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Investigating the effects of resistance training on the functions of GH/IGF1 axis and L-arginine supplementation

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ABSTRACT

Physical activity and diet are the factors that influence the body's structure. The purpose of this study was to compare the effects of four weeks of resistance training, and L-arginine supplement consumption on growth hormone (GH), and Insulin-like growth factor 1 (IGF-1) Axis.Forty amateur male bodybuilders (aged= 22.93 ±3.50yrs., Weight= 70.23 ±11.04 Kg), p articipated in thisstudy.Theywererandomly divided into four equal groups, Resistance (R), L-arginine (A), Resistance with L-arginine (RA), and Control (C). The Rgroup was assigned to a four week resistance training program ،three times/week, three sets of tenexercises with 6-10 repetitions, at the 80-95% 1RM(One RepetitionMaximum*), with 120 seconds rest between sets),Agroup is consumingl-L-arginine (0.1 g.kg^{-1}.day^{-1}), RA group resistance training with consuming L-L-arginine ,andCgroup continued their normal lifestyle without exercise training. GH, IGF1, IGFBP-III plasma levelswere measured before, and after the protocol.One-way ANOVA indicated significant change in GH, IGF, IGFBP-IIIbetween four groups, and Tukey test demonstrated significant increaseGH, IGF1, IGFBP-III plasma levels in R, and RA group.Based upon these findings, we concluded that resistance training at 80-95% 1RM intensity, and resistance training along with oral L-arginine showssignificantly increase secretion of GH, IGF-1, IGFBP-IIIin amateur males, but additionoralL-arginine toexercise programdo not show significant differenceinGH, IGF-1, and IGFBP-III.*

Key words: GH/IGF1 axis,L-arginine,resistance

INTRODUCTION

Regular resistance trainingcould cause hypertrophy in skeletal muscle(1).Exerciseas a potent physiological stimulus elevatesgrowth hormone (GH),andInsulin-like growth factor 1 (IGF-1) secretion(2). IGF-1 is the major mediator of the anabolic and growth-promoting effects of growth hormone (GH)(3). The competing processes of cellular proliferation, cellular differentiation, and the

increased protein synthesis required for muscle repair or hypertrophic adaptation is regulated by distinct roles of IGF-1 isoforms(4). The Insulin-like growth factor-binding protein III (IGFBP-III) as a carrier protein for IGF-1, and had a rolein growth modulators(5). During recent years non-medication based techniques including physical and herbal agents have been dramatically developed for the treatment of different disorders (6-17).

L-arginine is a key polypeptide in a wide variety of synthetic and metabolic processes, and has been suggested to become conditionally essential during metabolic stress (18). L- L-arginine consumption had a positive effect on fatigue at the recovery stage after maximal intensity exercise.(19)Skeletal muscle is the major site of L-arginine production andconsequently, the activity of skeletal muscle may directly influence those tissues that utilize it(20).There is evidence from studies in vitro that intramuscular L-arginine hasa role in the regulation of muscle protein synthesisand breakdown.(20)Strenuous physical exercise as well as exhaustive training programs, and other physical stress conditions leading to L-arginine depletiongenerally occur in conditions of metabolic acidosis, and could be considered as anovertrainingmarker.(21)Also, it has been shown muscle L-arginine formation was suppressed in severely hypercatabolic, and during prolonged severe stress(20).Soeters et al. noted in thelack of intracellular L-arginine , consumingL-arginine supplementation could be useful (22).NovaL-arginine synthesis with pharmacological or nutritional interventions could potentially counteract L-arginine depletion.(23)Welbourne demonstrated that a small oral L-arginine load is capable of elevating plasma GH(24). Biolo et al. mentined torhGH (releasing hormone Growth Hormone) administrationintheL-arginine release from muscle into circulation (25).

