Applied Nutriceuticals® Unpublished Research, Nov. 2009,

The Acute Effects of a Dietary Supplement on Serum Growth Hormone Levels in Weight-Trained Male Subjects

Tanis, D., Orrell, D., McAnulty, A., and Long, Dr. W.

Lab Corp® and Applied Nutriceuticals® Research, Charlotte, North Carolina 28269

Address all correspondence and requests for reprints to: Dirk Tanis, Jr., MSci, Department of Research, Applied Nutriceuticals®, 8112 Statesville Road Suite G, Charlotte, NC 28269.

Abstract

Many weight-trained men seek to raise circulating serum growth hormone (GH) levels, both through training, and supplementation. The major source of circulating GH is the pituitary. The known anabolic effects of GH on skeletal muscle, and the current rise in supplements on the current market that purport increases in GH and related body composition, has become a huge market in the United States. Most oral growth hormone supplements have been shown to be ineffective, due to various factors, and, aside from several medically-supervised challenge tests, injectible peptides have historically been the only way to increase GH levels. However, a dietary supplement formulation that recently hit the International market, HGH-Up™, containing L-Dopa, a Dopa Decarboxylase Inhibitor (DDCI), specific vitamins and minerals, and Huperzine-A, a potent acetylcholinesterase (AChE) and somatostatin inhibitor seems to be promising in allowing for the increase of Serum GH in weight-trained men. We sought to test this hypothesis in the study. **Methods:** 3 men (mean age, 33 ± 3.2 yr, range 22–44) with at least 5 years of weight-training experience were studied. Parameters measured were mean body weight (230.0 lbs ± 20.2 lbs.), mean body fat (10.2 % ± 0.92%), mean muscular mass (206.54 lbs. ± 18.5 lbs.), and mean fat mass (23.46 lbs ± 2.11 lbs). Serum GH levels were measured via bloodwork (LabCorp®) on two separate days, after an overnight fast. Serum GH levels were measured with (Test) and without (Baseline) having taken the supplement, with serum GH being measured at time (t)= -15, 45, 90, and 150 min. 4 separate blood draws per analysis period were taken; 8 total per subject over two separate days, and on the test day, subjects were given a 6 capsule dosage of the supplement (t=0). **Results:** Each of the 3 weight-trained men (100%) had frank increases in serum GH levels after a 6 capsule dosage of HGH-Up™ when compared to baseline values. Average baseline Serum GH for the entire group was 0.496 ng/mL ± 0.045 ng/mL (SEM). Average peak Serum GH following administration of

the supplement was 11.8 ng/mL ± 1.06 ng/mL, representing an average total rise of 2,379% in Serum GH values for the group.

Introduction

Human Growth Hormone (HGH) is a known anabolic agent found in the human body. We and others have found that adding supraphysiological doses of HGH can lead to an increase in muscle mass, a decrease in body fat, and increases in recovery time from strenuous weight training (28). A multitude of products currently exist on the sports supplement market that purport to increase HGH, and many of these products are completely ineffective, due to a variety of reasons (7, 31). However, a new supplement formulation that was recently released to the public, HGH-Up™ , containing L-Dopa, a Dopa Decarboxylase Inhibitor (DDCI), specific vitamins and minerals, and Huperzine-A, a potent acetylcholinesterase (AChE) and somatostatin inhibitor seems to be promising in allowing for the increase of Serum GH in weight-trained men (12,20,21,29,30,32,41). We therefore sought to test the hypothesis that HGH-Up™ could increase serum HGH levels. To stimulate GH secretion, we chose a dosage of 6 HGH-Up™, taken first thing in the morning, after an overnight fast. The same group of subjects received a series of blood draws (measuring serum GH levels) on two separate days- one testing period after taking HGH-Up™, and one testing period without taking HGH-Up™. Serum HGH levels were matched on time-related variables, with normal GH values upon the first four hours after waking being factored in, and reference values for serum GH levels over a 24-hour period for the age range included in our cohort were generated and listed below in Figure 2.

