Comparative effects of *Curcuma longa* and curcumin on paraquat-induced systemic and lung oxidative stress and inflammation in rats

Seyedeh Zahra Ghasemi¹,², Arghavan Memarzia¹,²,³, Sepideh Behrouz¹,², Zahra Gholamnezhad², Mohammad Hossein Boskabady¹,²*¹

¹Applied Biomedical Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
²Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
³Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran

**Abstract**

**Objective:** Comparative effect of *Curcuma longa* (*C. longa*) ethanolic extract and curcumin on paraquat (PQ)-induced systemic and lung oxidative stress and inflammation were evaluated in the present study.

**Materials and Methods:** Control animals were exposed to normal saline and PQ group to 54 mg/m³ PQ aerosols (8 times, each time for 30 min). Treatment groups were exposed to PQ and treated with 150 and 600 mg/kg/day *C. longa*, or 30 and 120 mg/kg/day curcumin after PQ exposure period for 16 days. Total and differential white blood cells (WBC) and oxidative markers were measured both in bronchoalveolar lavage (BALF) and blood at the end of the study.

**Results:** Total and differential WBC counts as well as malondialdehyde (MDA) level were significantly increased but total thiol content and the activities of catalase (CAT) and superoxide dismutase (SOD) were reduced in both the BALF and blood of the PQ group in comparison with the control group (p<0.05 to p<0.001). Both doses of *C. longa* and curcumin diminished MDA level, total and differential WBC counts in the blood and BALF but increased CAT and SOD activities in both of them compared to PQ group (p<0.05 to p<0.001). The effects of *C. longa* and curcumin high dose on most variables were markedly more than low dose (p<0.05 to p<0.001). Furthermore, the effects of curcumin on some variables were markedly more than *C. longa* (p<0.05 to p<0.001).

**Conclusion:** Both *C. longa* and curcumin improved PQ-induced systemic and lung inflammation and oxidative stress, but the effect of curcumin was more prominent.
**Curcuma longa** and curcumin influenced lung toxicity and inflammation

**Introduction**

Agrochemicals such as paraquat (PQ) have widely been used in agriculture. PQ is a herbicide (Dinis-Oliveira et al., 2008) that might induce a serious hazard to human health (Chen et al., 2009; Kim et al., 2008) and PQ poisoning severity is dependent on the doses used (de Maglia et al., 2000). The possible mechanisms of PQ toxicity is inducing inflammation and oxidative stress by the generation superoxide anion (Hu et al., 2019). PQ poisoning can leads to the disruption of nicotinamide adenine dinucleotide phosphate (NADPH) (Morán et al., 2010).

In the traditional medicine of southeast Asian countries such as India and China, *Curcuma longa* L. (*C. longa*) has been used for the treatment of common cold and asthma (Debjit Bhowmik et al., 2009). *C. longa* also, is used as a functional food and a spice in food preparation (Kocher et al., 2015). Curcumin (diferuloylmethane) (3–4%) is the main active constituent of the plant, which is responsible for its vibrant yellow color, consist of curcumin I, curcumin II and curcumin III (Kumar et al., 2011).

Different studies showed *C. longa* anti-inflammatory, anti-asthmatic (Chen et al., 2015; Shakeri et al., 2017), relaxant (Emami et al., 2017), antioxidant (Srinivas et al., 1992) and immunomodulatory effects by modulating the balance of regulatory T cells (Tregs) /T-helper (Th) in a mouse model of asthma (Shin et al., 2015).

Curcumin also showed anti-inflammatory (Jurenka, 2009), antioxidant (Trujillo et al., 2013), hepatoprotective (Koffler et al., 2000), relaxant (Emami et al., 2017), and anti-asthma properties (Shakeri et al, 2017; Boskabady et al., 2018) in various clinical and experimental studies. The anti-inflammatory, antioxidant, and immunomodulatory properties of *C. longa* and curcumin were reviewed recently, which documented their modulatory effects on various inflammatory mediators, cytokines and oxidant markers (Chainani-Wu, 2003; Memarzia et al., 2021).

In the present study, the effects of *C. longa* and curcumin on PQ-induced lung and systemic inflammation and oxidative stress in rat were examined.

**Materials and Methods**

**Animal and groups**

Thirty Wistar rats (male, weighted 200–250 gr) were purchased from the Faculty of Medicine animal house, Mashhad University of Medical Sciences (MUMS) and were maintained in plexiglass cages with free access to food and water, 22±2°C, humidity of 54±2%, and 12 hr light/dark cycle during the experimental period. The ethics committee of Mashhad University of Medical Sciences approved the animal experiments (IR.MUMS.MEDICAL.REC.1397.148).

| Table 1. Various studied groups, their exposing to saline or paraquat and treatment protocol |
|---------------------------------------------------------------|
| groups            | Exposure                        | Treatment     | Abbreviation |
| Control           | Aerosol of saline               | -             | C            |
| Paraquat          | Aerosol of paraquat, 54 mg/m³   | -             | PQ           |
| C. longa          | "                              | 150 mg/kg/day | Ci-L         |
| C. longa          | "                              | 600 mg/kg/day | Ci-H         |
| Curcumin          | "                              | 30 mg/kg/day  | Cu-L         |
| C. longa          | "                              | 120 mg/kg/day | Cu-H         |