By regardingresistance training as a stimulus for the production of GH, L-arginine metabolism in muscle mass, and also declinesL-arginine concentration in plasma as a result of muscular activity, we have hypothesized to maintainL-arginine muscle, and plasma level by consuming L-arginine as a supplement may have an effect on GH/IGF1 axis, and IGFBP-III as a markerto elevate serum IGF-1 and GH production.

In line with our recent studies on physical activity and anthropometric measures including weight changes [31,32], effect of endurance and resistance training on parameters related to sexual function in men[33] and on some of preinflammatory cytokines[34] and hormonal changes in different states [34-45] this study designed. The purpose of this study was to compare the effects of four weeks of resistance training, and L-arginine supplement consumption on growth hormone (GH), and Insulin-like growth factor 1 (IGF-1) Axis.

MATERIALS AND METHODS

This study was conducted from April 2013 to June 2013 at the Islamic Azad University, ayatollah amoli Branch.The participation in the study was voluntary. All subjects were informed of the objectives of this study. Each subject signed a written informed consent.

All subjects had not any symptoms of cardiovascular diseases, pulmonary disease, diabetes, high blood pressure, and their historically demonstrated that they had not taken any dietary supplements, and pharmaceutical drugs, or were not on any specific diet. Frothyamateur male body builders (aged= 22.93 ±3.50 yrs., weight= 70.24 ±11.04 Kg, height= 174.00±0.05 cm, and BMI= 24.20 ±4.00 $kg.m^{-2}$)were selected randomly from 40 eligible volunteers. They were randomly divided into four equal groups, Resistance training (R), L-arginine (A), Resistance training and L-arginine (RA), and Control (C) group.

The resistance group took part in Resistance training program for four weeks (three times / week). The duration of each session was 60-90 minutes. Each session was divided into three sections consisting of ten- minute warm up, 70- minute resistance training at the 80 -95% 1RM, and ten- minute cool down. The warm-up section consisted of stretching movement, rhythmic movement with low intensity. The resistance training section consisted of nine exercises (Staggered-Stance Squat,Barbell Bench Press, Barbell Behind Neck Press, DumbbellSide Bend, Dumbbellbiceps, Seated Barbell Shoulder Press, Deadlift, Half Squats, Standing Calve Raise) eachexercise performed in three sets. The cool down section

consisted of rhythmic movement with low severity, and stretching movement with deep breathing. L-arginine group consuming L-arginine (0.1 $g.kg^{-1}.day^{-1}$). The resistance training and L-arginine group took part in resistance training with consuming L-arginine (0.1 $g.kg^{-1}.day^{-1}$). The control group continued their normal lifestyle without exercise training or consumption l-L-arginine .

Body weight was measured on a digital scale (Tefal - WZ5100C0 with a precision to 100 grams, USA). To measure height, we used the stadiometer (Seca, Modell 214, Hamburg, Germany).Quetelet index ($kg.m^{-2}$) was used to calculate BMI(26). The body fat percentage based on weight, age, and thickness measurements of three skin folds (pectoral, abdomen, thigh) based on the Jackson-Pollock 3-point formula by using a caliper (Lafayette Skinfold Caliper II, Model 01128, USA)(26).

Venous blood samples were obtained from the antecubital vein of subjects in a seated position. Collecting blood samples were done at the same time of the day to reduce any diurnal variation of the hormonal response. Following overnight fasting 9-12 hours, the subjects came to the laboratory at 7:00 to 8:00 am, and took a rest for 30 min prior to the first blood collection. GH (µg/ml**)** was assessed by Enzyme-linked immunosorbent assay (ELISA) utilizing kits diaplas (USA), IGF-1 and IGFBP-III assessed by ELISA kit utilizing Mediagnost IGF-1 and Mediagnost IGFBP- III (Germany) respectively.

Relevant statistical analyses were performed using SPSS version16 on a personal computer ($P<0.05$ was considered to be statistically significant). Descriptive analysis were adopted for demographic, and clinical characteristics were reported as means ±SD (Standard Deviation).Before statistical analysis Kolmogorov-Smirnov test showed that the normal distribution of all variables, and Levene'stestwas used to show differingvariances between two groups before the start of the protocol($P>0.05$). T-dependence Test was used to show a significant difference between pre-test, and post- test of variables in each group ($P<0.05$).Analysis of covariance was used to compare post- test of variables between four groups. The power of tests was 0.80 ($P<0.05$).

