Research and Reports of Medicine

Research Article

Nutrition Interventions to Manage Sarcopenia: An Appraisal of the Existing Evidence

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Received: April 19, 2018; **Accepted**: May 2, 2018; **Published**: May 9, 2018

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Abstract

Sarcopenia is a common condition that can lead to serious adverse events in older adults. However, sarcopenia can be prevented and treated and nutrition plays a major role in its management. This article aims to appraise the scientific evidence on nutritional interventions to prevent and treat sarcopenia in older adults, highlighting the effect of an adequate caloric and protein intake, protein and amino-acid supplementation, micronutrients, and phospholipids. Unfortunately, clinical trials assessing the effect of these interventions on sarcopenia or muscle parameters are scarce, and the majority were not conducted in sarcopenic individuals.

Keywords: Sarcopenia; Older Age; Nutrition; Protein; Micronutrients; Muscle Mass

Introduction

Sarcopenia, currently defined as low muscle mass combined with loss of muscle strength and/or function,[1–3] is a frequent condition in older adults that leads to adverse outcomes and increases the onus of distinct sectors of society [4]. Due to the different definitions adopted in population-based studies, the prevalence of sarcopenia ranges from 1% to 29% in community-dwelling populations, and from 14% to 33% in long-term care populations [5]. In its current definition, sarcopenia is associated with disability, hospitalization, and mortality, although muscle strength alone has also been associated with fracture risk and cognitive decline [6] Moreover, sarcopenia shares common characteristics and pathophysiology with frailty, a condition of vulnerability to physical stressors, that also is associated with adverse outcomes [7].

Recent evidence points out to the role of nutrition interventions to prevent and treat sarcopenia in older adults. An altered nutritional status can contribute to chronic diseases progression and to the development of sarcopenia. Older adults present higher risk of malnutrition due to

clinical comorbidities, mental health disorders, and physiologic changes related to aging (reduced appetite, altered taste and smell sensation, slowed gastric emptying, and hormonal changes) [8–10]. All these conditions may diminish food ingestion or favor a less caloric diet, leading to weight loss, mostly due to lean mass depletion. In a longitudinal study investigating changes in body composition related to weight loss and weight gain in community-dwelling older adults, Newman et al. demonstrated that the proportion of lean mass that is lost with weight loss is higher than the proportion gained with weight gain. Therefore, weight loss, even with regain of weight, may contribute to sarcopenia in older adults [11] Nutrition may also act in other physiopathologic processes that lead to sarcopenia, such as chronic inflammation (related to aging and comorbidities), endocrine imbalances, and central and peripheral nervous system changes [1,12,13].

As sarcopenia is potentially preventable and treatable, the identification of sarcopenic individuals in clinical practice is critical. Among the current prevention and treatment options, nutrition plays a major role in the management of sarcopenia. However, the scientific evidence supporting nutrition is controversial due to abundant intervention possibilities. This article aims to appraise the scientific evidence on nutritional interventions to prevent and treat sarcopenia in older adults. Each section will assess the updated information on the association of distinct nutritional aspects with sarcopenia and will outline the existing evidence from clinical trials.

Caloric Intake

Low caloric intake is frequent among older adults and it is associated with body composition alterations, poor physical performance, disability and frailty [14]. If energy intake fails to achieve the metabolic needs, fat and muscle are catabolized to provide energy [14] Lower weekly consumption of calories was associated with sarcopenia in a cohort of Spanish older adults [15]. In a cross-sectional analysis of a cohort of British men, higher percent energy intake from carbohydrates decreased the odds of low mid-arm circumference and free-fat mass [16] Malnutrition was associated with a 1.9-times increase in prevalence of low grip strength in community-dwelling older adults in Indonesia [17]. In a prospective study with older nuns, an annual body weight loss of 3% or greater increased the risk of dependence in activities of daily living [18] . Korean sarcopenic older adults had lower energy intake in a 24-hour recall to assess nutritional status than non-sarcopenic individuals [19]. Additionally, a study found that community-dwelling older women with an energy intake of less than the recommended daily allowance (between 25 and 30 kcal/kg/day) had a 3-times increase in the composite risk of death, getting sick, or becoming frail than women with energy intake in the midrange [20].

At least 25 kcal/kg/day are needed to meet the daily energy requirement of older adults. Considering that the rest energy expenditure ranges from 20 to 28 kcal/kg of free fat mass/day, the total expenditure ranges from 1.23 to 1.36 times the rest energy expenditure of healthy and sick older adults, respectively [21]. An insufficient daily caloric ingestion will lead to loss of muscle mass. Moreover, a constant energy input is necessary to maintain motor activity and subsistence of skeletal muscle cells, and deficient energy may compromise mitochondrial metabolism in muscle fibers, leading to muscle fatigue and loss of strength [22]. However, evidence on the individual caloric increment effect on muscle mass, function, and physical performance is compromised because most trials adopt nutritional intervention that increase both caloric and protein intake. A meta-analysis that assessed the effect of oral nutritional supplements in the community-setting found that supplements increased body mass and fat mass in some trials, although there was insufficient information to form conclusions about the

effect of supplements on body composition in specific groups, such as older adults [23].

A relevant point when considering the use of caloric supplementations to treat sarcopenia is the recognition of sarcopenic obesity, the coexistence of sarcopenia and obesity, that is associated with higher risk of adverse outcomes than sarcopenia or obesity alone [24]. The management of sarcopenic obesity aims at increasing muscle mass and performance while losing fat mass [24], demanding a different approach in terms of daily caloric needs than sarcopenia alone. The combination of exercise training and caloric restriction seems to be an effective management strategy [25].

Protein Intake

Protein is essential to muscle mass synthesis, muscle metabolism process, and to counterbalance inflammatory and catabolic conditions related to acute and chronic illnesses that are frequent with aging [26]. The anabolic response to dietary protein is driven by available amino acids (especially leucine), physical activity, and hormonal signals mediated by insulin and insulin growth factor-1. Although this anabolic mechanism is restricted in older adults, probably due to alterations in cellular kinases (mechanistic target of rapamycin and NF kappa beta) concentrations and structure, [27] it can be galvanized by an increase in available amino acids [28].

