PI-4

THE EFFECTS OF ITOPRIDE ON PLASMA GUT-REGULATORY PEPRIDES AND STRESS-RELATED HORMONES LEVELS IN HEALTHY HUMANS. F. Katagiri, S. Inoue, Y. Sato, H. Itoh, PhD, M. Takeyama, PhD, Oita University Hospital, Oita, Japan.

BACKGROUND: Itopride, a gastrokinetic drug with anti-dopamine and anti-acetylcholinesterase activity, has recently been evaluated for its clinical usefulness in non-ulcer dyspepsia that is closely related to stress. Here, we studied the effects of itopride on human plasma gastrin-, somatostatin-, motilin- and CCK-like immunoreactive substance (IS), and ACTH-IS and cortisol under stress conditions using repetitive blood sampling in healthy subjects.

METHODS: Itopride at a dose of 150 mg or placebo was orally administered in five healthy male volunteers. The blood samples were taken before and till 240 min after administration, followed by the extracting procedure, and submitted to the high sensitive enzyme immunoassay system as previously developed.

RESULTS: Single administration of itopride caused significant ($P < 0.05$) increases in plasma somatostatin- and motilin-IS levels, and decreases in plasma CCK-IS levels, compared with placebo. Furthermore, itopride suppressed plasma ACTH-IS levels significantly.

CONCLUSION: In this study, we hypothesize that itopride which is used as a prokinetic drug via motilin, somatostatin and CCK, could also be used to treat stress-related diseases.

PI-5

INTRAVESICAL CORTICOTROPIN-RELEASING HORMONE (CRH) INDUCES MAST CELL-DEPENDENT VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) RELEASE FROM MOUSE BLADDER EXPLANTS. J. Cao, W. Boucher, J. M. Donelan, T. C. Theoharides, Departments of Biochemistry, Pharmacology and Experimental Therapeutics, Tufts University School of Medicine, Department of Pharmacology and Experimental Therapeutics, Tufts University School of Medicine, Boston, MA.

BACKGROUND/AIMS: Corticotropin-releasing hormone (CRH) is typically released from the hypothalamus, but has proinflammatory effects outside the brain. This action involves selective mast cell secretion of vascular endothelial growth factor (VEGF), which may be responsible for bladder glomerulations in interstitial cystitis (IC). Here we investigated the effect of CRH on VEGF release from mouse bladder explants and the role of mast cells.

METHODS: Bladders of C57BL/6, mast cell-deficient (W/W^v) and normal congenic (+/+) female mice were catheterized; after emptying the urine, normal saline or CRH was introduced for 45 min, the urine was removed and frozen. Mice were allowed to recover for 4 h before sacrifice. The bladder was removed, minced into pieces and cultured with or without CRH overnight. Urine and media were assayed for release of histamine, IL-6 or TNF-α and VEGF.

RESULTS: CRH (100 nM) increased histamine release in the urine and VEGF release in the medium from bladder explants of C57BL/6 or +/+ mice; VEGF in the medium from bladder explants of W/W^v mice was unaffected by CRH. There was no change in histamine and IL-6 release in medium and TNF-α was under detection level in the normal or W/W^v mice. No VEGF, IL-6 or TNF-α was detected in the urine before or after stimulation.

CONCLUSIONS: CRH induces mast cell-dependent VEGF release from bladder explants without IL-6 and TNF-α. This finding further implicates mast cells in the pathogenesis of IC that worsens by stress and provides for a therapeutic new target.

PI-6

OBSERVATION OF THE CRUOR TIME WINDOW OF HYDROXYSAFFLOR YELLOW A OF THE MICE IN VIVO. L. Zhifeng, L. Chunmei, L. Guisheng, L. Min, L. Ke*, School of Pharmacy, Yantai University, Yantai, Shandong Province, China.

AIM: To observe the cruor time window of Hydroxysaffior yellow A of the mice in vivo.

METHODS: 70 male mice were divided into 7 groups, with the dose of 5 mg/kg, the drug was administrated ip to the mice once a day, continuously for 3-days. After the last administration for 1h, 2h, 4h, 8h, 16h, 24h, the cruor time were observed.

RESULTS: The measured cruor time was markedly longer after the last administration in the 1h, 2h, 4h, 8h and 16h groups than control group (respectively 136.8±29.5 sec in 1h group and 97.6±24.3 sec in 16h group vs 65.2±22.9 sec of control), and the 24h group had no significant change.

CONCLUSIONS: The results showed that the treatment time window of Hydroxysafflor yellow A on cruor time of the mice in vivo may be continued to 16 hours after administration.

PI-7

AN OBSERVATION ON OUT OF RANGE SAFETY LABORATORY RESULTS IN HEALTHY MALE VOLUNTEERS OF AFRO-CARIBBEAN ETHNIC ORIGIN. L. Adams, MBChB, D. Wilbraham, MBBS, T. Mant, FRCP, Guy's Drug Research Unit, Quintiles, London, United Kingdom.

A retrospective analysis was performed on laboratory results obtained from 21 healthy male subjects of Afro-Caribbean origin. The purpose of the study was to compare these volunteers to a standard phase 1 unit reference range and to observe any differences. Pre-dose data was obtained from Afro-Caribbean subjects who had participated in phase 1 studies at Guy's Drug Research Unit, Quintiles over the last year.

Blood samples were obtained for biochemistry, haematology, urinalysis and coagulation profile. The samples were analysed in-house and the results compared to a valid reference range (not adjusted for ethnicity). No significant differences were noted observed on reviewing results for serum liver enzymes, urea and creatinine, clotting profile and urinalysis.

In Afro-Caribbean subjects, the total white blood counts were relatively low, the differential neutrophil count was also relatively low and serum sodium concentrations were relatively high. The mean serum creatine phosphokinase (CPK) was approximately 2,6 times higher than the mean reference range CPK.

Ethnicity should be considered when reviewing laboratory data in healthy male volunteer studies.