

AlphaSize™ Abstracts and References

Alpha-Glycerol Phosphoryl Choline

Hormones & Metabolic Research, 1992; 24: 119-121

Effects of an Acetylcholine Precursor on GH Secretion in Elderly Subjects.

Ceda G.P., Marzani G.P., Tontodonati V., Piovani E., Banchini A., Baffoni M.T., Valenti G., and Hoffman A.R.

Abstract:

GH secretion is under complex neurotransmitter and hormonal control. GH releasing hormone (GHRH) is released from the hypothalamus into the hypothalamic-hypophyseal circulation, stimulating pulsatile GH secretion. Hypothalamic somatostatin, on the other hand, inhibits GH release. GH stimulates the synthesis of insulin-like growth factor I in several peripheral tissues, which mediates some, but not all, of GH hormone action. Completing the feedback-loop paradigm, IGF-I directly interacts with specific IGF receptors on somatotropes, inhibiting further GH secretion. Moreover, IGF receptors are present in brain, and there is evidence that locally synthesized IGF-I can inhibit GHRH release and stimulate somatostatin secretion, thereby suppressing GH secretion. Finally, GH inhibits its own secretion at the level of the hypothalamus.

Drug Development Research, 1992; 26: 439-447

Chronic Treatment with an Acetylcholine Synthesis Precursor, Alpha-Glycerolphosphorylcholine, Alters Brain Parameters Linked to Cholinergic Transmission and Passive Avoidance Behavior.

Govoni S., Lopez C.M., Battaini F., and Trabucchi M.

Abstract:

Chronic treatment with an acetylcholine synthesis precursor, alpha-glycerolphosphorylcholine, alters brain parameters linked to cholinergic transmission and passive avoidance behavior. The present study extends previous observations on the acute treatment with alpha-glycerolphosphorylcholine (GPC), a putative acetylcholine (ACh) precursor, and investigates the effect of chronic treatment with this drug on scopolamine-induced amnesia and on ACh release in the rat. The drug acutely administered antagonizes the amnesic effect of scopolamine (0.75 mg/kg s.c.) in passive avoidance experiments. The effect peaked at 600-mg/kg i.g. and lasted up to 30 hr. Potassium-stimulated release of ACh from slices of hippocampus and cerebral cortex was measured after various doses of GPC. The dose curve study indicated that GPC was able to increase ACh release in the hippocampus already at the dose of 75-mg/kg i.g. The maximum effect was obtained with 300-mg/kg i.g. (147% of the control values). The increase of the ACh release reached a maximum 3 hr following the administration, then declined toward control values. In the cortex, the effect was much less pronounced and shorter than in the hippocampus. The repeated (100 and 300 mg/kg i.g. 22 days) GPC administration effectively antagonized scopolamine-induced amnesia, indicating that there was no tolerance to this effect of GPC. While both doses were behaviorally active only 300 mg/kg was able to increase ACh release from hippocampus (+ 271%) and cortex (+ 57%). The data support the hypothesis that GPC improves behavioral performance in passive avoidance through an action on cholinergic transmission. On the other hand, it should be stressed that the action on ACh release is observed in a narrow time window in contrast to the long lasting effect on behavior. It is tempting to speculate that the effect on ACh may be related to cortical activation and important but not sufficient to explain the antagonism of scopolamine-induced amnesia. Along this line other mechanisms, possibly triggered by the action on ACh; many contribute to mediate the behavioral effect of GPC.

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Alpha-Glycerol Phosphoryl Choline

International Journal of Clinical Pharmacology, Therapy and Toxicology, 1992; Vol. 30, No. 9: 331-335.

A comparative study of free plasma choline levels following intramuscular administration of L- α -glycerylphosphorylcholine and citicoline in normal volunteers.

Gatti G., Barzaghi N., Acuto G., Abbiati G., Fossati T., and Perucca E.

Abstract:

L- α -glycerylphosphorylcholine (a-GPC) is a recently developed cognitive enhancer whose mode of action is considered to involve the release of free choline, which is then utilized for acetylcholine and phosphatidylcholine biosynthesis in the brain. The purpose of this study was to evaluate the profile of free plasma choline levels following a single i.m. dose of a-GPC in 12 normal volunteers. Citicoline (CTC), which also acts as a choline precursor, was included for comparison purposes. Each subject was studied on three randomized occasions, (i) in a control day in the absence of drug administration (to evaluate the plasma level profile of endogenous choline), (ii) after i.m. a-GPC (1,000 mg) and (iii) after i.m. CTC (1,000 mg) respectively, with a washout period of at least 1-week between sessions. Blood samples for plasma choline HPLC determinations were collected at regular intervals over a 6 h period. In the control session, plasma choline levels remained stable during the sampling period. The administration of a-GPC was associated with a rapid rise in plasma choline, peak levels being usually observed at the first (0.25 h) or second (0.5 h) sampling time after the injection. Thereafter, the concentration of choline declined gradually and returned to near baseline values at the end of the observation period. After the administration of CTC, plasma choline levels showed a similar time course but were considerably lower than those observed after the administration of a-GPC. Pharmacokinetic parameters calculated after subtracting the zero time concentration from all post-drug values indicated that exogenously derived choline declined in plasma with a half-life of 0.5 to 6.2 h, without any significant difference between a-GPC or CTC. Choline AUC values after a-GPC were significantly higher than those observed after CTC, but the difference was no longer significant when AUC's were corrected for the different choline content of the two preparations (405 mg for a-GPC vs. 213 mg for CTC). It is concluded that the i.m. Administration of a-GPC provides an effective means of increasing plasma choline levels.

References

AMENTA F., DEL VALLE M., VEGA J.A., ZACCIO D., Age-related structural changes in the rat cerebellar cortex: effect of choline alfoscerate treatment. *Mech Ageing Dev.* 61: 173-186. 1991.

GATTI G., et al., A comparative study of free plasma choline levels following intramuscular administration of L- α -glycerylphosphoryl-choline and citicoline in normal volunteers. *International Journal of Clinical Pharmacology, Therapy, & Toxicology.* 30(9): 331-335. 1992.

SCHETTINI G., CICERANO U., PELLEGRINI G., SORICELLI A., POSTIGLIONE A., Effect of choline alfoscerate in elderly patients with primary degenerative deficiency. *Department of Human Communication Sciences, Section of Pharmacology, Institute of Internal Medicine and Dysmetabolic Diseases, Chair of Nuclear Medicine, Faculty of Medicine and Surgery, University "FedericoII" of Naples.*