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# A novel phospholipid delivery system of curcumin (Meriva®) preserves muscular mass in healthy aging subjects

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**Abstract. – OBJECTIVE: Curcumin is known to interrupt pro-inflammatory signalling and increases anti-oxidant protection, thus inhibiting the expression of inflammatory cytokines and the expression and function of inducible inflammatory enzymes. Together, these effects contribute to limit the onset and the progression of sarcopenia, due to the major role played by inflammation in the pathophysiology of this disease. This registry study evaluates the effects of Meriva® supplementation in otherwise healthy elderly subjects.**

**PATIENTS AND METHODS: This was a registry, supplement study, conducted in healthy subjects > 65 years with apparent loss of strength and tiredness who freely decided to start one of the following interventions: (1) standard management (exercise, balanced diet including proteins) (n = 33); (2) standard management + Meriva® one tablet/day (n = 31); (3) standard management + Meriva® one tablet/day + other supplementation (n = 22). A number of functional and biochemical parameters were evaluated at baseline and after three months (hand grip, weight lifting, time/distance before feeling tired after cycling, walking and climbing stairs; general fitness, proteinuria, oxidative stress, Karnofsky scale; left ventricular ejection fraction).**

**RESULTS: Significant improvements in all parameters, with respect to baseline values, were observed in the two supplementation groups ($p < 0.05$ for all comparisons). On the other hand, no improvement was observed in the standard management-only group. At three months, intergroup comparison revealed a statistical advantage in all parameters for both supplementation groups compared with the standard management-only group ($p < 0.05$ for all comparisons).**

**CONCLUSIONS: Our registry study shows that the addition of Meriva® – either or not combined with other nutritional supplements – to standardized diet and exercise plan contributes to improve strenght and physical performance in elderly subjects, potentially preventing the onset of sarcopenia.**

*Key Words:*
Curcumin, Meriva®, Nutritional supplementation, Registry, Sarcopenia.

## Introduction

Sarcopenia is a decrease in muscle mass often related with age or pathological conditions[1,2]. Due to increasing age of population, the prevalence of sarcopenia is increasing in Western countries. Moreover, sarcopenia can progress in its severity and impair the ability to perform daily acrivities, with a marked impact on quality of life[1,2]. Eventually, sarcopenia may lead to an increased risk of disability, falls and hospitalization[3].

Besides life style-related factors, as diet and physical activity, other mechanisms underlying the development of sarcopenia are not completely understood. However, they are thought to be multi-factorial, with chronic inflammation status playing a crucial role[4].

Nutritional interventions may provide an important contribution to prevent the development of sarcopenia[1]. Among different nutritional interventions, curcumin is known to exert a pleiotropic effect. Curcumin interrupts pro-inflammatory signalling and increases anti-oxidant protection by acting at distinct time-domain targets: (1) short time-domain targets such as pro-inflammatory enzymes (mPGES-1, 5-LO), and ion channels (TRPV1, TRPA1), and (2) long time-domain targets such as pro-inflammatory transcrip-


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tion factors (NF-kB, AP1, STAT, PPAR-g). As a net result, curcumin inhibits the expression of inflammatory cytokines (TNF-α, IL-1b, IL-6) and of the expression and function of inducible inflammatory enzymes (COX2 and mPG2S)[5-7]. In particular, NF-kB is involved in the development of muscle wasting during catabolic conditions such as sarcopenia; animal studies have shown that inhibition of NF-kB activity in skeletal muscle allows reducing protein degradation[8]. A similar effect is associated with the inhibition of other pro-inflammatory enzymes exerted by curcumin[8]. Moreover, curcumin contributes to reduce the inflammatory burden leading to muscle loss in sarcopenia patients by inducing an inhibition of p38 kinase activity, oxygen radical scavenging, and induction of the heat-shock response[8]. Together, these effects, and in particular the inhibition of NF-kB, do contribute to limit the onset and the progression of sarcopenia[8].

