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ORIGINAL ARTICLE

Influence of long-term administration of *Curcuma longa* extract on explorative activity in aged rats

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Abstract: The effects of long-term administration of a standardised extract of *Curcuma longa* on the explorative activity in aged 24-month-old male Wistar rats were estimated in a hole-board test. The animals received the extract orally for two months in rodent chow at doses of 10 and 50 mg/kg/day. The correlations between concentration of some neurotransmitters and amino acids in selected brain regions, as well as the level of corticosterone in plasma (described previously), and the parameters of exploration were calculated. The antioxidant processes (GSH, GST, CAT and MDA levels) in heart and skeletal muscles were also investigated. The results suggested that the explorative activity of plant extract-treated rats was enhanced; however, no correlations between brain neurotransmitter concentration or plasma corticosterone level and the parameters of explorative activity were observed. In biochemical investigation, chronic *C. longa* extract administration influenced antioxidant processes (CAT, GST and MDA levels) in skeletal muscles of aged rats, but not in the heart muscle.

Key words: *Curcuma longa*, curcumin, hole-board, head-dipping, glutathione, glutathione-S-transferase, malonyldialdehyde, catalase, aged rats

INTRODUCTION

Curcuma longa is a widely-used medicinal plant with well-known anti-neurodegenerative effects [1-3]. The most important constituents of the standardised extract of its dried rhizome are curcuminoids – polyphenols generally regarded as the most active of compounds [4]. Curcumin may influence intra- and extra-cellular mechanisms in the central nervous system that are responsible for the antioxidant and anti-inflammatory properties of the *C. longa* extract [5-12]. It is able to inhibit beta-amyloid formation [13-15], and reverse stress-induced impairment of neurogenesis [16], as well as the proliferative and proapoptotic mechanisms [17]. Curcumin also stops lipid peroxidation in animal brains [18]. It protects against heavy-metal neurotoxicity [19, 20], glutamate excitotoxicity [21, 22], ischemia [23,24] and hyperglycaemia [25]. Learning and memory processes are also improved in adult and old animals after curcumin administration [1, 26]. Some research has shown that curcumin may influence neurotransmission in CNS and alternate the behaviour in animal models of depression [16, 27-31], as well as in aged rats [1].

This study is concerned with the influence of the chronic pre-treatment of a standardised extract of *Curcuma longa* administered in 2 doses (10 and 50 mg/kg/b.w.) on the explorative activity of aged Wistar male rats, estimated in a hole-board testing. The correlations between previously investigated brain neurotransmitters, as well as plasma corticosterone level [1] and behavioural parameters of exploration in naturally-aged rats, were calculated. Since it is known that curcumin may change the antioxidant equilibrium in rodents' brains, and following their behaviour [10], the estimation of curcumin influence on the antioxidant processes in heart and skeletal muscles (that may also change rats' activity) was then performed.

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MATERIALS AND METHODS

Subjects. The behavioural effects after 2 months of a standardised extract of the *Curcuma longa* rhizome pre-treatment were analysed in a hole-board test in 24-month-old male Wistar rats. The body weight of the animals did not differ between control and experimental groups ($F_{2,20}$=0.32, p<0.73 and $F_{2,20}$=1.11, p<0.35 at the beginning and at the end of the experiment), and did not change significantly within the 2-months duration of extract intake. The rats were housed in typical plastic cages (26 × 42 cm, 18 cm high) with wood cuttings inside. They stayed in the special animal room under a 12:12 hours light/dark cycle with free access to water. The rats were acclimatised to laboratory conditions before the behavioural test. All the procedures took place between 08:00–16:00, and each rat was used only once in the hole-board. All animal testing was carried out according to the European Communities Council Directive (86/609/EEC) of 24 November 1986, after approval of the Ethical Committee for Animal Experiments at the Medical University of Warsaw.

The procedure of experiments – *C. longa* extract administration. In the experiment, the animals were fed with standardised extract of *Curcuma longa* rhizome (CPE-014, curcumin powder; Arjuna Natural Extracts Ltd., India) that contained 96% of the active ingredient – curcumin, estimated by spectrophotometer method, and 1.2% of volatile oils (turmerones).