The World Health Organization (WHO) recommends a minimum daily protein allowance of 0.8 g/kg of body weight for adults to maintain a zero nitrogen balance, irrespective of age [29]. A study that compared the required protein intake to maintain a zero nitrogen balance between young and older adults found no differences in daily needs between them [30]. However, the WHO recommendation is considered inadequate to prevent muscle loss with aging by many specialists in the field. Campbell et al showed that older adults receiving the WHO recommended daily allowance of protein for 14 weeks had a reduction in the mid-thigh muscle area measured by computed tomography scan [31]. Apart from affecting muscle mass and function, low protein intake also influence comorbidities and functional status of older adults. In a secondary analysis of observational studies in the Netherlands, 10% of community-dwelling frail older adults and 35% of institutionalized older adults had a daily intake of protein bellow the estimated average requirement of 0.7 g/kg of body weight/day [32]. Since low dietary protein intake is the main limiting factor to muscular synthesis, sarcopenia may be withhold with an adequate protein intake [27]. A longitudinal study with 2000 community-dwelling older adults found that after 3 years of follow up, participants with protein intake in the highest quintile lost 40% less muscle mass than participants in the lowest quintile [33]. Beasley et al. demonstrated that postmenopausal women with higher protein intake at baseline had better physical performance at baseline and slower decline of physical function and grip strength [34].Although evidence from observational studies supports that higher protein intake may prevent and treat sarcopenia, there is no consensus on the recommended daily protein allowance for older adults.

According to the “muscle full” concept, the muscle protein synthesis will enhance in response to the increment of protein intake until a maximum stimulating level is achieved [35]. In fact, a meta-analysis demonstrated that protein intake increased muscular protein synthesis when the protein dose was ≤ 0.8 g/kg body weight/day, but had no effect when the dose was > 0.8 g/kg body weight/day in older adults [36]. Defining the proper amount of protein intake is pivotal since an excess of amino acids may be harmful due to kidney overload, and increments in oxidation, in urea formation, and in gluconeogenesis [27]. A systematic review suggested that a daily protein allowance between 1.2 and 1.5 g/kg of body weight was safe, and showed some benefits in mortality and maintenance of muscle mass

and strength in observational studies with older adults [37]. The PROT-AGE, an international study group with the aim of developing updated evidence-based recommendations for optimal protein intake for older people, recommends an average daily protein intake of 1.0 to 1.2 g/kg of body weight to maintain or regain lean body mass and muscle function [26]. Older adults with acute or chronic illnesses, or in a regular exercise program should increase the daily intake to achieve at least 1.2 g/kg of body weight, with the exception of individuals with chronic kidney disease and creatinine clearance bellow 30 ml/min/1.73m^2 [26]. Although controversial, the usual recommendation is to divide the daily protein intake in equal amounts at breakfast, lunch, and dinner, with additional supplementation given between meals when needed [38].

Evidence on the effect of higher protein intake on muscle mass, strength, and physical performance brought out by clinical trials is conflicting due to the heterogeneity of study interventions and design. Studies adopt different inclusion criteria, and nutritional intervention strategies. Also, several trials explore the combined effect of nutritional intervention and exercise, with a systematic review showing inconsistent evidence of benefits on muscle mass and strength, and physical performance [39]. (Table 1) shows trials that adopted nutrition interventions based on higher protein intake or supplements composed by whole protein molecules. Most of the studies described in this article were not conducted on sarcopenic individuals, although they add information on the effect of protein supplementation on muscle mass, strength, or physical performance.

Table (1): Randomized clinical trials that assessed the effect of nutrition interventions based on higher protein intake or protein supplementation on muscle mass, strength, and function in older-adults

Community-dwelling participants						
Authors	**Country**	**Sample**	**Intervention**	**Control**	**Outcomes**	**Results**
Bunout et al., 2004[40]	Chile	98 older adults	Factorial 2X2 design: Twice-daily supplementation of 6.5g of protein and/or 1h of resistance exercise training twice a week for 18 months	No intervention	Body composition (DXA), limb strength (muscle tester), physical performance (12-min walking test)	No changes in fat-free mass. Limb strength and walking capacity increased only in the trained subjects.
Verdijk et al., 2009[41]	Netherlands	26 healthy older men	10g of protein supplementation before and immediately after resistance	Resistance exercise training program	Muscle strength (1-RM), body composition (DXA), cross-	Both groups improved muscle mass and strength without differences

			exercise training program 3 times a week for 12 weeks		sectional area of the quadriceps (CT scan), muscle biopsy	between groups
Lammes et al., 2012[42]	Sweden	96 community-dwelling frail older adults	Factorial 2X2 design: individual dietary counselling for 12 weeks to assure an energy intake of 1.5-times the rest metabolic rate for participants allocated to an exercise program and 1.4-times the rest metabolic rate for participants not allocated to exercise	General advice regarding diet and physical training	Body composition (DXA)	Nutritional counselling combined or not with exercise had no effect in fat free mass
Tieland et al., 2012[43]	Netherlands	65 frail and pre-frail older adults	Supplementation of 15g of protein twice daily	Placebo	Skeletal muscle mass (DXA), muscle fiber size (biopsy), strength (1-RM), and physical performance (SPPB)	Improvement in physical performance in the supplemented group. No difference between groups on the other outcomes
Chalé et al., 2013[44]	USA	80 mobility-limited older adults	Whey protein concentrate 40g/day and high intensity resistance training for 6 months	Iso-caloric supplementation and high intensity resistance training	Body composition (DXA), muscle strength and power for leg press and knee extensor (1-RM), thigh	Improvement in muscle mass, strength, and physical performance in both groups, without difference

					cross-sectional area (CT scan), physical function (chair-rise, stair-climb, 400-meter walk time)	between groups.
Kim and Lee, 2013[45]	South Korea	87 frail older adults	Supplementation of 400 kcal, 25g of protein, 9.4 of EAA, and micronutrients twice daily for 12 weeks.	Monthly visits by the same dietitian, without counseling.	Physical performance (SPPB, timed up-and-go test, one-legged stance test), muscle strength (hand-grip)	SPPB remained stable in the intervention group and it decreased in the control group. Lower decrease of usual gait speed in the intervention group. No differences in the other outcomes tested.
Arnarson et al., 2013[46]	Iceland	161 older adults	Supplementation of whey protein (20g of protein) after resistance training exercise 3 times a week for 12 weeks	Isocaloric carbohydrate after exercise	Muscle mass (DXA), quadriceps muscle strength (isokinetic dynamometer), physical performance (gait speed, timed up-and-go test, 6-min walk distance).	No difference between groups.
Fielding et al., 2017[47] and Englund et al., 2017[48]	USA and Sweden	149 older adults at risk of mobility-disability (SPPB score ≤ 9) and insufficient	Supplementation of whey protein 20g, vitamin D 800 IU, calcium 350 mg, and other vitamins and minerals 3 times a week,	Placebo administered after the exercise program	Physical performance (400 meters walk test, SPPB), muscle strength (isokinetic dynamometry	No differences between groups.

