Palestrica of the third millennium – Civilization and Sport
Vol. 18, no. 2, April-June 2017, 81–86

The effect of branched-chain amino acid and curcumin supplementation on exercise capacity

Efectul suplimentării cu aminoacizi cu catenă ramificată și curcumină asupra capacității de efort fizic

Radu Cîrjoescu [1], Nikolaos Mavritsakis [2], Simona Tache [1]
[1] *"Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania*
[2] *1 December 1918 University of Alba Iulia, Department of Physical Education and Sport*

Abstract

Background. Our experimental results regarding the effect of supplementation with a complex of branched-chain amino acids (BCAA) on aerobic exercise capacity as well as on serum and tissue indicators of the oxidant/antioxidant balance led us to study the effect of a BCAA and curcumin (CCR) supplement under the same conditions.

Aims. The increase in oxidative stress (OS) during intense physical exercise and the increase in antioxidant (AO) defense during moderate physical exercise led us to study the effect of BCAA and CCR supplementation on aerobic exercise capacity (AEC) and biochemical redox profile.

Methods. The research was performed in 7 groups (n=10 animals/group): group I – controls, group II – controls + exercise (5% load), group III – controls + exercise (10% load), group IV – CCR, group V – CCR + BCAA, group VI – CCR + BCAA + exercise (5% load), group VII – CCR + BCAA + exercise (10% load). AEC was determined by the swimming test; for the O/AO balance, malondialdehyde (MDA) and total sulfhydryl groups (SH) were determined.

Results. BCAA+CCR supplementation induces an increase in AEC after 28 days of BCAA and CCR administration. BCAA+CCR supplementation in sedentary animals has modulating effects on the O/AO balance, with an increase in serum and muscle OS, a stimulation of serum AO defense, and a decrease in muscle and liver AO defense. BCAA+CCR supplementation in exercise trained animals with a 5% load induces a decrease in serum and liver OS and an increase in muscle OS and AO defense, while in animals with a 10% load, it results in a decrease in muscle OS and an increase in liver OS.

Conclusions. The BCAA+CCR complex has ergotropic, trophotropic and OS reducing effects in exercise trained animals.

Key words: curcumin, amino acids, aerobic exercise capacity, oxidant/antioxidant balance, oxidative stress.

Rezumat

Premize. Rezultatele noastre experimentale privind efectul suplimentării cu un complex de aminoacizi cu catenă ramificată (BCAA) asupra capacității aerobe de efort și indicatorilor serici și tisulari ai balanței oxidanți/antioxidanți ne-au determinat să studiem și efectul unui supliment de BCAA și curcumină (CCR) în aceleași condiții.

Obiective. Creșterea stresului oxidativ (SO) în cursul efortului fizic intens și creșterea apărării antioxidante (AO) în efortul fizic moderat ne-au determinat să studiem efectul suplimentării cu BCAA și CCR asupra capacității aerobe de efort (CAE) și profilului biochimic redox.

Metode. Cercetările au fost efectuate pe 7 loturi (n=10 animale/lot): lotul I - martori, lotul II - martori + efort (încărcare 5%), lotul III - martori + efort (încărcare 10%), lotul IV - CCR, lotul V – CCR + BCAA, lotul VI - CCR + BCAA + efort (încărcare 5%), lotul VII CCR + BCAA + efort (încărcare 10%). CAE s-a determinat prin proba de înot, pentru balanța O/AO s-au determinat malondialdehida (MDA) și grupările sulfhidril totale (SH).

Rezultate. Suplimentarea cu BCAA+CCR determină creșterea CAE după administrarea timp de 28 zile cu complexul de BCAA și CCR. Suplimentarea cu BCAA+CCR la animalele sedentare are efecte modulatoare asupra balanței O/AO, cu creșterea SO la nivel seric și muscular, stimularea apărării AO la nivel seric și scăderea apărării AO la nivel muscular și hepatic. Suplimentarea cu BCAA+CCR la animalele antrenate la efort determină la animalele cu încărcare 5% scăderea SO la nivel seric și hepatic și creșterea SO și apărării AO la nivel muscular, iar la animalele cu încărcare de 10% scăderea SO la nivel muscular și creșterea SO la nivel hepatic.

Concluzii. Complexul BCAA+CCR are efecte ergotrope, trofotrope și de atenuare a SO la animalele antrenate la efort fizic.