The biochemical analysis was performed after the end of the experiment. The powdered chow was enriched with the curcumin extract, mixed carefully and after slight wetting, the fresh pellets of chow were formed by hand each day. The 24-months-old rats were given the chow for 60 days, and then for the duration of the behavioural testing in the experiment. The amount of chow for each rat daily was restricted to 20 g because in earlier pilot trials such an amount had been precisely estimated as completely eaten and sufficient. The feeding and rats' weight were continuously controlled within the experiments. The control rats (Con, n=7) were given standardised laboratory chow and the treated ones the same chow with addition of the extract at the concentrations of 350 (C10, n=8) and 1750 ppm (C50, n=8). The daily amounts of plant extract used during the entire experiment were in doses between 9.5-10.3 mg/kg (mean value 9.99, SD=0.28) and 48.0-51.5 mg/kg (mean value 49.59, SD=1.33) in the C10 and C50 group, respectively.

Behavioural assessment – Hole-board test. For estimating the explorative activity of the animals the hole-board test [32, 33] was used. The white wooden apparatus had 16 equidistant holes 40 mm in diameter in the board (1m × 1m). The holes were restricted to an inner area and consisted of 16 squares (0.2m × 0.2m), and an outer area with a width of 0.1m beyond the squares. The height of the walls of the testing box was 0.35m. Each single rat was located in the centre of the floor and allowed to explore the apparatus freely for 5 minutes during 3 consecutive days. The following behavioural parameters were taken into account: the number of head-dippings (with both eyes disappearing in the hole) and rearings (with two paws lifting over the board) to assess explorative activity, as well as the number of crossings (of the internal square borders) and total time spent on moving to estimate locomotor activity. The behaviour of the animals was recorded on a video camera situated above the testing box. After each trial, the apparatus was carefully cleaned with acetic acid and water.

Biochemical assessment. Biochemical measurements were carried out 24 hours after the last behavioural trial. The levels of reduced glutathione (GSH; nmol/mg), glutathione transferase (GST; µmol/min/mg), catalase (CAT; U/mg) and malonyldialdehyde (MDA; nmol/mg) in heart and skeletal muscle (*biceps femoris*) were measured according to the methods of Sedlak et al.[34], Habig et al. [35], Góth [36] and Okhawa et al. [37], respectively.

Statistical analysis. All the results were presented as mean values±standard error. Two-way repeated measures ANOVA (dose x day) was used to assess differences during hole-board testing. All *post-hoc* tests were performed using the Newman-Keuls and Fisher (LSD) test to identify any significant differences. Pearson`s correlation coefficients *R* were calculated with simple linear regression analysis based on the results of the parameters of exploration (number of head-dippings and rearings), and the level of selected monoamines and amino acids in tested brain regions (prefrontal cortex, hippocampus and striatum) evaluated in our previous research [1]. A similar analysis was conducted with the results of plasma corticosterone levels. All the hypotheses tested used a significance level of 0.05.

RESULTS

Hole-board results – the influence of chronic *C.longa* pre-treatment on explorative activity. The effects of chronic *Curcuma longa* pre-treatment on explorative activity in aged rats are shown in the Table 1. In the hole-board, the enhanced explorative activity but not the locomotor performance was observed.

Table 1 Effects of chronic oral administration of a standardised extract of C. longa on the results in hole-board (day 1-3) of aged Wistar male rats.

Group	Time spent on moving (s)	Time spent in the central area (s)	Head-dippings	Rearings	Crossings
Con	49.95±6.25	45.05±13.8	3.14±0.34	2.14±0.33	3.0±0.29
C10	65.46±9.21	34.29±11.94	5.29±0.64 [a]	4.37±0.44 [a]	2.96±0.21
C50	55.5±6.49	40.63±15.95	5.3±0.6 [b]	4.54±1.0 [b]	3.13±0.26

[a] C10 *vs* Con, p<0.05; LSD, [b] C50 *vs* Con, <0.05; LSD.