However, curcumin has a poor systemic bioavailability[9]. Several attempts have been made to overcome this limitation: in particular, dispersion of active molecules (typically belonging to the chemical class of polyphenols and triterpenes) with phospholipids under appropriate conditions leads to the formation of a delivery form named Phytosome®[10]. Among these complexes, the commercially available Phytosome® of curcumin, named Meriva®, has been studied for the treatment of a wide range of conditions compared versus non-formulated Curcumin[11-22].

On these bases, curcumin may represent a potential nutritional intervention to control sarcopenia in affected subjects, in particular for elderly. This registry study evaluates the effects of Meriva® supplementation in otherwise healthy elderly subjects, in order to preliminarily evaluate its efficacy in the management of sarcopenia.

## Patients and Methods

This was a registry, supplement study (see[23] for a complete description of such studies), conducted in healty subjects > 65 years who freely decided, after consultation at our Center for apparent loss of strength and tiredness, to start one of the following interventions: (1) standard management: exercise (Table I), balanced diet including proteins (both according to the instructions of trained specialists); (2) Group B: standard management + Meriva® one tablet/day (each tablet containing 1 g Meriva®); (3) standard management + Meriva® one tablet/day + other supplementation (Vitamin D 800 IU/day; Vitamin C 500 mg/day; Isoleucin 3 g/day; Carinitine 1 g/day). The participants were visited at baseline and after three months. No other treatments were needed or used during the observation period. All patients had a completely nomal cardiovascular system (as shown by ultrasound evaluation before inclusion).

The following evaluations were performed at baseline and at the end of the observation period: (1) hand grip, using standard digital Jamar dynamometers (Patterson Medical, Warrenvile, IL, USA) and assessed as the sum of three consecutive measurements in 1 minute; (2) weight lifting, assessed as the number of times the subject can lift a 2 kg manuber; (3) time/distance before feeling tired after cycling, walking and climbing stairs; (4) general fitness, by a numerical scale (0 = unable to move; 3 = normal); (5) proteinuria; (6) oxidative stress measurements, according to[24,25]; (7) Karnofsky scale; (8) measurement of left ventricular ejection fraction by ultrasounds.

Basic blood tests and the physiological parameters were also evaluated at inclusion and at the end of the observational period.

### Statistical Analysis

Data were analyzed by descriptive statistics. Intra- and inter-group comparisons were performed by the Mann-Witney test. A $p$ value < 0.05 was considered statistically significant.

## Results

In total, 86 registry subjects were followed up. Of these, 33 decided to follow standard manage-

**Table I.** Exercise program, performed every day.

| | | |
|---|---|---|
| *Endurance* | Cycling/Walinkg/Climbing stairs until exaustion | Daily |
| *Strenght* | Lifting low weights | 20 × arm, 20 × leg, three times daily |
| *Balance* | Walk along a 5-meter line | Daily |
| *Flexibility* | All main joints | 20 second×joint, twice daily |

**Table II.** Basline characteristics.

| | Standard management only | Standard management + Meriva® | Standard management + Meriva® + additional supplementation |
|---|---|---|---|
| Subjects | 33 | 31 | 22 |
| Females | 16 | 14 | 12 |
| Age, years (mean ± SD) | 72 (2) | 74 (1) | 73 (1) |
| BMI, kg/m$^2$ | 24.7 (1.0) | 24.3 (1.5) | 24.3 (1.2) |

SD: standard deviation.

ment only, 31 standard management+Meriva® and 22 took also the additional supplementation. No significant differences among groups were reported (Table II). No safety concerns or clinically relevant variations of laboratory parameters and vital signs were reported.

Table III summarizes the efficacy evaluations. Overall, significant improvements in all parameters, with respect to baseline values, were observed in the two supplementation groups; on the other hand, no improvement was observed in the standard management only group. At three months, inter-group comparison revealed a statistical advantage in all parameters for both supplementation groups compared with the standard management only group.

Compliance to supplementation was good with more than 95% of the supplements correctly used.

## Discussion

Sarcopenia represents a major clinical issue, given also the increasing prevalence of elderly people in the general population. This clinical condition can lead to a number of health problems, with a significant burden to the healthcare system.