		vitamin D)	administered after an exercise program for 6 months		of knee flexors and extensors), muscle mass (DXA, cross-sectional area of thigh by CT scan).	
			Long-term care participants			
Authors	**Country**	**Sample**	**Intervention**	**Control**	**Outcomes**	**Results**
Fiatarone et al., 1994[49]	USA	100 older adults with ability to walk 6 meters	Factorial 2X2 design: Nutritional supplement with 360 kcal (60% carbohydrate, 23% fat, and 17% protein) and/or high intensity progressive resistance training 3 times a week for 10 weeks	Placebo supplement and/or recreational therapy	Muscle mass (mid-thigh circumference, thigh cross sectional area on CT scan, body potassium), muscle strength (1-RM for hip and knee extensors), gait speed	Supplement had no effect on the outcomes.
Bonnefoy et al., 2003[50]	France	57 frail older adults	Factorial 2X2 design: supplementation of 15g of protein, 25g of carbohydrates, and 4.4g of lipids twice daily and/or exercise program for 9 months	Placebo and/or memory training	Fat-free mass (deduced from labelled total body water), muscle performance (torque and power of knee extension), physical performance (gait speed, stair walking, chair rise).	Improvement in muscle power with supplementation. No difference in the other parameters.

Rosendahl et al. 2006[51]	Sweden	191 older adults dependent in at least one ADL	Factorial 2X2 design: Supplement with protein 7.4g and carbohydrate 15.7g and/or high intensity functional exercise program for 3 months	Placebo and/or control activity while sitting.	Balance (Berg balance scale), gait speed, muscle strength (1-RM in a leg-press machine)	No effect of the nutrition intervention
Smoliner et al., 2008[52]	Germany	65 older adults malnourished or at nutritional risk	Enriched diet (higher caloric and protein intake) for 12 weeks	Standard diet	Body composition (BIA), hand-grip strength	No differences between groups.

BIA: bioelectrical impedance analysis; CT: computerized tomography; DXA: dual-energy X-ray absorptiometry; EAA: essential amino acids; 1-RM: one repetition maximum strength test; SPPB: Short Physical Performance Battery; USA: United States of America.

Essential amino acids

Essential amino acids (EAA) are not synthesized de novo by the human organism and must be obtained through the diet from animal and vegetable sources. As promotors of anabolic stimulus for muscle synthesis,[53] EAAs may be used to prevent and treat sarcopenia. Supplements rich in leucine, the main EAA that boosts muscular anabolism through up-regulation of messenger RNA translation and stimulation of insulin secretion, [14] seems to compensate the blunted response to amino acid ingestion in older adults [54]. However, there is no consensus on the optimal mixture of EAAs. A trial with older women found that low-doses of leucine-enriched EAA supplement after exercise stimulates muscular protein synthesis after exercise to levels equivalent to 40 g of Whey protein, a dose that maximally stimulates muscular protein synthesis in men [55]. A meta-analysis with 16 studies found that leucine supplementation increased lean mass in older adults when compared to placebo, and it was more effective in sarcopenic individuals [56]. Trials that assessed the effect of EAA on sarcopenia and its components (muscle mass, strength, and physical performance) are summarized in (Table 2).

Table (2): Randomized clinical trials that assessed the effect of nutrition interventions based on essential amino acids supplementation on sarcopenia or sarcopenia parameters

Authors	Country	Sample	Intervention	Control	Outcomes	Results
Godard et al., 2002[57]	USA	17 older men	12 g of EAA combined with progressive knee extensor	No supplementation and progressive knee extensor	Muscle strength (knee extensor:	All variables improved without differences between groups.

			resistance training program for 12 weeks	resistance training program	torque with a isokinetic and isotonic dynamometry, and 1-RM), cross-sectional area of the mid-thigh (CT scan)	
Børsheim et al., 2008[58]	USA	12 glucose intolerant older adults	11g of EAA and arginine twice daily for 16 weeks. Maintenance of usual diet and physical activity.	No control group	Body composition (DXA), muscle strength (1-RM for leg extension and flexion), physical performance (timed step test, time floor-transfer test, SPPB)	Increase in muscle mass and strength, improvement in gait speed and performance on the timed step test, and time floor-transfer test.
Dillon et al., 2009[59]	USA	14 older women	15g of EAA daily for 3 months	Placebo	Muscle mass (DXA and biopsy), muscle strength (1-RM)	Increase in muscle mass in the supplemented group and no difference in muscle strength between groups.
Kim et al., 2012[60]	Japan	155 sarcopenic older women	Factorial 2X2 design: Leucine-enriched EAA 3g twice daily and/or comprehensive exercise training program twice a week for 3 months	Health education	Muscle mass (BIA), muscle strength (knee extension), and physical performance (gait speed)	Muscle mass and gait speed increased with all 3 interventions, although muscle strength improved only with the combination of exercise and EAA supplementation
Bauer et al., 2015[61]	Belgium, Germany, Ireland, Italy, Sweden, and the United Kingdom	380 community-dwelling sarcopenic older adults	Supplement with Whey protein 20g, leucine 3g, carbohydrate 9g, fat 3g, vitamin D 800 IU, and a	Iso-caloric supplement	Muscle strength (hand-grip strength), physical performance (SPPB), muscle mass	Improvement of hand-grip strength and SPPB in both groups, without difference between groups. Muscle mass improved more in the intervention group.

	mixture of vitamins, minerals and fibers twice daily for 13 weeks.	(DXA)

BIA: bioelectrical impedance analysis; CT: computerized tomography; DXA: dual-energy X-ray absorptiometry; 1-RM: one repetition maximum strength test; SPPB: Short Physical Performance Battery; USA: United States of America; UK: United Kingdom.

Beta-hydroxy Beta-metilbutyrate

Beta-hydroxy-beta-metilbutyrate (HMB) – the leucine active metabolite – reduces protein degradation and increases protein synthesis and muscle cell´s cholesterol production, stabilizing cell membranes. It is hypothesized that HMB supplementation may be more effective than leucine supplementation because only 5 to 10% of the ingested leucine is converted into HMB [62]. Different studies demonstrated that HMB supplementation associated with resistance exercise increased muscle mass and strength, and attenuated sarcopenia development in older adults [63].

