EFFECT OF ACUTE EXPOSURE TO ALCOHOL AND ALCOHOLIC BEVERAGES ON GASTRIN AND HISTAMINE RELEASE FROM THE DOG STOMACH

S. Bertini, L. Intorre, E. Luchetti, G. Mengozzi and G. Soldani
Laboratory of Veterinary Pharmacology, University of Pisa, Viale Piagge 2, 56124 Pisa, Italy.

The mediator for the action of ethanol on the parietal cell of the stomach is not known. However, since the action of ethanol on gastric acid secretion was proposed to involve endogenous release of gastrin (G) and/or histamine (H), we decided to investigate the effects of alcohol and some alcoholic beverages (red wine and beer) on G and H release from the dog stomach. After performing a splenectomy in anaesthetized beagle dogs, the gastrosplenic vein draining the corpus of the stomach was cannulated for blood withdrawal in order to evaluate local release of such transmitters. H and G concentrations in plasma were determined by RIA. Results Acute intragastric administration of 200 ml of beer (4.8% ethanol) or red wine (12.5% ethanol) caused a significant ($P<.05$) enhancement in G and H concentrations in venous blood after 10 min. The increase in G and H concentrations was similar with both beer and wine and lasted about 60 min. By contrast, intragastric administration of pure ethanol in distilled water at the same concentrations of wine (12.5% v/v) or beer (4.8% v/v) did not significantly modify G and H release. Integrated H responses for 20 min to beer and wine paralleled G concentrations and were of the same magnitude as those induced by intravenous infusion of pentagastrin (1 µg/kg/h). Conclusions We conclude that: 1) beer and red wine are potent releaser of G and H; 2) the ethanol content of these drinks is not important for their stimulant effect; 3) some other components of beer and wine are responsible for G and H release from the dog stomach.

PHARMACOLOGICAL EFFICACY OF DELTA-SLEEP INDUCING PEPTIDE UNDER ACUTE PANCREATITIS

T.I.Bondarenko, V.I.Rusakov, Yu.A.Kalmykova, I.I.Mikhaleva
Department of Biochemistry and Microbiology of State University and Department of Surgical Diseases N 2 of Medical University, Rostov-on-Don, Russia

The system of regulatory peptides(RP) turned out to be one of the most important organism regulatory systems.The use of RP as drugs promises the most physiological and direct medical influences.Being oligopeptides similar with metabolic products RP are effective in very low doses and not toxic.The elucidation of the role of delta sleep inducing peptide(DSIP),an antistress and hypnogenic brain modulator,is of significant interest.Oedematic form of acute pancreatitis(AP) which was simulated by injection of I% solution of Trithon X-I00 into parenchyma of pancreas was used as an experimental model of the pathology.Administration of DSIP at the dose of I2 mkg/I00 g body weight to animals with AP 3 times after the operation results in inhibition of increased lipid peroxidation,erythrocyte membrane stabilization,activation ofantioxidant enzyme catalase,and inhibition of protein autolysis in pancreas,liver, kidney,and blood serum.Thus,the research has shown that DSIP inhibits starting and strengthening mechanisms of the pathology development.

GASTRIN-INDUCED SUPPRESSION OF RAT STOMACH ECL CELLS

D.Chen, C-M. Zhao, P. Norlén and R. Håkanson
Department of Pharmacology, University of Lund, S-223 62 Lund, Sweden