Cuvinte cheie: curcumină, aminoacizi, capacitate aerobă de efort, balanța oxidanți/antioxidanți, stres oxidativ.

Received: 2017, January 18; *Accepted for publication:* 2017, February 14
Address for correspondence: Ambulatory Sports Medicine Clinic, 19 Ludwig Roth Str., Cluj-Napoca
E-mail: rcirjoescu@yahoo.com
Corresponding author: Radu Cirjoescu, rcirjoescu@yahoo.com

Introduction

Curcumin (CCR) is the main active principle in the perennial plant Curcuma longa, whose rhizome has been used in Chinese and Indian medicine for more than 5000 years, the plant also being known as turmeric or Indian saffron. Curcumin extract (diferuloylmethane) is a yellow-orange water-insoluble, acetone, ethanol and dimethyl sulfoxide-soluble phytochemical component, which is present along with two other curcuminoids, demethoxycurcumin and bisdemethoxycurcumin, in the Curcuma longa rhizome.

Curcuminoids are exogenous natural antioxidants present as polyphenols in diet, in the form of a yellow pigment (Yilmaz Savcun G et al., 2013; Menon & Sudheer, 2007; Hemeida & Mohafez, 2008).

Curcumin has been used for hundreds of years as a spice (it is also known as the king of spices), a food colorant, a preservative, a source of industrial starch, a textile colorant, and in some cosmetic preparations.

Ayurvedic (traditional Indian) medicine and scientific studies over the past 20 years confirm and recommend curcumin for the prevention and treatment of many disorders.

Curcumin is considered to be the strongest natural anti-inflammatory agent, by regulation of many factors: cytokines, protein kinases, adhesion molecules, redox molecules and pro-inflammatory enzymes. Inflammation in its turn can aggravate cancer, cardiovascular diseases, diabetes, arthritis, autoimmune disorders, neurological diseases and pulmonary diseases (1).

Curcumin is a strong anticancer agent, preventing the formation and growth of tumor cells and metastasis (Kuttan et al., 2007; Tang, 2015; Sharna et al., 2004; Chen et al., 2016; Cheng et al., 2001; Shabana et al., 2015; Hadisaputri et al., 2015; Boyanapalli & Tony Kong, 2015; Guan et al., 2016).

Curcumin:

- reduces the effects of degenerative diseases, particularly Alzheimer's disease (Chen et al., 2013; Liu et al., 2014; Zhang et al., 20 06; Pulido-Moran et al., 2016; Goozee et al., 2016)
- has an anti-hyperalgesic effect (Singh & Vinayak, 2015)
- has an anti-parasitic effect (Novaes, 2016)
- protects and detoxifies hepatic cells (Hemeida & Mohafez, 2008; Pulido-Moran et al., 2016; Moghadan et al., 2015; Wang et al., 2005; Kim et al., 2016)
- has an antidepressant effect (Sanmukhani et al., 2009)
- plays a role in metabolic syndrome (Shabana et al., 2015; Boyanapalli et al., 2015; Yang et al., 2014)
- plays a role in cardiovascular disorders and reduces the risk of heart attack (Wongcharoen et al., 2012; Pulido-Moran et al., 2016)
- plays a role in digestive, gastrointestinal and hepatobiliary diseases (He et al., 2015)
- has an anti-allergic effect (Altintoprack et al., 2016; Chong et al., 2014)
- has an antifungal effect (Kim et al., 2003)

Hypothesis

Our experimental results regarding the effect of BCAA supplementation on aerobic exercise capacity as well as on serum and tissue indicators of the oxidant/antioxidant balance led us to study the effect of a BCAA and curcumin (CCR) complex under the same conditions.

We experimentally monitored the effect of supplementation with a BCAA + curcumin complex on:

- aerobic exercise capacity
- serum as well as muscle and liver tissue oxidant/antioxidant balance

Material and methods

Research protocol

a) Period and place of the research

The experimental study was performed in male Wistar rats from the Biobase of the "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca. The rats had a mean weight of 180-190 grams and were aged 16 weeks. The study was approved by the Ethics Committee, according to the Good Practice Guidelines. It complied with the requirements of the Declaration of Helsinki, Amsterdam Protocol, Directive 86/609/EEC and the regulations of the Bioethics Committee of the "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca. The studies were conducted in the Experimental Research Laboratory of the Physiology Department of the "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca.

b) Subjects and groups

The determinations were performed in 7 groups of rats (n =10 animals/group):

Group I – controls
Group II – controls + exercise (5% load)
Group III – controls + exercise (10% load)
Group IV – curcumin
Group V – curcumin + BCAA
Group VI – curcumin + BCAA + exercise (5% load)
Group VII – curcumin + BCAA + exercise (10% load)

Curcumin was administered in doses of 30 mg/kg body weight/day for 28 days, by oropharyngeal gavage. The administered curcumin is produced by Secom, and the product is found under the name of "Curcumin 95" – 500 mg.