RESULTS

Forty amateur male body builders (aged= 22.93 ±3.50 yrs., weight= 70.23 ±11.04 Kg, height= 174.00±0.05 cm, and BMI= 24.03 ±3.57 kg. m^{-2}, FP= 25.38±6.89%) completely took part in our study. Demographic, and clinical characteristics of all 40 subjects that completed the study period are given in table 1. Pre- tests, and post- tests as mean ±SD of variables (BMI, FP, GH, IGF-1, and IGFBP-III) in R, A, RA and C groups.

Table 1.Characteristics of variables as a Mean, and Standard Deviation in studying subjects

Variables		Mean ±SD. R	Mean ±SD A	Mean ±SD RA	Mean ±SD C
Weight (Kg)	Pre test	68.75 ±10.50	71.50 ±12.34	69.75 ±10.10	70.92 ±11.23
	Post test	69.80 ±10.80	71.83 ±14.50	70.23 ±10.80	70.80 ±12.52
BMI ($kg.m^{-2}$)	Pre test	23.65 ±3.50	24.72 ±3.50	23.85 ±3.60	23.92 ±3.70
	Post test	23.92 ±4.00	24.84 ±3.90	24.20 ±4.10	23.87 ±4.20
FP (%)	Pre test	24.21 ±6.00	26.36 ±4.50	25.80 ±4.54	25.16 ±4.54
	Post test	22.71 ±5.22	26.55 ±4.35	23. 51 ±6.41	25.21 ±4.93
GH (ng/ml)	Pre test	6.51 ±1.27	6.83 ±0.30	6.44 ±1.14	6.40 ±1.10
	Post test	14.36 ±0.83	6.30 ±0.80	12.50 ±2.40	6.43 ±0.70
IGF-1 (ng/ml)	Pre test	508.7 ±50.13	531.10 ±67.60	536.50 ±75.50	506.10 ±65.60
	Post test	576.2 ±56.02	516.20 ±35.60	620.90 ±138.78	514.0 ±40.90
IGFBP-III (ng/ml)	Pre test	5.27 ±1.10	5.96 ±0.70	5.74 ±0.90	5.50 ±1.08
	Posttest	7.30 ±0.96	5.19 ±0.80	6.39 ±0.62	4.92 ±0.80

BMI (Body Mass Index), GH (Growth Hormone), IGF-1 (Insulin-like growth factor 1), IGFBP-III (Insulin-like growth factor-binding protein III). Values expressed as Mean ±SD (Standard Deviation).

Resistance Training (R) (n = 10), L-arginine (A) (n = 10), Resistance with L-arginine (RA) (n = 10), Control group (C) (n = 10). P< 0.05.

KS test demonstrated distribution GH serum level in R (Z= 0.51, p= 0.89), A (Z= 0.82, p= 0.51), RA (Z= 0.32, p= 0.94), and C (Z= 0.85, p= 0.54), IGF-1 serum level in R (Z= 0.62, p= 0.73), A(Z= 0.53, p= 0.87), RA (Z= 0.10, p= 0.97), and C (Z= 0.12, p= 0.92), IGFBP-IIIserum level in R (Z= 0.63, p= 0.82), A(Z= 0.43, p= 0.91), RA (Z= 0.24, p= 0.85), and C (Z= 0.22, p= 0.88) in pre- test was normal distribution (p> 0.05).Levene'stest show there was no significant difference in variance of variables between two groups before the start of the protocol (P>0.05).

Characteristics of the T-dependence test have been in table 2 (p< 0.05).One way analysis have reported in GH (F= 6.05,p= 0.01*), IGF-1 (F= 4.19,p= 0.01*), and IGFBP-III(F= 5.59,p= 0.01*) (*P*<0.05).

