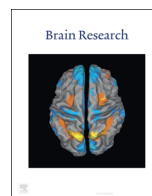




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## Research Report

# The therapeutic effect of curcumin in male albino rats and its putative mechanisms on cerebral microvascular flow



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## ABSTRACT

The present study aimed to investigate the therapeutic effect of curcumin on hypertension and its putative mechanisms in the cerebral microcirculation. The surgical preparation was made to generate a cranial window for observation of the capillary network in the cerebral cortex region. Digital image processing, intravital videomicroscopy, and laser Doppler flow meter were used in this investigation. The number of open capillaries, arterial blood pressure, red cell velocity, microvascular diameter, circulating endothelial cells, relative blood flow and frequency were determined. Control rats showed severe dysfunction in the microcirculation with increased blood pressure. In curcumin treated mice, the blood pressure significantly reduced compared to their respective controls. Curcumin significantly increased blood velocity and LDF flow in hypertensive and normotensive rats. Curcumin significantly altered the circulating endothelial cells and open capillaries number in the male albino rats. Our results suggested that the curcumin exerts its therapeutic effect in male albino rats by regulating vasomotion function, increasing blood perfusion, releasing the peripheral resistance and opening efficiently capillaries. Taking all these data together, it is concluded that the curcumin might be useful in the regulation of the cerebral microcirculatory function and hypertension.

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## 1. Introduction

Curcumin is a is the principal curcuminoid of turmeric, which belongs to a member of the ginger family. Turmeric exists as desmethoxycurcumin and bis-desmethoxycurcumin. The yellow color of turmeric due to natural phenols. Curcumin exists in various tautomeric forms, such as 1,3-diketo shape and two equivalent enol forms. The enol form is more energetically stable than keto form (Manolova et al., 2014). Curcumin is known to have antioxidant and anti-inflammatory potential (Dutta et al., 2005; Lim et al., 2005; Weber et al., 2005; Biswas et al., 2005). Curcumin has been reported as possible compound against cerebral ischemia, and cerebral vasospasm in subarachnoid hemorrhage-induced rats.

Curcumin is well known for its therapeutic potential for several diseases such as Parkinson's disease, Alzheimer's disease, epilepsy, multiple sclerosis, cerebral injury, cancer, allergy, asthma, bronchitis, colitis, rheumatoid arthritis, renal ischemia, psoriasis, diabetes, AIDS, depression, obesity and fatigue (Aggarwal and

Harikumar, 2009). The brain is one of the oxidative organs that consume 20% of the body's oxygen. Metals ions such as iron (Fe), zinc (Zn), and copper (Cu) accumulates in the brain during the normal aging process. Consequently, the brain is abundant in antioxidants that control and prevent the detrimental formation of reactive oxygen species (Smith et al., 2007). Curcumin is potent compound which contains activity in several neurologic diseases, such as multiple sclerosis (Natarajan and Bright, 2002), AD (Lim et al., 2001), epilepsy (Sumanont et al., 2006), Parkinson's disease (Zbarsky et al., 2005), cerebral injury (Ghoneim et al., 2002), age-associated neurodegeneration (Calabrese et al., 2003), schizophrenia (Bishnoi et al., 2008), Spongiform encephalopathies (Hafner-Bratkovic et al., 2008), depression (Xu et al., 2005) and neuropathic pain (Sharma et al., 2006).

Curcumin is an essential product of turmeric. There are several studies about curcumin effects on the inhibition of platelet, erythrocyte aggregation, the regulation of vascular tone, the release from arteriolar spasm and the reduction of leukocyte adherence. Curcumin provides the tissue imaging effects on the cerebrovascular and peripheral vascular insufficiency. Curcumin acts on arteries, veins and capillaries to lower the vascular resistance and to reduce the capillary hyperpermeability. Curcumin is a well-known compound as oxygen free radical scavengers and other compounds that are highly useful as a platelet activating factor inhibitors.

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We proposed a possible mechanism of vasomotion and cerebral microcirculation. Our present study was aimed to investigate the therapeutic effects of curcumin on hypertension of male albino rats.

## 2. Results

### 2.1. Effect of curcumin on arterial blood pressure

In 14 days treatment, curcumin significantly reduced the blood pressure from 242.6 to 221.2 and 180.7 mmHg at 60 and 120 mg/kg respectively ( $p < 0.05$ , Fig. 1). In 28 days treatment, curcumin significantly reduced the blood pressure from 240 to 210 and 155 mmHg at 60 and 120 mg/kg respectively ( $p < 0.05$ , Fig. 1).

### 2.2. Effect of curcumin on flow velocity

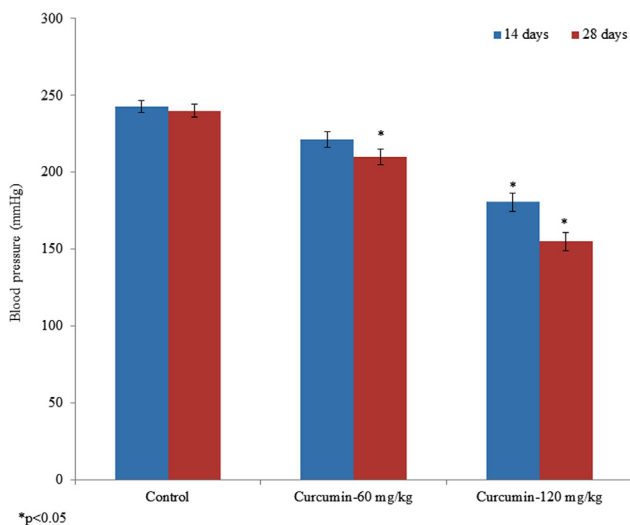
RBC velocity was very slow in the control rats. In 14 days treatment, curcumin significantly increased the blood velocity from 320 to 390 and 460  $\mu\text{m/s}$  at 60 and 120 mg/kg respectively ( $p < 0.05$ , Fig. 2). In 28 days treatment, curcumin significantly increased the blood velocity from 318 to 410 and 490  $\mu\text{m/sec}$  at 60 and 120 mg/kg respectively ( $p < 0.05$ , Fig. 2).