BCAA (Natural plus preparation) was administered by oropharyngeal gavage, in a dose of 0.1 ml per rat, the dose being calculated in relation to the daily dose recommended for humans. The ratio between amino acids (AA) in the preparation is 2:1:1 (1000 mg L-leucin, 500 mg L-isoleucin and 500 mg L-valin). The administered amount was 30 mg/animal/day for 28 days.

c) Tests applied

Aerobic exercise capacity (AEC) was determined by the swimming test, which was performed in a plastic pool, using the Nayanatara method (2005).

The AEC value was calculated by measuring the time period, expressed in seconds, from the introduction of the animals in the pool until their exhaustion (refusal to swim).

Exercise intensity was changed by loading the animals with different weights, 5% and 10% of the animal's weight, in the standard linear loading variant.

The duration of the experiment was 28 days. The studied days were day 1 (T1), day 14 (T14) and day 28 (T28).

Biochemical determinations were performed in the Laboratory for the Study of Oxidative Stress of the Physiology Department of "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca. For determination of the indicators of the blood O/AO balance, venous blood samples were collected from the retro-orbital sinus. From the collected blood, serum was separated by centrifugation, for the measurement of indicators.

Malondialdehyde (MDA) was measured using the fluorescence method, according to Conti et al., (1991). Concentration values were expressed in nmol/ml. Total sulfhydryl groups (SH) were determined using the Hu method (1994). Concentration values were expressed in µmol/ml.

d) Statistical processing

Statistical processing was performed with the StatsDirect v.2.7.2 software, using the OpenEpi 3.03 application and the Excel application (Microsoft Office 2010). The results were graphically represented using the Excel application (Microsoft Office 2010).

Results

a) Aerobic exercise capacity (Table I)

The statistical analysis of exercise capacity values, considering all groups, evidenced highly statistically significant differences between at least two of the groups at the time points T1, T14 and T28 ($p < 0.001$).

The statistical analysis of exercise capacity values, considering all time points, showed highly statistically significant differences between at least two of the studied time points in all groups ($p < 0.001$).

The statistical analysis of exercise capacity values for unpaired samples revealed the following:

- at T1

o highly statistically significant differences between groups III-VII ($p < 0.001$)

o statistically significant differences between groups VI-VII ($p < 0.05$)

- at T14 and T28 – highly statistically significant differences between groups III-VI, III-VII ($p < 0.001$).

The statistical analysis of exercise capacity values for paired samples evidenced the following:

- in group VI

o highly statistically significant differences between time points T1-T14 ($p < 0.001$)

o very statistically significant differences between time points T1-T28 and T14-T28 ($p < 0.01$)

- in group VII

o highly statistically significant differences between time points T1-T14 ($p < 0.001$)

o very statistically significant differences between time points T1-T28 and T14-T28 ($p < 0.01$).

b) Serum O/AO balance (Tables II and III).

The statistical analysis of MDA values, considering all groups with curcumin administration (with or without BCAA), showed very statistically significant differences between at least two of the groups ($p < 0.01$).

The statistical analysis of MDA values, considering all groups with curcumin and BCAA administration, evidenced very statistically significant differences between at least two of the groups ($p < 0.01$).

The statistical analysis of MDA values for unpaired samples indicated the following:

- highly statistically significant differences between groups IV-VI, I-V, I-IV, III-VII ($p < 0.001$)
- very statistically significant differences between groups II-VI ($p < 0.01$)
- statistically significant differences between groups V-VI, VI-VII ($p < 0.05$).

The statistical analysis of SH values, considering all groups with curcumin administration (with or without BCAA), indicated no statistically significant differences between the groups ($p > 0.05$).

The statistical analysis of SH values, considering all groups with curcumin and BCAA administration, revealed no statistically significant differences between the groups ($p > 0.05$).