A study compared an 8-week resistance exercise program combined with supplementation of HMB 3 g/day with resistance exercise and placebo in older adults. The supplemented group had higher fat-free mass gain and fat mass loss than the placebo group [64]. Another clinical trial compared the effect of a 12-week intervention of daily supplementation of HMB 2 g, arginine 5 g, and lysine 1.5 g with placebo in older women. The supplemented group improved physical performance on the get-up-and-go test, limb circumference, leg strength, and grip strength in comparison to the control group [65]. Baier et al. showed that one-year daily HMB supplementation (2-3 g) combined with arginine (5-7.5 g) and lysine (1.5-2.25 g) increased muscle mass in older adults in comparison to the placebo group, although there were no differences in physical performance between groups [66]. Finally, Berton et al. found that an 8-week course supplementation of HMB 1.5 g/day did not improve physical performance in older women that maintained their regular physical activity [67].

Creatine

Creatine – an endogenously synthesized amine stored mostly in skeletal muscle – provides rapid energy to muscle cells, maintaining intracellular ATP for immediate use during muscle contraction, a mechanism that is deficient in older adults [68]. Its supplementation enhances the ability to perform high-intensity exercise and increase training volume, which are stimulus for muscle protein synthesis [69]. A meta-analysis demonstrated that creatine supplementation in association with resistance training increased fat-free mass and had a greater effect on 30-s chair stand test than resistance training alone in older adults [69]. Low-dose, short duration courses of up to 3 g/day of creatine are considered safe for aged individuals, despite their diminished renal clearance and vulnerability to renal adverse effects related to the high nitrogen content of the substance [68].

Micronutrients

The intracellular excess of reactive oxygen species may damage molecules such as DNA, lipids, and proteins, leading to mitochondrial dysfunction and cellular apoptosis. Accumulated reactive oxygen species due to ineffective counterbalance defense mechanisms contribute to muscle atrophy and sarcopenia. Some vitamins and oligoelements are anti-oxidants and may

diminish oxidative stress damage to muscle cells [27]. The Women´s Health and Aging study originated a series of observational evidence on the effect of oxidative stress on physical performance in community-dwelling older women with some degree of disability. Analysis of this study demonstrated that protein carbonyl levels, a marker of oxidative damage to proteins, were cross-sectionally associated with lower grip strength, [70] and predicted slower grip strength and severe walking disability after 3 years of follow-up [71]. Also, low serum carotenoid levels, an indicator of low intake of fruits and vegetables, were associated with slower gait speed [72] and severe walking disability [73] after 3 years of follow up. Evidence derived from other studies are the following: community-dwelling older adults in the lower quartile of total plasma carotenoid were at higher risk of developing poor knee, hip, and grip muscle strength after 6 years; [74] and plasma vitamin C concentration was positively correlated with grip strength and ability to stand on one leg with eyes open [75].

Carotenoids

Carotenoids are supposed to modulate redox-sensitive transcription factors, such as NF-kB, that stimulate inflammatory cytokine production. Therefore, carotenoids may protect from the inflammatory mechanisms that originate sarcopenia. A diet rich in fruits and vegetables could prevent sarcopenia, although clinical trials are needed to test this hypothesis [27].

Vitamin D

Vitamin D levels have been associated with sarcopenia. In a cohort of Australian community-dwelling older adults, 25-hydroxyvitamin D levels ≤ 20 ng/ml were cross-sectionally associated with lower appendicular lean mass, physical activity, and leg strength. 25-hydroxyvitamin D levels at baseline also predicted leg strength after 2.6 years of follow-up [76]. In the Longitudinal Aging Study, participants with baseline 25-hydroxyvitamin D levels < 10 ng/ml were 2.57 times more likely to lose grip strength after 3 years, and 2.14 times more likely to lose muscle mass when compared with participants with 25-hydroxyvitamin D > 20 ng/ml [77]. Also, low 25-hydroxyvitamin D was a predictor of mobility disability in two cohorts of older adults [78,79]. However, a study with older men from Hong Kong did not find any association of vitamin D levels with changes in muscle mass or physical performance test after 4 years of follow-up [80].

Three recent meta-analysis assessed the effect of vitamin D supplementation, combined or not with calcium supplementation, on muscular strength. Muir and Montero-Odasso selected 13 articles and showed that supplementation of vitamin D improved muscle strength and balance [81]. The work of Beaudart et al. included 30 randomized clinical trials and found a small but positive effect on global muscle strength (mostly in older adults with 25-hydroxyvitamin D levels < 12 ng/ml), but not on muscle mass and power [82]. Stockton et al analyzed 17 randomized clinical trials and did not find any effect of vitamin D supplementation on muscle strength in individuals with 25-hydroxyvitamin D > 10 ng/dl. However, supplementation improved proximal muscle strength in individuals with vitamin D deficiency [83].

N-3 long chain polyunsaturated fatty acids (Omega 3)

A diet poor in N-3 polyunsaturated fatty acids and rich in N-6 polyunsaturated fatty acids is pro-inflammatory and may harm skeletal muscle and other tissues. A baseline cross-sectional analysis of a longitudinal study in community-dwelling older adults found that, among dietary factors obtained through food frequency questionnaire, fatty fish consumption was associated with grip strength [84]. A cross-

sectional study with oldest old participants found that a lower habitual intake of eicosapentaenoic and decosahexaenoic acids was associated with poor functional mobility in men [85]. Another study with community-dwelling and long term care older adults showed that a lower intake of omega 3 was associated with lower leg strength and poorer performance on the chair-rise test [86].

A randomized clinical trial compared the effect of a strength training program combined with fish oil supplementation with exercise only for 90 or 150 days in older women. The supplemented groups had greater increase in peak torque and rate of torque for knee extension and flexor, plantar, and dorsiflexor. Also, chair-rising performances in the supplemented groups were higher than in the exercise group [87]. Another clinical trial with older women showed greater improvement in gait speed after omega 3 supplementation in comparison to placebo. However, there was no effect of supplementation in grip strength and chair-rise [88]. The supplementation of fish oil-derived omega 3 for 6 months increased thigh muscle volume, and muscle strength in older adults compared to controls that received corn oil [89]. Finally, older adults with low appendicular lean mass that received omega 3 combined with vitamin E for 12 weeks had no increase in muscle mass, muscle strength and physical performance when compared to the control group, that received vitamin E alone [90].

