

approaches supported by mixtures of natural bioactive compounds should reveal more effectiveness than classical therapeutics for AD.

Methods: The polyphenolic profile of elderberry extract and of anthocyanin-enriched fraction was evaluated by HPLC-DAD, the optical properties by UV-vis and fluorescence spectroscopy and the redox behavior by cyclic voltammetry. Antioxidant properties were assessed in cell-free assays while the ability the elderberry extract to modulate the mitochondrial redox chain was evaluated in rat brain mitochondria.

Results: HPLC analyses showed that elderberry extract is a mixture of chemical compounds, particularly rich in anthocyanins. It exhibits intrinsic fluorescence properties with potential for bioimaging, reversible redox behavior and ability to scavenge DPPH, nitric oxide and superoxide radicals. The antioxidant, optical and redox properties of elderberry extract are strongly correlated to their content in anthocyanins. Bioenergetic studies show that elderberry extract has ability to promote the oxidation of NADH in aqueous phase and deliver electrons to ubiquinone or complex III in the inner-mitochondrial membrane, overcoming the complex I inhibition promoted by rotenone.

Conclusion: Elderberry anthocyanins have potential to be used in mitochondria-targeted formulations to modulate the pathophysiological changes underlying AD from their early stages.

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PS016

Effect of resveratrol on the cartilage and nociceptive system of Osteoarthritic animals



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Aim: This study aims to evaluate the effect of RV on the nociceptive behavior, histopathological alterations at the knee and DRG neurons of OA rats.

Introduction: Osteoarthritis (OA) is a common degenerative joint disease and arthritic pain is a prominent symptom associated with reduced quality of life. Peripheral pain mechanisms seem to be involved, with cartilage lesions showing a repercussion in Dorsal Root Ganglia (DRG) neurons. Resveratrol, a polyphenol with proven anti-inflammatory, anti-oxidant and neuroprotective properties, has been shown to prevent development of OA and act as an antinociceptive agent. However, its systemic effects once the disease has fully developed remain unclear.

Methods: To evaluate this, OA was induced in 18 male Wistar rats through intra-articular injection of mono-iodoacetate (MIA) (day 0). Animals were allowed to develop the disease for two weeks,

after which followed a 4-week-long treatment with resveratrol or vehicle, administered intraperitoneally twice daily (10 mg/kg). Nociceptive behavior was quantified weekly using the CatWalk and Knee-Bend tests. Animals were sacrificed one week after the last treatment administration, their knees were dissected for histopathological analysis, and the DRG were dissected and processed for immunohistochemical evaluation of activating transcription factor 3 (ATF-3) neuronal expression.

Results: Resveratrol was unable to prevent cartilage degeneration but it significantly decreased ATF-3 expression. The nociceptive behavior of OA animals treated with resveratrol decreased during the first three weeks of treatment, in comparison to day 14 (before treatment was initiated), as shown by Knee-Bend scores. However, this tendency reverted as the disease progressed.

Conclusion: These results indicate that resveratrol may have antinociceptive effects in the early stages of the disease development, but it might not play such a relevant role once the disease has progressed. Thus, further studies are needed to fully understand the possible role of resveratrol in the different stages of OA.

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PS173

Bupivacaine treatment enhances the regeneration of the lesioned external urethral sphincter of the rat



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Aim: In this study we intent to verify if bupivacaine treatment can be used to enhance the repair of the lesioned urethral sphincter in rat.

Introduction: Stress urinary incontinence (SUI) is a major and frequent urinary dysfunction. It has been associated with external urethral sphincter (EUS) weakness due to several causes. Among them, ischemia and nerve lesion frequently associated with child-birth. The current treatments are mainly surgical but are far from being satisfactory. The local anesthetic bupivacaine is known to exert myotoxic action, followed by muscle regeneration with increased strength. This effect was already used in ocular muscles to treat strabismus. In the present study we evaluated the effect of bupivacaine application in the recovery of the damaged EUS.

Methods: A lesion of the external urethral sphincter (urethrol-ysis) was performed in adult female Wistar rats using established protocols. Two weeks after the lesion, the animals were injected in the EUS with 0.4 ml of 0.5% bupivacaine. Ten days later, the whole urethra was removed, fixed and sectioned in paraffin wax. Sections

were stained with hematoxylin and eosin, Masson's trichrome and immunoreacted for markers of striated and smooth muscle (sarcomeric actin and smooth muscle actin, respectively).

