Pentadecapeptide BPC 157 Counteracts the Adverse Effects of Lithium Overdose in Rats

Filip Radevski^{*a*}, Zoya Jelovečki-Dokić^{*a*}, Marina Madunić^{*a*}, Slaven Gojković^{*a*}, Helena Žižek^{*a*}, Tajana Đurašin^{*a*}, Vilim Dretar ^{*a*}

^aDepartment of Pharmacology, School of Medicine, University of Zagreb

Filip Radevski 0000-0001-7556-1652 Zoya Jelovečki-Dokić 0000-0001-6758-4627, Marina Madunić 0000-0001-9555-3895, Slaven Gojković 0000-0003-4020-326X, Helena Žižek 0000-0001-9863-4164, Tajana Đurašin 0000-0002-6893-0875, Vilim Dretar 0000-0002-3969-712X

Key words: BPC, lithium, overdose, rats

INTRODUCTION We sought to determine whether stable gastric pentadecapeptide BPC 157 mitigates lithium intoxication in rats. METHODS: Lithium was applied at 500 mg/kg/day, intraperitoneally, once daily throughout 3 subsequent days. Medication used (in mg/kg) for the treatment group includes BPC 157 (0.01; 0.00001), L-NAME (5.0), L-arginine (100.0), applied alone and/or together, while control group rats received an equivolume of saline solution (5 mL/kg). At 20 minutes after drug application, we assessed muscular weakness (score 1-5) during the following 8 minutes. Then, for the next 5 minutes, we recorded an ECG. At 3 hours after that, the brain, the heart, the quadriceps muscle and the diaphragm muscle were used for histopathological analysis. RESULTS Consistently, lithium produced severe intoxication syndrome (muscular weakness and prostration, reduced quadriceps muscle fibers and diaphragm, myocardial infarction, and edema of various brain areas, most prominently in the cerebral cortex). The effects worsening with subsequent applications. L-NAME and L-arginine, given separately, both induced severe aggravation. This aggravation disappeared when L-NAME and L-arginine were given together. Contrarily, when given alone or together with NO-agents, BPC 157 reduced muscular weakness and prostration and muscle damage and mitigated lithium induced myocardial damage. BPC 157 reduced nerve damage and brain edema.

CONCLUSION BPC 157 could be used as therapy for lithium intoxication.