SUMMARY

The behaviour of L-rhamnose, a deoxyhexose which is synthesized in bacteria and plants but not in animal cells, in the mammalian organism, as well as its anticancer potency, is poorly known. In the present study, we examined the pharmacokinetics, behaviour on the blood-biliary barrier and the antineoplastic activity of L-rhamnose.

Our study is the first to describe in detail pharmacokinetic parameters and the biliary excretion of intravenously administered (100 $mg.kg^{-1}$) L-rhamnose in healthy and cholestatic rats. Despite the cumulative data having shown that this pathway takes only a negligible part of the applied dose of the sugar, the quick equilibration of L-rhamnose concentrations was seen between the plasma and bile which may be interesting for the future evaluation of biliary drug excretion with respect to bile production. We found that the dual-sugar permeability test with L-rhamnose and the disaccharide melibiose is a useful probe to describe the alteration of the blood–biliary barrier during acute extrahepatic cholestasis in rats. Using this test, we evidenced that the blood–biliary barrier becomes highly leaky in bile duct obstructed animals and that this impairment could be reliably measured during the first 60 min after administration of the probes. Importantly for sugar permeability studies in animals and humans, our data provide the evidence that overall results of intestinal mucosa integrity testing which are based on cumulative 5-h urine collection should not be altered by extrahepatic cholestasis.

The effect of unsubstituted deoxyhexoses, 2-deoxy-D-glucose (2-DG) and L-fucose, on tumor cells has been reported in several papers throughout the last decades. That of L-rhamnose has until today not been explored. We examined the effect of L-rhamnose on the DNA and protein synthesis, growth and the potential induction of apoptosis of tumor cells *in vitro*. Using 2-DG for comparison, we studied the effect of L-rhamnose in concentration up to 20 (32 resp.) $mmol.l^{-1}$ on the initial velocity of the incorporation of labeled precursors of DNA and proteins in short term cultures of mouse Ehrlich ascites tumor (EAT), a new mouse mammary adenocarcinoma MC29 and human HL-60 cells *in vitro*, and further, on cell proliferation and apoptosis induction in HL-60 cells. For the evaluation of the DNA and protein synthesis influencing, a method of dynamic monitoring of specific activities of DNA and protein fractions has been validated using conventional cytostatics, mitoxantrone and doxorubicin. The sensitivity of the new tumor MC29, syngenic in NMRI mice, was probed in an *in vivo* study with mitoxantrone. Neither cytotoxic nor cytostatic effects of L-rhamnose were observed with exception of slightly pronounced inhibition of DNA synthesis in EAT cells. From the lacking inhibition of the protein synthesis it can be considered that L-rhamnose does not interfere with the energy metabolism like 2-DG. Nevertheless, the hypothetical analogy of L-rhamnose to L-fucose in the influence on the behavior of tumor cells *in vivo* may retain unexplored potential of L-rhamnose that awaits future clarification.