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Effects of Curcumin Intake on CVD Risk Factors and Exercise-Induced Oxidative Stress in Healthy Volunteers—An Exploratory Study †

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Abstract: Background: Evidence suggests that turmeric or curcumin intake can improve antioxidant defense, blood pressure, ageing and gut microbiota. The effects of turmeric concentrate (curcumin) intake on cardiovascular risk factors and exercise induced oxidative stress were investigated. Methods: A randomized placebo-controlled study was performed to assess the effects of turmeric extract in healthy volunteers before and after a 30 min exercise bout. Participants ($n = 22$) were given either 500mg turmeric concentrate (Curcumin C3, Jarrow Formulas, Los Angeles, CA, USA) or placebo supplements. Anthropometry, blood pressure, pulse wave velocity (PWV), biomarkers of oxidative stress, perceived exertion and lipid peroxidation were assessed. Results: There were no significant differences in all baseline parameters between the placebo and the curcumin groups ($p > 0.05$). In the curcumin group, blood pressure response to exercise following curcumin intake was blunted and the increase was not significant compared to basal values. In the last run, there was a significant difference (before-after) between curcumin and placebo groups (Δ in SBP: 7.3 ± 6.8 vs. 13.8 ± 6.3 mmHg, $p = 0.007$, and Δ in DBP: 2.3 ± 6.9 V 8.0 ± 6.8mmHg, $p = 0.012$). Final PWV scores were reduced significantly in the curcumin group (7.2 ± 0.97 to 6.7 ± 0.77m/s, $p = 0.033$) and this reduction was significant compared to the control (Δ of 0.56 vs. 0.21m/s, $p = 0.04$). A significant increase was observed in urinary antioxidant power ($p = 0.031$) and total polyphenol levels ($p = 0.022$) post curcumin intervention, and those on the placebo did not show significant changes. The increase in exercise-induced MDA levels was blunted only in the curcumin group and before-after difference was significant compared to control (Δ of −0.81 vs. +0.205 μmole/day, $p = 0.032$). The distance ran by the participants taking curcumin was significantly longer ($p = 0.005$), and compared to placebo before-after difference was significant (Δ of −0.69 vs. +0.28km, $p = 0.014$). Conclusion: Our study suggests that turmeric concentrate intake can reduce blood pressure and improve antioxidant, anti-inflammatory status and arterial compliance. Curcumin may improve exercise performance and ameliorates oxidative stress. Larger studies are warranted to validate these findings and test other cardiovascular risk factors.

Keywords: Turmeric concentrate; curcumin; antioxidants; blood pressure; cardiovascular disease; oxidative stress

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1. Introduction

Regular physical exercise is known to convey several health benefits and considered to be good practice to combat many metabolic diseases including cardiovascular disease

(CVD), cancer, obesity, and diabetes [1–3]. However, strenuous and prolonged exercise generate inflammatory cytokines and reactive oxygen species (ROS) [4,5]. It has been reported that the negative effects associated with eccentric exercise such as inflammation and DOMS are caused by a large increase in inflammatory cytokines in the working muscle, plasma and brain generated as a result of oxidative stress which stimulates the production of free radicals [5,6]. Retamoso et al. [7] found that eccentric exercise may cause delayed onset muscle soreness (DOMS) causing discomfort of skeletal muscles. MDA is the most used biomarker of oxidative stress in several conditions such as cancer, chronic obstructive pulmonary disease, and cardiovascular diseases [8]. It is vital to monitor both SBP and DBP throughout exercise. In addition, pulse wave velocity (PWV) is regarded the gold standard measurement of arterial stiffness and it is generally assessed by using carotid-femoral or brachial-ankle approaches [9]. PWV rises with stiffening of the aorta and consequently causes an earlier return of reflected pressure waves from the periphery to the aorta which enhances aortic SBP and reduces DBP [10]. In CVD and hypertensive patients, the incidence of oxidative stress can be determined in biological fluids by the thiobarbitoric acid (TBARS) assay [8,11]. These patients also display impaired antioxidant defense, and in the heart, the production of ROS exceeds the capacity of the antioxidant defense mechanism to buffering the ROS resulting in cardiac dysfunction, ischemia-reperfusion injury, hypertrophy, cell death, and heart failure [11].

