

MP03-13

EFFECT OF *HIBISCUS SABDARIFFA* SUPPLEMENTATION ON METABOLISM AND BLADDER IN OBESE RATS

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INTRODUCTION AND OBJECTIVE: Obesity causes disorders such as increased inflammatory levels, type 2 diabetes, cardiovascular disease and kidney disorders. It is a risk factor for lower urinary tract symptoms (LUTS), such as overactive bladder and urinary incontinence, and has a high prevalence in the population, decreasing quality of life of patients. The ingestion of *Hibiscus sabdariffa* (HB) extract has several health benefits and also anti-obesogenic effects. Therefore, the aim of the present study was to assess whether the different medicinal properties attributable to *Hibiscus sabdariffa* would act to prevent or mitigate bladder changes induced by obesity induced by obesity in an experimental model.

METHODS: Forty-eight male *Wistar* rats were distributed in four different dietary interventions: G1, standard diet and water (n=12, controls); G2, standard diet and HB tea (n=12); G3 a palatable high-fat diet (DPH) and water (n=12); and G4, DPH diet and HB tea (n=12). The animals were monitored for body weight, HB feed, and water and tea intake, according to the allocated group. After 16 weeks, the animals were euthanized and the levels of creatinine, inflammatory cytokines, testosterone, cholesterol, triglycerides and electrolytes were evaluated. In addition, histopathological analysis of the animals' bladder was performed. Collagen III/I ratio were analyzed by hematoxylin/eosin and Picosirius red staining.

RESULTS: HB tea was able to reduce LDL cholesterol in the G4 group in comparison to G3 (5,62±1,19 Vs. 7,31±2,29, p<0.05). Leptin was shown to be elevated in the groups that received DPH. HB tea was able to decrease the levels of the pro-inflammatory cytokine IL-1 α in groups G2 and G4 (Table 1). It is noteworthy that G4 showed a decrease in the thickness of the bladder muscle fibers in comparison to the control group (0.36 Vs. 0.84, p=0.006), and a significant increase occurred in G3 in relation to G4 (0.50 Vs. 0.36, p=0.006). Furthermore, there was an increase in collagen fiber count in G4 when compared to G1 and G3 (7.93 Vs. 15.67, 17.38, p<0.001) and there was also a significant decrease in G2 group compared to G1 (11.72 Vs. 15.70, p<0.001).

CONCLUSIONS: We can conclude that HB has an anti-inflammatory role, is able to reverse hyperlipidemia in obese rats, and reduce deleterious effects of obesity on these animals' bladder.

Table 1: Median, minimum and maximum values of pro-inflammatory cytokines (pg/mL) measured in the blood plasma of rats, according to the study group.

Cytokines	Groups			
	G1	G2	G3	G4
Leptin	3157.54* (1731.8;8621.4)	2750.79# (704.4;5006.7)	8552.62 (2622.5;33347.1)	7537.30 (3434.2;16091.6)
IL-1 α	17.90 (1.03; 52.44)	6.74 $\&$ (0.50; 220.80)	16.98 (4.76; 47.66)	0.91 $\&$ (1.45; 56.57)

*p<0.01:G1XG3,G4 #p<0.01:G2XG3,G4;G1=G2 $\&$ p<0.05:G2XG1,G3;G2=G4 $\&$ p<0.05:G4XG1,G2,G3

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MP03-14

INHIBITION OF HUMAN DETRUSOR SMOOTH MUSCLE CELL GROWTH AND MODULATION OF CYTOSKELETAL ORGANIZATION BY IMMUNO-MODULATORY IMIDE DRUGS (IMiDS)

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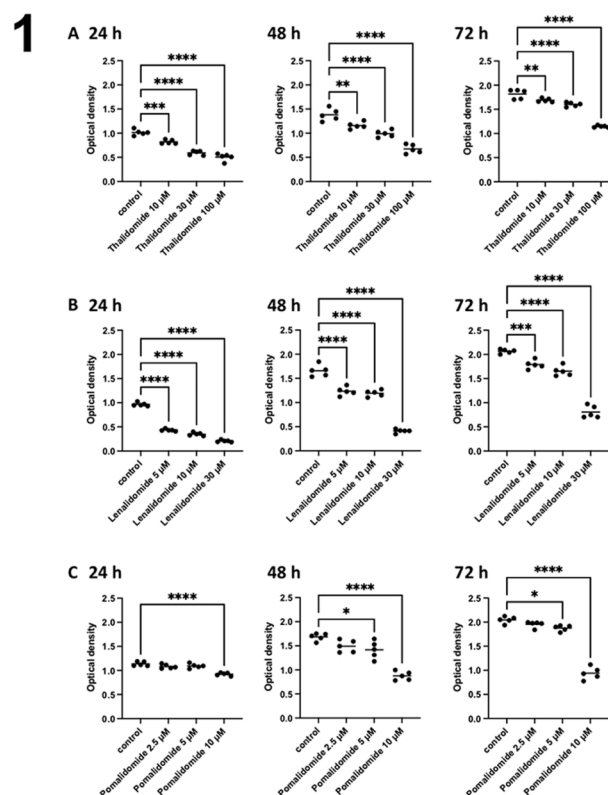
INTRODUCTION AND OBJECTIVE: While lower urinary tract symptoms (LUTS) consist of voiding (BPH) and storage disorders