The values of mean total head-dippings count (Days 1-3) were different among the groups (Con: 3.14±0.34, C10: 5.29±0.64, C50: 5.3±0.6), ($F_{2,20}$=3.37, p = 0.05). *Post-hoc* tests showed a significant decrease in mean total head-dippings for the C10 (p <0.05, LSD) and C50 (p <0.05, LSD) groups in comparison with controls. ANOVA analysis for a particular day of the experiment and head-dipping score was as follows: Day 1: $F_{2,20}$=2.67, p <0.09, Day 2: $F_{2,20}$=1.22, p <0.32, Day 3: $F_{2,20}$=1.4, p <0.27. The *post-hoc* analysis showed an increase of head-dippings count in C10 group *versus* control on 1st day (p <0.05, LSD).

The values of mean total rearing count (Days 1-3) were different among the groups (Con: 2.14±0.33, C10: 4.37±0.44, C50: 4.54±1.0), ($F_{2,20}$=3.13, p <0.06). *Post-hoc* tests showed a decrease in mean total rearing for the C10 and C50 (p <0.05, LSD) groups in comparison with controls. ANOVA analysis for a particular day of the experiment and rearing score were as follows: Day 1: $F_{2,20}$=2.01, p <0.16, Day 2: $F_{2,20}$= 2.47, p <0.1, Day 3: $F_{2,20}$=0.84, p <0.45.

In the hole-board, no differences in the motor activity of aged animals were observed.

The total number of crossings was the same in all tested groups of rats during the entire experiment (Con: 3.0±0.29, C10: 2.96±0.21 and C50: 3.13±0.26) ($F_{2,20}$=0.13, p <0.88). The total time spent on moving did not differ either (Con: 49.95±6.25 s, C10: 65.46±9.21 s, C50: 55.5±6.49 s) ($F_{2,20}$=1.29, p <0.3). The total time spent by animals in the central area of the testing box was the same (Con: 45.05±13.8 s, C10: 34.29±11.94 s, C50: 40.63±15.95 s) ($F_{2,20}$=0.09, p <0.9).

Neurotransmitter levels and explorative activity correlation. The number of head-dippings and rearings in the hole-board was compared with the levels of selected

amino acids and monoamines in the evaluated regions of the rats` brains (see also [1]). There was no correlation between selected brain neurotransmitter levels and either total number of head-dippings (except for serotonin in C10 group in the striatum $F_{1,6}$=25.3, p <0.002) and rearings in the hole-board (Table 2a and 2b).

Table 2 a The correlations between selected brain neurotransmitter levels and total number of head-dippings in the hole-board after chronic oral administration of a standardised extract of *C. longa* in aged Wistar male rats.

		Brain structure		
		cortex	hippocampus	striatum
5-HT	Con	R=-0.37; p<0.42	R=-0.19; p<0.69	R= 0.32; p<0.48
	C10	R= 0.23; p<0.58	R= 0.55; p<0.15	**R= 0.9; p<0.002**
	C50	R= 0.08; p<0.85	R= 0.15; p<0.73	R= 0.00; p<0.99
DA	Con	R=-0.06; p<0.89	R=-0.28; p<0.55	R= 0.28; p<0.55
	C10	R=-0.13; p<0.76	R=-0.15; p<0.72	R= 0.11; p<0.8
	C50	R= 0.19; p<0.64	R=-0.22; p<0.6	R=-0.36; p<0.39
Glutamic acid	Con	R=-0.37; p<0.41	R= 0.62; p<0.14	R= 0.62; p<0.14
	C10	R= 0.11; p<0.8	R=-0.02; p<0.97	R= 0.38; p<0.35
	C50	R= 0.29; p<0.49	R= 0.11; p<0.79	R= 0.28; p<0.5

Table 2 b The correlations between selected brain neurotransmitter levels and total number of rearings in the hole-board after chronic oral administration of a standardised extract of *C. longa* in aged Wistar male rats.