Mediterranean diet

Considered a key-factor for healthy aging, the Mediterranean diet contains large portions of vegetables (especially raw), fruits (including nuts), raw cereals, and fish, that contribute with micronutrients, such as vitamins, oligoelements, and polyunsaturated fatty acids. Older adults with higher adherence to a Mediterranean diet showed lower decline in physical performance tests after 9 years of follow-up, and lower risk of incident mobility disability [91]. Older women that adopted the diet also lost less muscle mass after 3 years of follow-up [92]. However, a prospective study in Hong Kong did not find association between higher adherence to Mediterranean diet and incident sarcopenia after 4 years of follow-up [93].

Phospholipids

Phospholipids are the major constituents of cell membranes. Phosphatidic acid, the smallest and simplest phospholipid, acts as a precursor for other lipids. There is also evidence that phosphatidic acid also has a role as an intracellular messenger, regulating protein signaling activity. One of the proteins regulated by phosphatidic acid is the mammalian/mechanistic target of rapamycin (mTOR), activating mTOR kinase activity, therefore stimulating muscular protein synthesis, and subsequent muscular hypertrophy [94]. Combined with resistance training exercise, another pathway to activate mTOR, supplementation of phosphatidic acid may prevent and recover muscle loss. Additionally, phosphatidic acid acts in neurotransmission [95] and could have a role in improving some neuronal alterations related to the aging process that contribute to the development of sarcopenia [13].

Few studies evaluated the effect of phosphatidic acid supplementation, and to the extent of our knowledge, none were conducted in sarcopenic subjects [96]. conducted a trial in 15 resistance trained men randomized to receive 750 mg of phosphatidic acid or placebo for 8 weeks, and found that it did not differentially affect muscle thickness and 1-RM (one-repetition maximum strength test) between groups.96 Similar results were obtained in another placebo-controlled clinical trial that administered smaller doses of phosphatidic acid for resistance trained men [97]. In contrast, a trial that compared the effect of exercise combined with a supplement composed mostly by phosphatidic acid and other m-TOR signaling substances, with exercise combined with placebo in 18 strength-trained men for 8 weeks, found that the supplemented group had higher

lean body mass and strength than the placebo group [98].

Phosphatidic acid may also act on neurotransmission. Since alterations in Another role of phospholipids in the management of sarcopenia is as delivery systems for biologically active substances with poor systemic bioavailability, such as curcumin (that may act through anti-inflammatory properties) [99], and sphingomyelin (that promotes skeletal muscle regeneration and increase muscle contractile force in rats) [100]. In a study, 86 older adults with complaint of loss of strength and tiredness were submitted to an exercise program associated with balanced diet or supplementation of a curcumin associated with phospholipids. The supplemented group improved strength and physical performance in comparison to the non-supplemented group [99].

Conclusions

Observational studies indicate benefits of different nutrition interventions in the prevention and treatment of sarcopenia. However, clinical trials are scarce and mostly not conducted in sarcopenic individuals, with controversial results. Sarcopenia is a prevalent condition that can lead to serious adverse outcomes in older adults. Well-designed and well-conducted clinical trials with sarcopenic individuals are pivotal to understand the role of nutrition interventions in the management of sarcopenia.

References

1. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. (2010) Sarcopenia: European consensus on definition and diagnosis. Age Ageing; 39(4): 412-423.
2. Fielding RA, Vellas B, Evans WJ, et al. (2011) Sarcopenia: An Undiagnosed Condition in Older Adults. Current Consensus Definition: Prevalence, Etiology, and Consequences. International Working Group on Sarcopenia. J Am Med Dir Assoc; 12(4): 249-256.
3. Chen LK, Liu LK, Woo J, et al. (2014) Sarcopenia in Asia: Consensus report of the Asian working group for sarcopenia. J Am Med Dir Assoc; 15(2): 95-101.
4. Morley JE, Anker SD, von Haehling S (2014) Prevalence, incidence, and clinical impact of sarcopenia: facts, numbers, and epidemiology—update 2014. J Cachexia Sarcopenia Muscle; 5(4): 253-259.
5. Cruz-Jentoft AJ, Landi F, Schneider SM, et al. (2014) Prevalence of and interventions for sarcopenia in ageing adults: A systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). Age Ageing; 43(6): 748-759.
6. Dodds RM, Roberts HC, Cooper C, et al. (2015) The Epidemiology of Sarcopenia. J Clin Densitom; 18(4): 461-466.
7. Morley JE, Vellas B, Abellan van Kan G, et al. (2013) Frailty consensus: A call to action. J Am Med Dir Assoc; 14(6): 392-397.
8. Favaro-Moreira NC, Krausch-Hofmann S, Matthys C, et al. (2016) Risk Factors for Malnutrition in Older Adults: A Systematic Review of the Literature Based on Longitudinal Data. Adv Nutr An Int Rev J; 7(3): 507-522.
9. Ahmed T, Haboubi N (2010) Assessment and management of nutrition in older people and its importance to health. Clin Interv Aging; 5: 207-216.
10. Inzitari M, Doets E, Bartali B, et al. (2011) Nutrition in the age-related disablement process. J Nutr Heal Aging; 15(8): 599-604.
11. Newman AB, Lee JS, Visser M, et al. (2005) Weight change and the conservation of lean mass in old age: the Health, Aging and Body Composition Study. Am J Clin Nutr; 82(4): 872-878.
12. Wang Y, Liu X, Qiu J, et al. (2017) Association between Ideal Cardiovascular Health Metrics and

Suboptimal Health Status in Chinese Population. Sci Rep; 7(1): 5-10.