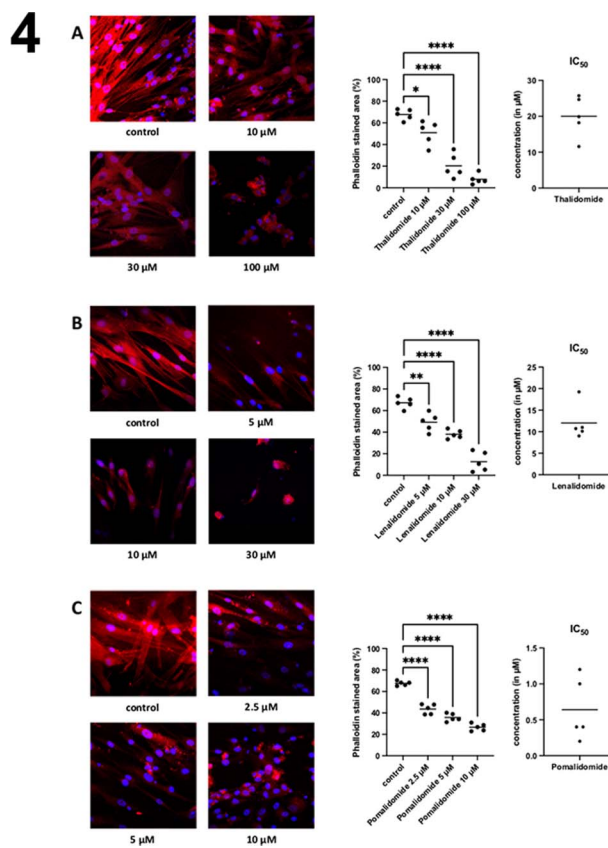
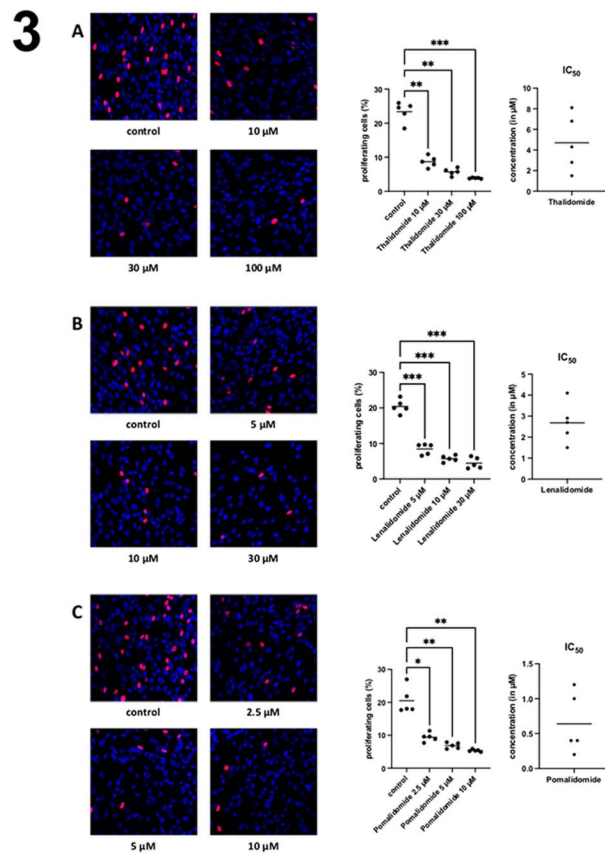
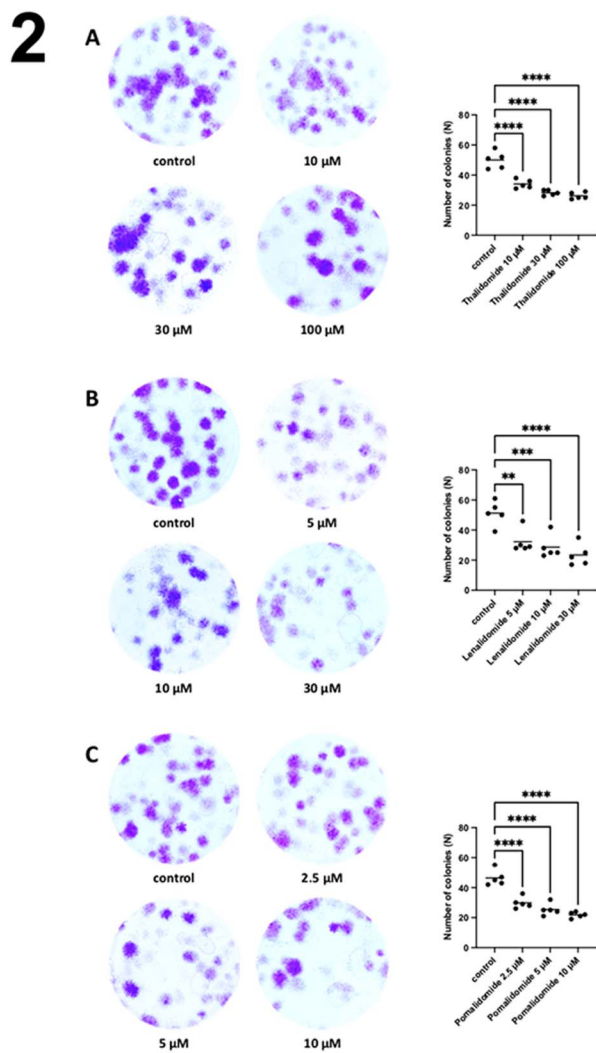
(OAB), new AUA and EAU guidelines take into account the mounting number of patients suffering from both, so called "mixed LUTS". Recently, we could show that IMiDs (thalidomide, lenalidomide and pomalidomide) inhibit prostate smooth muscle contraction, modulate cytoskeletal actin organization, and reduce prostate stromal cell growth at the same time, without showing cytotoxic effects. Based on these promising data, we now investigated the effects of IMiDs on cellular functions, including cytoskeletal organization, and growth in bladder cells.