Methods

Subjects

Three men between the ages of 22 and 44 yr (mean age, 33 ± 3.2 yr) were studied. There were no clinical, biochemical, or densitometric differences between those who underwent GH testing and those who did not. No patient had a history of thyroid dysfunction, glucocorticoid or anticonvulsant use, diabetes mellitus, gastrointestinal disease, gastrointestinal surgery, acromegaly, malignancy, or any other known metabolic disease. No patient had a history of alcoholism. All subjects were required to have at least 5 years of weight training experience. Parameters measured before the draw were mean body weight (230.0 lbs. ± 20.2 lbs.), mean muscular mass (206.54 lbs. ± 18.5 lbs.), mean body fat (10.2% lbs. ± 0.92%), and mean fat mass (23.46 lbs ± 2.11 lbs). There was no history of childhood GH deficiency or growth disturbance, no history of delayed

puberty, and no history of pituitary disease or deficiency. All subjects gave written informed consent.

Serum GH testing

There were two separate days of testing: Testing Day 1 (1), where each subject received a dosage of HGH-UP™, and Testing Day 2 (2), where none of the subjects received a dosage of the product. During testing days 1 and 2, 4 separate blood draws occurred on each day (via Lab Corp). At t=0 on Testing Day 1, each subject orally ingested six (6) capsules of HGH-Up™, and Serum GH levels were sampled at time (t)= -15, 45, 90, and 150 min. On Testing Day 2, Serum GH levels were sampled at (t)= 0, 45, 90, and 150 min, and with no oral ingestion of HGH-Up™ occurring. Studies were performed in the morning after an overnight fast, and the testing periods were separated by a period of 2 days.

Assays

Routine serum biochemical measurements were made using standard techniques. GH was measured by ICMA and expressed in nanograms per milliliter. All samples from each respective testing period were batched and assayed at the same time (36-40).

Body Mass Measurements

Body mass measurements (mean body weight, mean body fat, mean lean body mass, and mean fat mass) were taken on each subject. Body weight was recorded on a NIST-Calibrated Pelouze 4040 Scale, and body fat percentages were determined by using a set of NIST-Calibrated SKF Calipers. Measurements (7 total for each subject) were taken on the chest, abdomen, triceps, subscapula, suprailiac, midaxilla, and thigh. Results of the skin fold measurements were analyzed via the 7 SKF Jackson-Pollock Equation (43).

Results

Results of average GH (in ng/mL) taken via RIA during both periods of analysis are shown in Table 1. Subjects had no clinical evidence of anterior pituitary hormone abnormalities (3,5). For the group, mean body weight was 230.0 lbs. ± 20.2 lbs., mean muscular mass was 206.54 lbs. ± 18.5 lbs., mean body fat was 10.2% lbs. ± 0.92%, and mean fat mass was 23.46 lbs ± 2.11 lbs. These values are comparable to average for experienced weight-trained males of a comparable mean age (43).

Peak GH responsiveness was defined as the highest average level achieved by each group during either analysis period (1,2,4,44). All three patients responded maximally to the supplement, with a mean peak value of 11.8 ng/mL. Average baseline Serum GH for the entire group was 0.496 ng/mL ± 0.045 ng/mL, representing a increase above baseline of 2,379%. There was a steady curve of increase in each of the Test group

values post-administration of the supplement, with values increasing all the way through 150 minutes. All three subjects achieved peak GH at 150 min after dosing the supplement, and one subject responded as early as 30 min. after dosing. All three subjects reported feeling extreme hunger within 90 minutes of dosing the supplement, lasting until the end of the testing period.

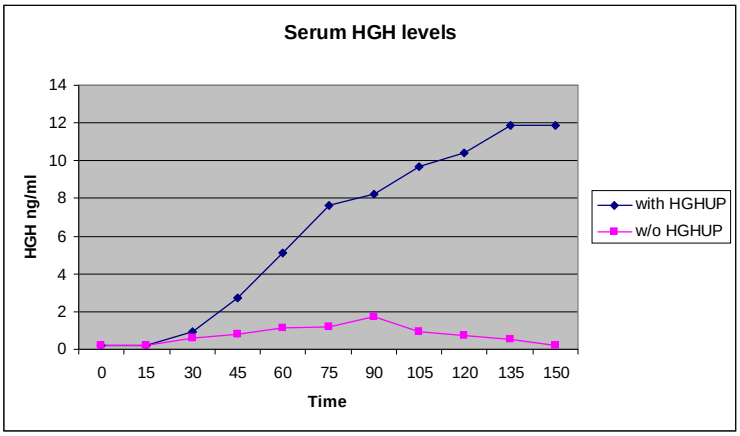

Figure 1. Peak responsiveness of GH to stimulation with (Blue; Test) or without (Pink; Baseline) HGH-Up. Data are shown as response to a single dose HGH-Up (0-150 min) in relation to baseline. Peak GH after taking HGH-Up was 11.8 ng/mL ± 1.06 ng/mL.