Curcumin is a natural polyphenol derived from the rhizome of *Curcuma longa* [12,13] and has antioxidative, anti-inflammatory, cardiovascular, mental wellbeing and ageing protective effects, and interacts with gut microbiota and several other actions [14–16]. Curcumin and turmeric extract have been shown to improve oxidative stress markers [17] by acting on cytokine/ROS-mediated inflammatory pathways to reduce the expression of NFkB/cyclooxygenase-2, enhancing antioxidants activity [18], and inhibiting the production of prostaglandin and NF-kB signaling [19]. In addition, curcumin may have musclo-protective effects against exercise induced muscle damage (EIMD) by inhibiting free radical formation in injured skeletal muscles [18,20]. The aim of this short preliminary study was to investigate the effects of turmeric extract (rich in curcumin) intake on exercise induced oxidative stress, blood pressure, PWV and lipid peroxidation in human volunteers.

2. Methods and Results

Study Design: We have adopted a randomized placebo-controlled parallel study to investigate the efficacy of curcumin supplementation on exercise-induced oxidative stress and blood pressure over a period of 11 days (Figure 1). The study was granted ethical approval by the Ethics Committee of Queen Margaret University (QMU); code, 11010149-Honors/Curcumin/DNBS/QMU Ethical Committee.

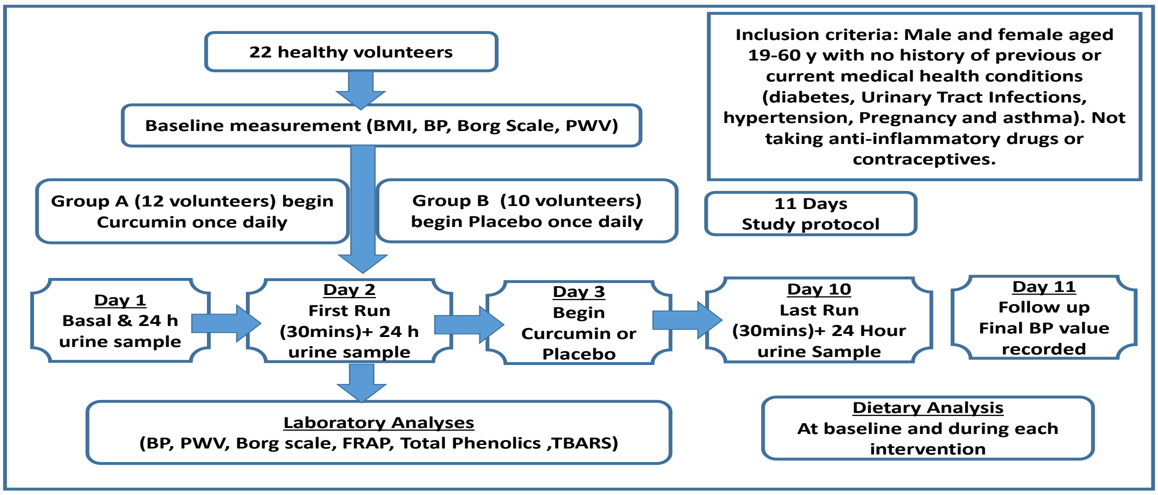

Figure 1. Study protocol demonstrating the trial arrangements and measurements performed for all participants.

Supplement: Each participant in both groups was supplied with 8 capsules, either Turmeric concentrate (Curcumin C3 Complex (500 mg), Jarrow Formulas, Los Angeles, CA, USA) or placebo capsules made by filling empty gelatin capsules with corn flour.