METHODS: Experiments were carried out in an immortalized line of cultured human bladder detrusor smooth muscle cells (HBdSMC). Cytoskeletal organization was visualized by phalloidin staining, while cell growth was assessed using an EdU and cell colony assay. Cell viability was quantified in CCK8 assay, and FACS.

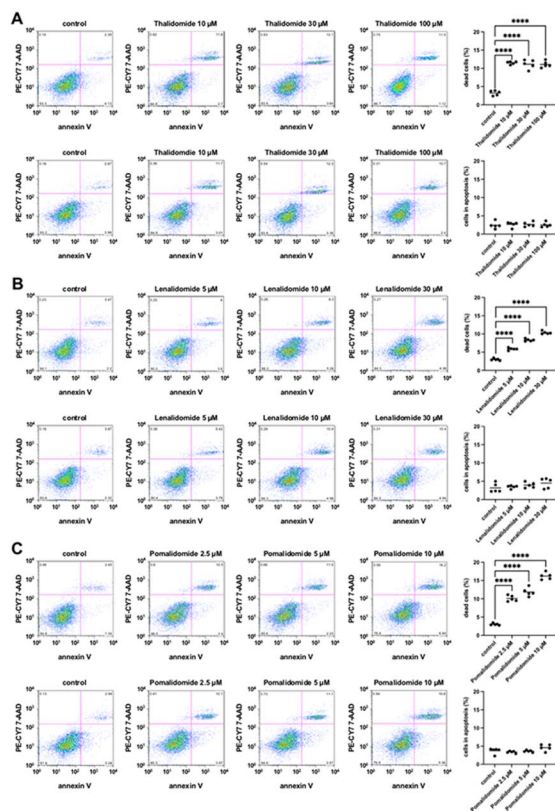
RESULTS: IMiDs ([A] thalidomide 10-100 μ M, [B] lenalidomide 5-30 μ M, and [C] pomalidomide 2.5-10 μ M) significantly reduced the number of viable WPMY-1 cells in a concentration- and time-dependent manner (Figure 1). Correspondingly, proliferation of WPMY-1 cells was significantly reduced in a concentration-dependent manner (Figure 2 and 3), without showing pro-apoptotic effects (Figure 4). In parallel, IMiDs induced cytoskeletal disorganization: while the cellular shape of control cells was characterized by many long and thin protrusions containing bundles of actin filaments, this structure collapsed after treatment with IMiDs (Figure 5).

