

The Reversible Mode of Action of YH1885

Lee SJ^o, Song KS, Hwang MS, Keum SH, Lee BY, Lee JW

Yuhan Research Center, Yuhan Corporation, #27-3, Tangjeong-Dong, Kunpo, Kyunggi-Do 435-715, Korea

YH1885 is a potent acid pump antagonist as an antiulcer agent being developed by Yuhan Research Center. We compared the mode of action of YH1885 and omeprazole on gastric vesicles isolated from pig by washout method. To examine the mode of action of YH1885 in animals, we measured the effect of 7 days repeat-dosed YH1885 on plasma gastrin level in rats and dogs. The H⁺/K⁺-ATPase activity of gastric vesicle treated by YH1885 was completely recovered after washout, while that treated by omeprazole was strongly suppressed even after washout as reported. Plasma gastrin levels in rats and dogs were reached peak levels at 4 hr after the drug treatment, then began to decrease to normal level until 24 hr after the treatment. Increasing extent of plasma gastrin level showed a tendency of dose-dependent manner. Furthermore plasma gastrin levels had never reached to steady state during the whole treatment period. These results indicated that YH1885 is a reversible acid pump antagonist.

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[PA1-14] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl. Bldg 3]]

Rhenium-188 tin colloid as a new radiation synovectomy agent

Ko JI^o, Lee JJ, Doh H, Son M, Chang MS, Kim WB, Jeong JM(1) and Song YW(2)

Research Laboratories, Dong-A Pharm. Co. Ltd., (1)Department of Nuclear Medicine, Seoul National University College of Medicine, (2)Department of Internal Medicine, Seoul National University College of Medicine

Radiation synovectomy has been shown to be an effective treatment for the rheumatoid arthritic knee. In this study, we performed toxicity, stability and biodistribution study to evaluate the suitability of rhenium-188 tin colloid as a synovectomy agent. Intravenous (i.v.) injection in ICR mice and intra articular injection in SD rats were conducted to evaluate the acute toxicity of rhenium-188 tin colloid. LD(50) value of rhenium-188 tin colloid in i.v. toxicity test was 60.9 mCi/kg. In rats, mild toxicity including skin and synovium inflammation was observed in the radioactivity of 15 mCi/kg at intra-articular injection site, but systemic toxicity was not observed. Also In vitro stability tests showed that rhenium-188 tin colloid remained in colloid form without critical size variation over a 2-day period. Intra-articular injection of rhenium-188 tin colloid into normal rat joints was followed by gamma counting to quantify the leakage. The mean retention percentage of rhenium-188 tin colloid in normal rat joint was 98.7% at 1 day. In addition, the biodistribution study in rats showed that the highest radioactivity outside the injected knees was in the liver. Our preliminary results indicate that rhenium-188 tin colloid may be an effective radiopharmaceutical for synovectomy.

[PA1-15] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl. Bldg 3]]

The chronic administration of green tea extract affects the levels of brain neurotransmitters in senescence accelerated mouse

Choi SJ^{o1}, Lee HY1, Han SS2, Song CW2, Yang SD2, Lee HS1

1College of Pharmacy, Wonkwang University, 2Experimental Animal Laboratory, Toxicology Research Center, Korea Research Institute of Chemical Technology

Studies on the effect of long term administration of green tea extract on the memory are limited. The green tea extract (0.2 % and 0.5 %) was administered in place of water for 6 months to senescence-accelerated mouse (SAM) R1 and P8. The changes in the levels of acetylcholine, choline, norepinephrine (NE), dopamine (DA) and serotonin (5-HT) in five forebrain regions (cortex, hippocampus, striatum, cerebellum and midbrain) were examined. Green tea administration in SAM-R1 and SAM-P8 decreased acetylcholine levels significantly in hippocampus, striatum and midbrain, respectively. The changes of DA, NE and 5-HT concentrations in SAM-R1 treated with green tea extract were negligible except the significant increase of 5-HT in the midbrain. In SAM-P8 treated with green tea extract, DA levels in the hippocampus and striatum were significantly decreased but 5-HT contents in cortex and midbrain were significantly increased. These results suggest that the improvement of the learning ability may be linked not to acetylcholine but to aminergic neurotransmitters. (This study was supported by HMP-97-ND-4-0027).

[PA1-16] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Isolation, chemical structure, and characterization of anti-inflammatory principle from cactus

Kahang JH^{O*}, Hwang SE*, Lee HE*, Kim MH*, Song YS*, Park EH*, Shin KH#

*College of Pharmacy, Sookmyung Women's University, #Natural Products Research Institute, Seoul National Univ., Seoul

Cactus (*Opuntia ficus-indica* var. *saboten Makino*) has been widely used as folk medicine. It was previously found that the ethanolic extract of cactus showed potent anti-angiogenic action. In the present study, the active principle of anti-angiogenic action was purified from cactus stems by solvent extraction and column chromatography, based on adjuvant-induced chronic inflammation model in mice with chemical and spectroscopic methods, the purified anti-angiogenesis component was identified to be β -sitosterol.

[PA1-17] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

The Effect of Higenamine on Endotoxin-induced Experimental Disseminated Intravascular Coagulation (DIC) in Rats

Pyo MK^{O1}, Park KM¹, Chang KC², Lee DH³, Ryu JC⁴, Yun-Choi HS¹

¹Natural Products Research Institute, Seoul National University; ²College of Medicine, Gyeongsang National University; ³Department of Chemistry, Sogang University; ⁴Doping Control Center, Korea Institute of Science and Technology

Disseminated intravascular coagulation (DIC) is a pathological syndrome which occurs following the uncontrolled activation of clotting factors and fibrinolytic enzymes throughout small blood vessels; fibrin is deposited, platelets and clotting factors are consumed, and fibrin degradation products inhibit fibrin polymerization, resulting in tissue necrosis and bleeding. The indications for DICs include a decrease in the number of platelets in blood, a decrease of fibrinogen level and an increase of fibrin/fibrinogen degradation product (FDP) level in blood, and an extension of prothrombin time (PT) and activated partial thromboplastin time (aPTT). These indices for LPS-induced DIC were improved by the administration of higenamine. Higenamine prevented the decrease of the number of platelets and the concentration of fibrinogen in blood, the increase of FDP level, and the extension of PT and aPTT induced by LPS. The parameters of multiple organ failure (MOF), such as serum glutamic oxalacetic transaminase (S-GOT), serum glutamic pyruvic transaminase (S-GPT) and blood urea nitrogen (BUN), were also assayed. Higenamine significantly suppressed the increase in S-GOT. The increase in S-GPT and BUN were also suppressed.