The statistical analysis of SH values for unpaired samples evidenced the following:

- highly statistically significant differences between groups I-IV ($p < 0.001$)
- very statistically significant differences between groups I-V, II-VI, III-VII ($p < 0.01$).

Table I

Comparative analysis of exercise capacity values (measured in sec) in the studied groups and statistical significance.

Time point	Group	Mean	SE	Median	SD	Min.	Max.	Statistical significance (p)		
T1	II	321	10.7703	310	34.0588	290	385	T1-T14-T28	II	< 0.001
	III	292	7.0427	292.5	22.2711	255	325		III	< 0.001
	VI	329	5.1403	324	16.2549	306	358		VI	< 0.001
	VII	346	5.1876	340	16.4046	329	375		VII	< 0.001
T14	II	428	11.0000	420	34.7851	385	482	II	T1-T14	< 0.01
	III	382	11.3490	385	35.8887	335	430		T1-T28	< 0.01
	VI	442	4.6857	444	14.8174	423	465		T14-T28	< 0.001
	VII	451	4.1740	450.5	13.1993	434	475	III	T1-T14	< 0.001
T28	II	525	8.2476	524.5	26.0811	495	560		T1-T28	< 0.001
	III	503	4.8120	504	15.2169	469	520		T14-T28	< 0.001
	VI	668	15.8808	654.5	50.2195	615	780	VI	T1-T14	< 0.001
	VII	678	7.6522	679	24.1983	640	710		T1-T28	< 0.01
Statistical significance (p)	Time point	II-III-VI-VII	II-III	VI-VII	II-VI	III-VII			T14-T28	< 0.01
	T1	< 0.001	NS	< 0.05	NS	< 0.001	VII		T1-T14	< 0.001
	T14	< 0.001	< 0.01	NS	NS	< 0.001			T1-T28	< 0.01
	T28	< 0.001	< 0.05	NS	< 0.001	< 0.001			T14-T28	< 0.01

Table II

Comparative analysis of malondialdehyde values (measured in nmol/ml) in the studied groups and statistical significance.

Group	Mean	SE	Median	SD	Min.	Max.	Statistical significance (p)			
I	1.467	0.0875	1.476	0.2768	1.002	1.944	VII-V-VI-VII	< 0.01	VI-VII	< 0.05
II	1.717	0.1675	1.545	0.5298	0.979	2.697	V-VI-VII	< 0.01	II-VI	< 0.01
III	2.023	0.0676	2.130	0.2138	1.712	2.238	IV-V	NS	III-VII	< 0.001
IV	3.349	0.2197	3.397	0.6948	2.133	4.194	IV-VI	< 0.001	I-IV	< 0.001
V	2.949	0.2269	3.043	0.7175	2.051	4.046	IV-VII	NS	I-V	< 0.001
VI	2.291	0.0557	2.308	0.1762	2.050	2.546	V-VI	< 0.05	nmol/ml	
VII	3.421	0.3445	3.207	1.0895	2.297	5.316	V-VII	NS		

Table III

Comparative analysis of SH values (measured in µmol/ml) in the studied groups and statistical significance.

Group	Mean	SE	Median	SD	Min.	Max.	*Statistical significance (p)*			
I	0.128	0.0123	0.124	0.0388	0.083	0.197	IV-V-VI-VII	NS	VI-VII	NS
II	0.150	0.0076	0.154	0.0239	0.111	0.179	V-VI-VII	NS	II-VI	< 0.01
III	0.166	0.0044	0.163	0.0140	0.143	0.192	IV-V	NS	III-VII	< 0.01
IV	0.198	0.0101	0.205	0.0320	0.144	0.239	IV-VI	NS	I-IV	< 0.001
V	0.188	0.0105	0.189	0.0333	0.139	0.238	IV-VII	NS	I-V	< 0.01
VI	0.193	0.0106	0.188	0.0337	0.136	0.234	V-VI	NS	µmol/ml	
VII	0.189	0.0051	0.185	0.0160	0.175	0.224	V-VII	NS		

c) Statistical correlation analysis (Table IV) between the values of the studied indicators showed the following:

• in group VI, an acceptable positive correlation between AEC-MDA;

• in group VII, an acceptable negative correlation between AEC-MDA.