13. Manini TM, Hong SL, Clark BC (2013) Aging and muscle: A neuron?s perspective. Curr Opin Clin Nutr Metab Care; 16(1) :21-26.
14. Cruz-Jentoft AJ, Kiesswetter E, Drey M, et al. (2017) Nutrition, frailty, and sarcopenia. Aging Clin Exp Res; 29(1): 43-48.
15. Coto Montes A, Boga JA, Bermejo Mill C, et al. (2017) Potential early biomarkers of sarcopenia among independent older adults. Maturitas; 104: 117-122.
16. Atkins JL, Whincup PH, Morris RW, et al. (2014) Low muscle mass in older men: The role of lifestyle, diet and cardiovascular risk factors. J Nutr Heal Aging; 18(1): 26-33.
17. Riviati N, Setiati S, Laksmi PW, et al. (2017) Factors Related with Handgrip Strength in Elderly Patients. Acta Med Indones; 49(3): 215-219.
18. Tully CL, Snowdon DA (1995) Weight change and physical function in older women: findings from the Nun Study. J Am Geriatr Soc; 43(12): 1394-1397.
19. Kim JE, Lee YH, Huh JH, et al. (2014) Early-stage chronic kidney disease, insulin resistance, and osteoporosis as risk factors of sarcopenia in aged population: The Fourth Korea National Health and Nutrition Examination Survey (KNHANES IV), 2008-2009. Osteoporos Int; 25(9): 2189-2198.
20. Vellas BJ, Hunt WC, Romero LJ, et al. (1997) Changes in nutritional status and patterns of morbidity among free-living elderly persons: A 10-year longitudinal study. Nutrition; 13(6): 515-519.
21. Gaillard C, Alix E, Sallé A, et al. (2007) Energy requirements in frail elderly people: A review of the literature. Clin Nutr; 26(1): 16-24.
22. Volkert D (2011) The role of nutrition in the prevention of sarcopenia. Wiener Medizinische Wochenschrift; 161(17-18): 409-415.
23. Stratton RJ, Elia M (2000) Are oral nutritional supplements of benefit to patients in the community? Findings from a systematic review. Curr Opin Clin Nutr Metab Care; 3(4): 311-315.
24. Molino S, Dossena M, Buonocore D, et al. (2015) Sarcopenic obesity: An appraisal of the current status of knowledge and management in elderly people. J Nutr Heal Aging; 20(7): 1-9.
25. Weinheimer EM, Sands LP, Campbell WW (2010) A systematic review of the separate and combined effects of energy restriction and exercise on fat-free mass in middle-aged and older adults: implications for sarcopenic obesity. Nutr Rev; 68(7): 375-388.
26. Bauer J, Biolo G, Cederholm T, et al. (2013) Evidence-based recommendations for optimal dietary protein intake in older people: A position paper from the prot-age study group. J Am Med Dir Assoc; 14(8): 542-559.
27. Bonnefoy M, Berrut G, Lesourd B, et al. (2015) Frailty and nutrition: Searching for evidence. J Nutr Heal Aging; 19(3): 250-257.
28. Bosaeus I, Rothenberg E (2016) Nutrition and physical activity for the prevention and treatment of age-related sarcopenia. Proc Nutr Soc; 75(2): 174-180.
29. WHO/FAO/UNU Expert Consultation (2007) Protein and amino acid requirements in human nutrition. World Health Organ Tech Rep Ser; 935:1-265.
30. Campbell WW, Johnson CA, McCabe GP, et al. (2008) Dietary protein requirements of younger and older adults. Am J Clin Nutr; 88(5): 1322-1329.
31. Campbell WW, Trappe TA, Wolfe RR, et al. (2001) The recommended dietary allowance for protein may not be adequate for older people to maintain skeletal muscle. Journals Gerontol - Ser A Biol Sci Med Sci; 56(6): M373-M380.

32. Tieland M, Borgonjen-Van Den Berg KJ, et al. (2012) Dietary protein intake in community-dwelling, frail, and institutionalized elderly people: Scope for improvement. Eur J Nutr; 51(2): 173-179.
33. Houston DK, Nicklas BJ, Ding J, et al. (2008) Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study. Am J Clin Nutr; 87(1): 150-155.
34. Beasley JM, Wertheim BC, Lacroix AZ, et al. (2013) Biomarker-calibrated protein intake and physical function in the women's health initiative. J Am Geriatr Soc; 61(11): 1863-1871.
35. Dideriksen K, Reitelseder S, Holm L (2013) Influence of amino acids, dietary protein, and physical activity on muscle mass development in humans. Nutrients; 5(3): 852-876.
36. Gweon HS, Sung HJ, Lee DH (2010) Short-term protein intake increases fractional synthesis rate of muscle protein in the elderly: meta-analysis. Nutr Res Pract; 4(5): 375.
37. Pedersen AN, Cederholm T (2014) Health effects of protein intake in healthy elderly populations: a systematic literature review. Food Nutr Res; 58: 1-39.
38. Morley JE, Argiles JM, Evans WJ, et al. (2010) Nutritional recommendations for the management of sarcopenia. J Am Med Dir Assoc; 11(6): 391-396.
39. Denison HJ, Cooper C, Sayer AA, et al. (2015) Prevention and optimal management of sarcopenia: a review of combined exercise and nutrition interventions to improve muscle outcomes in older people. [Review]. Clin Interv Aging; 10: 859-869.
40. Bunout B, Barrera G, de la Maza P, et al. (2004) Effects of nutritional supplementation and resistance training on muscle strength in free living elders. Results of one year follow. J Nutr Health Aging; 8(2): 68-75.
41. Verdijk LB, Jonkers RAM, Gleeson BG, et al. (2009) Protein supplementation before and after exercise does not further augment skeletal muscle hypertrophy after resistance training in elderly men. Am J Clin Nutr; 89(2): 608-616.
42. Lammes E, Rydwik E, Akner G (2012) Effects of nutritional intervention and physical training on energy intake, resting metabolic rate and body composition in frail elderly. A randomised, controlled pilot study. J Nutr Heal Aging; 16(2): 162-167.
43. Tieland M, van de Rest O, Dirks ML, et al. (2012) Protein Supplementation Improves Physical Performance in Frail Elderly People: A Randomized, Double-Blind, Placebo-Controlled Trial. J Am Med Dir Assoc; 13(8): 720-726.
44. Chalé A, Cloutier GJ, Hau C, et al. (2013) Efficacy of whey protein supplementation on resistance exercise-induced changes in lean mass, muscle strength, and physical function in mobility-limited older adults. Journals Gerontol - Ser A Biol Sci Med Sci; 68(6): 682-690.
45. Kim CO, Lee KR (2013) Preventive effect of protein-energy supplementation on the functional decline of frail older adults with low socioeconomic status: a community-based randomized controlled study. Journals Gerontol Ser A Biol Sci Med Sci; 68(3): 309-316.
46. Arnarson A, Gudny Geirsdottir O, Ramel A, et al. (2013) Effects of whey proteins and carbohydrates on the efficacy of resistance training in elderly people: Double blind, randomised controlled trial. Eur J Clin Nutr; 67(8): 821-826.
47. Fielding RA, Travison TG, Kirn DR, et al. (2017) Effect of structured physical activity and nutritional supplementation on physical function in mobility-limited older adults: Results

from the VIVE2 randomized trial. J Nutr Heal Aging; 21(9): 936-942.

