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Benefits of Supplementation with Herbal Medicines in Anabolic Hormone Replacement Related to Aging

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Abstract

Exercise can be carried out according to the morphological and physiological changes of the living organism over time. The increase in life expectancy is also an achievement along with functional decline and increased disease are observed. Aging in a healthy way for a general well-being, however, when aging is not successful, the elderly have a great tendency towards a functional, cognitive and other diseases, generating the total dependence of basic activities, thus determining the need care.

The present article had the objective of supplementation with phytotherapics in the anabolic hormone replacement related to aging. The study was based on the literature review, and a case study was done in the United States. Library of Medicine, Pub Direct, Science Direct, Cochrane Library, Electronic Scientific Library, Online Databases (SciELO), Scopus, Web of Science, Medline via Proquest and Periodics capturing the years between 2007 and 2019, using the terms of reference "Aging and Metabolic Alterations" "Aging and Phytotherapics" "Aging and *Tribulus terrestris*" "Aging and *Maca Peruvian*" "Aging and Ginseng", in addition we related the term hormone with each phytotherapeutic mentioned. They observe that the herbal remedies Tribulus terrestris, Maca peruana and Ginseng possess in their combination with the chemistry, anabolic, being thus, a supplementation with these products can allow an anabolic hormonal balance, generating the effect in the levels of catabolic hormones, providing a better This topic was extracted from population longevity.

1. Introduction

Aging refers to the progressive changes that occur in all cells, tissues and organs from the moment of conception until death and occurs at different rates in each individual. The proportion of elderly people in the world population has increased rapidly in recent years, especially due to the demographic explosion that occurred in past decades, the improvement in quality of life and health conditions and the decrease in birth rates (LIN et al, 2012; PRINCE *et al*, 2013, ALVES et al, 2007).

The increase in life expectancy promotes the need for macro-structural reorganization in several sectors, especially public social and health policies. A longer-lived population is also accompanied by a change in the prevalence of diseases, notably chronic non-communicable diseases, and functional disability. (ALVES *et al*, 2007).

According to the World Health Organization (WHO) and the United Nations Population Fund (UNFPA), an aging population is one of humanity's greatest trium-

phs and also one of our greatest challenges. Worldwide, the proportion of people aged 60 and over corresponds to the fastest growing age group. In 2012, the number of elderly people in the world was almost 810 million. This number is projected to more than double by 2050, reaching 2 billion, 80% of which in developing countries (WHO, 2015; UNFPA 2012).

It is estimated that, in 2025, Brazil will occupy the sixth place in the world in terms of the number of elderly people, reaching around 32 million people aged 60 and over. In 2050, children aged 0 to 14 years will represent 13.15%, while the elderly population will reach 22.71% of the total population (IBGE, 2013, 2015).

According to Brito (2008) and Kalache (2008), this population aging is considered one of the greatest public health challenges, as well as one of the most important structural phenomena that has impacted the Brazilian economy and society since the second half of the 20th century.

Faced with these changes, with population aging and increased life expectancy, factors, such as the significant reduction in the fertility rate associated with the strong reduction in the infant mortality rate, are decisive in this demographic transition (MORAES, 2012). Also noteworthy are the scientific and technological transformations that also directly impact people's daily lives (PEDRO, 2013).

The growing number of elderly people calls for the development of specific strategies that can offer adequate support to the growing population and their specific needs. In this perspective, the importance of the scope of Science and Technology (S&T) for the health sector in the development of benefits to society through the incorporation of new knowledge and technologies, sometimes based on traditional folk medicine, such as the use of of herbal medicines (SILVA *et al.*, 2014).

With the constant increase in life expectancy, disabling diseases associated with aging have become more prevalent. The prevalence of chronic diseases, the risks of physical limitations, cognitive loss, sensory decline and accident propensity and social isolation are

increasing. In addition to physical aspects, mental health is also compromised, with a consequent deterioration in the health of the elderly.