During the Baseline period, all three patients had minor fluctuations in GH levels, within the 0.2-2.5 ng/mL range, with a 2.5 ng/mL reading being the outlier, with the next largest value at 1.4 ng/mL. One subject reported feeling very sleepy and hungry during the baseline period, but there were no other complaints reported.

For the entire 2.5 h after having taken the supplement, the group of men produced an average of 3.72 ± 0.33 ng/mL per min of GH compared with production in the Baseline group of 0.38 ± 0.033 ng/mL per min. Total secretory output amounted to 558 ng/mL ± 50.22 ng/mL in the Test group, with a secretory output of 57 ng/mL ± 5.13 ng/mL in the Baseline group.

Discussion

The results of this investigation demonstrate that the supplement does raise mean serum GH in normal weight training males. The study was prompted by the massive amount of ineffective growth hormone products currently circulating on the supplement market. Consumers spend millions of dollars per year, only to get products that simply do not do what they claim, and this can have a deleterious effect on the sports supplement market as a whole, both in terms of reputation and overall consumer purchasing.

The increased levels of GH observed in each of the 3 subjects, especially on the second and third respective draws, indicate that the supplement shows extreme promise in this market. Increased GH can have numerous positive effects in terms of body fat loss and increased anabolism, and an orally viable non-prescription supplement that can allow end users a plausible alternative to prescription/pharmaceutical chemical intervention (20,33,35). This alone was a compelling reason to study potential GH secretory dynamics in a group of male weight trainers to explore how the supplement could manipulate GH in a time-dependant manner.

GH responses in the first 120 minutes after ingestion of the supplement were comparable with the results in Page *et. al* , who an analysis on GH-provocative challenge tests with 500 mg of oral L-Dopa in normal adult subjects (44). Subjects in this study reported an average increase to 17.6 ng/mL ± 7.4 ng/mL of GH at 90 minutes after administration, and a similar study by Etah *et al.* performed via RIA reported an average GH level of 5.7 ± 1.0 ng/mL 90-120 minutes after L-Dopa administration (45). In this study, subjects reported an average increase to 8.0 ng/mL ± 0.72 ng/mL during the draw at 90 minutes, which is significantly higher than the Etah study, but fairly close in line with the extrapolated Page study. The magnitude of our subjects' responses— about half that of Page's group— is likely to have occurred because of their use of an RIA to measure GH, whereas we used an ICMA. ICMA was selected as the means of assay due to its better ability to pick up L-Dopa-induced GH increases- IRMA and RIA tend to have substantial issues with this, unfortunately (6,36-38). In respect to this fact, GH values obtained by RIA are approximately twice those obtained by ICMA (in ng/mL), an observation that places the data of Page *et al.* in line with the data reported here (44). This can further be extrapolated to the results of the study as well- when matched to this variable (ICMA to RIA), GH responses for the time period are actually around 4,700% greater at 150 minutes for subjects in the Test group.

This brings up an interesting point concerning dose/response to L-Dopa: that the substance is most effective when conversion of L-Dopa to dopamine is mediated by a decarboxylase inhibitor (19,24). Decarboxylase inhibitors are generally administered at the same time as L-Dopa in order to reduce conversion of the L-dopa into dopamine in the periphery (2,3). (−)-epigallocatechin-3-O-gallate (EGCG), which is found in high amounts in the green tea extract used in the supplement**,** is a fairly potent decarboxylase inhibitor (19,24). The decarboxylase-inhibiting qualities of EGCG have been documented in several recent studies, in that EGCG seems to prevent L-dopa from converting into dopamine and allowing significant levels of L-dopa to reach the brain and increase growth hormone levels (2,3,19,24). This can potentially boost GH levels even higher than indicated in L-Dopa challenge studies, simply due to more intact L-Dopa crossing the BBB (2,3,19,22,23,24,25,26).

