

of trypsin was 50%, of bromelain, 45%, of amylase, 42%, of chymotrypsin, 38%, and of papain, 26%; that of lipase was not measurable. The highest proportion of undigested high molecular enzyme in serum was found after oral application of amylase (77%), trypsin (54%), and bromelain (52%); all other values were below 30%, including lipase (0%). Treatment of the edema of the hind limbs of rats with bromelain reduced the edema significantly (50%) within week 1 compared with the control animals.

From this observation, it can be concluded that enzymes applied orally can be absorbed from the gut partially in the undegraded form, and can significantly reduce inflammation and accelerate tissue repair.

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65 Hepatotrophic Effect of Folinic Acid

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In previous studies, we have demonstrated that normothermic liver ischemia hinders hepatic regeneration following 70% hepatectomy or CsA administration. This effect was partially reversed by antioxidant drugs. Of all the drugs tested, folinic acid showed the greatest effect, restoring the normal regenerative response. In the present work, we have tried to clarify whether folinic acid exerts its action through a pure antioxidant effect or has some additional hepatotrophic effect.

Material and Methods. Eighty Sprague-Dawley rats (250 g, male) were used. The different procedures were performed on ether-anesthetized rats through a midline laparotomy. Hepatic ischemia was induced for 15 min by clamping the porta hepatis with Yassargil clips. The superior mesenteric artery and the celiac trunk were also clamped to avoid splanchnic congestion. Folinic acid (2.5 mg/kg) was administered through the left femoral vein by means of a perfusion pump, just prior to reperfusion. When necessary, hepatectomy was performed just after reperfusion. All animals were sacrificed 24 h later, and fragments of liver were quickly removed and embedded in paraffin. The DNA contents of 100 hepatocytic nuclei were measured by means of a microcytospectrophotometer (Feulgen reaction). The regenerative capacity was expressed as the percentage of regenerating hepatocytes (% RH) and the regenerative gradient (ratio of DNA content of regenerating to static hepatocytes). The results were statistically compared using the rank sum test.

Experimental series: (1) normoperfused livers (control); (2) folinic acid administration; (3) 40% hepatectomy (Hep.); (4) 40% Hep. + folinic acid; (5) 70% Hep.; (6) 70% Hep. + folinic acid; (7) ischemic livers + 70% Hep.; and (8) ischemic livers + 70% Hep. + folinic acid.

Results. % RH at each stage: (1) 1.211%; (2) 5.071%; (3) 23.00%; (4) 25.65%; (5) 22.27%; (6) 41.03%; (7) 8.852%; and (8) 29.10%. RG at each stage: (1) 2.161; (2) 1.756; (3) 1.754; (4) 1.700; (5) 1.607; (6) 1.562; (7) 1.739; and (8) 1.955.

Conclusions. (1) Folinic acid showed a hepatotrophic effect, inducing hepatic regeneration on resting liver (1.211 vs. 5.071, $p < 0.005$), and also improving the % RH after partial hepatectomy (22.27 vs. 41.03, $p < 0.005$). (2) Folinic acid administration on normoperfused livers decreased the RG (2.161 vs. 1.752, $p < 0.0005$) as did the proved regenerative stimuli (partial hepatectomies). (3) Folinic acid increased the regenerative response following normothermic liver ischemia (8.82 vs. 29.10, $p < 0.0005$), reaching regenerative levels similar to those of normoperfused livers (22.27, $p = 0.146$). (4) Finally, folinic acid administration prior to reperfusion is effective in abrogating the deleterious effect of normothermic hepatic ischemia on hepatic regeneration.

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66 Kinetic Analysis of Work-cost Performance of the Liver

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Both increased energy metabolism during liver regeneration and decreased energy metabolism in jaundice deteriorate easily, resulting in liver failure. To clarify the impaired functional reserve in these opposing pathological conditions, energy transfer function in the rabbit liver was studied in terms of ADP_f , ADP, ATP, Km and V_{max} of mitochondrial ATP synthesis, v/V_{max} and $\Delta v/\Delta ADP_f$. As the physiological ATP synthesis velocity (v) is determined by ADP_f , the ratio ($\Delta v/\Delta ADP_f$) of increase in work output of ATP synthesis (Δv) relative to increase in biochemical input of ADP_f (ΔADP_f) indicates the work-cost performance of the liver.

Methods. Jaundiced rabbit liver at 24 h after bile-duct ligation and regenerating liver at 24 h after 70% hepatectomy were studied. Sham-operated rabbit was employed as a control. Free cytosolic ADP (ADP_f) was calculated from the measured components and equilibrium constants of the glyceraldehyde-3-phosphate