Effect of Natural and Synthetic Peptides on the Biological Function of Leukemic Cells*

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A. Introduction

The goal of this work was to study the influence of some naturally occurring peptides and their analogs on the impaired biological properties of blood cells derived from leukemic patients. The effect of human tuftsin and of the insect neuropetide, proctolin, and their synthetic derivatives on the phagocytosis of granulocytes and the influence of proctolin and its analogs on the blastic transformation of lymphocytes were investigated.

B. Material and Methods

The phagocytic activity of granulocytes was determined in 30 patients with acute lymphoblastic leukemia (ALL). The lymphocyte transformation test was performed in 25 children with ALL and in a control group, consisting of 30 healthy children aged 2–12 years.

The phagocytic activity test was done according to the Steuden method, using ^{14}C-labeled *Staphylococcus aureus* 519 in the presence of tuftsin and its derivatives: Arg-tuftsin, Pro-Arg-tuftsin, Lys-Pro-Arg-tuftsin, and tuftsinyl-tuftsin [2–4]. The lymphocyte transformation test was performed using ^{14}C-thymidine in the presence of proctolin (Pr) and its derivatives: [Dopa^2]-Pr, (Homo-Arg)^1-Pr, [Phe(p-OMe)^2]-Pr, [Cha(-40Me)^2]-Pr, [Phe(p-NMe$_2$)^2]-Pr and [Phe(p-NO$_2$)^2]-Pr [1]. Both tests were performed in the initial phase of ALL and during complete remission on cytostatic therapy (Fig. 1).

A high stimulatory effect of tuftsin on the impaired PMN phagocytosis of patients in the initial phase of ALL was observed (67.4%). The influence of tuftsin on the phagocytic activity of granulocytes of ALL patients in remission was less striking. Tuftsin caused a decrease of phagocytosis of PMN in healthy children (Fig. 2).

The elongation of the tuftsin chain from the amino end resulted in a proportional decrease of the stimulatory activity of the subsequent peptides (Fig. 3).

It was found that proctolin restores the impaired phagocytosis of the ALL granulocytes to the normal level. A modification of the natural structure of proctolin by subsequent replacement of the -ON group in the aromatic ring of tyrosine by the -OMe, -NMe$_2$, and -ON$_2$ groups caused a lowering of this stimulatory effect. The proctolin analogs with 4-OMe-cyclohexyl and pNH$_2$-phenylalanyl did not influence the phagocytic activity of granulocytes (Fig. 4).

It was observed that the stimulatory effect of proctolin and its derivatives on the transformation rate of cultured lymphocytes was higher in those derived from patients who were in the initial stage of ALL than in those derived from patients in remission. Stimulation was higher in the presence of the analogs [Phe(p-NMe$_2$)^2]-Pr and (Homo-Arg)^1-Pr (63% and 59%). A less striking influence