48. Englund DA, Kirn DR, Koochek A, et al. (2017) Nutritional Supplementation With Physical Activity Improves Muscle Composition in Mobility-Limited Older Adults, The VIVE2 Study: A Randomized, Double-Blind, Placebo-Controlled Trial. J Gerontol A Biol Sci Med Sci; 73(1):95-101.
49. Fiatarone MA, O'Neill EF, Ryan ND, et al. (1994) Exercise training and nutritional supplementation for physical frailty in very elderly people. N Engl J Med; 330(25): 1769-1775.
50. Bonnefoy M, Cornu C, Normand S, et al. (2003) The effects of exercise and protein–energy supplements on body composition and muscle function in frail elderly individuals: a long-term controlled randomised study. Br J Nutr; 89(5): 731-738.
51. Rosendahl E, Lindelöf N, Littbrand H, et al. (2006) High-intensity functional exercise program and protein-enriched energy supplement for older persons dependent in activities of daily living: A randomised controlled trial. Aust J Physiother; 52(2): 105-113.
52. Smoliner C, Norman K, Scheufele R, et al. (2008) Effects of food fortification on nutritional and functional status in frail elderly nursing home residents at risk of malnutrition. Nutrition; 24(11-12): 1139-1144.
53. Volpi E, Kobayashi H, Sheffield-Moore M, et al. (2003) Essential amino acids are primarily responsible for the amino acid stimulation of muscle protein anabolism in healthy elderly adults. Am J Clin Nutr; 78(2): 250-258.
54. Leenders M, van Loon LJ (2011) Leucine as a pharmaconutrient to prevent and treat sarcopenia and type 2 diabetes. Nutr Rev; 69(11): 675-689.
55. Wilkinson DJ, Bukhari SSI, Phillips BE, et al. (2017) Effects of leucine-enriched essential amino acid and whey protein bolus dosing upon skeletal muscle protein synthesis at rest and after exercise in older women. Clin Nutr; S0261-5614(17): 31340-31347.
56. Komar B, Schwingshackl L, Hoffmann G (2015) Effects of leucine-rich protein supplements on anthropometric parameter and muscle strength in the elderly: A systematic review and meta-analysis. J Nutr Heal Aging; 19(4): 437-446.
57. Godard MP, Williamson DL, Trappe SW (2002) Oral amino-acid provision does not affect muscle strength or size gains in older men. Med Sci Sports Exerc; 34(7): 1126-1131.
58. Børsheim E, Bui Q-UT, Tissier S, et al. (2008) Effect of amino acid supplementation on muscle mass, strength and physical function in elderly. Clin Nutr; 27(2): 189-195.
59. Dillon EL, Sheffield-Moore M, Paddon-Jones D, et al. (2009) Amino acid supplementation increases lean body mass, basal muscle protein synthesis, and insulin-like growth factor-I expression in older women. J Clin Endocrinol Metab; 94(5): 1630-1637.
60. Kim HK, Suzuki T, Saito K, et al. (2012) Effects of exercise and amino acid supplementation on body composition and physical function in community-dwelling elderly Japanese sarcopenic women: A randomized controlled trial. J Am Geriatr Soc; 60(1): 16-23.
61. Bauer JM, Verlaan S, Bautmans I, et al. (2015) Effects of a Vitamin D and Leucine-Enriched Whey Protein Nutritional Supplement on Measures of Sarcopenia in Older Adults, the PROVIDE Study: A Randomized, Double-Blind, Placebo-Controlled Trial. J Am Med Dir Assoc; 16(9):740-747.
62. Hickson M (2015) Nutritional interventions in sarcopenia: A critical review. Proc Nutr Soc; 74(4): 378-386.
63. Holeček M (2017) Beta-hydroxy-beta-methylbutyrate supplementation and skeletal muscle in healthy and muscle-

wasting conditions. J Cachexia Sarcopenia Muscle; 8(4): 529-541.

64. Vukovich MD, Stubbs NB, Bohlken RM et al. (2001) Body composition in 70-year-old adults responds to dietary beta-hydroxy-beta-methylbutyrate similarly to that of young adults. J Nutr; 131(7): 2049-2052.
65. Flakoll P, Sharp R, Baier S, et al. (2004) Effect of β-hydroxy-β-methylbutyrate, arginine, and lysine supplementation on strength, functionality, body composition, and protein metabolism in elderly women. Nutrition; 20(5): 445-451.
66. Baier S, Johannsen D, Abumrad N, et al. (2009) Year-long changes in protein metabolism in elderly men and women supplemented with a nutrition cocktail of β-hydroxy-β-methylbutyrate (HMB), L-arginine, and L-lysine. J Parenter Enter Nutr; 33(1): 71-82.
67. Berton L, Bano G, Carraro S, et al.(2015) Effect of oral beta-hydroxy-beta-methylbutyrate (HMB) supplementation on physical performance in healthy old women over 65 years: An open label randomized controlled trial. PLoS One; 10(11).
68. Andres S, Ziegenhagen R, Trefflich I, et al. (2017) Creatine and creatine forms intended for sports nutrition. Mol Nutr Food Res; 61(6).
69. DEVRIES MC, PHILLIPS SM (2014) Creatine Supplementation during Resistance Training in Older Adults—A Meta-analysis. Med Sci Sport Exerc; 46(6): 1194-1203.
70. Howard C, Ferrucci L, Sun K, et al. (2007) Oxidative protein damage is associated with poor grip strength among older women living in the community. J Appl Physiol; 103(1): 17-20.
71. Semba RD, Ferrucci L, Sun K, et al. (2007) Oxidative Stress and Severe Walking Disability among Older Women. Am J Med; 120(12): 1084-1089.
72. Alipanah N, Varadhan R, Sun K, et al. (2009) Low serum carotenoids are associated with a decline in walking speed in older women. J Nutr Heal Aging; 13(3): 170-176.
73. Semba RD, Varadhan R, Bartali B, et al. (2007) Low serum carotenoids and development of severe walking disability among older women living in the community: The Women's Health and Aging Study I. Age Ageing; 36(1): 62-67.
74. Lauretani F, Semba RD, Bandinelli S, et al. (2008) Low plasma carotenoids and skeletal muscle strength decline over 6 years. Journals Gerontol - Ser A Biol Sci Med Sci; 63(4): 376-383.
75. Saito K, Yokoyama T, Yoshida H, et al. (2012) A significant relationship between plasma vitamin C concentration and physical performance among Japanese elderly women. J Gerontol A Biol Sci Med Sci; 67(3): 295-301.
76. Scott D, Blizzard L, Fell J, et al. (2010) A prospective study of the associations between 25-hydroxy-vitamin D, sarcopenia progression and physical activity in older adults. Clin Endocrinol (Oxf); 73(5): 581-587.
77. Visser M, Deeg DJH, Lips P (2003) Low Vitamin D and High Parathyroid Hormone Levels as Determinants of Loss of Muscle Strength and Muscle Mass (Sarcopenia): The Longitudinal Aging Study Amsterdam. J Clin Endocrinol Metab; 88(12): 5766-5772.
78. Houston DK, Tooze JA, Davis CC, et al. (2011) Serum 25-Hydroxyvitamin D and Physical Function in Older Adults: The Cardiovascular Health Study All Stars. J Am Geriatr Soc; 59(10): 1793-1801.
79. Houston DK, Neiberg RH, Tooze JA, et al. (2013) Low 25-hydroxyvitamin D predicts the onset of mobility limitation and disability in community-dwelling older adults: The health ABC study.