It has been proposed that nutritional supplementation can have a role in the prevention and management of sarcopenia[1]. Our registry study, conducted in healty elderly subjects complaining for strength loss and physical tiredness, lends further support to this assumption.

In fact, the addition, to standardized diet and exercise, of nutritional supplementation with Meriva®, either or not combined with other supplements, resulted in statistically significant and

**Table III.** Efficacy evaluations. All data are expressed as mean (SD).

| | Standard management only (n = 33) | | Standard management + Meriva® (n = 31) | | Standard management + Meriva® + additional supplementation (n = 22) | |
|---|---|---|---|---|---|---|
| | Baseline | 3 months | Baseline | 3 months | Baseline | 3 months |
| Hand grip, kg | 32.2 (2.1) | 31.8 (2.0) | 31.2 (1.5) | 33.9 (1.8)* | 32.8 (1.7) | 35.4 (1.1)* |
| Weight lifting | 12 (2) | 11 (1) | 13 (1) | 16 (2)* | 11 (1) | 16 (2)* |
| Time/distance before eeling tired, minutes (meters for the walking test) | | | | | | |
| Cycling | 2’ 20” (18”) | 2’ 16” (12”) | 2’ 29” (18”) | 3’ 11” (11”)* | 2’ 14” (13”) | 3’ 44” (21”)* |
| Walking | 234 (21) | 239 (12) | 251 (11) | 311 (14)* | 244 (18) | 319 (24)* |
| Climbing stairs | 58” (6”) | 69” (5”) | 54” (6”) | 75” (3”)* | 51” (5”) | 69” (2”)* |
| General fitness, score | 1.1 | 1.1 | 1.2 | 2.2* | 1.1 | 2.5* |
| Proteinuria, mg/die | 244 (37) | 239 (46) | 239 (28) | 154 (39)* | 233 (34) | 158 (39)* |
| Oxidative stress, carr units | 368 (24) | 359 (26) | 379 (31) | 334 (26)* | 377 (28)* | 336 (23)* |
| Karnofsky scale, units | 75.4 (3.2) | 72.2 (1.3) | 76.2 (3.4) | 81.1 (2.0)* | 75.3 (1.8) | 83.4 (2.2)* |
| Left ventricular ejection fraction, % | 54.8 (0.2) | 55 (0.4) | 56.2 (0.5) | 59.8 (0.3)* | 57.1 (0.6) | 62.4 (1.0)* |

*$p < 0.05$ *vs*. baseline and *vs*. standard management-only.

clinically relevant improvements in a number of functional and physiological parameters without any safety concern. On the other hand, stardard management only was not associated with any significant improvement over a 3 months' period.

Our findings can be due, at least in part, to the recognized anti-inflammatory effects of Meriva®[5,6,8], which target systemic inflammation, one of the main contributors to the onset of sarcopenia[4]. Moreover, in animal models curcumin was shown to promote protein regeneration and reduce muscle loss[26].

Remarkably, subjects who decided to take supplementation reported a reduction of oxidative stress, which remains a major determinant of sarcopenia development. This kind of cellular damage has a role in enhancing tiredness and weakness, also in healty subjects[27,28], overall potentially contributing to the onset of sarcopenia. Further studies on the effect of oxidative stress and anti-oxidant compounds in sarcopenia patients can be of the highest interest. Moreover, the effects of nutritional supplementation were also evident in improving left ventricular ejection fraction: while all subjects had normal values of this parameter at baseline, this finding may suggest more specific studies in patients with impaired left ventricular function.

## Conclusions

Our registry study shows that the addition of Meriva® – either or not combined with other nutritional supplements – to standardized diet and exercise plan contributes to improve strenght and physical performance in elderly subjects, potentially preventing the onset of sarcopenia. We believe that Meriva®, in the context of an integrated approach[29-33], holds the potential to have a role in the management of this condition.

### Conflict of Interest

FF and ST are employees of Indena S.p.A. LG is a consultant of Indena S.p.A.

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