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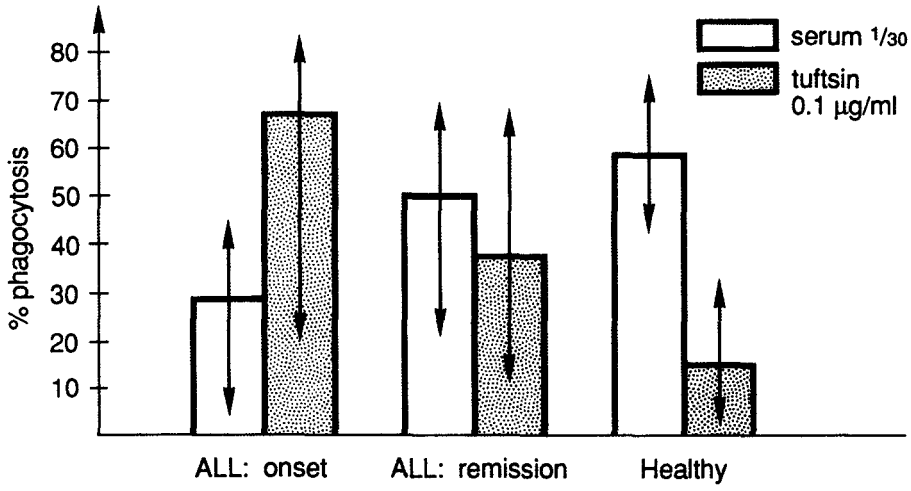
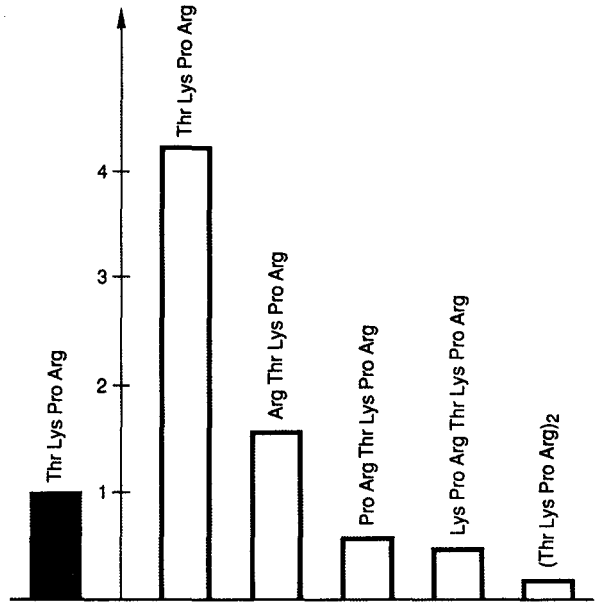
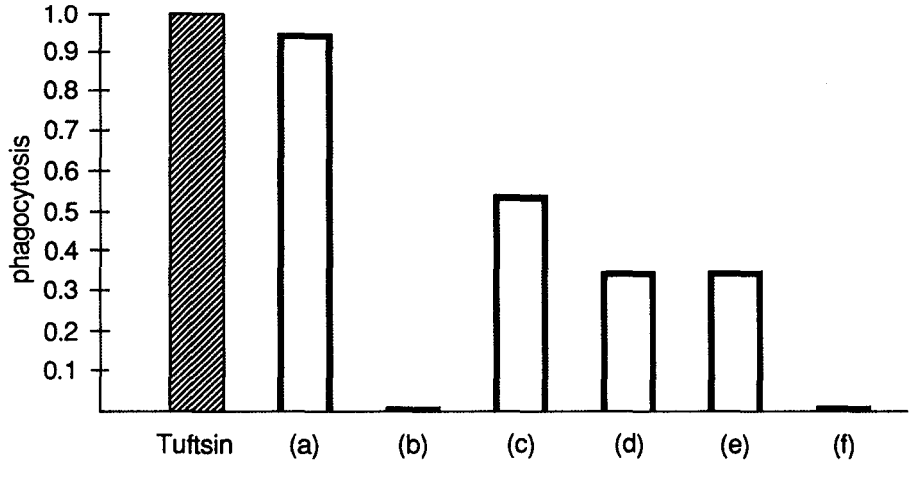


Fig. 1. Influence of tuftsin on the phagocytosis of ALL-affected and healthy PMN



	ALL: onset	Remission	Healthy
Tuftsin	4.3	2.4	1.0
Arg-tuftsin	1.6	2.0	1.1
Pro-Arg-tuftsin	0.6	0.5	0.7
Lys-Pro-Arg-tuftsin	0.5	0.2	0.3
Tuftsinyl-tuftsin	0.2	0.1	0.0

Fig. 2. Stimulatory effects of tuftsin and its analogs on the phagocytosis of ALL-affected and healthy PMN



a – Proctolin (Pr)
b – [Phe – $(pNH_2)^2$] – Pr
c – [Phe – $pOMe^2$] – Pr
d – [Phe – $(pNMe_2)^2$] – Pr
e – [Phe – $(pNO_2)^2$] – Pr
f – [Cha – $(4\text{-}OMe)^2$] – Pr

