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The synergy of Antiepileptic action of Rapamycin, Pioglitazone, and Minocycline on acute seizures in mice

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One-third of patients with epilepsy are resistant to antiepileptic drugs (AED). Combined treatment with neuromodulators with antiseizure action, which are not classical AED, is promising for searching for more effective antiepileptic therapy. The purpose of this study was to investigate the pronouncement and type of interaction of complex administration of rapamycin – blocker of mTOR, pioglitazone - agonist of PPAR-gamma, and minocycline hydrochloride – suppression of microglia upon acute seizures.

Methodology & Theoretical Orientation: the effectiveness of antiseizure action of neuromodulators administered in different dosages estimated as a number of mice prevented from generalized cloned-tonic fits induced with pentylenetetrazol (PTZ, 70.0 mg/kg, i.p.). Drugs were dissolved in DMSO and administered intraperitoneally daily for one week before testing with PTZ. Control rats were treated with DMSO. Data were analysed using the Synergy Finder web application (version 2.0) (<https://synergyfinder.fimm.fi/synergy/>). Results were estimated as synergy when summary Bliss synergy scores exceeded ten when applied to the most synergistic 3-by-3 dose window in a dose-response matrix. Less than -10: the interaction between two drugs is likely to be antagonistic; From -10 to 10: the interaction between two drugs is likely to be additive.

Findings: Bliss Synergy score was 19.0 and favoured the presence of the synergy between combined administration of investigated compounds (Fig.1). Pioglitazone combined with minocycline also demonstrated synergy (16.7), while rapamycin, pioglitazone, and rapamycin with minocycline interaction were characterized as an additive (9.7 and 4.7 score correspondently).

Conclusion & Significance: Combined treatment with rapamycin, pioglitazone, and minocycline caused synergetic preventive effects upon generalized cloned-tonic seizures induced with PTZ in mice. Gained data revealed the strengthening of seizure protective action of investigated compounds while the antagonistic interaction was absent.



Figure 1. Type of interaction of between rapamycin, pioglitazone and minocycline on the model of acute seizures caused with pentylenetetrazol in mice.

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Recent publications

1. Poshyvak OB (2021) The synergy of rapamycin and pioglitazone antiseizure action in pentylenetetrazol (PTZ)-kindled rats Pharmacology online 2: 680–689.
2. Poshyvak OB, Pinyazhko OR, Godlevsky LS (2021) Oxidative stress suppression contributes to antiseizure action of axitinib and rapamycin in pentylenetetrazol-induced kindling. Ukrainian Biochem J 93(2): 53-60.
3. Poshyvak OB, Pinyazhko OR, Godlevsky LS (2021) Axitinib displays antiseizure activity on pentylenetetrazol - Induced kindling model. Pharmacology online 1: 200-213.

Biography

Prybolovets is interested in Neuroscience, Epilepsy, Seizures. She has participated in main neuroscience conferences such as Neuronus, INS, World congress of Neurology as a main speaker and presenter of oral abstracts and poster presenter. Planning to become a Neurologist specialist, and participate in PhD programs in UAE, Dubai.

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