		Brain structure		
		cortex	hippocampus	striatum
5-HT	Con	R= 0.52; p<0.24	R= 0.36; p<0.43	R= 0.49; p<0.26
	C10	R= 0.31; p<0.46	R= 0.55; p<0.16	R= 0.44; p<0.27
	C50	R= 0.00; p<0.99	R= 0.28; p<0.51	R=-0.07; p<0.88
DA	Con	R=-0.58; p<0.18	R=-0.33; p<0.46	R=-0.1; p<0.83
	C10	R= 0.2; p<0.63	R= 0.47; p<0.24	R=-0.36; p<0.39
	C50	R=-0.23; p<0.58	R=-0.43; p<0.29	R=-0.01; p<0.99
Glutamic acid	Con	R=-0.23; p<0.62	R=-0.37; p<0.41	R= 0.29; p<0.53
	C10	R=-0.38; p<0.35	R=-0.23; p<0.58	R= 0.53; p<0.18
	C50	R= 0.37; p<0.36	R=-0.46; p<0.25	R=-0.22; p<0.6

Plasma corticosterone levels and explorative activity correlation. The total number of head-dippings and rearings in the hole-board was compared with the level of plasma corticosterone (see also [1]). There was no correlation between plasma corticosterone levels and total number of head-dippings (Con: $F_{1,5}$=1.2, R=0.44, p <0.32; C10: $F_{1,6}$=0.025, R=-0.065, p <0.88; C50: $F_{1,6}$=0.2, R=-0.181, p <0.68) and rearings (Con: $F_{1,5}$=0.88, R=0.388, p <0.39; C10: $F_{1,6}$=0.39, R=-0.25, p <0.55; C50: $F_{1,6}$=0.38, R=0.245, p <0.56) in the hole-board.

Antioxidant and antitoxic activity in heart and skeletal muscles. There were differences in glutathione-s-transferase, catalase and malonylodialdehyde content in the femoral skeletal muscles between the groups of aged rats (Table 3). The increased levels of CAT ($F_{2,20}$=4.99, p <0.01; C10: 13.07±1.19 U/mg, p <0.01, NK test, C50: 11.04±1.3, p <0.05 *vs.* Con: 7.49±1.21), and GST ($F_{2,20}$=27.82, p <0.0000; C10: 0.098±0.003 µmol/min/mg, p <0.0001, NK test, C50: 0.094±0.002, p <0.0001 *vs.* Con: 0.075±0.003), and MDA ($F_{2,20}$=4.0, p<0.04; C10: 0.11±0.009 nmol/mg, p <0.05, NK test, C50: 0.1±0.01, p <0.05 *vs.* Con: 0.064±0.015) were seen

Table 3 Effects of chronic oral administration of a standardised extract of *C. longa* on the GSH, GST, CAT and MDA levels in heart and skeletal muscles of aged Wistar male rats.

		GSH nmol/mg	GST µmol/min/mg	CAT U/mg	MDA nmol/mg
Heart muscle	Con	2.28±0.24	0.25±0.009	34.05±2.32	0.12±0.006
	C10	2.22±0.19	0.26±0.01	32.85±1.35	0.11±0.005
	C50	2.4±0.29	0.28±0.007	36.13±1.72	0.12±0.003
Skeletal muscle	Con	1.63±0.12	0.075±0.003	7.49±1.21	0.064±0.015
	C10	1.69±0.09	0.098±0.003[c]	13.07±1.19[b]	0.11±0.009[a]
	C50	1.77±0.24	0.094±0.002[c]	11.04±1.3[a]	0.1±0.01[a]

[a] p<0.05; NK, [b] p<0.01; NK, [c] p<0.001; NK *vs.* Con.

in both extract-fed groups of rats in comparison to control group. The concentration of glutathione in the skeletal muscles of all aged animals was the same in all tested animals ($F_{2,20}$=0.18, p <0.8). No differences of any checked parameters were found in the heart muscles between all estimated groups: CAT ($F_{2,20}$=0.89, p <0.43), GST ($F_{2,20}$=2.04, p <0.16), GSH ($F_{2,20}$=0.15, p <0.87), MDA ($F_{2,20}$=1.17, p <0.33) (Table 3).