CONCLUSIONS: IMiDs impair human detrusor smooth muscle growth, which is paralleled by a breakdown of the cytoskeleton, which may inhibit exaggerated bladder smooth muscle contraction in OAB. Urodynamic effects in vivo and a possible application in LUTS appear possible. Together with our previous data, this may suggest a possible novel drug class in LUTS treatment.





5



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MP03-15
THE INFLUENCE OF STROKE LATERALITY ON FUNCTIONAL BRAIN ACTIVITY DURING MICTURITION: A URODYNAMIC-FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY

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INTRODUCTION AND OBJECTIVE: Hemispheric differences in brain function account for the differential effects of stroke laterality on various domains of cognition, sensory-motor function, and decision making. Similarly, the size and location of stroke determine the type and severity of bladder dysfunction in patients with neurogenic lower urinary tract dysfunction (NLUTD). However, the changes in functional brain activity in relation to the side of stroke are yet to be understood. This study aimed to determine the differential patterns of micturition-related neural activity in right- vs. left-sided strokes.

METHODS: Patients with a history of chronic (>1yr) ischemic or hemorrhagic strokes and NLUTD were enrolled. Patients underwent urodynamic assessment while micturition-related brain activity was simultaneously assessed using functional magnetic resonance imaging with the blood-oxygen-level-dependent (BOLD) technique. Statistical parametric mapping (SPM) was used to assess the changes in BOLD signal during a 10-second period of maximum urgency. The signal intensity was compared between left- versus right-sided strokes, with age, gender, and time since stroke as covariates. Statistically significant clusters were identified using a p value of <0.001 and cluster size of >25 voxels.

RESULTS: A total of 23 patients (16 men, 69.57%; mean age 53.61±9.82) were enrolled, of whom 16 (69.57%) suffered from right-sided strokes. Analysis of the BOLD signal changes during the period of maximum urgency yielded increased intensity in patients with left-sided strokes in eight areas spanning the anterior cingulate (Brodmann area 32), inferior frontal gyrus, middle frontal gyrus, and

limbic area (cingulate gyrus) on the left hemisphere; frontal sub-gyral area on the right; and superior frontal gyrus (Brodmann area 8) bilaterally. Two clusters located in the left cerebellar anterior lobe and right limbic lobe (posterior cingulate) showed decreased BOLD signal in left-sided strokes compared to right-sided counterparts.

CONCLUSIONS: This study demonstrated the differences in micturition-related brain activity between left- and right-sided strokes and identified ten areas of differential activity. Patients with right-sided strokes demonstrated markedly diminished brain activity in several brain regions that are known to play a role in LUT control. Consistent with the inherent functional differences across the brain hemispheres, stroke laterality is correlated with the changes in brain activation during micturition.

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MP03-16
PHENOTYPING OVERACTIVE BLADDER PATIENTS: MAY MOLECULAR CHARACTERIZATION WITH URINARY BIOMARKERS BE OF HELP?

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INTRODUCTION AND OBJECTIVE: The objective of this study was to evaluate the association between the level of 5 urinary markers (NGF, BDNF, TIMP-2, TGF-B1, and PGE2) and the characteristics of patients with overactive bladder underpinned by detrusor overactivity (OAB-DO) and their possible association with response to treatment

METHODS: A single-center prospective study was conducted between March 2015 and June 2017 including all consecutive patients with OAB referred for urodynamics in whom filling cystometry evidenced detrusor overactivity. At the end of the inclusion period, the urine samples were unfrozen to assess the level of NGF, BDNF, TIMP-2, PGE2, TGF-B1 using dedicated ELISA kits. The association between urinary marker levels and patient characteristics was investigated.

RESULTS: Forty-three patients were included all with non-neurogenic OAB underpinned by detrusor overactivity on urodynamics. Patients with affective disorders (anxiety, depression) had significantly higher levels of NGF/Cr (2.04 vs. 0.07 pg/mg creatinine; p=0.006) and significantly lower levels of PGE2/Cr compared to other patients (40.6 vs. 83.4 pg/mg creatinine; p=0.008). There were no other statistically significant associations between urinary markers and patient characteristics. There was also no association between urinary marker levels and response to anticholinergics. In contrast, patients who responded to posterior tibial nerve stimulation (PTNS) had significantly lower BDNF/Cr levels (3.5 vs. 7.6 pg/mg creatinine; p=0.03).

CONCLUSIONS: In this study there was a molecular signature in the subgroup of patients with affective disorders with significantly higher NGF and significantly lower PGE2 levels compared to other OAB-DO patients. These results reinforce the hypothesis of an OAB phenotype associated with anxiety/depression with a specific pathophysiology. BDNF/Cr may be predictive of response to PTNS.