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Amantadine Hydrochloride Improves Cognitive and Motor Deficits after Fluid Percussion Injury of Cerebral Cortex in Rats

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Backgrounds:

Amantadine hydrochloride, a weak NMDA receptor channel blocker, has been the subject of considerable interest and clinical use for patients with prolonged disorders of consciousness after traumatic brain injury (TBI). Preliminary studies have shown that amantadine hydrochloride accelerated the pace of functional recovery during active treatment in patients. To date, no studies have explored the potential for amantadine hydrochloride to provide behavioral recovery in chronic treatment.

Materials and Methods:

Using male Sprague-Dawley rats, we employed the 6 atm fluid percussion traumatic brain injury model to treat with saline or amantadine hydrochloride that was released 3.6 mg/kg per hour for each rat for 7 weeks by using subcutaneous mini-osmotic pump after a week of injury. Novel object recognition (NOR) and fixed-speed rotarod (FSRR) behavioral tests were used to determine whether the treatment enhanced cognitive and motor deficits recovery every week after injury.

Results:

Cognitive and motor behavior were impaired in NOR and FSRR behavioral tests after injury. Treatment with amantadine hydrochloride persistently improved the impairments in both NOR and FSRR behavioral tests after TBI.

Conclusion:

Persistent treatment of amantadine hydrochloride could ameliorate cognitive and motor deficits caused by traumatic brain injury.

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The protective effect of 5-lipoxygenase inhibitor in animal models of Parkinson's disease

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Background

Neuroinflammation and oxidative stress are the important factors inducing neurodegeneration in age-related neurological disorders. 5-lipoxygenase (5-LOX) is the enzyme that can insert oxygen into the molecule of arachidonic acid and thereby synthesize inflammatory leukotrienes or 5-HETE. 5-LOX is expressed in central nervous system neurons and may participate in neurodegenerative disease.

Materials & Methods:

In the present study, we studied the effect of pharmacologic inhibition of 5-lipoxygenase activating protein by MK-886 on the rat neuron glia co-culture and MPTP injected mice.

Results:

It was found here that 5-LOX was over-expressed in astrocyte after injection of MPTP to C57BL6 mice. We thus evaluated whether the inhibitors of 5-lipoxygenase is a possible neuroprotective agents in midbrain culture of rat. MK-886, a specific 5-LOX activating protein (FLAP) inhibitor, significantly increased the [^{3}H] dopamine uptake, which is a functional indicator of the integrity of dopaminergic neurons, in mesencephalic neuron-glia co-cultures after MPP^+ treatment. In addition we found that LTB_4, one of 5-LOX downstream product, enhanced MPP^+-induced neurotoxicity. However, LTD_4 and 5-HETE did not exert similar potentiating effect. Furthermore, MK-886 reduced the level of LTB_4 in MPTP-induced Parkinsonism mice and exert the neuroprotection.

Conclusion:

These experiments indicate that 5-LOX inhibitors may be useful to developed as a novel neuroprotective agent and LTB_4 may play important pathological role in Parkinson's disease.

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A study for the preparation of biodegradable microspheres

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Purpose:

In this study, we evaluated a new drug delivery system for cancer radiotherapy using a biodegradable PLGA microspheres consisting of therapeutic radionuclide.

Materials and Methods:

In this experiment, PLGA (50/50)and PVA(2wt%) were proved to have the better result for manufacturing the microsphere and the PLGA microspheres were conjugated with DOTA for the labeling of In-111. The following instruments were used to analyze the material and its particle size, including (1) GPC(2) SEM (3) FT-IR, (4) NMR and (5) XPS.

Result:

The selected particles size for the microsphere was ranged between 25±10μm~47±10μm. We modified DOTA-PLGA- microspheres by EDC/NHS mixed solution. By using the 0.2 N sodium acetate solution as environment buffer in In-111 labeling DOTA-PLGA-microsphere preparation and the labeling rate of 90%.

Conclusion:

In this experiment, PLGA (50/50) and PVA (2wt%) were proved to have the better result for manufacturing the microsphere and in the In-111 labeling rate of 90%. In the future, we would use In-111/Y-90-DOTA-PLGA-microspheres to evaluate the therapeutic potential in hepatoma animal model via transcatheter arterial embolization pathway.

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B7, a Novel Anthraquinone Derivative, Inhibit Telomerase and HDAC Activities in Hepatoma Cells Apoptosis

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Backgrounds:

After screening hundreds of anthraquinone derivatives, we found B7 possesses significant cytotoxic effects on different cell line including, HT29, HepG2 and A549. Increasing evidence indicates that HDAC inhibitors show anticancer activity in cell culture and animal models of carcinogenesis. Moreover, the intimate connection between telomerase regulation and cancer is now well established. Consequently, we exploring the role of DNA histone deacetylase(HDAC) and telomerase in B7 induced hepatoma cell apoptosis.

Materials and Methods:

The human hepatocellular carcinoma cell line (HepG2), human lung cancer adenocarcinoma cell line (A549) and human colon cancer cell (HT29) were cultured and seeded in 24-well plate for 24 h prior to B7 addition. The cell viability was estimated by XTT and methylene blue assay at indicated exposure time. Levels of specific proteins expression were detected by Western blotting analysis. DNA strand breaks were determined by alkaline comet single-cell gel electrophoresis and the stained with SYBR Green. The SYBR Green RTQ-TRAP assay was conducted with dilution of HepG2 protein extracts. The change in CT value related to fixed fluorescence intensity (ΔRn) can estimate telomerase activity.

Results:

Our data have demonstrated that B7 increased apoptosis signals, caused DNA damage and activated acetyl-histone H3 as a dose-dependent manner. Telomerase repeat amplification plot also showed that B7 cause significant inhibition on telomerase activity as dose-response manner.

Conclusion:

Our results have indicated that in addition to DNA damage, we found the activities of HDAC and telomerase were decreased in B7 induced hepatoma cells apoptosis. These outstanding anticancer activities made B7 as a potential compound to fight cancer.

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