Effects of therapeutic ribose levels on human lymphocyte proliferation in vitro

W. Pliml¹, T. von Arnim², C. Hammer³

¹ Medizinische Klinik, Klinikum Innenstadt, Ludwig-Maximilians-Universität München
² Medizinische Klinik I, Klinikum Großhadern, Ludwig-Maximilians-Universität München
³ Institut für Chirurgische Forschung, Klinikum Großhadern, Ludwig-Maximilians-Universität München

Summary. Ribose has been used successfully in the treatment of ischemic heart disease and muscular enzyme deficiencies, and its administration also facilitates the diagnosis of coronary artery disease by influencing thallium-201 scintigraphy. Concerns about the safety of ribose therapy have been triggered by reports about inhibitory effects of ribose on cell proliferation in vitro. This study examines possible side effects of ribose on human lymphocytes. Unstimulated and mitogen-stimulated human lymphocytes were incubated with ribose concentrations associated with high-dose oral administration, i.e., 3.5 mM, and with two- (7 mM) and tenfold (35 mM) higher concentrations. Cell cultures with matching glucose concentrations served as controls. Incorporation of [3H]thymidine into cells was used to measure cell proliferation. No significant inhibition of human lymphocyte proliferation in vitro was observed in mitogen-stimulated cells. Unstimulated cultures showed significant inhibition only at 35 mM ribose. It is concluded that ribose plasma levels associated with high-dose oral administration do not inhibit human lymphocyte proliferation in vitro. No evidence was found that short-term ribose therapy is harmful to human lymphocytes.

Key words: (D-)Ribose – Ribose side effects – Human lymphocytes – Ribose therapeutic use

Materials and methods

Blood from ten healthy volunteers (six women, four men) aged 21–41 years (mean 30.3) was collected aseptically from an arm vein and immediately heparinized. Within 1 h lymphocytes were separated by Ficoll-Isopaque gradient centrifugation, washed three times in culture medium (Iscoves, Behringwerke) and resuspended at a concentration of 10⁶ cells/ml. Of this cell suspension 0.2 ml, containing 2 x 10⁵ cells, was seeded in the wells of a round-bottomed culture plate (Nunc). Mitogens and D-ribose (Pharma-Waldhof) or glucose was added. The final ribose concentrations were 3.5, 7.0, and 35.0 mM with matching glucose concentrations. Phyto-
Results

Ribose concentrations of 3.5 mM, which corresponds to peak plasma levels achieved with high-dose oral administration in humans, and 7 mM did not inhibit \(^{3}H\)thymidine incorporation either in unstimulated or in mitogen-stimulated human peripheral blood lymphocytes (Fig. 1). None of the ribose concentrations tested (3.5, 7.0, and 35 mM) had any inhibitory effect in lymphocytes stimulated with phytohemagglutinin (Fig. 1b) or in those stimulated with pokeweed mitogen (Fig. 1c). A significant inhibition (\(P = 0.0001\) versus glucose; \(P = 0.001\) versus baseline) was found at a concentration of 35 mM ribose in unstimulated lymphocytes (Fig. 1c). Reduced counts in the ribose group at 7 mM were statistically nonsignificant (Fig. 1c). None of the control cultures supplemented with matching concentrations of glucose showed any significant inhibition.

Discussion

The clinical use of ribose requires information about possible side effects that might be harmful to patients. This study investigated ribose-induced inhibition of human lymphocyte proliferation in vitro. Earlier laboratory work unrelated to therapeutic interventions using ribose concentrations of up to 100 mM had indicated pronounced inhibitory effects. The purpose of this study was to examine