It is known that with advancing age, especially over 50 years, there is a decline in anabolic hormones such as Testosterone, Growth Hormone, Insulin, Vitamin D and Estradiol and an increase in catabolic hormones such as Glucocorticoids, Catecholamines, Cytokines and Interleukins. This hormonal imbalance leads to consequences on body structure and functioning, directly affecting people's health and longevity (DOHERTY, 2003; MORLEY, 2008).

Thus, an alternative of hormonal balance is configured to supplementation with herbal medicines that have active ingredients in their chemical composition capable of inducing such an effect, directly influencing the anabolic and catabolic hormonal balance in the search for organic integrity related to longevity. The objective of this work is to describe the benefits of herbal supplementation of ginseng, Peruvian maca and tribulus terrestris in the adequacy of anabolic hormone rates in the elderly.

2. Methodology

This study consists of a literature review, where an electronic search was performed in the United States Library of Medicine (PubMed), Science Direct, Cochrane Library, Scientific Electronic Library, Online databases (SciELO), Scopus, Web of Science, Medline via Proquest and Periodicos Capes covering the years between 1994 and 2019, using the terms of reference "Aging and Metabolic Changes" "Aging and Herbal Medicine" "Aging and Tribulus terrestris" "Aging and Peruvian Maca" "Aging and Ginseng", in addition we list the term hormone with each herbal medicine mentioned.

3. Development

3.1 Nutritional State and Aging

As you get older, the number of physical limitations you are exposed to increases, which redu-

ces people's quality of life. In the West, 30% of the aging population are faced with these limitations, which vary in severity, increasing the chances of exposure to falls, comorbidities and premature death (TIELAND; TROUWBORST, CLARK, 2017).

There is no standard aging process for all individuals, so establishing markers that relate to pathologies associated with aging is a good method of assessing biological deterioration regardless of chronological age (BANERJEE *et al,* 2011).

Research carried out in places with a longer population also shows that traditional diets that are more natural and rich in vegetables, away from ultra-processed foods are a common habit of long-lived elderly people. They tend to follow the traditional eating habits of the place, such as the Mediterranean diet, without conforming to new patterns and fads, maintain low levels of stress and participate in community routines, practicing light to moderate physical activity (REDDY and CHAIBAN, 2017).

In addition, these factors can be intensified, contributing to exposure to weaknesses and limitations when it is necessary to use medication for a prolonged period or permanently, because despite the increase in life expectancy, the high rates of non-chronic diseases still remain. Transmissible diseases, which makes the use of medications more and more compromising the metabolism and absorption of nutrients in older patients (VITOLO, 2008).

3.2 Metabolic Endocrine Changes in Aging

The endocrine function has a regulating action on reproduction, metabolism, development, growth, as well as on the aging process, being considered an important marker for a long life to also mean a qualitatively interesting life (LÓPEZ-OTÍN et al, 2016, GUARENTE, 2014). It is known that the hormonal decline according to Figure 3 is a condition inherent to the human organism.

The aging process is associated with changes that include a decline in neuromuscular function and a consequent reduction in muscle mass and strength. Sar-

copenia is a central phenomenon in the aging process, as it can be aggravated by other changes triggered by aging. This sarcopenia that begins around the third or fourth decade of life, leading to progressive disability and loss of autonomy (WOO, 2007).

The mechanisms that occur with aging and that contribute to the development of sarcopenia are multiple and include: increased apoptosis and mitochondrial dysfunction in myocytes, neurodegenerative processes (loss of α motoneurons), reduced levels of anabolic hormones (testosterone, estrogens, hormone growth, insulin growth factor-1), increased production of pro-inflammatory cytokines (TNF-α, IL-6), oxidative stress due to the accumulation of free radicals, physical inactivity and inadequate nutritional intake (RASMUSSEN *et al*, 2006).