Journals Gerontol - Ser A Biol Sci Med Sci; 68(2): 181-187.

80. Chan R, Chan D, Woo J, et al. (2012) Not all elderly people benefit from vitamin D supplementation with respect to physical function: Results from the osteoporotic fractures in men study, Hong Kong. J Am Geriatr Soc; 60(2): 290-295.
81. Muir SW, Montero-Odasso M (2011) Effect of vitamin D supplementation on muscle strength, gait and balance in older adults: A systematic review and meta-analysis. J Am Geriatr Soc; 59(12): 2291-2300.
82. Beaudart C, Buckinx F, Rabenda V, et al. (2014) The effects of vitamin D on skeletal muscle strength, muscle mass and muscle power: a systematic review and meta-analysis of randomized controlled trials. J Clin Endocrinol Metab; 99: jc20141742.
83. Stockton KA, Mengersen K, Paratz JD, et al. (2011) Effect of vitamin D supplementation on muscle strength: A systematic review and meta-analysis. Osteoporos Int; 22(3): 859-871.
84. Robinson SM, Jameson KA, Batelaan SF, et al. (2008) Diet and its relationship with grip strength in community-dwelling older men and women: The Hertfordshire cohort study. J Am Geriatr Soc; 56(1): 84-90.
85. Takayama M, Arai Y, Sasaki S, et al. (2013) Association of marine-origin N-3 polyunsaturated fatty acids consumption and functional mobility in the community-dwelling oldest old. J Nutr Heal Aging; 17(1): 82-89.
86. Rousseau JH, Kleppinger A, Kenny AM (2009) Self-reported dietary intake of omega-3 fatty acids and association with bone and lower extremity function. J Am Geriatr Soc; 57(10): 1781-1788.
87. Rodacki CLN, Rodacki ALF, Pereira G, et al. (2012) Fish-oil supplementation enhances the effects of strength training in elderly women. Am J Clin Nutr; 95(2): 428-436.
88. Hutchins-Wiese HL, Kleppinger A, Annis K, et al. (2013) The impact of supplemental N-3 long chain polyunsaturated fatty acids and dietary antioxidants on physical performance in postmenopausal women. J Nutr Heal Aging; 17(1): 76-80.
89. Smith GI, Julliand S, Reeds DN, et al. (2015) Fish oil-derived n-3 PUFA therapy increases muscle mass and function in healthy older adults. Am J Clin Nutr; 102(1): 115-122.
90. Krzyminska-Siemaszko R, Czepulis N, Lewandowicz M, et al. (2015) The Effect of a 12-week omega-3 supplementation on body composition, muscle strength and physical performance in elderly individuals with decreased muscle mass. Int J Environ Res Public Health; 12: 10558-10574.
91. Milaneschi Y, Bandinelli S, Corsi AM, et al. (2011) Mediterranean diet and mobility decline in older persons. Exp Gerontol; 46(4): 303-308.
92. Isanejad M, Sirola J, Mursu J, et al. (2017) Association of the Baltic Sea and Mediterranean diets with indices of sarcopenia in elderly women, OSPTRE-FPS study. European Journal of Nutrition; Pp: 1-14.
93. Chan R, Leung J, Woo J. (2016) A Prospective Cohort Study to Examine the Association Between Dietary Patterns and Sarcopenia in Chinese Community-Dwelling Older People in Hong Kong. J Am Med Dir Assoc; 17(4): 336-342.
94. Shad BJ, Smeuninx B, Atherton PJ, et al. (2015) The mechanistic and ergogenic effects of phosphatidic acid in skeletal muscle. Appl Physiol Nutr Metab; 40(12): 1233-1241.
95. Raben DM, Barber CN (2017) Phosphatidic acid and neurotransmission. Adv Biol Regul; 63: 15-21.
96. Gonzalez AM, Sell KM, Ghigiarelli JJ, et al. (2017) Effects of phosphatidic acid supplementation on muscle thickness

and strength in resistance-trained men. Appl Physiol Nutr Metab; 42(4): 443-448.

97. Andre TL, Gann JJ, McKinley-Barnard SK, et al. (2016) Eight weeks of phosphatidic acid supplementation in conjunction with resistance training does not differentially affect body composition and muscle strength in resistance-trained men. J Sport Sci Med; 15(3): 532-539.
98. Escalante G, Alencar M, Haddock B, et al. (2016) The effects of phosphatidic acid supplementation on strength, body composition, muscular endurance, power, agility, and vertical jump in resistance trained men. J Int Soc Sports Nutr; 13(1).
99. Franceschi F, Feregalli B, Togni S, et al. (2016) A novel phospholipid delivery system of curcumin (Meriva®) preserves muscular mass in healthy aging subjects. Eur Rev Med Pharmacol Sci; 20(4): 762-766.
100. Ishida Y, Kiyokawa Y, Asai T, et al. (2016) Ameliorating Effects of Sphingomyelin-Based Liposomes on Sarcopenia in Senescence-Accelerated Mice. Biol Pharm Bull; 786(39): 786-793.