Anthropometry and Physiological Measurements: Measurements of Body Mass Index (BMI) was facilitated by recording the weight and height of each subject day 1 of the study allowing to calculate their BMI using the equation: [BMI = Weight (kg)/height $(m)^2$]. Arterial compliance measured by pulse wave velocity (PWV) was performed between the carotid and femoral artery (PWVcf) by means of a validated Vicorder™ device (Skidmore Medical Limited, Bristol, UK). Blood pressure (BP) was measured and average of 3 SBP and DBP readings were calculated. A Borg rating of perceived exertion scale (1–10) was used to measure each subject's level of exertion and intensity during each of the 30 min runs [21].

Urinary Biomarkers assays: Urinary Polyphenols Levels, Urinary FRAP excretion, and MDA concentration were measured.

3. Discussion

This short study has highlighted some of the beneficial effects of curcumin supplements in healthy volunteers. The present study confirms the antioxidant and anti-inflammatory properties of curcumin as evidenced in the significant increase in antioxidant concentrations (FRAP) and total poly-phenol levels in the urine samples of the curcumin group [16,22] (Table 1). Studies have confirmed that polyphenols possess antioxidant and free radical scavenging properties, which reduce low-density lipoprotein (LDL) oxidation [23]. We believe that the increase in antioxidant and polyphenol concentrations might have provided a protective mechanism against vascular dysfunction by neutralizing free radicals and reducing BP during exercise [24] (Table 2 and Table 3).

This supports the data of published studies that showed curcumin intake was able to reduce BP [25]. Other CVD parameters that may be of relevance; Arterial stiffness compliance as measured by PWV_{cf} was significantly reduced after curcumin intake indicating its cardiovascular beneficial effects [26].Turmeric extract intake has attenuated the exercise-induced increase of lipid peroxidation (Table 4). In addition, Borg score of perceived exertion was lowered and thus the curcumin group felt they were able to run at a greater intensity during the last run compared to their first run [27] (Table 5). The limitations in this present study were that of short duration with low number of participants, and the study implemented a parallel design due to the notion that both crossover and parallel designs offer advantages and disadvantages (Table 6). Finally, the influence of oral bioavailability of turmeric and curcumin should be considered in relation to gut microbiota of individuals [28].

Table 1. Total Polyphenol concentration of 24 h urine samples measured in GAE/day. Data presented as (mean ± SD). Significance of data is measured against the basal concentration of each group (*p* value ≤ 0.05).

	Intervention	**Polyphenol Concentration (mg GAE/day)**	***p*-Value**
Basal	Placebo	293.3 ± 73.3	-
	Curcumin	276.3 ± 92.2	0.275
First Run (Pre-Intervention)	Placebo	304.8 ± 95.2	0.659
	Curcumin	282.7 ± 85.7	0.772
Last-Run (Post-Intervention)	Placebo	318.4 ± 57.1	0.254
	Curcumin	405.9 ± 132.6	0.022

Table 2. SBP and DBP readings recorded for all participants at basal, first run and last run before and after the exercise. It also shows the Δ change (mmHg) in SBP and DBP between pre-exercise and post exercise. Significance levels: * < 0.05; ** <0.01; *** <0.001; ^{NS} > 0.05.

Curcumin	**SBP**			**DBP**		
	Pre Exer	**Post Exer**	**Δ Change**	**Pre Exer**	**Post Exer**	**Δ Change**
Basal	121.8 ± 12.0	-		75.5 ± 6.9	-	
First run	124.3± 11.8	139.8 ±14.5 ***	15.5 ± 9.6	74.5 ± 5.4	81.8 ± 6.0 **	7.3 ± 7.2
Last run	126.4 ± 13.5	133.7 ± 15.3 *	7.3 ± 7.0 *	76.3 ± 8.6	78.6 ± 7.2 ^{NS}	2.3 ± 6.9 *
Placebo	**Pre Exer**	**Post Exer**		**Pre Exer**	**Post Exer**	
Basal	120.6 ± 12.2	-		73.9 ± 7.5	-	
First run	123.6 ± 14.2	138.1 ±12.5 ***	14.5 ± 6.1	73.4 ± 3.1	80.6 ±5.1 ***	7.2 ± 4.8
Last run	123.5 ± 13.0	137.3 ± 11.6 **	13.8 ±6.3 ^{NS}	70.1 ± 7.8	78.1 ± 6.2 *	8.0 ± 6.8 ^{NS}