Of all these factors responsible for the sarcopenia of aging, physical inactivity and inadequate nutritional intake, in addition to being related to the main cellular mechanisms underlying sarcopenia, they are modifiable factors that deserve special importance as an intervention strategy in order to delay progression of sarcopenia. Resistance exercise is the best type of exercise to increase muscle mass and strength although aerobic exercise also has important benefits. The increase in the quantity and quality of proteins in the diet becomes one of the most important strategies to avoid sarcopenia (SONG *et al*, 2004).

Although sarcopenia is present in all of these processes, there are marked differences in its underlying mechanisms. Thus, while in the sarcopenia of aging, the decrease in protein synthesis is one of the important mechanisms, in the sarcopenia associated with hunger or chronic disease it is the increase in the muscular catabolic process that is the cause (ZAMBONI *et al*, 2008). The sarcopenia of aging is part of a complex and natural process of aging, where several mechanisms and alterations are involved and, as such, has a multifactorial etiology.

The loss of muscle proteins that results from an imbalance between protein synthesis and degradation contributes to the development of sarcopenia (DIRKS

and LEEUWENBURGH, 2005). Muscle atrophy occurs when protein degradation exceeds protein synthesis. In fact, there is evidence that aging is associated with a decreased rate of synthesis of muscle proteins, myofibrillar proteins (actin / myosin) and mitochondrial proteins (DOHERTY, 2003).

During aging, there are several factors that contribute to changes in protein synthesis and turnover, among which are: "aging anorexia" that is related to lower protein intake; the decrease in the postprandial anabolic response, low-grade chronic inflammation; oxidative stress and hormonal changes (NEWMAN *et al,* 2005).

Aging is also related to increased resistance to other anabolic stimuli, notably insulin. The impact of insulin resistance on age-related muscle loss has recently been proposed since the increase in intracellular fat in muscle fibers is known to be associated with an increased risk of insulin resistance with aging (BARBIERI *et al*, 2003).

There is evidence that the increase in fat mass, particularly the increase in abdominal fat, and the reduction of sex hormone levels with age contribute to the increase in pro-inflammatory cytokines that occurs with aging (SHRAGER *et al*, 2007).

Pro-inflammatory cytokines (TNF, IL1 and IL6) directly promote muscle breakdown by increasing proteolysis and decreasing protein synthesis. The activation of the ubiquitin-proteosome pathway, responsible for proteolysis, and the decrease in the production of IGF-1 are two of the mechanisms that lead to the loss of muscle mass by a high level of cytokines (SHRAGER *et al*, 2007). An indirect effect of TNF on muscle protein metabolism may be its ability to inhibit the action of insulin (PHILIPS AND LEEUWENBURGH, 2005).

According to Hughes and colleagues in 2002, aging is associated with a decrease in levels of free testosterone and adrenal androgens including DHEA (dihydroepiandrosterone), which contributes to the decrease in muscle mass and bone density. In elderly women, bioavailable testosterone levels also decrease, particularly in the years immediately after

menopause begins (NAIR, 2005; MORLEY, 2008). Several studies demonstrate that testosterone increases muscle mass and strength by stimulating the activation of satellite cells and protein synthesis, this increase in muscle strength and physical performance has been seen in male patients who receive testosterone administration due to hypogonadism (MORLEY, 2008).

In women, associated with menopause, there is also a decrease in estrogens, which are hormones that also have anabolic effects on muscle, possibly as a result of their conversion to testosterone (DOHERTY, 2003).

Estrogens and testosterone can also inhibit the production of IL-1 and IL-6, which suggests that the decrease in the levels of these hormones can have an indirect catabolic effect on the muscle (DOHERTY, 2003). During perimenopause, impairment in muscle performance has been observed, accompanied by a rapid and dramatic decrease in hormone production by the ovary. This suggests that female sex steroid hormones play an important role in regulating muscle performance in middle-aged women and in elderly women, suggesting that hormone replacement therapy can mitigate the loss of muscle mass that occurs in the perimenopause period (DOHERTY, 2003).

