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Pregnenolone as an Effective Prohormone for Multiple Therapeutic Uses

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ABSTRACT

If there is a deficit of endogenous steroid hormones, chemical derivatives can be used. However, an endogenous prohormone of the steroid hormones, namely pregnenolone, could also be applied. It was discovered and synthesized 90 years ago. Since then, many publications have demonstrated its positive effects, as it enables the endocrine glands to increase the production of corticoids and sex hormones. It is also effective as a neurosteroid against brain disorders. The widespread use of pregnenolone is therefore indicated.

Keywords: pregnenolone, sex hormones, steroid hormones, anti-ageing

INTRODUCTION

Pregnenolone is an endogenous prohormone. Pregnenolone was first synthesized by Adolf Butenandt et al. in 1934 (Butenandt & Westphal, 1934) and was then called the "mother hormone" of steroid hormones. Pregnenolone (P5), or pregn-5-en-3β-ol-20-one, is an endogenous steroid and precursor/metabolic intermediate in the biosynthesis of most of the steroid hormones, including the progestogens, androgens, estrogens, glucocorticoids, and mineralocorticoids (Henderson, Weinberg, & Wright, 1950; Marx et al., 2011; Vallée, Mayo, & Le Moal, 2001). In addition, pregnenolone is biologically active in its own right, acting as a neurosteroid (Vallée, 2016).

It is produced in the adrenal glands, the brain and the peripheral nervous system. Pregnenolone levels decrease with age: we produce 60 % less pregnenolone at 75 than at 35. However, plasma concentrations can also fall due to depression, anxiety, stress, toxin exposure and hypothyroidism.

Pregnenolone is formed from cholesterol by hydroxylation at C20 and C22 with subsequent cleavage of the side chain. The conversion is catalyzed by the enzyme cholesterol monooxygenase in the mitochondria and controlled by the pituitary hormones ACTH, FSH, LH (Figure 1) (Data sheet, n.d.; Pregnenolone biosynthesis, n.d.; Rassow et al., 2012).

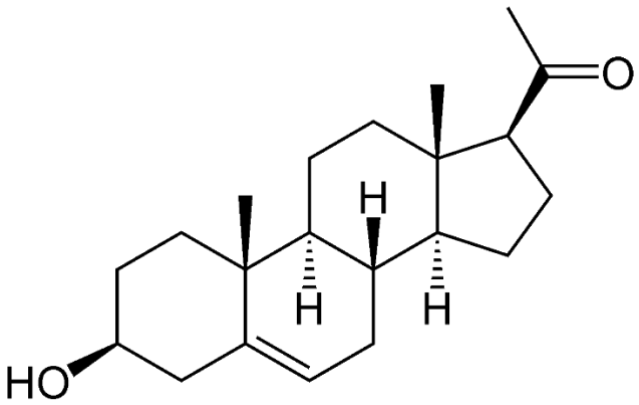

Figure 1: Structure of Pregnenolone

INVESTIGATIONS

In 1944, Pincus showed in a study with American army pilots that pregnenolone reduces feelings of stress and fatigue without any significant side effects (9.) In the 1950s, pregnenolone was tested on healthy volunteers to investigate its effect on learning and memory capacity, among other things. A significant improvement in performance was observed (McGavack, Chevalley, & Weissberg, 1951; Henderson, Weinberg, & Wright, 1950).

Several studies from the 1950s have proven its effectiveness in relieving the symptoms associated with rheumatoid arthritis: Less joint pain, tenderness, paralysis with improved strength and variety of movement (Guest et al., 1950; Freeman et al., 1950). This is thought to result from an increase in corticoids when pregnenolone is offered to the adrenal glands.

In the 1990s, pregnenolone attracted particular interest because it significantly improves learning and memory skills. American biochemists found that intravenous administration of pregnenolone into several parts of the brain of old mice significantly increased their memory abilities (Roberts, 1995; Flood, Morley, & Roberts, 1992). Broué et al. (2007) showed that the pregnenolone level in the nerve cells of mice decreases with age. As a result of the pregnenolone injections, these old animals showed the same spatial memory abilities as those of young mice.

Numerous experiments have been conducted to assess the effect of pregnenolone on memory loss due to Alzheimer's disease (Roberts, 1995; Mayo et al., 2005).

In 2007, Professor Baulieu's team (Bicêtre Hospital, Paris), in collaboration with American researchers (California University, USA), showed that pregnenolone increases the lifespan of a worm (Caenorhabditis elegans) by 15%. This is one of the most spectacular breakthroughs in the knowledge of ageing processes (Broué et al., 2007).

In older people, pregnenolone improves spatial memory and color perception in men and language memory in women (Saint Louis University, USA). The scientists suspect that restoring pregnenolone levels from adolescence can prevent age-related depression and significantly improve libido and well-being (Ducharme et al., 2010).

Taking pregnenolone, especially from the age of fifty, normalizes the levels of steroid hormones and raises them to the level of younger and healthier people. Post-menopausal women are often deficient in progestogens, a common cause of osteoporosis. Here, pregnenolone is a therapeutic agent of choice. Xiao et al. demonstrated that pregnenolone can induce glioma cells to undergo apoptosis, an interesting area of research (Xiao et al., 2014).

DISCUSSION

Pregnenolone enables a gentle therapy with few side effects for deficiencies in the following hormones: progestogens, androgens, oestrogens, glucocorticoids and mineralocorticoids. Since such deficiencies have increased in frequency today and the use of synthetically produced artificial analogs is rich in side effects, there is a broad field of application for pregnenolone. It should not go unmentioned that geriatrics as a whole can benefit from it, especially in the prevention of dementia and Alzheimer's disease.

