EFFECT OF PIDOTIMOD, A NEW IMMUNOSTIMULATING AGENT, ON SOME ASPECTS OF IMMUNE RESPONSE. IN VITRO STUDY.

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KEY WORDS
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INTRODUCTION

PIDOTIMOD is a synthetic compound which showed a positive effect on some immune functions both in animals and in humans (increased response to phytohaemagglutinin, increased cytotoxic activity of NK cells, normalizing of CD4/CD8 ratio of lymphocyte subpopulations, increased cutaneous responses to common antigens), [1-2]. In our study, PIDOTIMOD has been evaluated in experimental models, exploring several aspects of immune reaction.
The following aspects have been studied in detail:

- PIDOTIMOD effect on E-rosette forming lymphocytes, testing the drug both on cells of patients affected by immunologic disorders which depress this function spontaneously, and on pharmacologically depressed lymphocytes treated in vitro with adenosine;
- PIDOTIMOD effect on lymphocyte subpopulations and receptors: the whole T lymphocyte population (CD3), the helper/inducer (CD4) and citotoxic/suppressor (CD8) subsets, B lymphocytes (CD19), IL-2 receptor (CD25) and HLA-DR (HLA-DR) as markers of cell activation;
- PIDOTIMOD effect on complement system explored both through classic and alternate pathway;
- PIDOTIMOD effect on some PMN functions and in particular the oxidative metabolism evaluated as O_2^- production and phagocytosis evaluated as chemiluminescence associated with phagocytosis.

MATERIALS AND METHODS

Lymphocyte test: E-rosette forming cells (ERFC): Jondal's method modified.
Lymphocyte subpopulations and receptors: monoclonal antibodies (Ortho) and FACScan (Becton-Dickinson).
Complement activity: classic pathway: Mayer's method modified. Alternate parthway: Pillemer's method modified.
PMN functions: oxidative metabolism: O_2^- generation by spectrophotometric method.
Phagocytosis: induced by yeast and evaluated by chemiluminescence (RLU x 10^3 cells).
Pharmacological study: increasing concentrations of PIDOTIMOD were incubated before evaluating the various functions.

RESULTS

PIDOTIMOD was able to correct the inhibition of the E-rosette forming cells both spontaneously and pharmacologically induced; the drug maximum activity was at concentrations ranging from 50 to 100 μg/ml, reaching statistically significant values, compared with the basal ones. About lymphocyte subsets, we found that the drug did not modify either the whole T and B lymphocyte populations (CD3 and CD19) or the subsets (CD4 and CD8); on the contrary, an increased expression of IL-2 and HLA-DR receptors (CD25 and HLA-DR) was found. This finding might be very important, being these receptors the expression of a functional activation (Fig.1) Moreover, PIDOTIMOD showed an important effect on complement system: it potentiated in a significant way the complement activation both through the classic and the alternate pathway; the active doses ranged from 10 to 100 μg/ml. Regarding PMN functions, no effect was shown on O_2^- production, while PIDOTIMOD was able to potentiate phagocytosis significantly (active concentrations ranging from 10 to 50 μg/ml).

CONCLUSIONS

Our findings showed that PIDOTIMOD has an important effect on some aspects of the immune response, as previously shown by other authors [1-2]. In particular, the drug seems to play an important role especially on lymphocyte functions; in fact, it is able to correct the E-rosette forming deficiency and to induce lymphocyte activation, as meant by the increased expression of IL-2 and HLA-DR receptors. An

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important effect of PIDOTIMOD is also shown both in PMN functions, where phagocytosis was affected positively, and in humoral immunity, where a potentiating effect of complement system was found.
In conclusion our study confirmed that PIDOTIMOD may play an important role as immunomodulator, especially in cell-mediated immunity.

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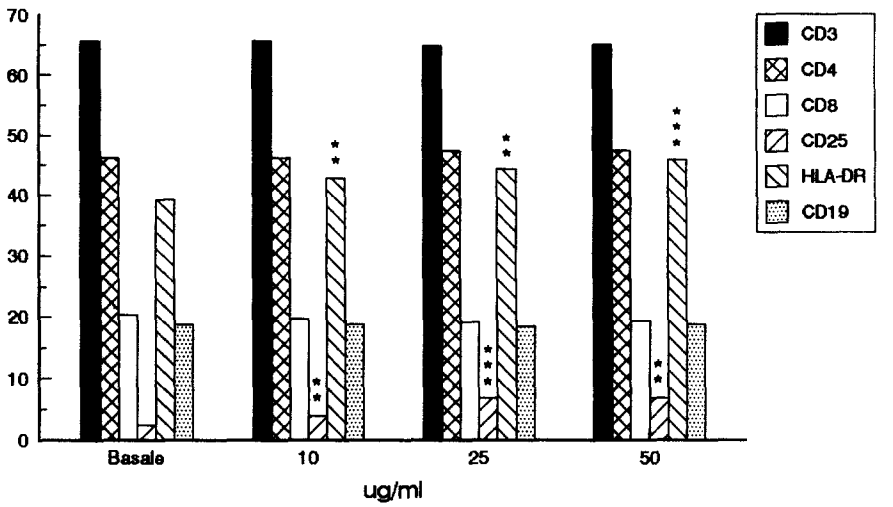

Fig.1 - Effect of PIDOTIMOD on lymphocyte subpopulations and receptors.