It is observed that the advancement of the age group directly influences the decline in the anabolic hormonal rate of people, in this perspective we find herbal medicines, which have phytosteroid and phytoestrogen in their chemical composition capable of contributing to the maintenance of anabolic hormonal rate.

3.2 Phytotherapy and its Endocrine Actions

Phytotherapic means that medicine obtained using exclusively active vegetable raw materials. It is characterized by knowledge of the effectiveness and risks of its use, as well as by the reproducibility and constancy of its quality. Its effectiveness and safety, being validated through ethnopharmacological surveys of use, technoscientific documentation in publications or phase 3

clinical trials (RDC nº 48/04 - Anvisa).

Herbal medicines are an important source of innovation in health (MINISTÉRIO DA SAÚDE, 2006). Therefore, traditional herbal medicine, which uses centuries of experience, still plays an important complementary role in improving human health (POKRYWKA et al, 2014).

In this sense, it constitutes an alternative therapy modality in the face of health needs, with its increasing use in the elderly population of several countries (MARLIÉRE et al, 2008).

The advances that have taken place in the scientific area have allowed the development of phytotherapies that are known to be safe and effective, as well as a strong tendency to search, by the population, for less aggressive therapies (YUNES; PEDROSA, CECHINEL FILHO, 2001). Since the elderly, in general, use a high number of medications and for a prolonged period, which makes them more vulnerable to the risks associated with polypharmacy (ALEXANDRE, BAGATINE and SIMÕES, 2008).

Herbs have been used throughout history to improve physical performance, but scientific scrutiny with controlled clinical trials has only been used recently to study such effects. The herbal approach has been put in place to improve the health of men and women. “Currently, the use of medicinal and herbal plants is a worldwide practice, being encouraged by the World Health Organization (WHO), especially in developing countries” (MATTOS et al. 2016).

The following herbs are currently used to improve organic performance (BUCCI, 2000).

3.2.1 Composition and Therapeutic Property of Tribulus terrestris

Tribulus is an herbaceous plant in the family Zygophyllaceae, cultivated annually or occasionally perennial. It grows in semi-arid regions in various parts of the world, such as the USA, Australia, Eastern Europe, the Mediterranean region of Europe, Africa, China and India (DINCHEV et al., 2008). In Brazil, it is born occasionally in the Northeast, in se-

mi-arid regions in areas of the caatinga (SILVA et al, 2014). It has seeds with three thorns and yellow flowers, and grows to a meter in height (POKRYWKA et al, 2014). The fruit odor is slightly aromatic and the taste is slightly acidic (CHHATRE *et al*., 2014).

It has been used since ancient times in traditional folk medicine. Studies describe the chemical composition of Tribulus containing steroids, saponins, flavonoids, alkaloids, unsaturated fatty acids, vitamins, tannins, resins, potassium nitrate, aspartic acid and glutamic acid. This plant has several medical advantages, including antimicrobial, antibacterial, antioxidant and antitoxic activities used in the treatment of cardiovascular diseases, diabetes (POKRYWKA *et al,* 2014; ALMASI *et al*, 2016). Such a product comprises about 20 species in the world, of which three species, viz. Tribuluscistoides, Tribulusterrestris and Tribulusalatus are common in India. Among them, T. terrestris (TT) is a medicinal herb used by Ayurvedic seers, as well as by modern herbalists (CHHATRE *et al,* 2014).

Steroidal saponins are considered the factor responsible for the biological activity of products derived from this plant. Activity depends on the concentration and composition of active saponins, and the composition of saponins and the content of TT from different geographic regions are not the same (DINCHEV *et al,* 2008; CHHATRE et al, 2014). The two main components of the saponin fraction of TT are protodioscin and protogracillin.