Table IV

Statistical correlation analysis between the values of the serum indicators of the O/AO balance

Items		Group VI		Group VII	
AEC	MDA	0.2675	**	-0.3567	**
	SH	0.2188	*	-0.2371	*

Correlations: **** very good, *** good, ** acceptable, * weak

Discussions

The effect of BCAA and CCR supplementation on AEC. Chronic supplementation with a BCAA and CCR complex induced at 28 days (T28): a significant increase in AEC in group VII compared to group II, and in group VII compared to group III.

BCAA and CCR supplementation in sedentary animals (group V) compared to controls (group I) induced a significant increase in MDA and SH groups.

BCAA and CCR supplementation in exercise trained animals compared to supplemented sedentary animals induced a decrease in serum MDA in group VI compared to group V.

BCAA and CCR supplementation in exercise trained animals determined the following significant changes in redox homeostasis compared to unsupplemented trained animals:

- in group VI compared to group II, an increase in serum MDA and SH was evidenced;

- in group VII compared to group III, an increase in serum MDA and SH was observed.

The comparative effect of BCAA+CCR supplementation compared to BCAA supplementation on AEC in exercise trained animals:

- in group VI compared to group V, significant increases were found at 14 days (T14) compared to initial values (T1), and at 28 days (T3) compared to values at 14 days (T2);

- in group VII compared to group VI, significant increases were found at 14 days (T2) compared to initial values (T1), and at 28 days (T3) compared to values at 14 days (T2).

The comparative effect of BCAA and CCR supplementation compared to BCAA supplementation on serum redox homeostasis in exercise trained animals:

- in group VI compared to group V, a significant increase in MDA and SH was observed;

- in group VII compared to group VI, a significant increase in MDA was detected.

The dual effect of curcumin in redox homeostasis.

Curcumin has a strong antioxidant effect by:

a) fighting oxidative stress in two ways:

- by preventing the formation of free radicals;

- by suppressing/removing the formed free radicals, particularly superoxide anion and hydroxyl radical (Thiyagarajan & Charma, 2004; Epstein et al., 2010; Jagetia & Rajanikant, 2015; Farooqui, 2016);

b) modulating AO enzymes: superoxide dismutase, catalase, glutathione peroxidase, reductase and transferase (Singh, 2015; Altintopbrak et al., 2016; El-Bahr, 2015; Panahi et al., 2016).

The pro-oxidant effect of curcumin consists of rapid production of free radicals, a dose-dependent effect (Marathe et al., 2011).

Literature data on CCR supplementation and physical exercise are available.

In athletes, an increase in physical strength and performance (Franceshi et al., 2016), no exercise-induced changes in serum and muscle OS markers (Drobnic et al., 2014); and a decrease in OS (Takashi et al., 2014; Kawanishi et al., 2013) were observed.

In animals, a protective effect against muscle damage during eccentric exercise was evidenced, independently of

redox homeostasis (Boz et al., 2014), as well as a reduction of OS (Roshan et al., 2011; Dabidi, 2013).

Although the AO effect of some complex preparations based on CCR in pathological situations is well demonstrated, under physiological physical exercise conditions, we found no evidence in this respect.

Conclusions

1. The BCAA+CCR complex induces an increase in AEC in exercise trained animals.

2. BCAA+CCR supplementation in sedentary animals has modulating effects on the O/AO balance, with an increase in serum OS levels and a stimulation of AO defense.

3. BCAA+CCR supplementation determines a decrease in serum OS in exercise trained animals with a 5% load.

4. The BCAA+CCR complex has ergotropic, trophotropic and OS reducing effects in exercise trained animals.

Conflicts of interest

Nothing to declare.

Acknowledgements

The article is part of the first author's PhD thesis, presented at the "Iuliu Haţieganu" University of Medicine and Pharmacy in Cluj-Napoca.

References

Altintoprack N, Kar M, Acar M, Berkoz M, Muluk NB, Cingi C. Antioxidant activities of curcumin in allergic rhinitis. Eur Arch Otorhinolaryngo. 2016;273(11):3765-3773. DOI:10.1007/s00405-016-4076-4.

Boyanapalli SS, Tony Kong AN. "Curcumin, the king of spices": Epigenetic Regulatory Mechanisms in the Prevention of Cancer, Neurological, and Inflammatory Disease. Curr Pharmacol Rep. 2015;1(2):129-139. DOI:10.1007/s40495-015-0018-x.