Another noteworthy observation is the continuation of the increase in serum GH up to 150 minutes, to an average of 11.8 ng/mL ± 1.06 ng/mL. This is important for several reasons: one, there seems to be a secondary, higher peak in GH levels at 150 min. This is very important, because GH levels may indeed actually rise further past what was indicated in the study, if given additional time. We believe that this has to do with the

half-lives of the different components in the product. L-Dopa seems to be the primary player in the first 90-120 minutes, as it has a half-life (t½) of about 90 minutes, and this has been validated by the dose-response curve in several different human studies (1,2,3,4). In these, studies, however, once the peak GH is attained at 90 minutes, there tends to be a rapid decrease in GH levels post-challenge, normally returning to baseline by t=180 (1,2,3). The exact opposite occurred during the study, and we feel that the longer half life of Huperzine-A (t½= 4 hours) may offer an explanation for the increase/peak in GH levels through 150 minutes, and possibly longer (8,9,10,11,16). Huperzine-A is a strong inhibitor of somatostatin via increasing hypothalamic cholinergic tone via acetylcholinesterase (AChE) inhibition (8,9,13,14,34). Somatostatin release is controlled in large part by the cholinergic system, as the cholinergic system is responsible for regulating the amount of acetylcholine found in the body at any given time (10,15,27). Acetylcholine is a neurotransmitter responsible for muscular activation in the peripheral nervous system, and tends to be excitatory in the central nervous system (CNS) (9,10). The CNS component of acetylcholine mediates the cholinergic system, and this is important because the cholinergic system is responsible for mediating growth hormone response. The mechanism through which this is accomplished is simple: by increasing acetylcholine levels, there will be an increase in mean serum GH (9,10,11,12). Somatostatin is the key inhibitory pituitary hormone to GH, and by manipulating somatostatin levels (via AChE inhibitors), GH can be increased markedly (12,13,14). Increased serum GH from the supplement allows for increased anabolism, better recovery, and increased muscle mass. In the case of the supplement, the pharmacology lends itself to an initial increase in GH via increased L-Dopa levels, and then a secondary increase in GH levels, possibly for up to 8 hours, due to subsequent somatostatin inhibition from the AChE inhibitor Huperzine-A (17,19). This also allows for increased mean serum GH, both per minute, and peak, through increasing or "fattening" the dose-response curve significantly (16,30,31). The anabolic effects of growth hormone seem to be more highly correlated with higher mean 12-24 hour serum GH levels, rather than higher peak GH levels over shorter intervals. Thus, by the aforementioned means, it may be surmised that the product could indeed raise serum GH levels in 8 hour or greater increments, thus making it a very useful anabolic agent, at least in terms of a viable non-prescription source of GH (16,19,31).

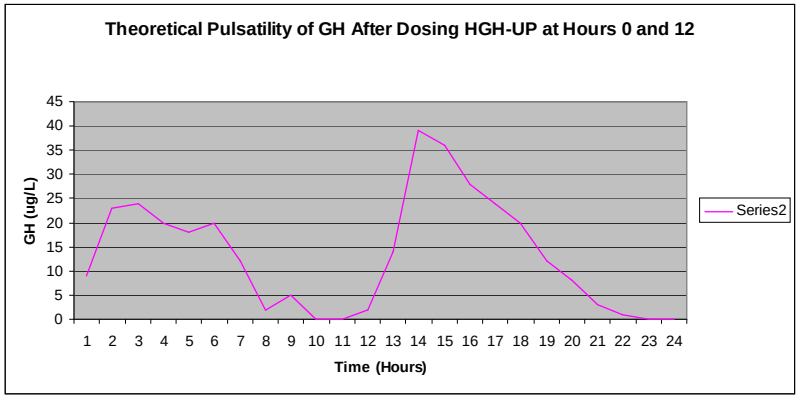

Figure 2. Theoretical GH output in response to stimulation with HGH-Up matched for RIA (note adjusted values). Data are shown as response to a single dose HGH-Up at t=0 and t=12.