DISCUSSION

The results of this research show that the long-term administration of standardised *C. longa* extract (with curcuminoids as major active components) influences the explorative activity in aged rats.

In the hole-board, the biggest number of head-dippings as well as rearings were seen in pre-treated aged rats in comparison to control, and regarded as an increase in exploration. The frequency of dipping is one of the measures of directed exploration and was independent from the general locomotor activity [32]. Because of better results from pre-treated rats in a water maze (decreased latency and distance to the visible platform [1]), it is possible to assume that curcumin may also affect some sensorimotor functions. The extract pre-treatment still had no influence on the speed of swimming in the water maze [1]. This suggests that curcumin may rather improve the motivation of tested animals in behavioural performance.

Concomittantly, it should be taken into account that the behavioural tasks that depend on voluntary exploration of an apparatus may also be affected by anxiety states [38]. The high levels of head-dipping may indicate neophilia (an attraction to novel objects) or decreased anxiety; the low ones may be attributed either to lack of a curiosity-based approach or they may result from enhanced fear. Takeda et al. [39] have indicated that the anxiolysis in animals may be reflected by an increase in head-dippings. Brown and Nemes [40] suggested recently that head-dipping should be considered as influenced both by neophilia and neophobia (fear-based avoidance) and estimated in the connection with other behavioural tests. In our investigations, the time that animals spent in the central area of the hole-board (assumed as aversive to rodents) did not differ within all tested groups. As this parameter is regarded as a reflexion of fear; therefore, it is possible that aged rats had similar anxiety levels. In conclusion, it is possible that their motivation may differ.

The higher level of stress is also related to elevated plasma corticosterone [41]. The exposure to the novel open field resulted in its increase [42]. But the aged animals pre-treated with *C. longa* extract that were examined by us in water

maze and hole-board had significantly decreased plasma corticosterone levels compared to the control rats [1]. This is consistent with an observation that stress-induced increases in serum corticosterone concentrations were reduced in curcumin treated rats [31, 43, 44]. In our research the levels of plasma corticosterone did not correlate with previously estimated total latency to the visible platform but the control group had longer total escape latency in the visible platform test to the cue alongwith higher hormone levels ($F_{1,5}$=8.16, p<0.036, R=0.787). The levels of plasma corticosterone did not correlate with the total number of head-dippings and rearings in plant-extract treated rats either.

Chronic *C.longa* extract administration to aged rats did not influence the locomotor activity evaluated as swimming velocity in water maze [1] and time spent on moving in hole-board. It is consisted with Kumar et al. [45] who assessed the locomotor activity in young Wistar male rats and observed no differences between curcumin-treated (30 and 60 mg/kg, p.o. for 6 weeks) and control animals. Awasthi et al. [46] reported that curcumin pre-treatment did not differentiate the spontaneous locomotor activity in streptozocin-injected and control mice. There are also reports of the protective ability of curcumin against the toxicity of exogenous compounds that may affect moving performance. Curcumin (100 mg/kg b.w., p.o. for 28 days) protected rats against arsenic toxicity that led to decrease in locomotor activity, grip strength and rota-rod performance [47]. Curcumin may also attenuate aluminium-induced alterations in behavioural performance estimated in the open field – ambulation and defecation index [48]. Shukla et al. [49] observed that curcumin pre-treatment (100 mg/kg b.w., p.o. for 5 days before middle cerebral artery occlusion) improved rota-rod performance and grid walking in comparison to untreated ischemic rats.

It is widely-known that curcumin exerts multiple neuroprotective effects in central nervous system. The effects of long-term administration of *Curcuma longa* extract on the levels of brain monoamines and aminoacids has been already discussed in our previous report [1] in the view of the improvement of spatial memory in aged Wistar male rats. The activity of dopaminergic, serotoninergic and noradrenergic systems is supposed to be of some importance in explorative behaviour in rodents [50, 51].

