INHIBITION OF PSORIATIC SKIN ALKALINE PHOSPHATASE BY LEVAMISOLE

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Summary

The inhibition of psoriatic skin alkaline phosphatase by the anthelmintic drug levamisole was studied. It was shown that "in vitro" levamisole is an extremely effective inhibitor of the enzyme. A possible role of levamisole in the treatment of psoriasis is suggested.

It has been demonstrated that the alkaline phosphatase level of the psoriatic plaque is tremendously elevated as compared to normal skin.[1] Inhibitors of alkaline phosphatase can have therapeutic implications as the physiological role of alkaline phosphatase in the skin may be related to the keratinization of epidermis and in the endothelium of small vessels its function could be that of aiding the transfer of materials to and from the vessels.[2] Biochemical and cytochemical studies have shown that the anthelmintic drug levamisole is a potent, non competitive, organ specific inhibitor of alkaline phosphatase from a variety of organs.[3] It was therefore planned to study the inhibition of psoriatic skin alkaline phosphatase by levamisole.

Material and methods :

Skin biopsies of uniform thickness and 5 mm diameter were taken by a trephine after a subcutaneous injection of 2% xylocaine hydrochloride. These were quickly washed and transferred to a glass mortar precooled to (—20C°). Biopsies from 10 patients were pooled and homogenized by grinding with 5 ml, 0.05 M glycine buffer pH 10.5. The homogenate was centrifuged at 4000 r.p.m. and the clear supernatant used for enzyme assay. Enzyme activity was measured according to the method of Bessey et al[4].

Briefly the reaction mixture (1.1) ml) contained glycine-3 0.05M, $Mgcl_2$ 5×10^{-4} M, p-nitrophenyl phosphate (Sodium salt) 5.5×10^{-3} M, homogenate 0.1 ml and various concentrations of the drug levamisole. Incubation was done at 37°C for 4 hrs. The reaction was stopped by adding 5 ml 0.02 N sodium hydroxide and the O. D. of the solution measured at 400 mu. Appropriate blanks and controls were also run and the percent inhibition of activity at various concentrations of inhibitor calculated.

Results :

Our results are shown in Fig. 1. Measurable inhibition of activity occurs at extremely low concentrations of levamisole (0.0125 M) percent. Inhibition increased with higher concentrations of levamisole and 83% of the activity was inhibited with 0.2 M levamisole.

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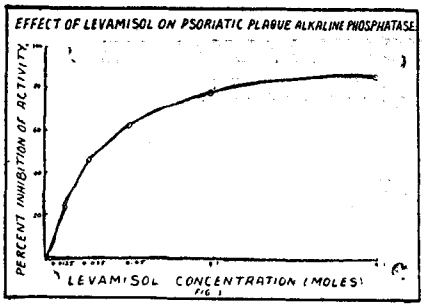

FIG. 1

Discussion :

To date there is no completely satisfactory systemic therapy for control of psoriasis. Drugs currently employed for controlling psoriasis like corticosteriods, methotrexate, azaribine and hydroxyurea have limited use because of their serious side effects. Photochemotherapy has recently been shown to be effective for controlling psoriasis[5] but is inconvenient to the patients who have to come daily to the hospital for exposure to U. V. light. We have previously shown that the alkaline phosphatase level of the psoriatic plaque is nearly 4 times that of normal skin. Mammalian alkaline phosphatase also acts as a pyrophosphatase[6] and may be involved in the polymerization of D.N.A. in the cell. In the endothelium of small vessels alkaline phosphatase could have the function of aiding the transfer of materials to and from the vessels[2]. In view of the above observations inhibition of skin alkaline phosphatase could have therapeutic implications for the treatment of psoriasis. Our studies confirm the effectiveness of levamisole in inhibiting the alkaline phosphatase of the psoriatic plaque in vitro and suggest a possible role of this drug for the treatment of psoriasis.

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