In the venture towards the development of potent multi-target ligands, a series of twelve benzothiazole derivatives were synthesized employing synthetic hybrid compounds, logically designed to integrate into a single molecular framework consisting of at least two different pharmacophoric moieties. **Enzyme based drug screening** assays specific for Alzheimer's disease were performed. All derivatives showed Acetylcholine esterase (AChE) inhibitory activity. Compounds 11 (IC$_{50} = 0.421$ μM) and 13 (IC$_{50} = 3.641$ μM) were potent, mixed-type and selective AChE inhibitors, binding at the both catalytic and peripheral anionic site of the enzyme. Treatment with compounds 11 and 13 at 50 μM with Aβ reduced the aggregation propensity of Aβ by 80.708% and 74.49% respectively, observed by the reduced fluorescence intensity of Thioflavin T. **Confocal** laser scanning microscopy, **Transmission electron** microscopy, and **Infrared** spectroscopic analysis also substantiated the Aβ fibril formation hampering ability of the compounds. Furthermore, disaggregation assay showed decrease in the fluorescence intensity after treatment with compounds 11 and 13 with Aβ fibrils, suggesting these can also disaggregate the matured fibrils. Besides, these derivatives were found to be non-neurotoxic agents in human neuroblastoma SHSY5Y cells.

Further, **in vitro** and **in vivo** investigations are under study. These results support our assertion that these compounds may constitute novel multi-functional agent for AD treatment.

https://doi.org/10.1016/j.ibror.2019.07.1569

P32.85

**Evaluation of the role of ellagic acid on spatial memory activity and oxidative responses in pentyleneetrazole chronic epileptic rat model**

Philemon Paul Mshelia 1,∗, Nuhu m. Danjuma 2, Rabiu A. Magaji 3, Tavershima Dzenda 4

1 Abubakar Tafawa Balewa University, Zaria, Nigeria 2 Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria, Nigeria 3 Department of Human Physiology, Ahmadu Bello University, Zaria, Nigeria 4 Department of Veterinary Physiology, Ahmadu Bello University, Zaria, Nigeria

Ellagic acid (EA) is a natural flavonoid abundant in plants and fruits that offers neuroprotection in animals. This study assessed the effect of pretreatment with EA (15, 30 and 60 mg/kg) in pentyleneetrazole (PTZ)-kindled rats and its role in memory using the Y-maze and elevated plus maze for memory. The effects of the pre-treatment with the EA on kindling – induced memory impairment, oxidative stress and neurotransmitters were evaluated. Male Wistar rats (weighing 200–300 kg) were injected with PTZ (35 mg/kg, s.c) once every alternate day (48 ± 2) until they were kindled. Memory impairment was assessed using the elevated plus maze and Y-maze tests. Oxidative stress biomarkers (malondialdehyde, MDA), antioxidant enzymes (superoxide, SOD and catalase, CAT) and neurotransmitters (Glutamate and Y-amino-butyrac acid, GABA) of the whole brain were assayed at the end of the experiments using relevant kits. One way ANOVA followed by Tukey post hoc analysis were used for statistical analysis. In the present study, PTZ increased ($P < 0.05$) glutamate and MDA with consequent reduction ($P < 0.05$) in GABA. EA showed anti-seizure ability in all treated groups and increased ($P < 0.05$) antioxidant enzymes activities. In conclusion, our study suggests that EA has anti-epileptogenic like effect on PTZ-induced kindling in rats and improved memory. The mechanism of action of EA could be due to its antioxidant properties.

https://doi.org/10.1016/j.ibror.2019.07.1570

P32.86

**Neuroprotective role of pioglitazone in reversing hippocampal insulin resistance in Amyloid-β fibrils induced animal model of Alzheimer's disease**

Syed Obaidur Rahman 1, Suhel Parvez 2, Bibhu Prasad Panda 1, Abul Kalam Najmi 1,∗

1 School of Pharmaceutical Education and Research (SPER), Jamia Hamdard, New Delhi, India 2 School of Chemical and Life Sciences, Jamia Hamdard, New Delhi, India

**Background:** Complications of the Alzheimer’s disease (AD) have made the development of its therapeutic intervention quite a challenging task. Numerous studies have supported the hypothesis that central insulin resistance plays a significant role in AD. Serine phosphorylation of Insulin Receptor Substrate-1 (IRS-1) has been found to be a contributing factor in neuronal insulin resistance. Pioglitazone (PIO) is a peroxisome proliferator-activated receptor gamma (PPAR-γ) activator, known for its significant anti-diabetic functions, has also demonstrated neuroprotective actions.

**Methods:** In the present study, AD was induced by i.c.v administration of amyloid-β (1-42) fibrils in Wistar rats. After 7 days of recovery, rats were treated with 10 mg/kg and 20 mg/kg of PIO orally for 28 days. Behavioral analysis was done in the last week of our experimental study. On the 36th day, rats were sacrificed and their hippocampus was separated from the whole brain, then homogenized and stored for biochemical estimations.