Table 3. Mean of antioxidant concentrations of urine samples obtained from the FRAP assay. Data presented as (mean ± SD). Significant difference is measured against the basal concentration of each group (*p* ≤ 0.05).

	Intervention	Antioxidant Concentration (mmol Fe^{+2}/day)	*p*-Value
Basal	Placebo	3.04 ± 0.57	-
	Curcumin	2.81 ± 1.8	0.216
First Run (Pre-Intervention)	Placebo	3.05 ± 0.42	0.956
	Curcumin	3.12 ± 1.29	0.558
Last-Run (Post-Intervention)	Placebo	3.43 ± 1.22	0.839
	Curcumin	3.75 ± 0.94	0.031

Table 4. TBARS as determinant of lipid peroxidation was assessed by the estimation of MDA levels (µmole/day). Data is presented as (mean ± SD). Significant differences are measured against the basal concentration of each group.

	Intervention	MDA Concentration (µmol/day)	*p*-Value
Basal	Placebo	2.263 ± 0.74	-
	Curcumin	2.249 ± 0.91	0.825
First Run (Pre-Intervention)	Placebo	3.422 ± 0.97	0.026
	Curcumin	3.472 ± 1.2	0.002
Last-Run (Post-Intervention)	Placebo	3.627 ± 1.43	0.040
	Curcumin	2.662 ± 0.68	0.328

Table 5. Mean exercise and perceived exertion parameters of participants before and after the intervention. Data presented as (mean ± SD). Significant difference in the last run is measured against that in first run ($p \leq 0.05$).

Curcumin	**First Run**	**Last Run**	***p*-Value**
Distance (km)	3.66 ± 0.81	3.97 ± 0.94	0.005
Speed (km/h)	7.32 ± 1.61	7.45 ± 1.99	0.227
Borg Scale	4.08 ± 1.38	3.51 ± 1.1	0.131
Placebo	**First Run**	**Last Run**	***p*-Value**
Distance (km)	3.38 ± 0.84	3.66 ± 0.72	0.186
Speed (km/h)	6.85 ± 1.67	7.22 ± 1.44	0.219
Borg Scale	4.13 ± 1.69	4.06 ± 0.95	0.924

Table 6. Baseline demographics of all participants participated in the curcumin and placebo groups. Data presented as (mean ± SD).

	Placebo (n = 10)	Curcumin (n = 12)	Significance *p*-Value
Age	21.8 ± 2.2	22.1 ± 1.7	0.729
BMI (kg/m^2)	24.7 ± 3.8	25.8 ± 5.3	0.524
Caffeine intake (cups/day)	0.8 ± 1.1	1.2 ± 1.1	0.336
Baseline PWV (m/s)	7.49 ±0.6	7.51 ±0.9	0.564
Exercise (h/week)	2.6 ± 1.3	1.8 ± 1.6	0.452
SBP (mmHg)	120.7 ±12.4	123.4 ±15.2	0.871
DBP (mmHg)	73.9 ± 7.5	75.5 ± 6.9	0.682

4. Conclusions

Our study has demonstrated that curcumin possesses antioxidant and anti-inflammatory properties which have proven to lower blood pressure and improve CVD risk factors, exercise performance and ameliorates oxidative stress. Larger studies investigating the effects of turmeric extract or curcumin on oxidative stress, exercise performance and other cardiovascular parameters are warranted.

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