Table 2.Characteristics of T-dependence test in studying subjects

Group / Variable	R		A		RA		C	
	t	p	T	P	t	p	t	p
GH (ng/ml)	22.95	0.01*	0.98	0.23	29.93	0.01*	0.07	0.94
IGF-1 (ng/ml)	3.84	0.01*	1.32	0.10	6.70	0.01*	0.56	0.58
IGFBP-III (ng/ml)	1.86	0.09	1.72	0.10	3.77	0.01*	1.48	0.17

GH (Growth Hormone), IGF-1 (Insulin-like growth factor 1), IGFBP-III (Insulin-like growth factor-binding protein III). Resistance Training (R) (n = 10), L-arginine (A) (n = 10), resistance with L-arginine (RA) (n = 10), Control group (C) (n = 10). P< 0.05.

Tukey test as a post hoc test of one way analysis in GH showed that there was a significant difference between R-RA (m= 1.22±0.68, p= 0.09), RA-A (m= 6.25±0.68, p= 0.01*), R-A(m= 15.20±0.68, p= 0.01*), RA-C (m= 14.15±0.68, p= 0.01*), R-C (m= 7.93±0.68, p= 0.01*), G-C (m= 0.87±0.68, p= 0.88) (*P*<0.05).

Tukey test as a post has the one way analysis in IGF-1showed there was a significant difference R-RA (m= 1.46±40.28, p= 0.01*), RA-A (m= 324.25±40.28, p= 0.01*), R-A(m= 164.20±40.28, p= 0.01*), RA-C (m= 324.15±40.28, p= 0.01*), R-C (m= 166.93±40.28, p= 0.01*), G-C (m= 2.20 ±40.28, p= 0.96) (*P*<0.05).

Tukey test as a post has the one way analysis in IGFBP-III showed there was a significant difference R-RA (m= 1.46 ±0.62, p= 0.07*), RA-A (m= 2.57 ±0.62, p= 0.01*), and RA-C (m= 2.60±0.62, p= 0.01*), whereas there was no significance difference between R-A(m= 1.31±0.62, p= 0.25), R-C (m= 1.24±0.62, p= 0.28), and G-C (m= 0.17±0.62, p= 0.89) group (*P*<0.05).

DISCUSSION

There was a significant increase in GH after four- week resistance training in our study. The change rates of GH in R, A, RA, and C groupswere120.58%, -7.75%, 94%, and 0.4% respectively.T-dependence test demonstrated a significant increase in GH serum level in R andRA groups (p< 0.05), and Tukey test as a post hocof One way analysis demonstrated there was no significant difference between R-RA, andA-C groups(*P*<0.05), so oral L-arginine as supplement had no significant effect on GH serum level.

Kochańska-Dziurowicz et al. showed an intense exercise led to a significant increase in GH concentration.(27) Whereas Voss et al. demonstrate that a period of heavy, long-term exercise with changes in plasma volume does not significantly increase the GH.(28)GH is widely abused by athletes specially to increase lean body mass and improve anaerobic exercise capacity, whereas it has suggested improving the athletic performance of professional male (29). Athletes muscle resistance, power, and aerobic exercise capacity are not enhanced by GH administration (30). Regarding the risks of adverse

effects of long-term abuse of GH like acromegaly, and increased morbidity and mortality(30) and also the use of GH in different clinical purposes like its effect on immunological function,(31) resistance training as a stimulator to increase produce GH is the safest method to increase GH. Althoughexercise-inducedincreasesinGH levels, but itsincrease is not as well asdue to exogenous GHusage.The advantage of endogenousGH is the lack of side effects, and had a role in adjustingreactionson other tissues.Increase GH level in response to exercise may to recruitment actin and myosin in muscle fibers. The rest interval between sets is a significant agent on the magnitude of acute GH responses.(32)The intensity of exercise and the rest time is the main factor as a stimulatorHypothalamus-Pituitary axis(33) and its effect to recruitactin and myosin (attach – detachment)and maximum shortening velocity of filaments in muscle fiber.(34)Also the age, sex, baseline of other hormones specially sex hormones, and disorder of sex releasinghormones are effectivefactorsonGH,also GH isaffectedbytheresultsinduce by exercise in each situation mentioned above.

