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# Anserine and carnosine supplementation in the elderly: Effects on cognitive functioning and physical capacity

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ABSTRACT

The aim of this study was to investigate the potential beneficial effects of dietary anserine and carnosine (CRC) supplementation on cognitive functioning and physical activity of the elderly. The fifty-six subjects (65+) were allocated to the CRC group or placebo group at a 1:1 ratio. The double-blind procedure was used. Data were collected at the baseline and after 13-weeks of supplementation. In the follow up procedure fifty one subjects took part. Chicken meat extract (CME) containing 40% of CRC components (2:1 ratio of anserine to carnosine) was administered 2.5 g per day which allowed to rich the level of 1 g CRC in dipeptides supplement. The cognitive function, physical capacity, body measurements, blood pressure and heart rate (HR) were assessed. After supplementation Body Mass Index (BMI) decreased significantly ($p < 0.05$) in the CRC group performance comparing the placebo group. In two of six Senior Fitness Test the scores increased significantly ($p < 0.05$) in CRC group comparing to the placebo group. The perceived exertion differed significantly ($p < 0.05$) at the baseline and after follow up at the CRC group. The mean values of the Short Test of Mental Status (STMS) scores showed the significant ($p < 0.04$) increase only in CRC group, in the subscores of construction/copying, abstraction and recall. Conducted anserine and carnosine supplementation in the elderly brings promising effects on cognitive functioning and physical capacity of participants. However, further studies are needed.



## 1. Introduction

Carnosine (β-alanyl-L-histidine) is an endogenous and water-soluble dipeptide first discovered in Russia in 1900 by Gulevitsch (Gariballa & Sinclair, 2000). Carnosine has been reported to be present in the skeletal muscles of many vertebrates. In bird muscles another dipeptide, anserine (β-alanyl-), which is synthesized either from β-alanine and 1-methylhistidine (1-MH) or is created by the N-methylation of β-alanyl-L-histidine, predominates. Both components, also including homocarnosine, are called carnosine related compounds-CRC. There are high levels of CRC in muscles, but also in the central nervous system of vertebrates, mainly in glia and neurons of the olfactory epithelium and bulbs (Budzeń & Rymaszewska, 2013; Jackson & Lenny, 1996). CRC are absorbed in the small intestine and penetrate the blood–brain barrier (Teuscher et al., 2004), but there is a difference in catabolism between carnosine and anserine. Products of carnosine hydrolysis, i.e. beta alanine and histidine, are used in the body for the synthesis of various metabolites, while 1-MH, being one of the products of anserine catabolism, is excreted mainly in urine (Kubomura, Matahira, Masui, & Matsuda, 2009). The concentration of carnosine in tissues depends on the diet (Gariballa & Sinclair, 2000).

CRC are reported to play an important physiological role in the body. They have antioxidant properties, cytosolic buffering capabilities and maintain an acid–base balance in excitable tissues of animals and humans. Carnosine is an antiglycating agent that sugarmediate protein crosslinking. It has metal ion-chelating properties (copper-, calcium- and zinc-chelating), extends the life of cells in cell culture conditions and regulates the activity of calcium channels in skeletal muscles (Aydyn, Kusku-Kiraz, Dooru-Abbasoolu, & Uysal, 2010; Gariballa & Sinclair, 2000; Hipkiss, 1998, 2009; Zieba, 2007). It is a potentially therapeutic agent of many diseases, present in pathogenesis of oxidative and carbonyl stress.

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Studies conducted on rats and mice show that carnosine has a neuroprotective potential against cerebral ischemia, and indirectly reduces the mortality of the animal (Dobrota et al., 2005; Rajanikant et al., 2007; Stvolinsky, Kukley, Dobrota, Mezesowa, & Boldyrev, 2000; Zemke, Krishnamurthy, & Majid, 2005). Data derived from the study on the carnosine administration therapy among patients with chronic discirculatory encephalopathy stress that carnosine enhances the efficacy of basal therapy of these patients (Federova et al., 2009). The carnosine level in tissues decreases with age and is the effect of a decline in the buffering capacity of the muscle (Tallon, Harris, Maffulli, & Tarnopolsky, 2007). According to del Favero et al. (2012), beta-alanine supplementation increases the carnosine level in skeletal muscles among the elderly and improves their exercise capacity. Anserine could also be used therapeutically due to its slower than carnosine degradation by plasma (Peters et al., 2011).

Some biochemical processes related to neurodegeneration, including Alzheimer Disease, are still unknown, but they probably include the metabolism of amino acids and dipeptides (Advokat & Pellegrin, 1992; Bowen, 1990; Fonteh, Harrington, Tsai, Liao, & Harrington, 2007; Molina et al., 1998).

According to cell studies using neurons, carnosine prevents cell death (Marchis et al., 2000). These properties of carnosine imply that it is an anti-aging agent, and various nutritional supplement manufacturers claim its benefits in treating neurodegenerative diseases, such as Alzheimer disease (Boldyrev, Gallant, & Sukhich, 1999; Stuerenburg, 2000).

