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Glycyl-glutamine: A new hope in the treatment of depression?Sinan Cavun, Gulce Sevdar, M Sertac Yilmaz, Levent R Buyukuysal and Sami Aydin
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Statement of the Problem: Depression is the 4th leading cause of disability and death all around the world and it is expected to be the 2nd cause after 2020. Globally, more than 300 million people of all ages suffer from depression. The high rate of patients who still have not responded to depression treatment makes it necessary to perform preclinical research. The current medications used in depression treatment are also very troublesome drugs in respect of the adverse effects they cause. The risks and adverse effects of antidepressants currently used for depression treatment spread in a large range from sexual problems to death. In the current brain microdialysis studies from our laboratory, it is shown that glycyl-glutamine (Gly-Gln) augments serotonin release in the brain. It is well known that serotonin is a hormone that makes people feel happy, energetic and lively. In this study, we aim to investigate antidepressant effects of Gly-Gln dipeptide because of its enhancing effects on serotonin levels.

Methodology: These studies have been performed by the "forced swimming test" method which is the most applied animal model used in antidepressant treatment surveys. Using the swimming test, the dose response study, comparison with Gly-Gln cleavage products and fluoxetine, as well as locomotor activity test was performed.

Findings: In this sense, animal studies performed with "glycyl-glutamine" showed that it is tremendously effective against depression.

Conclusion: The most important feature of Gly-Gln is being a molecule, which can be synthesized in our body endogenously, and it is comes off while β -endorphin is being burned in the body. Therefore, Gly-Gln is extremely safe with its adverse effects. There isn't any adverse effect observed during the toxicological studies. This result is important for considering Gly-Gln as a potential antidepressant.

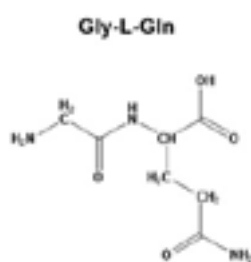


Figure 1: Chemical composition of glycyl-glutamine.

Recent Publications

1. M Guclu, S Kiyici, Z Gul and S Cavun (2017) Exenatide treatment causes suppression of serum fasting ghrelin levels in patients with type 2 diabetes mellitus. *Endocrine Connections* EC-17-0242.
2. N F Basaran, R L Buyukuysal, M S Yilmaz, S Aydin, S Cavun, et al. (2016) The effect of Gly-Gln [β -endorphin 30-31] on morphine-evoked serotonin and GABA efflux in the nucleus accumbens of conscious rats. *Neuropeptides* 58:23-29.
3. S Kiyici, N F Basaran, S Cavun and V Savci (2015) Central injection of CDP-choline suppresses serum ghrelin levels while increasing serum leptin levels in rats. *European Journal of Pharmacology* 764:264-270.
4. N F Basaran, R L Buyukuysal, W R Millington and S Cavun (2010) Glycyl-
5. glutamine (β -endorphin30-31) inhibits morphine-induced dopamine efflux in the nucleus accumbens. *Naunyn-Schmiedeberg's Archives of Pharmacology*, 381(5):467-475.

6. S Cavun, G Göktalay and W R Millington (2005) Glycyl-glutamine, an endogenous β -endorphin-derived peptide, inhibits morphine-induced conditioned place preference, tolerance, dependence, and withdrawal. *Journal of Pharmacology and Experimental Therapeutics* 315(2):949–958.

Biography

Sinan Cavun, after graduating from the Uludag University, Faculty of Medicine in 1993, completed his Doctoral Education in 1999. He has been working in the field of Pharmacology for a total of 17 years. He worked for eight years in Hospital Medicine Management as a Team Leader. He has focused on neuropharmacology, particularly on depression and neuroendocrine regulation. As a result of his work, he has a European patent in this regard (use of Gly-Gln in the treatment of depression).

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