It is observed that protodiocin works by increasing the conversion of testosterone to the potent dehydrotestosterone, which stimulates the production of red blood cells in the bone marrow, together with the development of muscles, contributing to the improvement of blood circulation and oxygen transport. Systems that are essential for maintaining health (CHHATRE *et al*, 2014). Other compounds of TT gitonin and tribulosaponins A and B also have similar effects to testosterone due to the similarity of their chemical composition. The main effect of tribulus supplementation is the increase in anabolic testoste-

rone and androgenic action through the activation of endogenous testosterone production (ZHU, et al 2017). In this sense, TT is presented as a testosterone booster, which can be a way to improve androgenesis (POKRYWKA *et al,* 2014).

Typically, TT extracts are offered by the pharmaceutical market as a separate product with no additional components or as a constituent of various nutritional supplements.

3.2.1 Composition and Therapeutic Property of Peruvian Maca

Peruvian Maca has Peruvian origin from the central Andes, having in its chemical composition Steroids; Phenolic Compounds; Flavonoids; Tannins; Glycosides; Saponins; Secondary Aliphatic Amines; Tertiary Amines; Alkaloids; Anthocyanidins; Dextrins; Glycosinolates. Being known for improving memory, and with it learning (DINI *et al,* 1994). In addition to being an effective solution for fatigue, it improves physical endurance. It consists of nutritional components, the primary metabolites and secondary metabolic compounds have been identified as phenolic compounds, to which biological and medicinal properties have been attributed, among them macaenes, macamides, glucosinalates maca and alkaloids, which are found in maca. It has aphrodisiac properties, contributing to the increase in sexual desire, stimulating hormonal production, influencing body metabolism, stimulating muscle mass gain and acting positively during menopause (TROYA-SANTOS, 2017).

A field research carried out in October 2016, controlled by students from an academy in Cambuquira, Minas Gerais. For the research to take place, it was necessary 16 students practicing bodybuilding, they would have the objective of demonstrating that the use of Peruvian Maca and Tribulus terrestris would influence the body composition of bodybuilding practitioners and improve the libido of those who consumed it. Thus, they were randomly selected in two groups that one received a placebo and the other received

tribulus capsules associated with the Peruvian Maca (produced in a handling pharmacy) that would be 750mg to 1500mg / day for tribulus and 1000mg to 3000mg / days for Peruvian Maca. The duration of therapy was 30 days, and all individuals underwent physical evaluation before and after treatment, following the following protocols: The Body Mass Index (BMI), using the cutoff points recommended by (WHO, 2003). At the end of this period they diagnosed that there was no change in body composition and there was also no improvement in libido, but they noticed an improvement in physical performance.

A survey conducted with 16 students practicing bodybuilding through a randomized controlled study, selecting adult male students aged between 18 and 40 years, who trained at least three times a week. The results were evaluated using a questionnaire and physical evaluation. After 30 days from the beginning of the administration of the substances, the results were analyzed and there were no significant changes in the physical parameters of the study participants. Some variables may have influenced the result of the present study. Among them, we can mention: the sample size; the selected indicators and factors exogenous to the experiment, for example, the participants' diet, which was not fully controlled. As for the questionnaire, 83.3% of the participants in Group C (control) said they had improved libido and physical performance and in the TM Group (Tribulus + Maca) 100% of the participants said they had improved physical performance and 37.5% improved their libido. The study demonstrated that the use of Tribulus Terrestris and Lepidium meyenii Walp (Maca Peruvian) did not influence the body composition of bodybuilding practitioners, but promoted an improvement in physical performance and libido (PEREIRA, 2017).

Peruvian maca is traditionally dried and ground for trade. The traditional drying and grinding process carried out was evaluated and, after analyzing the chemical composition of the final product, Esparza *et al* (2015), found values of macamides much

higher than the count of the same component in the fresh litter.

The importance of the drying process is justified because the final activity of its bioactive compounds is subject to the action of hydrolytic enzymes. In addition, the traditional process of drying the litter gives greater stability to the plant's alcohols and aldehydes (Esparza *et al,* 2015). The analysis is promising since the bioactive and phytochemical compounds of maca, not being lost in the drying and milling treatment, can be consumed and achieve their specific actions within the body, either via supplementation in capsules or as part of a balanced diet.