Hipkiss noticed that the brain parts affected in the early stages of Alzheimer's disease are also those, in which carnosine is typically found in high concentrations (Hipkiss, 2007). This suggests that, when the level of carnosine decreases with age, it is these areas of the brain that are the most vulnerable to damage associated with Alzheimer's disease. Fonteh et al. showed a decrease in histidine in cerebro-spinal fluid (CSF) of patients with probable Alzheimer Disease (pAD) and a decrease in carnosine in their plasma. This implies that pAD patients could not control peroxidation events properly. The observed decreased capacity to prevent oxidation can result in an increased degeneration of nerve cells, resulting in a decline in cognitive and mental functions (Fonteh et al., 2007). Further assumption can be that supplementation in diet could reduce or even decelerate such processes.

Moreover, in the brains of patients with Alzheimer's disease, characterized by the presence of a pathological form of amyloid beta protein and intracellular lesions made up largely of the cytoskeletal protein tau, some accumulation of heavy metal ions can also be observed (Taylor, Hardy, & Fischbeck, 2002). Carnosine binds to metal ions and given the above observations CRC, due to their ability to participate in chelating metals, have a potential as a therapeutic agent of degenerative diseases, as an inhibitor of the toxicity of amyloid beta, as well as to be a "scavenger" of free radicals (Hipkiss, 2009; Corona et al., 2011).

In this study, we investigated the potential benefits of dietary anserine and carnosine supplementation (1 g per day, based on a 2:1 ratio of anserine to carnosine) on the cognitive functioning and physical activity. The assessment of the impact of supplementation on cognition was also carried out taking into account the age of the subjects, as the level of carnosine may decrease with age and cause increased sensitivity to the deterioration of cognitive function.

## 2. Materials and methods

The trial was conducted in a nursing home in Wroclaw, Poland. To be included in the study, subjects had to be at least 65 years old. Also, the subjects were not engaged in any physical exercises program for at least 1 year before recruitment. The exclusion criteria were: a Mini Mental State Examination (MMSE) score below 15, the presence of neurological, orthopedic or psychiatric diseases (psychotic disorders, mood disorders), addiction to alcohol, a medical history of eating disorders, cancer, intestinal diseases, stomach and duodenal ulcers, gastrointestinal bleeding, malabsorption syndrome, liver diseases, gastrointestinal inflammation and the use of nutritional supplements within the past 6 months (e.g. protein, amino acids and creatine). A MMSE score below 15 was chosen by the authors a priori as an exclusion criterion in order to keep a uniform methodology. Below this score, communication with subjects is so difficult that it would be impossible to carry out other psychometric tests. Respondents did not undergo any physiotherapy during the time of the supplementation and did not do any regular physical activity. 70 nursing home residents were recruited for the study. Of the 60 residents meeting the eligibility criteria, 4 were excluded because of a MMSE score below 15. The subjects were randomized using the matched design randomization that subjects were paired by sex before the CRC group and placebo group allocation at a 1:1 ratio. The patient allocation status was delivered to the head nurse after the first phase of the procedure. Participants and researchers were blinded to the group allocation. In total, 56 subjects were recruited and 51 of them took part in the follow up procedure: 26 (13 female and 13 male) were placed in the CRC group and 25 (13 female and 12 male) were allocated in the placebo group.

The diet of subjects was in accordance with the energy supply needs, suited to their age, weight, height and lifestyle. The percentage composition of different nutrients was 1.5 g of protein, 2.5 g of carbohydrates/kg body weight body weight and 1 g fat/kg body weight. Furthermore, the amount of calcium in the diet was 1.5 g/kg body weight.

The Ethics Committee of the Wroclaw Medical University approved the study protocol, and all subjects gave their informed consent in writing after the purpose of the study had been explained.

CME containing 40% of CRC components (2:1 ratio of anserine to carnosine) was prepared following breast meat extraction with water (cold and at 80 °C) and spray drying. A hydrolysate obtained after chicken meat enzymatic treatment was used as a placebo. Both supplements i.e. placebo and CME were administered 2.5 g per day, which allowed to reach the level of 1 g CRC in dipeptide supplements resuspended in soup. Supplementation was carried out for 13 weeks (93 days).

### 2.1. Measurements

The cognitive function, presence of depressive symptoms, physical capacity, body measurements, blood pressure and HR were assessed at baseline (PRE) and at 13-week follow up of supplementation (POST). Trained research assistants, blinded to group allocations, collected demographic and behavioral measurements at baseline and at a 13 week follow up. Behavioral measurements included: the MMSE and the STMS to assess cognitive functions, the Geriatric Depression Scale (GDS) to assess the presence of depressive symptoms, the Clinical Dementia Rating (CDR) to evaluate the severity of dementia.

All subjects underwent the MMSE, a brief 30-point questionnaire test that is used to screen for cognitive impairment (Folstein, Folstein, & McHugh, 1975) and the STMS 38-point cognitive screening scale (Tang-Wai et al., 2003). According to its authors, the STMS is a highly sensitive psychometric screening test to identify patients with mild cognitive impairment. Considering depressive symptoms as the most frequent mental health problem among older people, the GDS – a 30-item self-report assessment used to identify depression in the elderly – was used (Yesavage et al., 1983). The CDR was used only as a descriptive data because it synthesized information obtained from the clinical assessment