Results: Two weeks after urethrolisis, a marked reduction of muscle fibers in the EUS was detected. A recovery was evident in lesioned, bupivacaine injected animals when compared with lesioned and saline-injected controls.

Conclusion: Our data show that bupivacaine application in the lesioned external urethral sphincter accelerates its recovery. This finding opens a therapeutic opportunity to treat stress urinary incontinence.

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PS074

In vivo and in silico study of allicin as a stroke prevention



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Aim: To prove allicin effect to prevent stroke in insilico and invivo method.

Introduction: Stroke is a disease that can cause permanent disability, even death. Atherosclerosis is one of the cause of stroke. One way to prevent stroke is to treat atherosclerosis using allicin. Allicin works by inhibiting Integrin Alpha Beta-3 and ApoE proteins. Therefore, allicin can be considered as an alternative in stroke prevention.

Methods: This is true experimental study with two methods. Allicin was taken from pubchem, while ApoE with code (1EA8), Integrin Alpha Beta-3 with code (1JX5) taken from protein data bank. Afterwards, the ligands and macromolecule were docked with Pyrx. Analysis was done using Discovery Studio. Pharmacokinetic study, allicin compounds were analyzed with ACD/I-Lab. During invivo study, rats were induced with high fat diet for 8 weeks and were given allicin with dose 5, 10, 20 mg/kg BW during 6 weeks. Rat blood, carotid artery, and brain were analyzed for lipid profile, foam cells in blood vessels, and immunohistochemically to see BDNF.

Results: Pharmacokinetic results showed that allicin has oral bioavailability above 70%, distributed through lipoproteins and a few albumins. Allicin can penetrate through membrane and cytoplasm, affecting its target. Pharmacodynamically, allicin can bind to active site of ApoE on 149 leucine, and to active site of ApoE on 173 serine. Allicin bound with active site of ApoE will increase ApoE expression, thus lowering lipid profile except HDL. Meanwhile, allicin bound with active site of Integrin Alpha Beta-3 blocked platelet aggregation. Decreasing Integrin Alpha Beta-3 was proven by invivo results where foam cells were decreasing. These events caused a decrease foam cell in common artery, causing no brain hypoxia and increased BDNF. Invivo test showed a decrease in foam cells on 10 mg/kg BW. On the contrary, the brain showed an increase in BDNF amount on 20 mg/kg BW.

Conclusion: Based on insilico and invivo studies, allicin can be considered as a preventive treatment to stroke by inhibiting atherosclerosis development by increasing ApoE, lowering Integrin Alpha Beta-3 protein, and increasing BDNF.¹⁻⁵

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PS148

Anxiety-like behavior in elevated plus maze upon sleep fragmentation of one light phase of rats' circadian cycle



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Aim: To assess anxiety-like behavior in rats after twelve hours of sleep fragmentation during the light phase of sleep-wake cycle, using the elevated plus maze test.

Introduction: Hallmark of sleep fragmentation is set of frequent, brief arousals, which modulates sleep architecture without significant diminishment of total sleep time. Anxiety is recognized as comorbidity in numerous disorders, including some of those related to sleep quality. Sleep fragmentation may be appropriate model of sleep alteration pattern in some disorders, yet its effects on behavioral alterations have not been broadly investigated.

Methods: Sleep fragmentation was achieved by treadmill method lasting for 12 h, during the light phase of the day (starting at 8 AM). Wistar albino male rats were randomly divided into: sleep fragmentation group (SF, $n=8$, treadmill programmed to alternately work 30 s ON and 90 s OFF every 2 min); activity group (AC, $n=8$, treadmill programmed to alternately work 10 min ON and 30 min OFF); and treadmill control group (TC, $n=8$, rats stayed in the treadmill set to OFF mode and conditions equivalent to cages). Immediately after the sleep fragmentation regimen, elevated plus maze test was performed. To assess anxiety-like behavior, we measured time spent in the open arms, as well as number of transitions between open and closed arms.

Results: SF group spent significantly less time in the open arms compared to both, AC and TC group ($p < 0.001$). SF rats also had significantly less number of transitions between closed and open arms of the maze, compared to AC and TC group ($p < 0.05$). Moreover, no significant difference was observed in any of the measured parameters between TC and AC group.

Conclusion: The results of our study indicate that acute 12-h sleep fragmentation induced anxiety-like behavior in rats in elevated plus maze. Further research should help us better understand impact of this phenomenon on psychiatric disorders.

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