Clinical studies that compared the effects of maca in groups that used maca and compared with groups that used placebo, compiled by Lee *et al.* (2011) in a literature review article, found positive effects of using maca for menopausal symptoms. broad spectrum.

Although there are several studies relating maca to menopausal effects supporting the wide use of its bioactive principles by Andean popular wisdom, there is no consensus regarding the quantification of consumption necessary to obtain its effects (LEE *et al,* 2011).

3.2.1 Composition and Therapeutic Property of Ginseng

About 2000 years ago, in Asia, the first record of ginseng for therapeutic use was found. In 1761, the first American species of ginseng were discovered in North America. Soon after, in 1843, ginseng was given the botanical name "Panax", a Greek word that means "everything cures". There are several ginseng, the best known of which are: Panax ginseng (Asian ginseng), Panax quinquefolius (American ginseng) and Panax japonicus (Japanese ginseng). The action of each one will depend on the active principles, and the most well-known bioactive components are ginsenosides, polysaccharides, peptides, fatty acids and saponins (DIAS, FORTES, 2018).

The main bioactive compound that accounts for the medicinal attributes of ginseng is the ginsenoside, however, it should be noted that the amount and composition of ginsenosides are signifi-

cantly influenced by species, age, part of the plant, cultivation method, harvest season, preservation method and geographic distribution. The main effects of Panax ginseng are the increase in the immune system, the antibacterial activity, the antitumor, anticarcinogenic, anti-inflammatory, antioxidant, hypotensive, hypoglycemic and neuroprotective effects, in addition to beneficial effects in the conditions of fatigue and erectile dysfunction (DIAS, FORTES, 2018).

In the chemical composition of ginseng we find Phytosterols (beta-sitosterol) and Phytoestrogens (estrone), so the effects of these compositions are described as stimulating and relaxing the central nervous system, stimulating muscle vigor; cardiac tonic, lowers blood glucose levels, helps the body withstand daily pressure, has antiviral, anti-aggregating, antioxidant action and improves states of weakness such as: after an illness or in old age, increase stamina as well how to improve the body's response to stress, increasing physical and cognitive capacities (FERNANDES, 2011).

In vitro studies have revealed that ginseng root extract facilitates synaptogenesis in neuronal cell cultures of the cerebral cortex. Following this evidence, new in vivo and in vitro studies describe the benefits of phytotherapics in the prophylaxis and palliative care of neurodegenerative pathologies, namely in Parkinson's, Alzheimer's and Huntington's diseases (FERNANDES, 2011).

4. Final Considerations

Aging is an inherent condition in all individuals, however how aging will be established, which may result in natural aging (senescence) or sickness (senility) will depend on the individual's various living conditions.

Although the quality of aging is largely related to the quality of food, it is possible to relate the use of dietary supplements with a proven action of bioactive phytochemicals capable of actions similar to the anabolic hormones in decline in the body.

The action of tribulus terrestris is, above all, in the modulation of testosterone, responsible for the

androgenic potential attributed to the compound by popular wisdom. Its reflex effects of improving the feeling of vitality, can give the user greater disposition for the day's activities and even physical activity, contributing to a more active aging.

Although there is no evidence regarding the quantification of Peruvian maca adequate for the purpose of hormonal modulation and symptoms in menopause, there are also no studies that rule out its effectiveness in relation to the use that traditional Andean medicine suggests of the plant. Its actions in menopausal symptoms and spermatogenesis have promising scientific documentation.

In this regard, we observed that the herbal medicines Tribulus terrestris, Peruvian Maca and Ginseng have in their chemical composition substances with anabolic efficacy such as phytosterols and phytoestrogens, so supplementation with these products may allow a better anabolic hormonal balance, generating direct influence on the levels of catabolic hormones, providing better organic integrity, a factor directly linked to population longevity.

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