growth factor, we determined the effectiveness of recombinant human hepatocyte growth factor (rh-HGF) protein in diabetic mice.

METHODS: Diabetes was induced by intraperitoneal injection of streptozotocin into 8-week-old C57BL/6 male mice. At 8 weeks after the induction of diabetes, the animals were divided into 4 groups: control nondiabetic mice and diabetic mice receiving two successive intracavernous injections of phosphate-buffered saline (days -3 and 0; 20 μL), a single intracavernous injection of rh-HGF protein (day 0; 4.2 μg/20 μL of PBS), or two successive intracavernous injections of rh-HGF protein (days -3 and 0; 4.2 μg/20 μL, respectively). Two weeks after treatment, we measured erectile function by electrical stimulation of the cavernous nerve. The penis was harvested for histologic and biochemical studies.

RESULTS: Repeated intracavernous injections of rh-HGF protein induced significant restoration of erectile function in diabetic mice (90% of control values), whereas a single intracavernous injection of rh-HGF protein elicited modest improvement. Rh-HGF significantly increased the content of endothelial cells, pericytes, and smooth muscle cells and decreased the generation of reactive oxygen species (superoxide anion and peroxynitrite) and extravasation of oxidized LDL in diabetic mice. Rh-HGF protein also promoted tube formation in primary cultured mouse cavernous endothelial cells and pericytes in vitro.

CONCLUSIONS: Re-establishment of functional and structural cavernous vasculature by use of potent angiogenic factor protein, HGF, is a highly promising treatment modality for ED from vascular causes.

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MP89-04

CF602 IMPROVES ERECTILE DYSFUNCTION IN DIABETIC RATS

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INTRODUCTION AND OBJECTIVES: Among the most important factors to affect erectile function is nitric oxide (NO) which is released by endothelial cells that line the corpus cavernosum and control smooth muscle relaxation and vascular inflow. Release of NO is diminished in patients with diabetes leading to erectile dysfunction.

CF602 is an allosteric compound known to modulate the A3 adenosine receptor (A3AR) binding site and confer the endogenous ligand adenosine to bind to the receptor with higher affinity. Adenosine is known to increase arterial blood flow and intracavernous pressure, thereby inducing penile erection. The advantage of allosteric modulators over synthetic agonists is their capability to target specifically pathological areas where adenosine levels are increased whereas normal body cells and tissues are refractory to the allosteric modulators due to low adenosine levels. In this study we show that the A3 adenosine allosteric molecule CF602 significantly improved erectile dysfunction in diabetic rats via a definitive mechanistic pathway.

METHODS: Streptozotocin (STZ) was administered IP in a dose of 60mg/kg in citrate buffer to Sprague Dawley male rats. Only animals with blood glucose level higher than 250 mg/dL were included in the study. CF602 was administered orally, twice daily for 24 hours or 5 days. Intracavernuous pressure (ICP)/Main arterial pressure (MAP) was used to determine erectile function one hour post last CF602 administration. The cavernous nerve was exposed and electro stimulation (20 Hz, 5V, 60 second duration) was applied. Immuno-histochemestry staining of Masson Trichrome, VEGF and eNOS were performed.

RESULTS: CF602 showed significant improvement in ICP (with no interfere in MAP) in both the 1 and the 5 days treated groups, demonstrating a 188% ($p<0.01$) and 250% ($p<0.001$) increase in penile ICP, respectively compared to placebo. Furthermore, CF602 reversed the damage in the smooth muscle via an increase in the expression levels of VEGF and eNOS.

CONCLUSIONS: CF602 treatment results in a significant improvement in erectile dysfunction and increased levels of VEGF and eNOS. These data position CF602 as a potential drug candidate for the treatment of erectile dysfunction in adult males with diabetes.

Source of Funding: CanFite Biopharma Ltd

MP89-05

EFFECT OF ICARISIDE II ON MIR-126 PATHWAY ON HUMAN CAVERNOUS ENDOTHELIAL CELLS EXPOSED TO A DIABETIC-LIKE ENVIRONMENT

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INTRODUCTION AND OBJECTIVES: To investigate the status of miR-126 and its targeting Spred1 under the stimulation of glucose and Age-BSA and to explore the effect of icariside II (ICA II) on the diabetic endothelial dysfunction of human cavernous endothelial cell (HCECs) by using the miR-126 pathway.

METHODS: Purified HCECs were divided into three groups: normal group + BSA (NC group), Glucose + Age - BSA group (DM group), ICA II treatment group (DM + ICA II group). Western blot to detect the expression of eNOS, RAGE protein expression so as to make sure the success of model construction; Immunofluorescence assay to study the proliferation of (HCECs); Real time PCR to detect the expression of miR-126 and Spred1; Western blot to detect the expression of the Spred1?c-Raf?MEK1/2?Erk1/2. Tube Formation Assay and Scratch assay were performed to detect the angiogenesis of HCECs under the diabetic-like environment.

RESULTS: Under the model, the expression of eNOS in DM group significantly reduced compared with that of NC group and the expression of RAGE in DM group is significantly increased compared with that of NC group ($p<0.05$), but the DM + ICA II group showed higher eNOS expression and lower RAGE expression compared with those in the DM group. The Ki67 expression in DM group is lowered than that in NC group; whereas the Ki67 expression in DM + ICA II group is higher when compared with that in DM group. The expression of miR-126 in DM group is significantly reduced compared with that of NC group but the DM + ICA II group showed higher miR-126 expression compared with that in the DM group. Western blot results showed Spred1 expression increased under the diabetic condition and its downstream target genes c-Raf?MEK1/2?Erk1/2 expression decreased obviously, but ICA II adding into the DM group could reverse these results effectively. Tube Formation Assay and Scratch assay also showed ICA II could promote the tube formation and cell proliferation in impairment of endothelial dysfunction of DM group.

CONCLUSIONS: Under the simulation of Age-BSA and glucose, HCECs occurred the endothelial dysfunction and the angiogenesis were repressed; ICA II could restore the HCECs functions by miR-126 / Spred1 / c-Raf / MEK1/2 / Erk1/2 pathway. ICA II may be a promising therapeutic compound to treat endothelial dysfunction in the future.

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MP89-06

THERAPEUTIC EFFECTS OF ADIPOSE-DERIVED STEM CELLS-BASED MICRO-TISSUES ON ERECTILE DYSFUNCTION IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

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INTRODUCTION AND OBJECTIVES: This study aimed to explore the therapeutic effects of adipose-derived stem cells (ADSCs)-based micro-tissues (MTs) on erectile dysfunction (ED) in streptozotocin (STZ) induced diabetic rats.

METHODS: Fifty-six 8-week-old Sprague-Dawley rats received intraperitoneal injection of STZ (60mg/kg) and eight weeks later, the