Recently it reported the effect of L-arginine on fatigue(19), but there was no similar investigation to control GH/IGF1 axisin plasma level by considering oral L-arginine consumption.

Some studies demonstrated GH stimulates the synthesis, and regulation of IGF-1 in most tissues. IGF-1 is thought to be a potential to develop skeletal muscle, and regulate muscle hypertrophy(3, 4).We had a significant change in IGF-1in our study. The change rates of IGF-1 in R,A, RA, and C groups were 13.3%, -2.0%, 15.6%, and 1.5% respectively. T-dependence test demonstrated a significant increase in IGF-1serum level in R, and RA groups ($p< 0.05$). Kochańska-Dziurowicz et al. showed IGF-1 concentration did not change after intense exercise(27). Copeland et al. demonstrate that among recreational female runners, an ultra-marathon,IGF-1 decreased after ultra-marathon race in menopausal women, and remained lower in recovery,(35)also Eliakim et al. reported 14% drop in circulating IGF-1 in healthy adolescent females after exercise.(36)IGF system changes are associated with catabolic state, and differences in results may beduetoage, andintensities of physical activityamongstudies.Hypoactivity of the GH-IGF-1 axis could explain age-related.(37)Interestingly,theovarian hormonal function is an important contributing factortoGH/ IGF-1axis, whereas Milewiczmentioned 17b-estradiol may be as important contributor to IGF-1 plasma level as age in hypo estrogenic, hypo gonadotropic women(38).Sexualdifferences, sex hormones, and their effects on body composition (the effect of testosterone on muscle mass, metabolic changes, fat distribution due to progesterone)are important factors which are involvedinstudieswithcontradictoryresults. Eliakimetal.emphasize ongenderdifferencesinthe IGF axis changes, he noted that after exercise training significant increase muscle volume in weight-stable and IGF-1in adolescent males,(39)whereas Roberts et al. mentionedthere was no significant difference in IGF-1 in Vastuslateralis muscle biopsies among younger (18-25 years), and older (60-75 years) male groups, in baseline and after resistance training at an intensity of 80% 1RM,alsoin both age groups IGF-1 remained stable throughout the intervention.(40)

The result of the study showed a significant change in IGFBP-III. The change rates of IGFBP-III in R,A, RA, and C groups were 38.51%, -12.91%, 11.32%, and -10.54%, respectively. The T-dependence test demonstrated a significant increase in IGFBP-III serum level in RA group ($p< 0.05$). Tukey test as a post hoc emphasis this fact ($p<0.05$). It seems logical the increase in GH associated with IGF-1 and IGFBP-III. In humans, almost 80% of circulating IGF-1 is carried by IGFBP-III. IGFBP-IIIis regulated mainly by GH, but also to some degree by IGF-1.(41)In the plasma, 99% of IGFBPs modulate the availability of free IGF-1 to the tissues.

Rosa et al. reported combined resistance, and endurance training significantly increased GH level in both endurance- resistance, and resistance- endurance groups compared with baseline values, and also IGFBP-III concentrations significantly increased in the endurance- resistancegroup after the exercise trainings, but did not change significantly in the resistance - endurance group(42), so the design of protocol of training could have an important role in hormonal changes.These resultsdemonstrate the physical activity can have a significant effect onGH, IGF-1, and IGFBP-III levels after the exercise which depend on the time, and the amount of work done.

