8th CROATIAN CONGRESS OF PHARMACOLOGY with international participation

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FINAL PROGRAMME AND ABSTRACT BOOK

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S1.4. POTENTIAL HARMFUL EFFECTS OF THE NOVEL ANTI-DIABETICS, INHIBITORS OF SODIUM-GLUCOSE COTRANSPORTERS SGLT1 AND SGLT2

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Introduction: In diabetics, major organs that contribute to glucose handling are small intestine (SI; SGLT1-mediated glucose absorption), kidneys (SGLT1- and SGLT2-mediated glucose reabsorption), and liver (glucose transport supposed to be SGLTs-independent). Recently, novel phlorizin-derived antidiabetic drugs (inhibitors of SGLT2 or both SGLT2+SGLT1) were developed aiming to lower blood glucose by inhibiting the SGLTs-mediated transport in SI and kidneys. However, SGLTs are insufficiently explored in other organs; where present, these drugs could affect their function and patient's health.

Material and methods: SGLT1 and SGLT2 mRNA and protein expression were explored, respectively, with quantitative RT-PCR and immunocytochemistry in various organs from humans, rats, and wild type (WT) and SGLT1 knockout (KO) mice.

Results: In all three species, SGLT2 mRNA and protein were detected only in kidneys, while SGLT1 was expressed in various organs. In WT, but not in KO mice, variable expression of SGLT1 mRNA and protein was found in SI, kidneys, salivary glands, prostate, tongue, optical nerve, uterus, pancreas, liver, and periurethral gland; lungs, heart, seminal vesicles, and brain were variably positive for mRNA and negative for protein. In rats, the SGLT1 protein was located in SI, kidneys, submandibular glands, lungs, heart, and brain. In humans, the SGLT1 mRNA and protein were detected in SI, kidneys, liver, lungs, and heart,

Conclusions: In contrast to selective SGLT2 inhibitors that will inhibit only the transporter in kidneys, the numerous extrarenal SGLT1 localizations represent potential targets for the novel, dual (SGLT2+SGLT1) inhibitors with unpredictable health consequences.

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