Fig. 3. Influence of proctolin and its analogs, relative to that of tuftsin, on the phagocytic activity of ALL-affected PMN

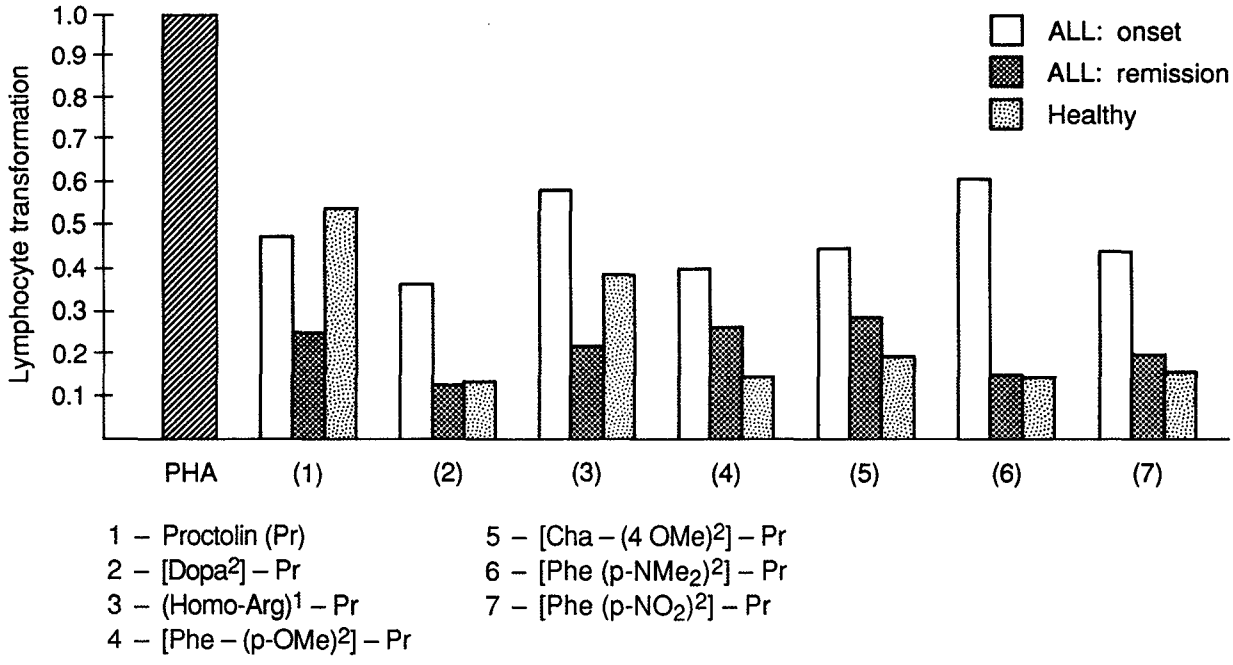


Fig. 4. Transformation of lymphocytes from ALL-affected and healthy children in the presence of proctolin and its analogs

on mitogenic activity was noticed when the other proctolin analogs were used (20%–30%).

C. Concluding Remarks

The high stimulatory effect of tuftsin and proctolin on the phagocytic activity of PMN derived from ALL patients was shown. A reduction in the phagocytosis of granulocytes of healthy subjects after preincubation with tuftsin, proctolin, and their analogs was observed, suggesting a regulatory effect of these peptides. The stimulating influence of tuftsin analogs on phagocytosis decreased with the elongation of the peptide chain at the N-terminal. A higher mitogenic effect of proctolin and its analogs was observed in cultured ALL lymphocytes compared with those of healthy children, which suggests a selective cytokinetic activity of the peptides studied.

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