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DBM-819, given intraduodenally, inhibited basal acid secretion with an ED50 value of 3.5 mg/kg. In addition, DBM-819 reduced either histamine or pentagastrin-stimulated gastric acid secretion with ED50 values of 4.0 and 5.1 mg/kg, respectively. Duration of the anti-secretory effect was about 18 h upon oral administration. Oral administration of DBM-819 dose dependently protected the gastric lesions induced by ethanol, NaOH, indomethacin and aspirin, and the duodenal ulcer induced by cysteamine, with ED50 values of 7.0, 20, 3.1, 4.0 and 6.0 mg/kg, respectively. Taken together, these results suggest that DBM-819 acts as an orally effective anti-ulcer agent in vivo, and that DBM-819 could be developed as a new therapeutic agent for peptic ulcer disease.

[PE1-25] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Effect of the pretreatment with prokinetic agents on gastric emptying as estimated from serum concentrations of orally administered ranitidine in humans

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To comparatively investigate the effect of two prokinetic drugs, cisapride and metoclopramide, on gastric emptying and intestinal transit by assessing the serum concentration of ranitidine following oral administration to healthy volunteers. Six healthy male subjects participated in a three-way cross-over study. Cisapride or metoclopramide was administered orally 30 min prior to an oral administration of ranitidine. Serum concetrations of ranitidine were determined by an HPLC method, and compared with the control group of no receiving the pretreatment. Pharmacokinetic parameters, including AUC_{inf}, C_{max}, T_{max} and $T_{1/2}$ were obtained by standard methods. In addition, the effects of these prokinetic drugs on the in vitro apparent permeability of ranitidine across the rat jejunum in the Ussing chamber, and on the in vivo intestinal transit of charcoal meals in rats were also examined. T_{max} of ranitidine in human subjects was shortened significantly by the either of the pretreatments. Even the AUC_{inf} of ranitidine was also decreased significantly in the case of cisapride pretreatment. However, no changes were observed for the values of C_{max} and $T_{1/2}$ by the pretreatments. Rat studies revealed that cisapride and metoclopropamide had no influence on the in vitro permeability of ranitidine or the in vivo intestinal transit of charcoal meals. We conclude that these prokinetic agents accelerate the gastric emptying of ranitidine, thereby decreasing the AUC_{inf} of ranitidine in the case of cisapride pretreatment. We hypothesize that the saturation of the carrier system, which is responsible for the intestinal absorption of ranitidine, is responsible for the decrease in the AUC_{inf}.

[PE1-26] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Inhibitory Effect of Curcumin on Experimental Hepatic Fibrosis <I>in vivo </I>and <I>in vitro</I>.

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Background/Aims. : In an earlier our report, we reported Curcumin had the protection effects on acute or subacute Carbon tetrachloride-induced liver damage in rats. In this present study, the

aim was to investigate that curcumin can influence the early phase of fibrogenesis in animal model of fibrosis induced by carbon tetrachloride, to investigate whether curcumin could act mainly by direct action on cultured rat hepatic stellate cells in vitro, and thus to estimate the posibilities as a candidate for therapeutics agent of hepatic fibrosis.
Methods : Effects of curcumin were investigated by histological and immunohistochemical examination in a carbon tetrachloride model of hepatic fibrosis in rats . Futhermore we also examined the effects of curcumin on cultured rat hepatic stellate cells, which play an important role in the pathogenesis of hepatic fibrosis, activation to investigate whether it could act mainly by direct action on hepatic fibroblastic cells.
Results : Histological and Immunohistological examination showed that curcumin reduced the accumulation of collagen and the number of smooth muscle alpha actin positive-stellate cells in the liver. In *in vitro* study, Moreover, curcumin reduced platelet derived growth factor-induced proliferation, smooth muscle-alpha actin expression, collagen synthesis in a dose-related manner in cultured rat hepatic stellate cells.
Conclusins : These results indicated that curcumin can inhibit hepatic fibrosis as a potent inhibitor of hepatic stellate cells and thus may become a valuable anti-fibrogenic agents

[PE1-27] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Transferrin as a targeting ligand for DNA/cationic liposome complex

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Among the promising cancer therapy is targeting of the drug to tumor cells via receptor specific ligands. The use of cationic liposomes as nonviral vehicles for gene delivery is becoming increasingly prevalent in the field of gene therapy. Transferrin(Tf) has been used as a ligand for delivering liposomes mostly due to the increased number of transferrin receptors(TfR) found on tumor cells as compared to normal cells. Liposomes were prepared by reverse-phase evaporation method using dimethyldioctadecyl amoniumbromide(DDAB), cholesterol(Chol), and maleimide delivatized phospholipid(MPB-PE). Tf was conjugated to liposomes via the reaction of a MPB-PE with a thiol introduced into the protein by a heterobifunctional cross-linking agent, N-succimidyl-3-(2-pyridyldithio)propionate(SPDP). Physico-chemical characterization of Tf-liposomes was done using scanning electron microscope(SEM), transmission election microscope(TEM) and zeta-sizer. Mean diameter of liposome or Tf-liposome was about 150nm. The transfection efficiency of Tf-liposome mesured by β-galactosidase expression from pCMVβ-gal in HeLa cells was compared to Lipofectin by using 5-bromo-4-chloroindol-3-yl beta-D-galactopyranoside ('X-Gal') staining and chlorophenol red beta-D-galactopyranoside.

[PE1-28] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Preparation and Characterization of Poly(D,L -lactide-co-glycolide) Microspheres containing PEGylated Peptide

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Biodegradable poly(D,L-lactide-co-glycolide) (PLGA) microspheres containing polyethylene glyco (PEG)-modified peptides were prepared by solvent evaporation/extraction method. Insulin and salmon calcitonin were used as model peptides, which were bioconjugated with succinimidyl succinate monomethoxy-PEG (SS-mPEG) to improve biological stability. The release test was