EFFECT OF WATER SOLUBLE VITAMINS AND THEIR ANALOGUES ON GROWTH OF CANDIDA ALBICANS. III. PARA-AMINO BENZOIC ACID, NICOTINIC ACID, INOSITOL AND THEIR ANALOGUES

by

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(31.X.1963)

(with 9 figs.)

INTRODUCTION

A study of the vitamin requirements of Candida albicans employing wide ranges in vitamin concentration in basal mineral synthetic medium revealed that pyridoxamine and pyridoxine acted as metabolites (LITTMAN & MIWATANI 1963a). Both of these compounds shortened the lag phase of the organism and reversed the toxicity of the anti-nuclear compounds, 5-fluorouracil and 5-fluoro-2'-deoxyuridine. Alterations in the biotin structure caused pronounced effects upon its growth stimulatory activity. The organism was noted to possess a complete dependency for biotin and to be partially dependent upon vitamin B₁₂ and thiamine (LITTMAN & MIWATANI 1963b). Twenty-seven different substituted pyrimidines, thiazoles and related thiamine compounds were utilized by the organism. Additional studies of the effects of p-aminobenzoic acid, nicotinic acid, inositol, their analogues, and other water soluble vitamins on Candida albicans are reported herewith.

METHODS

Five strains of C. albicans of human origin were employed in the vitamin studies: American Type Culture Collection (ATCC) #10231, Communicable Disease Center (CDC) #B3 and #B37,
and Mount Sinai Hospital strains (MS) #33 and #191. The vitamin depletion of the cultures, preparation of inoculum, basal culture medium, methods of incubation and methods of growth measurements were identical with those described in previous publications (LITTMAN & MIWATANI 1963a, 1963b).

**Para-aminobenzoic Acid**

Addition to, or omission from, a vitamin mixture of 5 µg p-aminobenzoic acid/ml (PABA) did not materially alter the growth response of five strains of *C. albicans* in basal synthetic medium containing 50 µg biotin/ml (LITTMAN & MIWATANI, 1963a). Nevertheless, when PABA was incorporated in biotin basal synthetic medium in ascending concentrations (5 to 50 µg/ml), moderate stimulation of growth did occur (Table I and Fig. 1). The optimal concentration of PABA proved to be 30 µg/ml. To help corroborate that PABA was utilized as a vitamin by *C. albicans*, sodium gantrisin [N¹—(3,4-dimethyl-5-isoxazolyl) sulfanilamide], a PABA antimetabolite for *C. albicans*, was applied to the organism. The incorporation of 15 mg sodium gantrisin/ml in biotin basal synthetic medium caused marked inhibition of growth of vitamin depleted cells of *C. albicans*, CDC #B37 (Fig. 2). Addition of 30 µg PABA/ml initially, and after 18 hours of incubation, to these inhibited cells caused complete reversal of growth inhibition after 72 hours of incubation.

![Chemical structures](image)

**Table I**

<table>
<thead>
<tr>
<th>PABA Concentration (µg/ml)</th>
<th>Candida albicans #CDC-B3</th>
<th>Candida albicans #CDC-B37</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Days on Shaker</td>
<td>Days on Shaker</td>
</tr>
<tr>
<td></td>
<td>1 2 3 4 5</td>
<td>1 2 3 4 5</td>
</tr>
<tr>
<td>0</td>
<td>79 50 38 21</td>
<td>76 50 38 21</td>
</tr>
<tr>
<td>5</td>
<td>77 53 33 23</td>
<td>76 50 38 21</td>
</tr>
<tr>
<td>10</td>
<td>77 53 34 22</td>
<td>78 54 38 20</td>
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<tr>
<td>30</td>
<td>74 49 20 17</td>
<td>78 55 39 21</td>
</tr>
<tr>
<td>50</td>
<td>71 44 28 21</td>
<td>72 47 30 22</td>
</tr>
</tbody>
</table>

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\[ \text{NH}_2 \quad \text{—} \quad \text{COOH} \]

\[ \text{NH}_2 \quad \text{—} \quad \text{SO}_2 \text{NH} \quad \text{N—} \quad \text{CH}_3 \quad \text{CH}_3 \]

\[ p\text{-Aminobenzoic acid} \]

\[ \text{Gantrisin [Sulfisoxazole; } \text{N¹—(3,4-Dimethyl-5-isoxazolyl)} \text{ sulfanilamide]} \]