It contradicts logic that artificial hormones are often prescribed, but not nature-identical hormones. Let's take the thyroid gland as an example: L-thyroxine is given for hypothyroidism. However, if it is the result of an iodine deficiency, the "prohormone" iodine would be indicated, combined with selenium, possibly also the amino acid L-tyrosine. This principle applies to endocrinology as a whole: if there is a deficiency of an end hormone, the use of a body-identical prohormone should be considered instead of an artificial variant.

CONCLUSIONS

It is understandable that treatment with endogenous substances is not in the interests of the pharmaceutical industry, as they cannot be patented and are marketed cheaply as OTC products. However, this is not justifiable in the case of pregnenolone and requires amendment. There is sufficient scientific evidence to support the frequent use of this "mother hormone". The author has only had positive experiences with it, including as an anti-ageing agent.

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REFERENCES

Broué, F., Liere, P., Kenyon, C., & Baulieu, E. E. (2007). A steroid hormone that extends the lifespan of Caenorhabditis elegans. *Aging Cell*, *6*(1), 87-94.

Butenandt, A., & Westphal, U. (1934). Zur Isolierung und Charakterisierung des Corpus-luteum-Hormons. *Berichte der deutschen chemischen Gesellschaft (A and B Series)*, *67*(8), 1440-1442. https://doi.org/10.1002/cber.19340670831

Data sheet. (n.d.). 5-Pregnen-3β-ol-20-one. Retrieved from Sigma-Aldrich.

Ducharme, N., Banks, W. A., Morley, J. E., Robinson, S. M., Niehoff, M. L., & Mattern, C. (2010). Brain distribution and behavioral effects of progesterone and pregnenolone after intranasal or intravenous administration. *European Journal of Pharmacology*, *641*(2-3), 128-134. https://doi.org/10.1016/j.ejphar.2010.05.033

Flood, J. F., Morley, J. E., & Roberts, E. (1992). Memory-enhancing effects in male mice of pregnenolone and steroids metabolically derived from it. *Proceedings of the National Academy of Sciences*, *89*(5), 1567-1571.

Freeman, H., Pincus, G., Johnson, C. W., Bachrach, S., McCabe, G. E., & MacGilpin, H. A. R. O. L. D. (1950). Therapeutic Efficacy of Δ5-Pregnenolone in Rheumatoid Arthritis: Preliminary Observations. *Journal of the American Medical Association*, *142*(15), 1124-1128.

Guest, C. M., Kammerer, W. H., Cecil, R. L., & Berson, S. A. (1950). Epinephrine, pregnenolone and testosterone in the treatment of rheumatoid arthritis. *Journal of the American Medical Association*, *143*(4), 338-344.

Henderson, E., Weinberg, M., & Wright, W. A. (1950). Pregnenolone. *The Journal of Clinical Endocrinology*, *10*(4), 455-474. https://doi.org/10.1210/jcem-10-4-455

Marx, C. E., Bradford, D. W., Hamer, R. M., Naylor, J. C., Allen, T. B., Lieberman, J. A., ... & Kilts, J. D. (2011). Pregnenolone as a novel therapeutic candidate in schizophrenia: emerging preclinical and clinical evidence. *Neuroscience*, *191*, 78-90. https://doi.org/10.1016/j.neuroscience.2011.06.076

Mayo, W., Lemaire, V., Malaterre, J., Rodriguez, J. J., Cayre, M., Stewart, M. G., ... & Abrous, D. N. (2005). Pregnenolone sulfate enhances neurogenesis and PSA-NCAM in young and aged hippocampus. *Neurobiology of Aging*, *26*(1), 103-114.

McGavack, T. H., Chevalley, J., & Weissberg, J. (1951). The use of Δ5-pregnenolone in various clinical disorders. *The Journal of Clinical Endocrinology*, *11*(6), 559-577.

Pincus, G., & Hoagland, H. (1944). Effects of administered pregnenolone on fatiguing psychomotor performance. *J Aviation Med*, *15*, 98-115.

Pregnenolone biosynthesis. (n.d.). R-HSA-196108. Retrieved from Reactome.Org

Rassow, J., Hauser, K., Netzker, R., & Deutzmann, R. (2012). *Biochemistry* (3rd ed.). Thieme-Verlagsgruppe. ISBN 978-3-13-125353-8.

Roberts, E. (1995). Pregnenolone—from Selye to Alzheimer and a model of the pregnenolone sulfate binding site on the GABAA receptor. *Biochemical Pharmacology*, *49*(1), 1-16.

Vallée, M. (2016). Neurosteroids and potential therapeutics: focus on pregnenolone. *The Journal of Steroid Biochemistry and Molecular Biology*, *160*, 78-87. https://doi.org/10.1016/j.jsbmb.2015.09.030

Vallée, M., Mayo, W., & Le Moal, M. (2001). Role of pregnenolone, dehydroepiandrosterone and their sulfate esters on learning and memory in cognitive aging. *Brain Research Reviews*, *37*(1-3), 301-312. https://doi.org/10.1016/S0165-0173(01)00135-7

Xiao, X., Chen, L., Ouyang, Y., Zhu, W., Qiu, P., Su, X., ... & Yan, G. (2014). Pregnenolone, a cholesterol metabolite, induces glioma cell apoptosis via activating extrinsic and intrinsic apoptotic pathways. *Oncology Letters*, *8*(2), 645-650. https://doi.org/10.3892/ol.2014.2147