Exhaustive training is associated with a chronic reduction in plasma concentrations of L-arginine .(21) The intramuscular concentration of L-arginine is known to be related to the rate of the protein synthesis,and there is also some evidences that L-arginine produced by muscle is an important fuel, which regulates human metabolism, alters glycogen depleted muscles, and plays the role of L-arginine in promoting glycogen synthesis, so increased gluconeogenesis(18).Agostiniet al. reported increased L-arginine availability may contribute to decreased inflammation, which associated with optimal training,(21) so this could have an effect on muscle work capacity, and greater tolerate of resistance training,andtheeffect on the adaptation rate in muscle, which could include GH/IGF1 axis, but the results demonstrated L-arginine consumption had no significant effect on GH, IGF1, and IGFBP-III. The measure of the L-arginine serumlevel could help explain our study result. The lack of L-arginine (intracellular, plasma) measured was the limitation of this study, and another limitation factor was the lack of control of subjects feeding, whereassome studies noted changes in serum levels L-arginine in starving- feeding, and the role of carbohydrate in maintaining or depletingL-arginine resources.

CONCLUSION

Based upon these findings, we concluded that resistance training at 80-95% 1RM intensity,increasesignificantly secretion of GH, IGF-1, IGFBP-III in amateur males, oralL-arginine had no significant differenceinGH/IGF-1 axis, and also there was no significant difference between resistance training,andresistance training along with oral L-arginine in GH, IGF-1, and IGFBP-IIIchanges. We concluded resistance training is the stimulator to GH/IGF-1 axis in comparisonwithL-arginine supplements as a peptide to control the GH/IGF-1 axis on proteinssynthetize in muscles.

REFERENCES

1. Phillips SM. A brief review of critical processes in exercise-induced muscular hypertrophy. *Sports Med* 2014;44:71-77.

2. Glaser S, Friedrich N, Ewert R, et al. Association of circulating IGF-I and IGFBP-3 concentrations and exercise capacity in healthy volunteers: results of the Study of Health in Pomerania. *Growth Horm IGF Res* 2010;20:404-410.

3. Laron Z. Insulin-like growth factor 1 (IGF-1): a growth hormone. Molecular pathology : MP 2001;54:311-316.

4. Philippou A, Maridaki M, Halapas A, Koutsilieris M. The role of the insulin-like growth factor 1 (IGF-1) in skeletal muscle physiology. *In Vivo* 2007;21:45-54.

5. Juul A, Dalgaard P, Blum WF, et al. Serum levels of insulin-like growth factor (IGF)-binding protein-3 (IGFBP-3) in healthy infants, children, and adolescents: the relation to IGF-I, IGF-II, IGFBP-1, IGFBP-2, age, sex, body mass index, and pubertal maturation. *J Clin Endocrinol Metab* 1995;80:2534-2542.

6. Davi Vieira Teixeira da Silva, Carlos Adam Conte-Junior, Vânia Margaret Flosi Paschoalin and et al. Hormonal response to L-arginine supplementation in physically active individuals. Food Nutr Res. 2014; 58: 10.3402

7. Alvares TS, Conte-Junior CA, Silva JT and Paschoalin VM. L-arginine does not improve biochemical and hormonal response in trained runners after 4 weeks of supplementation. Nutr Res. 2014 Jan;34(1):31-9

8. Forbes SC, Harber V and Bell GJ. Oral L-arginine before resistance exercise blunts growth hormone in strength trained males. Int J Sport Nutr Exerc Metab. 2014 Apr;24(2):236-44

9. Collier SR, Collins E, Kanaley JA. Oral arginine attenuates the growth hormone response to resistance exercise. J Appl Physiol (1985). 2006 Sep;101(3):848-52.