**Results:** PIO significantly reversed the cognitive and memory impairment, as assessed by Morris water maze test, in Aβ (1-42) fibrils infused Wistar rats. PIO also significantly attenuated Aβ (1-42) level, IRS-S307 activity, GSK-3β activity, TNF-α level, AChE level, nitrite level and oxidative stress in the hippocampus. Histopathological evaluation, done through H&E and Congo red staining, also demonstrated neuroprotective and anti-amyloidogenic effects of PIO in the hippocampus.

**Discussions:** Our study concludes protective action of pioglitazone against hippocampal insulin resistance and Alzheimer’s disease complications, supporting the potential role of hippocampal insulin resistance targeting against the AD.

https://doi.org/10.1016/j.ibror.2019.07.1571

P32.87

**The role of DNA damage in TDP-43-associated Amyotrophic Lateral Sclerosis (ALS)**

Shaﬁ Jamalı 1,∗, Anna Konopka 1, Adam Walker 2, Julie Atkin 1

1 Macquarie University, Sydney, Australia 2 Queensland Brain Institute, The University of Queensland, Queensland, Australia

Almost all cases of ALS (97%) are associated with pathological forms of TAR-DNA binding protein 43 (TDP-43), which mislocalizes from the nucleus to the cytoplasm and forms inclusions containing misfolded TDP-43. However, it remains unclear how TDP-43...

P32.88

Fingolimod improves the functional recovery of optic pathway and alleviates the expression level of histone deacetylase/sphingosine 1 phosphate receptor 1 in focal demyelination model of rat’s optic chiasm

Mona Hashemian1, Hadi Parsian1, Farzin Sadeghi2, Maryam Ghasemi-Kasman2, Mahdi Pouramir2,

1 Student Research Committee, Babol University of Medical Sciences, Babol, Iran, Babol, Iran
2 Neuroscience Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran, Babol, Iran
3 Department of Clinical Biochemistry, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran, Babol, Iran
4 Department of Medical Microbiology, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran, Babol, Iran

Fingolimod (FTY720) as a sphingosine 1-phosphate (S1P) receptor agonist, has been introduced as the first oral medicine for relapsing-remitting multiple sclerosis (MS). Besides immunomodulatory role, FTY720 exerts beneficial effects on remyelination process in central nervous system (CNS). In this study, the effect of FTY720 on conductivity of visual signals, myelin repair, glial activation and expression levels of histone deacetylase 1 (HDAC1)/S1P1R has been evaluated in lysolecithin (LPC)-induced demyelination model in optic chiasm. In order to induce demyelination model, LPC (1%, 2 µl) was injected into rat’s optic chiasm. Visual evoked potential recording (VEP) was used to measure the latency of visual waves. The extent of demyelination area and levels of glial activation were assessed using immunostaining. Gene expression analysis was performed to evaluate the expression levels of HDAC1, S1P1R and Olig2 in the optic chiasm. Analysis of electrophysiological data showed that injection of LPC increased the latency of visual signals and application of FTY720 significantly improved the functional recovery of visual pathway and alleviated the levels of glial activation in the optic chiasm. FTY720 enhanced the myelin repair and upregulated the expression level of Olig2. Additionally, the expression levels of HDAC1/S1P1R were significantly reduced in animals treated with FTY720. Cumulatively, the results of the present study demonstrate that FTY720 application improves the functional recovery of optic pathway through enhancement of remyelination, alleviation of glial activation and downregulation of S1P1R/HDAC1.

https://doi.org/10.1016/j.ibror.2019.07.1572

P32.89

Ursin reduce neuronal loss and astrocytes activation in chemical kindling model of epilepsy

Seyed Raheleh Ahmadian1, Maryam Ghasemi-Kasman2, Mahdi Pouramir2,

1 Student Research Committee, Babol University of Medical Sciences, Babol, Iran, Babol, Iran
2 Cellular and Molecular Biology Research Institute, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran, Babol, Iran
3 Cellular and Molecular Biology Research Center, Health Research Center, Babol University of Medical Sciences, Babol, Iran, Babol, Iran

Background: Epilepsy is one of the most common chronic neurological disorders, which provoke progressive neuronal degeneration and memory impairment. In recent years, application of herbal compounds with anti-inflammatory properties, such as Ursin has been introduced as useful agent in reducing of the epilepsy symptoms. In this study, the effect of Ursin application on spatial memory improvement, neuronal density and astrocyte activation were evaluated in pentylenetetrazol (PTZ)-induced kindling model.

Methods: Male NMRI mice have received the daily injection of Ursin at dose of 25 and 50 mg/kg. All interventions were injected intraperitoneally (i.p.), 10 days before PTZ administration and the injections were continued until 1 h before each PTZ injection. Spatial learning and memory was evaluated using Morris water maze test after the 11th PTZ injection. Animals have received 13 injections of PTZ and then, brain tissues were removed. Immunostaining against NeuN and GFAP respectively as mature neuronal and astrocyte markers were performed on brain sections.

Findings: Our results showed that Ursin administration reduced the seizures behavior and prevented cognitive impairment in fully kindled animals. Immunostaining data demonstrated that the level of neuronal loss and astrocyte activation were reduced in animals under treatment of Ursin.

Conclusion: Overall, the results of this study suggest that Ursin administration effectively ameliorates memory impairment and alleviates the level of neuronal death and astrocyte activation in PTZ-induced kindling model.

https://doi.org/10.1016/j.ibror.2019.07.1574