This 8 hour-plus half-life could have some added positive implications for physique enhancement, in that some studies have indicated that taking an acetylcholine esterase inhibitor (in the case of the supplement, Huperzine-A) before sleep will result in dramatically reduced somatostatin levels and dramatically increase serum GH levels, as somatostatin seems to be the major inhibitory factor in sleep-related GH pulses (9,10,16,17,19). When AChE is inhibited by pryridostigmine (an AChE inhibitor very similar to Huperzine-A) GH pulse mass is increased, and mean serum GH almost *doubled* in several studies. In terms of potency, Huperzine-A has actually been shown to be more potent than pyridostigmine bromide in terms of AChE inhibition. There has also been a very popular trend recently of bodybuilders taking Huperzine-A along with injectible synthetic growth hormone, because the compound is so effective at inhibiting somatostatin and increasing serum GH (9-12). Also, EGCG has also been shown to significantly increase the effects of Huperzine A on acetylcholine esterase inhibition by increasing the transport of Huperzine-A by serum albumin, thus making this MOA potentially even more effective, for an even longer period of time, due to the long half-life of the Huperzine-A, and its positive effects on GH levels during sleep (17,18).

Acknowledgments

We thank LabCorp® for assisting with the assays and blood work.

References

1. Hanew, K., Tanaka, A, and Utsumi, A. *Plasma GH responses to GHRH, arginine, L-dopa, pyridostigmine, sequential administration of GHRH and combined administration of PD and GHRH in Turner's syndrome*. J. Endocrinol. Invest. 1998. Feb.; 21(2): 72-77.
2. Schönberger W, Grimm W, Ziegler R. *The effect of nacom (L-dopa and L-carbidopa) on growth hormone secretion in 75 patients with short stature.* Eur J Pediatr. 1977 Dec 30;127(1):15-9.
3. Schönberger W, Ziegler R, Brodt B, Grimm W. *HGH secretion after oral application of L-dopa and L-carbidopa*. Eur J Pediatr. 1976 Jun 8;122(3):195-200.
4. Fevang FO, Stoa RF, Thorsen T, Aarskog D. *The Effect of L-dopa with and without decarboxylase inhibitor on growth hormone secretion in children with short stature*. Acta Paediatr Scand. 1977 Jan; 66(1):81-84
5. Philippi H, Pohlenz J, Grimm W, Koffler T, Schönberger W. *Simultaneous stimulation of growth hormone, adrenocorticotropin, and cortisol with L-dopa, carbidopa, and propranolol in children of short stature.* Acta Paediatr, 2000 Apr;89(4):442-446.
6. Gordon M, Markham J, Hartlein JM, Koller JM, Loftin S, Black KJ. *Intravenous levodopa administration in humans based on a two-compartment kinetic model.* J. Neurosci Methods, 2007 Jan 30:159(2):300-307. Epub 2006 Aug 24
7. *Pyridoxine (B6) suppresses the rise in prolactin and increases the rise in growth hormone induced by exercise*. 1982 Aug 12;307(7):444-5.
8. Gordon RK, Haigh JR, Garcia GE, Feaster SR, Riel MA, Lenz DE, Aisen PS, Doctor BP. *Oral administration of pyridostigmine bromide and huperzine A protects human whole blood cholinesterases from ex vivo exposure to soman*. Chem Biol Interact. 2005 Dec 15;157-158:239-46. Epub 2005 Oct 26.