10. Forbes SC, Bell GJ. The acute effects of a low and high dose of oral L-arginine supplementation in young active males at rest. Appl Physiol Nutr Metab. 2011 Jun;36(3):405-11

11. Sunderland KL, Greer F, Morales J. VO2max and ventilatory threshold of trained cyclists are not affected by 28-day L-arginine supplementation. J Strength Cond Res. 2011 Mar;25(3):833-7

12.Kanaley JA. Growth hormone, arginine and exercise. Curr Opin Clin Nutr Metab Care. 2008 Jan;11(1):50-4.
13. Halson SL. Sleep in elite athletes and nutritional interventions to enhance sleep. Sports Med. 2014 May;44 Suppl 1:S13-23.
14. Nieman D. *Exercise Testing & Prescription*: McGraw-Hill Education; 2010.
15. Kochanska-Dziurowicz AA, Janikowska G, Bijak A, et al. The effect of maximal physical exercise on relationships between the growth hormone (GH) and insulin growth factor 1 (IGF-1) and transcriptional activity of CYP1A2 in young ice hockey players. *J Sports Med Phys Fitness*2015;55(3):158-163.
16. Voss SC, Robinson N, Alsayrafi M, et al. The effect of a period of intense exercise on the marker approach to detect growth hormone doping in sports. *Drug Test Anal* 2014;6:582-586.
17. Liu H, Bravata DM, Olkin I, et al. Systematic review: the effects of growth hormone on athletic performance. *Annals of internal medicine* 2008;148:747-758.
18. Birzniece V, Nelson AE, Ho KK. Growth hormone administration: is it safe and effective for athletic performance. *Endocrinology and metabolism clinics of North America* 2010;39:11-23.
19. Ramos S, Gray B, Van Driel M, et al. Recombinant human growth hormone—Effects on cytokine production in healthy young males. *Journal of Science and Medicine in Sport* 2010;13:e10-e1.
20. Bottaro M, Martins B, Gentil P, et al. Effects of rest duration between sets of resistance training on acute hormonal responses in trained women. *Journal of Science and Medicine in Sport* 2009;12:73-78.
21. Traustadottir T, Bosch PR, Cantu T, et al. Hypothalamic-pituitary-adrenal axis response and recovery from high-intensity exercise in women: effects of aging and fitness. *The Journal of clinical endocrinology and metabolism* 2004;89:3248-3254.
22. Canepari M, Rossi R, Pellegrino MA, et al. Effects of resistance training on myosin function studied by the in vitro motility assay in young and older men. *Journal of applied physiology* 2005;98:2390-2395.
23. Copeland JL, Verzosa ML. Endocrine response to an ultra-marathon in pre- and post-menopausal women. *Biol Sport* 2014;31:125-131.
24. Eliakim A, Brasel JA, Mohan S, et al. Physical fitness, endurance training, and the growth hormone insulin-like growth factor I system in adolescent females. *Journal of Clinical Endocrinology & Metabolism* 1996;81:3986-3992.
25. Arvat E, Ceda G, Ramunni J, et al. The IGF-I response to very low rhGH doses is preserved in human ageing. *Clin Endocrinol* 1998;49:757-763.
26. Milewicz T, Krzysiek J, Sztefko K, et al. 17beta-estradiol regulation of human growth hormone (hGH), insulin-like growth factor-I (IGF-I) and insulin-like growth factor binding protein-3 (IGFBP-3) axis in hypoestrogenic, hypergonadotropic women. *Endokrynol Pol* 2005;56:876-882.
27. Eliakim A, Brasel JA, Mohan S, et al. Increased physical activity and the growth hormone-IGF-I axis in adolescent males. *Am J Physiol* 1998;275:R308-314.
28. Roberts MD, Dalbo VJ, Sunderland KL, et al. IGF-1 splice variant and IGF-1 peptide expression patterns in young and old human skeletal muscle prior to and following sequential exercise bouts. *Eur J Appl Physiol* 2010;110:961-969.
29. Kanety H, Karasik A, Klinger B, et al. Long-term treatment of Laron type dwarfs with insulin-like growth factor-1 increases serum insulin-like growth factor-binding protein-3 in the absence of growth hormone activity. *Acta endocrinologica* 1993;128:144-149.
30. Rosa C, Vilaca-Alves J, Fernandes HM, et al. Order effects of combined strength and endurance training on testosterone, cortisol, growth hormone and IGFBP-3 in concurrent-trained men. *J Strength Cond Res* 2015;29(1):74-79.
31. Hosseini S, Gorjian M, Rasouli L, Shirali S. A Comparison between the Effect of Green Tea and Kombucha Prepared from Green Tea on the Weight of Diabetic Rats.