Boz I, Belviranli M, Okudan N. Curcumin Modulates Muscle Damage but not Oxidative Stress and Antioxidant Defense Following Eccentric Exercise in Rats. Int J Vitam Nutr Res. 2014;84(3-4):163-172. DOI: https://doi.org/10.1024/0300-9831/a000203.

Chen CQ, Yu K, Yan OX, Xing CY, Chen Y, Yan Z, Shi YF, Zhao KW, Gao SM. Pure curcumin increases the expression of SOCS1 and SOCS3 in myeloproliferative neoplasms through suppressing class I histone deacetylases. Carcinogenesis. 2013;34(7):1442-1449. DOI:10.1093/carcin/bgt070.

Chen Y, Pan L, Jiang M, Li D, Jin L. Nanostructured lipid carriers enhance the bioavailability and brain cancer inhibitory efficacy of curcumin both in vitro and in vivo. Drug Deliv. 2016;23(4):1383-1392. DOI:10.3109/10717544.2015.1049719.

Cheng AL, Hsu CH, Lin JK, Hsu MM, Ho YF, Shen TS, Ko JY, Lin JT, Lin BR, Ming-Shiang W, Yu HS, Jee SH, Chen GS, Chen TM, Chen CA, Lai MK, Pu YS, Pan MH, Wang YJ, Tsai CC, Hsieh CY. Phase I clinical trial of curcumin, a chemopreventive agent, in patients with high risk or pre-malignant lesions. Anticancer Res. 2001;21(4B):2895-2900.

Chong L, Zhang W, Nie Y, Yu G, Liu L, Wen S, Zhu L, Li C. Protective effect of curcumin on acute airway inflammation of allergic asthma in mice trhough Notch1-GATA3 signaling pathway. Inflammation. 2014;37(5):1476-1485. DOI:10.1007/s10753-014-9873-6.

Conti-Tronconi BM, Diethelm BM, Wu XD, Tang F, Bertazzon T, Schröder B, Reinhardt-Maelicke S, Maelicke A. Alpha-bungarotoxin and the competing antibody WF6 interact with different amino acids within the same cholinergic subsite. Biochemistry. 1991;30(10):2575-2584.

Dabidi RV, Hosseinzadeh S, Mahjoub S, Hosseinzadeh M, Myers J. Endurance exercise training and diferuloyl methane supplement:changes in neurotrophic factor and oxidative stress induced by lead in rat brain. Biol Sport. 2013;30(1):41-46. DOI:10.5604/20831862.1029820.

Drobnic F, Riera J, Apendino G, Togni S, Franceschi F, Valle X, Pons A, Tur J. Reduction on delayed onset muscle soreness by a novel curcumin delivery system (Meriva®): a randomized, placebo-controlled trial.J Int Soc Sports Nutr. 2014;11-31. DOI:10.1186/1550-2783-11-31.

El-Bahr SM, Embaby MA, Al-Azraqi AA, Abdelghany AM, Hussein YA. Effect of Curcumin on Aflatoxin B1-Induced Toxicity in Rats:A Biochemical and Histopathological Study. Int J Biochem Res & Review. 2015;5(1):63-72.

Epstein J, Sanderson IR, Macdonald TT. Curcumin as a therapeutic agent: the evidence from in vitro, animal and human studies. Br J Nutr. 2010 Jun;103(11):1545-1557. DOI:10.1017/S0007114509993667

Farooqui AA. Therapeutic Potentials of Curcumin for Alzheimer Disease. Springer Int Pub Ag. 2016.

Franceschi F, Feregalli B, Togni S, Cornelli U, Giacomelli L, Eggenhoffner R, Belcaro G. A novel phospholipid delivery system of curcumin (Meriva) preserves muscular mass in healty aging subjects. Eur Rev Med Pharmacol Sci. 2016;20(4):762-766.

Goozee KG, Shah TM, Sohrabi HR, Rainey-Smith SR, Brown B, Verdile G, Martins RN. Examining the potential clinical value of curcumin in the prevention and diagnosis of Alzheimer's disease. Br J Nutr. 2016;115(3):449-465. DOI:10.1017/S0007114515004687.

Guan F, Ding Y, Zhang Y, Zhou Y, Li M, Wang C. Curcumin Supresses Proliferation and Migration of MDA-MB-231 Breast Cancer Cells through Autophagy-Dependent Akt Degradation. Plos One. 2016;11(1):e0146553. DOI:10.1371/journal.pone.0146553.