9. Wang R, Yan H, Tang XC. *Progress in studies of huperzine A, a natural cholinesterase inhibitor from Chinese herbal medicine.* Acta Pharmacol Sin. 2006 Jan;27(1):1-26
10. Kelijman M, Frohman LA. *The role of the cholinergic pathway in growth hormone feedback*. J Clin Endocrinol Metab. 1991 May;72(5):1081-7
11. Liang YQ, Tang XC. *Comparative studies of huperzine A, donepezil, and rivastigmine on brain acetylcholine, dopamine, norepinephrine, and 5-hydroxytryptamine levels in freely-moving rats*. Acta Pharmacol Sin. 2006 Sep;27(9):1127-36
12. Giustina A, Bossoni S, Bodini C, Doga M, Girelli A, Buffoli MG, Schettino M, Wehrenberg WB. *The role of cholinergic tone in modulating the growth hormone response to growth hormone-releasing hormone in normal man*. Metabolism. 1991 May;40(5):519-23
13. Friend K, Iranmanesh A, Login IS, Veldhuis JD *Pyridostigmine treatment selectively amplifies the mass of GH secreted per burst without altering GH burst frequency, half-life, basal GH secretion or the orderliness of GH release.* Eur J Endocrinol. 1997 Oct;137(4):377-86
14. Dinan TG, O'Keane V, Thakore J. *Pyridostigmine induced growth hormone release in mania: focus on the cholinergic/somatostatin system*. Clin Endocrinol (Oxf). 1994 Jan;40(1):93-6
15. Thakore JH, Coffey I, Dinan TG. *Time dependency of pyridostigmine-induced growth hormone response.* J Basic Clin Physiol Pharmacol. 1994 Apr-Jun;5(2):117-2
16. Li YX, Zhang RQ, Li CR, Jiang XH. *Pharmacokinetics of huperzine A following oral administration to human volunteers.* Eur J Drug Metab Pharmacokinet. 2007 Oct-Dec;32(4):183-7.
17. Haigh JR, Johnston SR, Peppernay A, Mattern PJ, Garcia GE, Doctor BP, Gordon RK, Aisen PS. *Protection of red blood cell acetylcholinesterase by oral huperzine A against ex vivo soman exposure: next generation prophylaxis and sequestering of acetylcholinesterase over butyrylcholinesterase*. Chem Biol Interact. 2008 Sep 25;175(1-3):380-6.
18. Xiao J, Chen X, Zhang L, Talbot SG, Li GC, Xu M. *Investigation of the mechanism of enhanced effect of EGCG on huperzine A's inhibition of acetylcholinesterase activity in rats by a multispectroscopic method*. J Agric Food Chem. 2008 Feb. 13:56(3) 910-915.
19. Zhang L, Cao H, Wen J, Xu M. *Green tea polyphenol (-)-epigallocatechin-3-gallate enhances the inhibitory effect of huperzine A on acetylcholinesterase by increasing the affinity with serum albumin.*
20. Berdanier, Carolyn D.; Dwyer, Johanna T.; Feldman, Elaine B. (2007). Handbook of Nutrition and Food. Boca Raton, Florida: CRC Press.
21. Saxena S and Dixit V.K: *Role of total alkaloids of Mucuna pruriens Baker in spermatogenesis in male rats*, Indian Journal of Natural Products. 1987, 3(2), 3-7.
22. Tharakan B, Dhanasekaran M, Mize-Berge J, Manyam BV. *Anti-Parkinson botanical Mucuna pruriens prevents levodopa induced plasmid and genomic DNA damage.*Phytother Res. 2007 Dec;21(12):1124-6.
23. Shukla KK, Mahdi AA, Ahmad MK, Jaiswar SP, Shankwar SN, Tiwari SC .*Mucuna pruriens Reduces Stress and Improves the Quality of Semen in Infertile Men* .Evid Based Complement Alternat Med. 2007 Dec 18. [Epub ahead of print