### 2.3. Effect of curcumin on diameter

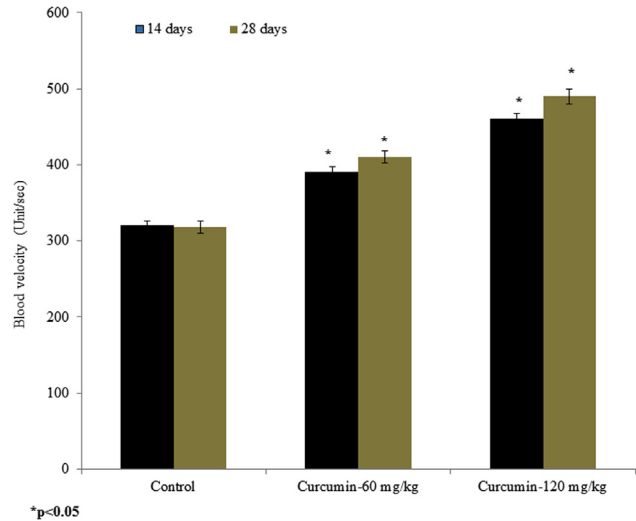
Curcumin treatment produced significant changes in the microvascular diameter. In 14 days treatment, curcumin significantly increased the diameter from 20 to 25 and 31  $\mu\text{m}$  at 60 and 120 mg/kg respectively ( $p < 0.05$ , Fig. 3). In 28 days treatment, curcumin significantly increased the diameter from 21 to 29 and 33  $\mu\text{m}$  at 60 and 120 mg/kg respectively ( $p < 0.05$ , Fig. 3).

### 2.4. Effect of curcumin on frequency

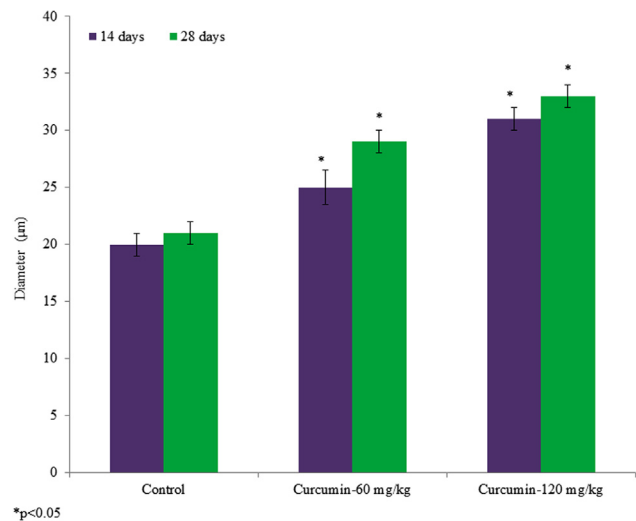
Curcumin treatment produced significant changes in the rate. In 14 days treatment, curcumin significantly increased the rate from 2.6 to 3 and 3.5 cycle/min at 60 and 120 mg/kg respectively ( $p < 0.05$ , Fig. 4). In 28 days treatment, curcumin significantly increased the frequency from 2.7 to 3.2 and 3.6 cycle/min at 60 and 120 mg/kg respectively ( $p < 0.05$ , Fig. 4).



**Fig. 1.** The effect of curcumin on the blood pressure of male albino rats. Curcumin 60 and 120 mg/kg was given to the rats for 14 and 28 days. The change in mean arterial blood pressure expressed as mean + SEM,  $*p < 0.05$ .



**Fig. 2.** The effect of curcumin on the blood velocity in male albino rats. Curcumin 60 and 120 mg/kg was given to the rats for 14 and 28 days. The change in mean blood velocity expressed as mean + SEM,  $*p < 0.05$ .



**Fig. 3.** The effect of curcumin on the diameter of male albino rats. Curcumin 60 and 120 mg/kg was given to the rats for 14 and 28 days. The change in mean diameter expressed as mean + SEM,  $*p < 0.05$ .

### 2.5. Effect of curcumin on amplitude

Curcumin treatment produced significant changes in the amplitude. In 14 days treatment, curcumin significantly increased the amplitude from 19 to 26 and 33% at 60 and 120 mg/kg respectively ( $p < 0.05$ , Fig. 5). In 28 days treatment, curcumin significantly increased the amplitude from 20.2 to 29 and 35% at 60 and 120 mg/kg respectively ( $p < 0.05$ , Fig. 5).

### 2.6. Effect of curcumin on open capillaries

Curcumin treatment produced significant changes in the open capillaries. In 14 days treatment, curcumin significantly increased the number of open capillaries from 9 to 12 and 15  $\text{n/mm}^2$  at 60 and 120 mg/kg respectively ( $p < 0.05$ , Fig. 6). In 28 days treatment, curcumin significantly increased the open capillaries from 10 to 14 and 17  $\text{n/mm}^2$  at 60 and 120 mg/kg respectively ( $p < 0.05$ , Fig. 6).

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