Hadisaputri YE, Miyazaki T, Suzuki S, Kubo N, Zuhrotun A, Yokobori T, Abdulah R, Yazawa S, Kuwano H. Molecular characterization of antitumor effects of the rhizome extract from Curcuma zedoaria on human esophageal carcinoma cells. Int J of Oncology. 2015;47(6):2255-2263. DOI:10.3892/ijo.2015.3199.

He Y, Yue Y, Zheng X, Zhang K, Chen S, Du Z. Curcumin, inflammation, and chronic diseases: how are they linked. Molecules. 2015;20(5):9183-9213. DOI:10.3390/molecules 20059183.

Hemeida RA, Mohafez OM. Curcumin attenuates methotraxate-induced hepatic oxidative damage in rats. J Egypt Natl Canc Inst. 2008;20(2):141-148.

Hu ML. Measurement of protein thial groups and glutathione in plasma. Methods enzymol. 1994; 233:380-385.

Jagetia GC, Rajanikant GK. Curcumin Stimulates the Antioxidant Mechanisms in Mouse Skin Exposed to Fractionated γ-Irradiation. Antioxidants (Basel). 2015; 4(1):25-41. DOI: 10.3390/antiox4010025

Kawanishi N, Kato K, Takahashi M, Mizokami T, Otsuka Y, Imaizumi A, Shiva D, Yano H, Suzuki K. Curcumin attenuates oxidative stress following downhill running-induced muscle damage. Biochem Biophys Res Commun. 2013;441(3):573-578. DOI:10.1016/j.bbrc.2013.10.119.

Kuttan G, Kumar KB, Guruvayoorappan CKim MK, Choi

GJ, Lee HS. Fungicidal property of Curcuma longa L. rhizome-derived curcumin against phytopathogenic fungi in a greenhouse. J Agric Food Chem. 2003;51(6):1578-81. DOI:10.1021/jf0210369.

Kuttan R. Antitumor, anti-invasion, and antimetastatic effects of curcumin. Adv Exp Med and Biology. 2007;595:173-184.

Liu ZJ, Liu HQ, Xiao C, Fan HZ, Huang Q, Liu YH, Wang Y. Curcumin protects neurons against oxygen-glucose deprivation/reoxygenation-induced injury through activation of peroxisome proliferator-activated receptor-γ function. J Neurosci Res. 2014;92(11):1549-1559. DOI:10.1002/jnr.23438.

Marathe SA, Dasgupta I, Gnanadhas DP, Chakravortty D. Multifaceted roles of curcumin: two sides of a coin. Expert Opin Biol Ther. 2011; 11(11):1485-1499. DOI:10.1517/14712598.2011.623124.

Menon V, Sudheer AR. Antioxidant and anti-inflammatory propreties of curcumin. Adv Exp Med Biol. 2007;595:105-125. DOI:10.1007/978-0-387-46401-5_3.

Moghadam AR, Tutunchi S, Namvaran-Abbas-Abad A, Yazdi M, Bonyadi F, Mohajeri D, Mazani M, Marzban H, Los MJ, Ghavami S. Pre-administration of turmeric prevents methotrexate-induced liver toxicity and oxidative stress. BMC Complement Altern Med. 2015;15:246. DOI:10.1186/s12906-015-0773-6.

Nayanatara AK, Nagaraja HS, Anupama BK. The effect of repeted swimming stress on organ weights and lipid nperoxidation in rats. J Phys Biomed Sci, 2005;18(1):3-9.

Novaes RD, Sartini MV, Rodrigues JP, Goncalves RV, Santos EC, Souza RL, Caldas IS. Curcumin Enhances the Anti-Trypanosoma cruzi Activitu of Benznidazole-Based Chemotherapy in Acute xperimental Chagas Disease. Antimicrob Agents Chemother. 2016;60(6):3355-3364. DOI:10.1128/AAC.00343-16.

Panahi Y, Hosseini MS, Khalili N, Naimi E, Soflaei SS, Majeed M, Sahebkar A. Effects of supplementation with curcumin on serum adipokine concentrations: A randomized controlled trial. Nutrition. 2016;32(10):1116-1122. DOI:10.1016/j.nut.2016.03.018.