The ECL cells are histamine-containing enterochromaffin-like cells in the acid-producing part of the stomach. They respond to gastrin with release of histamine and pancreastatin, activation of histidine decarboxylase (HDC) and growth. The effect of gastrin on the ECL cells is mediated by gastrin/CCK-B receptors. The present study examines the dose- and time-response relationships of rat stomach ECL cells to gastrin. Human Leu^{15}-gastrin-17, given by continuous intravenous infusion to fasted rats for 3 h, activated the HDC in a dose-dependent manner. The ED_{50} value was 0.2 nmol $kg^{-1}h^{-1}$ (corresponding to a serum gastrin concentration of approx. 250 pmol l^{-1}) and the ED_{100} value was 3-5 nmol $kg^{-1}h^{-1}$ (serum gastrin concentration of 500-700 pmol l^{-1}). The time-response relationship was studied first with an ED_{100} dose of gastrin. The activation of HDC by the ED_{100} dose reached a maximum 3 h after start of the infusion (25-35 pmol $CO_2mg^{-1}h^{-1}$ in fasted rats and 60-70 pmol $CO_2mg^{-1}h^{-1}$ in freely rats) and remained at this level for 16 h. Twenty-four h after start of the infusion, the HDC activity had declined to the pre-stimulation level in freely fed rats and to a level slightly higher than the pre-stimulation level in fasted rats. The enzyme activity remained suppressed thereafter (6 days in freely fed rats and 36 h in fasted rats). The maximum activation of HDC induced by ED_{50} gastrin was much higher than that induced by ED_{100} gastrin (140-150 pmol $CO_2mg^{-1}h^{-1}$ by ED_{50} and 60-70 pmol $CO_2mg^{-1}h^{-1}$ by ED_{100}) and the enzyme activity remained elevated throughout the experiment (6 days in freely fed rats). In conclusion, the activity of the ECL cells is suppressed in response to a sustained challenge with ED_{100} gastrin but not with ED_{50} gastrin.

ACTION OF A CALCIUM CHANNEL BLOCKER, PINAVERIUM BROMIDE, ON THE CCK-MEDIATED COLONIC MOTOR RESPONSE TO A MEAL IN RATS.

J. Fioramonti, M.O. Christen*, I. Dupré, L. Buéno
Department of Pharmacology, INRA, Toulouse and *Solvay Pharma/LTM, Suresnes, France.

Pinaverium bromide is a calcium-channel blocker used in the treatment of the irritable bowel syndrome. It has been recently shown that pinaverium bromide as well as other calcium antagonists, such as diltiazem, inhibit the contraction of intestinal smooth muscle cells induced by CCK. The aim of this study was to determine whether pinaverium bromide inhibits the postprandial colonic motor response that is controlled by a mechanism involving CCK.

In 2 groups of 6 rats equipped with nichrome electrodes, myoelectric activity of the proximal colon was recorded, after a 15h fast, for 15 min before and 60 min after a 3 g meal (group 1) or i.v. administration of CCK at a dose of 2 µg/kg (group 2). The effects of pinaverium bromide given orally (2, 5, 10 and 50 mg/kg), 1h before the meal or CCK, were compared to those of the CCK-A and -B antagonists, devazepide and L365260 (100 µg/kg, i.p.), and those of the calcium antagonist, diltiazem (10 mg/kg, per os).

Before the meal, the frequency of colonic spike bursts was 9.4±1.5/10 min. For the 10 min after the 3 g meal and CCK administration (2 µg/kg) the spike burst frequency reached 21.5±1.8 and 15.7±2.3/10 min, respectively. The postprandial spike frequency was significantly ($P<0.05$) reduced, in a dose-related manner, by pinaverium bromide (from 26.4 to 75.2 % for doses ranging from 2 to 50 mg/kg). It was reduced by 34.7, 28.1 and 19.8 % after devazepide (100 µg/kg), L365260 (100 µg/kg) and diltiazem (10 mg/kg), respectively. The colonic response to CCK was reduced by pinaverium bromide at the dose of 2 mg/kg (81.4 %) with a maximal effect (-116.3 %) at the dose of 5 mg/kg. It was also significantly reduced (-74.4 %) by L365260, but not by devazepide and diltiazem.

Ca-antagonists such as pinaverium bromide and diltiazem reduce the colonic response to eating in rats, but only pinaverium inhibits the CCK component of this response. This may be due to pharmacokinetic differences and emphasizes the interest of a GI selective calcium antagonist such as pinaverium bromide.