32. Abedi A, Shirali S, Jamshidnezhad J, Vakili M, Hosseini S, Sharafi M. The Effect of Mobile Phone Short Messages System on Physical Activity and Anthropometric Measures among Postmenopausal Women. 2014, 4(9) pp. 31-39.
33. Barari A, Ayatollahi A, Shirali S, Ghasemi M, Hosseini S, Ekrami A, Khandan Del A. Effect of Endurance and Resistance Training on Parameters Related to Sexual Function in Men. Medical Laboratory Journal, 2014, 8 (3)(47-53).
34. Barari A, Alavi S, Shirali S, Ghazalian F. Effect of short-term endurance training and silymarin consumption on some of preinflammatory cytokines, growth mediators and immune system performance. Annals of Biological Research 3 (6), 2933-7.
35. Chashmpoosh M, Shirali S, Abyaz S, Shirali A. The effect of work shift and short sleep duration on hormonal changes in Ahvaz airport personals. Persian Journal of Medical Sciences (PJMS), 2015, 2(3).
36. Shirali S, Daneghian S, Barari A, Masoumi H, Rezaee H, Rahimi R. The Effects of Six Weeks Plyometric Training and Mistletoe Supplementation on Changes of Cytokines Levels and Performance in Basketball Players. The AYER, 2015, 1(267-276).
37.Ebrahimi E, Shirali S, Talaei R. The Protective Effect of Marigold Hydroalcoholic Extract in STZ-Induced Diabetic Rats: Evaluation of Cardiac and Pancreatic Biomarkers in the Serum. Journal of Botany, Volume 2016 (2016), Article ID 9803928, 6 pages.
38.Shirali S., Bathaie S. Z., and Nakhjavani M., "Effect of crocin on the insulin resistance and lipid profile of streptozotocin induced diabetic rats," Phytotherapy Research, vol. 27, no. 7, pp.1042–1047, 2013.
39.Shirali S., Bathaie S. Z., and Nakhjavani M. and Ashoori M., "Effects of saffron (Crocus sativus L.) aqueous extract on serum biochemical factors in streptozotocin-induced diabetic rats," Iranian Journal of Medicinal and Aromatic Plants, 2012, vol. 28, pp. 293–308.
40. Sharifat M, Shirali S and Ebadi P, "Investigation of changes in levels of AGEs and β2-microglobulin in patients with type 2 diabetes," Journal of Academic and Applied Studies, 2014, vol. 4, no.9, pp. 1–10.
41. Mahdizadeh R., Shirali S and Ebadi P, "Investigation of imbalance of trace elements in patients with type 2 diabetesmellitus," Journal of Academic and Applied Studies, vol. 4, no. 9, pp. 11–21,2014.
42. Barari A, Fakori Joybari M, Shirali S, Shojaee M, and Khandandel A,"Effect of eight-week consumption of purslane extract on peroxidane/antioxidant balance in women with type 2 diabetes,"Medical Laboratory Journal, vol. 8, no. 2, pp. 1–7, 2014.
43. Bathaie S. Z., Mokarizade N., and Shirali S., "An overview of the mechanisms of plant ingredients in the treatment of diabetes mellitus," Journal of Medicinal Plants, vol. 11, no. 44, pp. 1–24,2012.
44. Mahdizadeh R., Sharifat M, Shirali S, Tarrah A. (2015). Investigation of changes in levels of serum elements, lipid profile and advanced glycation end product in patients with type 2 diabetes. International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS). 2015, 4(7): 244-261.
45. Chashmposh M, Shirali S, Ebrahimi E, Barari A .Correlation Between Hormonal and Neurochemical Changes and Depression With Menopausal STATUS: A Systematic Review. Women's Health Bulletin. 2015, 2 (3).