Pulido-Moran M, Moreno-Fernandez J, Ramirez-Tortosa C, Ramirez-Tortosa MC. Curcumin and Health. Molecules. 2016 21(3):264. DOI:10.3390/molecules21030264.

Roshan VD, Assali M, Moghaddam AH, Hosseinzadeh M, Myers J. Exercise training and antioxidants: effects on rat heart tissue exposed to lead acetate. Int J Toxicol. 2011;30(2):190-196. DOI:10.1177/1091581810392809.

Sanmukhani J, Satodia V, Trivedi J, Patel T, Tiwari D, Panchal B, Goel A, Tripathi CB. Efficacy and safety of curcumin in major depressive disorder: a randomized controlled trial. Phytother Res. Apr. 2014 28(4):579-585. DOI:10.1002/ptr.5025.

Shabana MH, Shahy EM, Taha MM, Mahdy GM, Mahmoud MH. Phytoconstituents of Curcuma longa L aqueous ethan extract and its immunomodulatory effect on diabetic infected rats. Egyptian Pharm J. 2015;14(1):36-43. DOI: 10.4103/1687-4315.154713.

Sharma RA, Euden SA, Platton SL, Cooke DN, Shafayat A, Hewitt HR, Marczylo TH, Morgan B, Hemingway D, Plummer SM, Pirohamed M, Gescher AJ, Steward WP. Phase I clinical trial of oral curcumin: biomarkers of systemic activity and compliance. Clin Cancer Res. 2004;10(20):6847-6854.

Singh AK, Vinayak M. Curcumin attenuates CFA induced thermal hyperalgesia by modulation of antioxidant enzymes and down regulation of TNF- α, IL-1β and IL-6. Neurochem Res. 2015 Mar;40(3):463-472. DOI:10.1007/s11064-014-1489-6

Takashi M, Suzuki K, Kim HK, Otsuka Y, Imaizumi A, Miyashita M, Sakamoto S. Effects of curcumin supplementation on exercise-induced oxidative stress in humans. Int J Sports Med.2014;35(6):469-475. DOI:10.1055/s-0033-1357185.

Tang Y. Curcumin Targets Multiple Pathways to Halt Hepatic Stellate Cell Activation:Updated Mechanisms In Vitro And In Vivo. Dig Dis Sci. 2015;60(6):1554-1564. DOI:10.1007/s10620-014-3487-6

Thiyagarajan M, Sharma SS. Neuroprotective effect of curcumin in middle cerebral artery occlusion induced focal cerebral ischemia in rats. Life Sci. 2004 Jan 9;74(8):969-985.

Wang M, Ruan Y, Chen Q, Wang Q, Cai J. Curcumin induced HepG2 cell apoptosis-asociated mitochondrial membrane potential and intracellular free Ca(2+) concentration. Eur J Pharmacol. 2011;650(1):41-47. DOI:10.1016/j.ejphar.2010.09.049.

Wongcharoen W, Jai-Aue S, Phrommintikul A, Nawarawong W, Woragidpoonpol S, Tepsuwan T, Sukonthasarn A, Apaijai N, Chattipakorn N. Effects of curcuminoids on frequency of avute myocardial infarction after coronary artery bypass grafting. Am J Cardiol. 2012;110(1):40-44. DOI:10.1016/j.amjcard.2012.02.043.

Yang YS, Su YF, Yang HW, Lee YH, Chou JI, Ueng KC. Lipid-lowering effects of curcumin in patients with metabolic syndrome: a randomized, double-blind, placebo-controlled trial. Phytother Res. 2014 Dec;28(12):1770-1777. DOI:10.1002/ptr.5197.

Ylmaz Savcun G, Ozkan E, Dulundu E, Topaloglu U, Sehirli AO, Tok OE, Erkan F, Sener G. Antioxidant and anti-inflammatory effects of curcumin against hepatorenal oxidative injury in an experimental sepsis model in rats. Ulus Travma Acil Cerrahi Derg. 2013;19(6):507-515.

Zhang L, Fiala M, Cashman J, Sayre J, Espinosa A, Mahanian M, Zaghi J, Badmaev V, Graves M, Bernard G, Rosenthal M. Curcuminoids enhance amyloid- β uptake by macrophages of Alzheimer's disease patients. J Alzheimers Dis. 2006;10(1):1-7.

Websites

(1) www.herbagetica.ro Accessed in January 2016