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Sensitisation for Specific Lysis in Target-Effektor-System with Derivatives of Chelidonium majus Alkaloids - Ukrain.

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Previous in vitro and in vivo studies and clinical results with immune-deficiency syndrome patients treated with Ukrain, a semisynthetic drug from alkaloids of Chelidonium majus L. and thiophosphoric acid (1) showed immune-stimulating and immune-modulating properties in various test systems. The experiments described here were designed to examine the possibilities of influence of the biocatalyst Ukrain in vitro system environments on certain cell-systems, such as effector-target.

As in the whole body environment immune mechanisms are very complex, depending on a lot of known factors like hormonal, neurogen and even psychic interconnections, in vitro experiments are more likely to show quantitative data in a comprehensive matter and so allow easy analysis of the different, well-defined determinants. The environment may be clearly defined and the level of expressions shown exactly. The often contrasting immunoregulatory activities may be well illustrated in model systems in which the main interferences are excluded.
Yac-1 cells (lymphomas), P815 (mast cell tumor) and WEHI (fibrosarcoma) were firstly tested as target in the Ukrain concentration of 0.1 and 100 ug/ml in the medium.
The following results were obtained:

after 5h incubation:	control	0.1 ug	100 ug
YAC-1	6.2	6.9	6.0
P815	5.9	5.9	5.2
WEHI	5.1	5.6	4.3
20h incubation:			
YAC-1	12	12	8.5
P815	14	13	8.6
WEHI	11	13	9.0
15h incubation:			
YAC-1	15	16	10
P815	20	19	12
WEHI	13	14	9.8

The higher the value of the lytic units the more efficient the NK population may work.
Especially YAC-1 cells, useful indicators for Natural Killer Cell activity are sensitive to Ukrain and P815, indicators for macrophage activity are already sensitive in the range of 0.1 ug/ml Ukrain concentration.
Sensitisation of tumor cells through Ukrain in concentrations (100 ug/ml) results in higher susceptibility against NK cells and macrophages.

Results:

Target:	control	1ug	100ug
YAC-1			
4h incub.	24.6	22.7	23.6
18h incub.	187.8	132.2	256.1
P815			
4h incub.	5	5	5
18h incub.	29.7	27.6	54.0

In another experiment (A.Liepins, Faculty of Medicine, St. John's, Newfoundland, Canada, personal communication) Ukrain was used in the concentration of 1,73 ug/ml where it enhanced the cytolytic response of spleen cells from alloimmunized C57/bl/6 mice. Similarly, the peritoneal exudate cells from these mice, which showed a cytolytic activity of approximately 8.0% in the absence of Ukrain, was also enhanced, but less than spleen cells. This data indicates that primed spleen cells have potentially cytolytic cells which respond more efficiently to Ukrain.
Spleen cells were collected at day 18 after alloimmunization and cultured in normal DMEM and FCS for 4 days in vitro or cultured in DMEM and 10 units/ml of rIL-2 which increased their cytolytic activity (controls). However, in the presence of Ukrain all types of spleen cells showed a dose-dependent increase in cytolytic activity, except perhaps at the highest dose (12.5 ug/225 ul).
The cytolytic activity of spleen cells was tested at various times after alloimmunization in order to determine whether there is an optimum time when spleen contains more Ukrain-responsive lymphocytes. On day 18 after alloimmunization the spleen cells respond to Ukrain with the highest increase of cytolytic activity (48 fold).
This data could partially explain the positive results in cancer patients treated with Ukrain (2) and suggest the direct influence of this preparation on target and effector cells. In a clinical study with small cell lung cancer (3) 50 percent of the patients treated with Ukrain are still in remission after 22 months.

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