Glu period. The increasing of ATP content by NO_2^- ions is due to their capacity to accept electrons from the IV complex (cytochrome oxidase) of the respiratory chain in mitochondria.

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P13. Cortexin and combination of nitrite with cortexin decrease swelling and destruction of cerebellar neurons in hemorrhagic stroke

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Background: Endogenic peptides are recognized as signal molecules in interneuronal and neuroeffector transmission, playing the roles of neuromodulators, neurotransmitters, or physiologically active substances with cerebroprotective and antiseizure activity. Nitric oxide (NO) has similar properties when its concentration does not exceed physiological levels. The purpose of this work was to study mechanisms of neuroprotective action of peptide-based drugs cortexin and combination of nitrite with cortexin in epilepsy-prone rats of Krushinsky–Molodkina (K-M) strain developing hemorrhagic stroke to acoustic stress.

Methods: We used the methods of spectrophotometry, spectrofluorimetry, EPR spectroscopy, HPLC, electron and optical microscopy, ELISA methods and behavioral tests. Male 4.5-month-old rats of the K-M strain were used for the study. The animals were selected for the experiments in accordance with their age, body weight, and sex from a population of K-M rats. 39 male rats weighing 260 ± 40 g were used for the study of the cortexin and combination of nitrite with cortexin effects on the progress of hemorrhagic stroke. The animals were divided into 3 groups. The experimental animals (13) of the first group were intraperitoneally injected with the neuropeptide cortexin dissolved in physiological solution at a dose of 0.02 mg/100 g body weight. The experimental animals (13) of the second group were intraperitoneally injected with nitrite (0.5 mg/100 g) + cortexin (0.02 mg/100 g) body weight. Thirteen control rats were intraperitoneally injected with the same volume of physiological saline. Hemorrhagic stroke was modeled in accordance with the standard scheme: rats of K-M strain were put into a chamber and underwent acoustic stress [1–3].

Results: Cortexin has proved to protect genetically predisposed K-M rats to cerebral hemorrhagic stroke. Pretreatment with nitrite + cortexin resulted in decreased mortality and hemorrhage area in the K-M rats. Cortexin lowered the level of autoantibodies to glutamate receptors in the blood and reduced NO content in the blood of K-M rats. It has been shown that cortexin decreases swelling and destruction of the cerbellar neurons in rats with hemorrhaqic stroke. In the cerebellum of the experimental animals treated with cortexin + nitrite, we observed changes that indicated positive influence of this combination on the structure of cerebellar granule cells.

Conclusion: The sequences of events and the mechanisms of neuroprotective action of cortexin and combination of cortexin with nitrite are not completely understood. However, the data of experiments of separate treatment with peptide-based drugs such cortexin and experiments of combination – NO-generating compounds or inhibitors of NO-synthase + cortexin may supplement our knowledge about cortexin and cortexin + nitrite action mechanisms.

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P14. Dietary nitrite and oleic acid attenuate colonic inflammation in experimental colitis

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Background: Nitric oxide, nitrite (NO_2^-) and related compounds can undergo nitration reactions with unsaturated fatty acids (e.g. oleic acid) thereby forming electrophilic nitrated fatty acids (NO_2-FAs), which can activate anti-inflammatory pathways.

Aim: Here we examined the *in vivo* formation and therapeutic effects of NO_2-FAs from dietary oleic acid, alone or in combination with nitrite, in a model of ulcerative colitis involving administration of dextran sulphate sodium (DSS, 2%).

Methods and results: Female Balb/c mice were treated with native oleic acid (100 mg/kg/day, diet), without or with inorganic nitrite (1 mg/kg, drinking water). At the end of the experiment (7 days) the extent of inflammation was measured as follows: colon length, Disease Activity Index (DAI), colonic expression of p65 and iNOS, and heme oxygenase-1 (HO-1) mRNA and protein levels.

The DSS group developed colitis as evident by a marked reduction in colon length, as well as an increase in DAI and tissue expression of p65 and iNOS, compared to the control group. Dietary administration of OA ameliorated colitis symptoms as evident by a reduction of DAI, p65 and iNOS colonic expression, and prevention of the DSS-induced colon shortening. Interestingly, co-administration of OA and NO_2^- improved these parameters, suggesting either a synergistic effect or endogenous formation of nitrated oleic acid (OA-NO_2). In support of the latter, oral gavage with nitrite and an unsaturated fatty acid to healthy control mice resulted in detectable formation of nitro fatty acids in the gastrointestinal tract. Moreover, the levels of HO-1 were increased in the presence of oleic acid and nitrite. As it has been shown that OA-NO_2(but not OA) induces HO-1 expression, this also supports endogenous nitration of oleic acid.

Conclusions: Dietary administration of oleic acid and nitrite attenuates DSS-induced colitis. Mechanistically, the observed effects may be related to nitrite-mediated formation of anti-inflammatory nitroalkenes. These results may have nutritional implications, in particular in relation to a traditional healthy diet such as the Mediterranean diet. Of note is that the levels of oleic acid and nitrite used correspond to the daily amount of olive oil (oleic acid) and vegetables (nitrate/nitrite) provided by a typical Mediterranean diet.

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P15. Effects of hemodialysis on the nitric oxide congeners nitrite and nitrate: Implications for cardiovascular health in dialysis patients

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Context: High cardiovascular death rates for patients on hemodialysis remain a serious problem. Cardiovascular mortality is considered the main cause of death in patients receiving dialysis and is 10 to 20 times higher in such patients than in the general population. To date there is no molecular mechanism that has been shown to explain this increased mortality although nitric oxide has been implicated.

Objective: To determine the scavenging effects of dialysis on steady state concentrations of nitrite and nitrate in patients' plasma and saliva which may reduce total body NO availability.

Design: Dialysis patients were enrolled and patients' baseline blood and saliva was collected for nitrite and nitrate analysis. Blood was also collected as it exited the dialysis unit as it was flowing back to patient. Blood and saliva was again collected from the patients after 4–5 h of dialysis for comparison to baseline before dialysis.

Setting: Moncrief Dialysis Center in Austin Tx.

Results: Beginning plasma nitrite and nitrate from patients was 0.21 ± 0.03 μM and 67.25 ± 14.68 μM, respectively. Blood coming immediately from the dialysis unit had 57% less nitrite and 84% less nitrate returning to the patient only 0.09 ± 0.03 μM nitrite ($p = 0.0008$) and 11.04 μM nitrate ($p = 0.0003$). After 4–5 h of dialysis new steady state plasma levels of nitrite and nitrate were significantly lower than baseline 0.09 ± 0.01 μM ($p = 0.0002$) and 16.72 ± 2.27 μM ($p = 0.001$), respectively. Dialysis also resulted in a significant reduction in salivary nitrite (232.58 ± 75.65 μM to 25.77 ± 10.88 μM; $p = 0.01$) and nitrate (500.36 ± 154.89 μM to 95.08 ± 24.64 μM; $p = 0.01$).

Conclusions: Our results demonstrate that the dialysis process removes as much as 90% of the steady state nitrite and nitrate. Chronic and persistent depletion of plasma and salivary nitrite and nitrate likely reduces NO biology and may be the under-