The increase in dopamine transmission results in a decrease in head-dippings in some research or it has any influence in the others. The reward-seeking is connected with higher brain dopamine levels [51]. Further examinations are needed to assess the detailed role of dopamine in the hole-board behaviour [32, 33, 52, 53]. The pharmacological-induced enhancement in dopaminergic transmission causes the increase in locomotion. In our research performed on aged animals, the differences between groups in dopamine concentrations were observed only in the prefrontal cortex (ANOVA), but in *post-hoc* testing none of the experimental group had significantly different dopamine level when compared to controls [1]. The absence of any significant alterations in dopamine metabolism in the striatum suggests that curcumin does not directly affect the locomotor functions of pre-treated animals, as also observed in behavioural testing. However, curcumin may elevate brain dopamine levels in younger stressed rodents [29, 30], but in aged animals the ability of its pre-treatment to affect dopamine levels may be decreased. Xu et al. [54] indicated that in olfactory bulbectomy depression model in young animals the level of dopamine in the prefrontal cortex was elevated after administration of 10 mg/kg of curcumin; however ,the influence of the bigger dose was not analysed.

In our report we have observed that *C. longa* extract significantly enhanced serotonin concentration in the prefrontal cortex and hippocampus [1]. The majority of known data indicate the age–related decrease in brain 5-HT levels (e.g. [55]). Activation of serotoninergic receptors in the prefrontal cortex may potentiate cognitive abilities in animals [56]. The serotonin system seems also to be essential for emotional stress and plays an important role in the pathology of depression. The reduction of 5-HT brain levels was linked with anxiolytic-like effects. In the forced swimming test in rodents the serotoninergic system seemed to be involved in the antidepressant-like effect of curcumin [27, 29, 30, 54], which was possibly mediated through interaction with 5HT1A/1B and 5HT-2C receptors [16, 57], and improvement of adenylyl cyclase-cAMP pathway [31]. Curcumin in a dose-dependent manner prevented the decreased level of 5-HT and consequently reduced the excytotoxicity and oxidative damage related to the depletion of serotonin in the brain [28, 30]. The changes in serotonin transmission may also influence the explorative activity in rodents [53, 58]. The improved cued navigation and augmented explorative activity in our research might be connected with altered serotonin neurotransmission, but increased serotonin levels in the prefrontal cortex and in hippocampus did not correlate either with total latency in the visible platform test in the water maze, or with the total number of head-dippings and rearings in the hole-board.

Curcumin reveals an antioxidant action in various tissues and cells [10, 59-62]. It may work as a reactive oxygen species (ROS) scavenger (peroxyl or hydroxyl radicals), change the cellular ROS as well as non-protein thiols levels (e.g. GSH) or antioxidant enzyme contents (e.g. catalase), up-regulate some second phase detoxyfying enzymes or inhibit ROS-induced lipid peroxydation [63-69]. On the other hand, curcumin is able to promote an oxidative stress toxicity in prolifering or transformed cells that leads to their damage and is responsible for its anticancer activity [17, 70-73]. Some recent research has shown that curcumin actions are related to its concentrations – it may act as an antioxidant at low concentrations but as an prooxidant at high ones [74-76]. Therefore, it may be stated that the action of curcumin depends on its concentration and on the cell type; however, the mechanism for these differences remains unclear as yet.

In this experiment, 2-month *Curcuma longa* extract pre-treatment (10 and 50mg/kg) did not change the concentration of glutathione, neither in the skeletal muscles nor in the heart muscle of aged rats. The increased GSH concentrations, a main nonenzymatic antioxidant and GST cofactor, could augment the ability of scavenging the free oxygen radicals. Curcumin in the dose of 15mg/kg given twice orally did not alter the GSH concentration in the myocardium of young rats versus control animals, but it might protect its ischemic-induced decrease [77]. Tanwar et al. [76] observed the protective action of curcumin against glutathione content depletion in heart muscle after isoprenaline-induced myocardial ischemia (100 and 200mg/kg, p.o., for 2 weeks), but not after a higher dose (400 mg/kg). Available data indicate that curcumin may increase glutathione content in other tissues and organs – liver, kidneys [78] or brain [79, 80]. It may also protect GSH depletion in brain, induced by streptozocin injection [46, phenytoin [79] as well as kainic acid administration [81]. Kumar et al. [45] reported that curcumin given chronically to

young rats (30 and 60 mg/kg, p.o.) did not change significantly *per se* the content of brain GSH, but it could prevent aluminium-dependent alterations of its levels.

