., a sudden drop in the rate below the control was observed after 3 and 4½ hours respectively.

Discussion

There is a certain R. Q. for each substrate utilized during respiration, e.g. Carbohydrates have R. Q. 1. In the present investigation the R. Q. values of *Candida albicans* recorded high values. They were above 2 in all the experiments. Such values obtained indicate that fermentation runs parallel with respiration.

Lampen *et al*¹³ showed that the exposure of the yeast cells to nystatin causes an initial stimulation of oxygen consumption by the cells which is followed by a total cessation of respiration, at which point the cells are no longer found to be viable. On the other hand, the results of the present work show that nystatin inhibits the oxygen consumption of *Candida albicans* cells, and the increase in its concentration increases the inhibition of oxygen consumption. Such inhibition is possibly due to alteration of cell permeability to small ions which allow cellular potassium to escape from the cells, thereby halting glycolysis¹⁴. It is also believed that the medicament exerts its primary pharmacological action on the plasma membrane of the susceptible organism by binding to sterol sites on their surface¹⁵.

It is clear that hydrocortisone enhanced oxygen consumption (Fig. 4 page No. 66) by *Candida albicans* cells. This could be explained on the assumption that steroid hormones have the ability to induce marked changes in enzymes and some of these changes are in activity of microsomal oxidases, for which steroids themselves can serve as substrate¹⁶. Such enhancement of respiration by hydrocortisone accompanied by another enhancement of

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Fig. 1

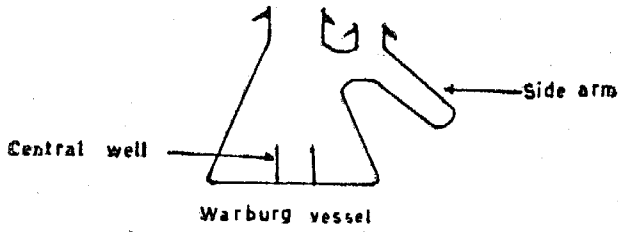


Fig. 2

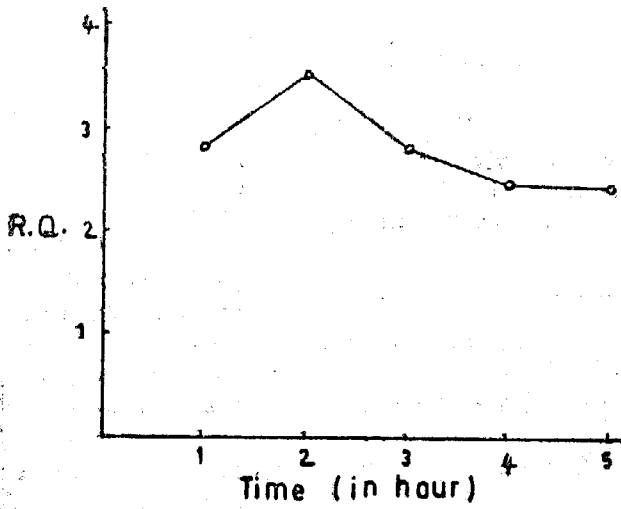
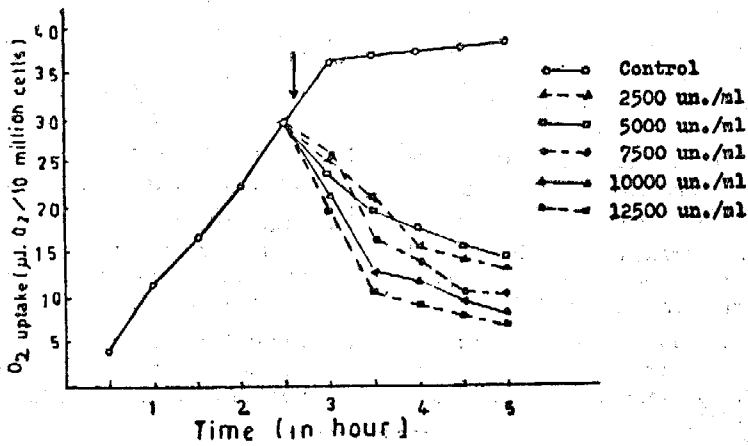
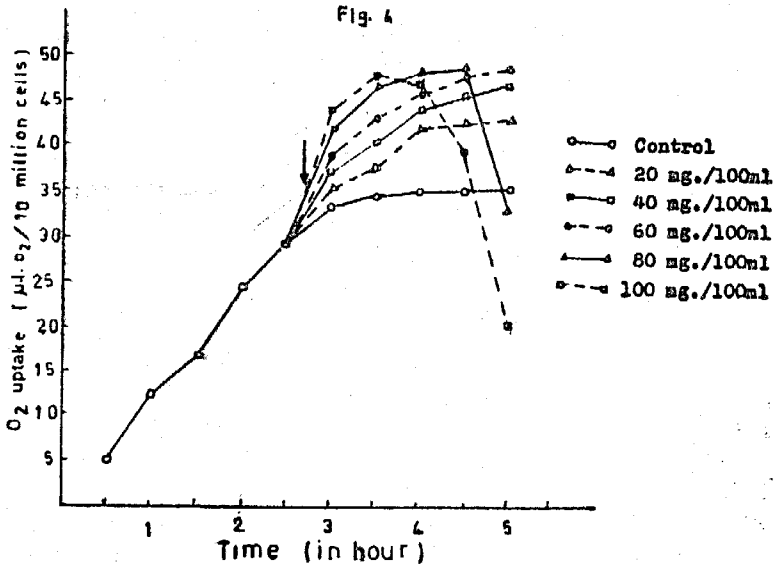


Fig. 2. Changes in R.Q. value

Fig. 3





growth as proved in vivo^{9,17} and in vitro⁹ studies could be the underlying factor of enhancing the candidiasis by corticosteroids.

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