24. Bertoldi M, Gonsalvi M, Voltattorni CB. *Green Tea polyphenols: Novel irreversible inhibitors of dopa decarboxylase* Biochem Biophys Res Commun. 2001 Jun 1;284(1):90-3.
25. Vaidya RA, Aloorkar SD, Sheth AR, Pandya SK. *Activity of bromoergocryptine, Mucuna pruriens and L-dopa in th control of hyperprolactinaemia.* Neurol India. 1978 Dec;26(4):179-82.
26. Vaidya RA, Sheth AR, Aloorkar SD, Rege NR, Bagadia VN, Devi PK, Shah LP. *The inhibitory effect of the cowhage plant- mucuna pruriens-and L-dopa on chloropromazine-induced hyperprolactinemia.* Neurol India. 1978 Dec;26(4):177-8.
27. Epelbaum J, Guillou JL, Gastambide F, Hoyer D, Duron E, Viollet *Somatostatin, Alzheimer's disease and cognition: An old story coming of age?* C. Prog Neurobiol. 2009 Jul 10.Strowski MZ, Blake AD. *Function and expression of somatostatin receptors of the endocrine pancreas.* Mol Cell Endocrinol. 2008 May 14;286(1-2):169-79.
28. Haff, G. *Lecture Notes for Graduate Study: Hormonal Parameters Relevant to Training*. Appalachian State University, 2000.
29. Khoo, B. and Grossman, A. *Normal Physiology of the Hypothalamus and Anterior Pituitary*. St. Bartholomew's Hospital, West Smithfield, London. Neuroendocrinology, Hypothalamus, and Pituitary. 2007 Ch. 1 Lecture.
30. Various sources. *Anecdotal Information concerning the usage of AChE inhibitors with synthetic GH.*
31. Applied Nutriceuticals Research. *Unpublished alpha testing for new somatotropin-enhancing sports supplement*. Charlotte, NC. 2009
32. Nikolaeva AA, Koroleva SV, Ashmarin IP. *[Research of interactions in the dopamine-serotonin-somatostatin system promises new outlook in fundamental and practical respects]* Nikolaeva AA, Koroleva SV, Ashmarin IP. Eksp Klin Farmakol. 2009 Mar-Apr;72(2):60-4. Review
33. Cordido F, Isidro ML, Nemiña R, Sangiao-Alvarellos S.*Ghrelin and growth hormone secretagogues, physiological and pharmacological aspect.* Curr Drug Discov Technol. 2009 Mar;6(1):34-42.
34. Clemmons DR, Van Wyk JJ. 1984 Factors controlling blood concentration of somatomedin C. Clinics in endocrinology and metabolism. 13:113–143.[CrossRef][Medline]
35. Frantz AG, Kleinberg DL, Noel GL. 1972 Studies on prolactin in man. Recent Prog Horm Res. 28:527–590.
36. Carlsson LM, Rowland AM, Clark RG, Gesundheit N, Wong WL. 1991 Ligand mediated immunofunctional assay for quantitation of growth hormone binding protein in human blood. J Clin Endocrinol Metab. 73:1216–1223.[Abstract/Free Full Text]
37. Bowsher RR, Apathy JM, Ferguson AL, Riggin RM, Henry DP. 1990 Cross-reactivity of monomeric and dimeric biosynthetic human growth hormone in commercial immunoassays. Clin Chem. 36:362–6.[Abstract/Free Full Text]
38. Chevenne D, Beau N, Leger J, Porquet D. 1993 Variability of serum human growth hormone levels in different commercial assays: specificity of growth hormone-releasing hormone stimulation. Horm Res. 40:168–172.[CrossRef][Medline]
39. Rahim A, Toogood AA, Shalet SM. 1996 The assessment of growth hormone status in normal young adult males using a variety of provocative agents. Clin Endocrinol (Oxf). 45:557–562.[Medline]
40. Reutens AT, Veldhuis JD, Hoffman DM, Leung KC, Ho KKY**.** 1996 A highly sensitive growth hormone (GH) enzyme-linked immunoabsorbent assay uncovers increased contribution of a tonic mode of GH secretion in adults with organic GH deficiency. J Clin Endocrinol Metab. 81:1591–1597.[Abstract]
41. Modi KP, Patel NM, Goyal RK. *Estimation of L-dopa from Mucuna pruriens LINN and formulations containing M. pruriens by HPTLC method* Chem Pharm Bull (Tokyo). 2008 Mar: Dec;21(12): 1124-6.
42. Unnithan A.R. and Tandon V.L: *Role of growth hormone in spermatogenesis in male rats*. Indian Journal of Experimental Biology**.** 1982,20,734-737.
43. Baumgartner, T., and Jackson, A. *Measurement for Evaluation of Body Build and Composition.* Englewood Cliffs, NJ: Prentice Hall, 1974.
44. Page MD, Dieguez C, Valcavi R, Edwards C, Hall R, Scanlon MF.Clin Endocrinol (Oxf). *Growth hormone (GH) responses to arginine and L-dopa alone and after GHRH pretreatment.* 1988 May;28(5):551-8. Department of Medicine, University of Wales College of Medicine, Health Park, Cardiff, UK.
45. Etah S. Kurland, Fredriech K. W. Chan, Clifford J. Rosen and John P. Bilezikian. *Normal Growth Hormone Secretory Reserve in Men with Idiopathic Osteoporosis and Reduced Circulating Levels of Insulin-Like Growth Factor-I.* The Journal of Clinical Endocrinology & Metabolism Vol. 83, No. 7 2576-2579. Copyright © 1998 by The Endocrine Society