We have also observed that both the doses of plant extract increased the activity of glutathione-s-transferase (GST) and catalase (CAT) in the skeletal muscles, but not in the heart muscle of aged rats. GSTs are important second phase enzymes that protect cells against electrophile compounds toxicity. The elevated GST levels in our research may facilitate such a defence. Catalase catalyzes the removal of hydrogen peroxide, an important reactive oxygen species. Elevated CAT activity in the tissues of *C. longa* extract-treated aged rats may be related to the greater ability of scavenging the free oxygen radicals by curcuminoids. The published data on the influence of curcumin on the activity of GST and CAT are not consistent. El-Demerdash et al. [82] reported that curcumin administration (15mg/kg p.o. for 30 days) enhanced the GST and CAT activity in various tissues and organs (plasma, liver, testes, brain , kidneys and lungs) of young male SD rats. On the contrary, curcumin given to young Wistar male rats (30 and 60 mg/kg, p.o. for 6 weeks) did not affect significantly the content of brain GST and CAT [45]. It could, however, protect against alterations of their levels induced by aluminium compounds. Curcumin in the dose of 15mg/kg given twice orally did not alter the GST and CAT activity in the myocardium of young rats versus control animals, but it may protect its ischemic-induced decrease [77]. There are also data on the inhibition of GST family enzymes activity by curcumin and its analogues that may play a role in chemotherapy [83].

The malonylodialdehyde (MDA) levels, related to the rate of lipid peroxidation, were not altered in the heart muscle, but seemed to be enhanced in skeletal muscles of aged rats after chronic administration of 10 and 50mg of *Curcuma longa* extract. There seems to be no data available on curcumin influence on lipid peroxydation within skeletal muscles. Manikandan et al. [77] noticed that curcumin (15mg/kg, p.o., given twice) did not change the MDA levels in the myocardium and plasma of young rats when compared with controls. It is able to decrease the MDA content in myocardium and plasma of animals exposed to isoprenaline-induced ischemic insult in comparison to untreated ischemic controls. The effects of the curcumin usage may be dose-dependent as was shown in isoprenaline-induced model of myocardial necrosis in rats by Tanwar et al. [76]. The lower doses of curcumin (100 and 200 mg/kg, p.o. for 2 weeks) led to a decrease in thiobarbituric acid reactive substances –TBARS in the myocardium when compared with ischemic controls, but at the highest dose (400 mg/kg) this protection remained ineffective. Hence, the authors concluded that curcumin potentiated the endogenous antioxidant system at lower concentrations, but augmented ROS induction at higher dose leading to myocardial damage. Ali et al.[84] observed that tetrahydrocurcumin pre-treatment may protect against enhanced lipid peroxidation in the course of experimental myocardial infarction, and suggested the influence of THC on myocardial antioxidant status. In aged rats, curcumin (30mg/kg) inhibited lipid peroxidation in various brain regions [10]. In young rats, the chronic curcumin treatment (30 and 60 mg/kg) did not significantly increased MDA brain content; however, there were visible dose-dependent trends for increase [45]. Curcumin administration (20 and 50 mg/kg p.o. for 2 weeks) prevented also the increase of MDA brain content in streptozocin-treated mice [46].

CONCLUSION

In conclusion, our study revealed that *C. longa* extract pre-treatment may affect the explorative performance in aged rats, however, without correlation with the changed brain neurotransmitter concentration as well as plasma corticosterone level. Chronic extract administration in the doses of 10 and 50 mg/kg/b.w. may also influence the antioxidant processes in the skeletal muscles of aged rats, but does not affect the heart muscle.

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