Animals in control (C) group were exposed to normal saline and to paraquat (PQ, Sigma Aldrich Co, China,) aerosol (with dose of 54 mg/m³) in PQ group, (every other day, 8 times, 30 min in each time), (Burleigh-Flayer & Alarie, 1987) during 16 days. PQ or saline aerosols were delivered to head box of animal dimensions 15×18×30 cm (Amin et al., 2021). Four groups were treated with 150 and 600 mg/kg/day *C. longa* extract (Shakeri et al., 2017) or 30 and 120 mg/kg/day curcumin (Shakeri et al., 2018) for 16 days by gavage after the end of PQ exposure period (Heydari et al., 2019) (n=5 in each group). *C. longa* and curcumin were administered by gavage.
Rats were randomly allocated to six groups (n=5 in each group) as described in Table 1. The method of animal exposure to PQ and saline aerosols as well as the method of treating animal to *C. longa* and curcumin were briefly described in the legend of Figure 1 (Amin et al., 2021).

**Plant and extract**

*C. longa* rhizomes (100 gr) were homogenized with ethanol 96% (Sigma-Aldrich Chemical Co., St. Louis, MO, USA) at a ratio of 1:10 (plant: ethanol) at 37°C for 3 days and occasionally shook. The extract was filtered and concentrated (under reduced pressure at 45°C in an Eyela, Heidolph, Schwabach, Germany) rotary evaporator as described previously (Shakeri F, Boskabady MH., 2017). The extract yield was 15% (1.5 gr out of 10 gr rhizomes powder). Qualitative and quantitative determination of curcumin in the extract was also described in our previous study (Shakeri et al., 2017).

**Blood and bronchoalveolar lavage fluid preparation**

At the end of the treatment period, the animals were anesthetized by intraperitoneal (i.p.) injection of 1.6 gr/kg of urethane. The blood samples were taken from the heart and one ml of the blood samples were dispensed into the anticoagulant containing for WBC counting. For measurement oxidative stress markers, the serum of the remaining blood samples was prepared and stored at −70°C.

Bronchoalveolar lavage fluid (BALF) was prepared as follows, after removal of the lungs from the chest BALF was obtained by washing the right lung with 1 ml normal saline for five times (total 5 ml) through tracheal cannula. The BALF was then centrifuged at 2500 rpm at 4°C for 10 min (Saadat et al., 2020). Cellular deposition was used for total and differential WBC count, and the collected supernatant was stored at −70°C for measurement of oxidative stress markers.

**Counting of total and differential white blood cell (WBC)**

Total WBC in the BALF and blood was counted using a hemocytometer (in a Burker chamber) in duplicate. From the cell pellet of the BALF and blood sample, a smear was prepared and stained with Wright-Giemsa for the differential WBC count. Differential MBC counts were then determined according to standard morphologic protocol under the light microscope (Saadat et al., 2019).
Curcuma longa and curcumin influenced lung toxicity and inflammation

Oxidant markers measurement
The level of MDA and activities of CAT and SOD were measured according method described in our previous study (Saadat et al., 2019).

Statistical analysis
The results were compared among different groups using one-way analysis of variance (ANOVA) and Tukey’s multiple comparison test. Data were shown as mean±SEM. The value of p<0.05 was considered as the level of statistical significance.

Results
The results of WBC (total and differential)
The effects of paraquat
Exposure of rats to inhaled PQ (54 mg/m³) resulted in a significant increase in total and all differential WBC both in the BALF and the blood except lymphocyte count in the blood (p<0.05-p<0.001, Figures 2-5).

The effects of C. longa extract treatment
Treatment with high dose of the C. longa extract significantly decreased neutrophil count in the blood and the BALF and eosinophil count in the BALF (p<0.05 for all cases), (Figures 2-5). The effect of high dose of the extract on neutrophil count both in the blood and in the BALF was significantly higher than its low dose (p<0.05 for the BALF and p<0.01 for the blood), (p<0.05 for the BALF and p<0.01 for the blood). In the blood, the effect of the extract high dose on monocyte count was significantly higher than its low dose. However, in the BALF there were not significant differences between two doses of the C. longa extract on that of WBC (total and differential counts (Figure 2).

![Figure 2](image-url)

Figure 2. White blood cells (WBC, total and differential) counts in blood of the control group (C), group exposed to 54 mg/m³ paraquat aerosol (PQ), and groups exposed to PQ and treated with 150 and 600 mg/kg/day C. longa or 30 and 120 mg/kg/day curcumin (Cl-L, Cl-H, Cu-L and Cu-H respectively), (in each group, n = 5). *p<0.05 compared to the control group; +p<0.05 and ++p<0.01 compared to the PQ group; $p<0.05 and $$p<0.01 comparison between two doses of C. longa, and curcumin; # p<0.05 and ## p<0.01, comparison between C. longa and curcumin. The results are shown as mean±SEM. One-way ANOVA and Tukey’s test was applied for comparisons among different groups.
Figure 3. Eosinophil and monocyte counts in white blood cells (WBC) in blood of the control group (C), group exposed to 54 mg/m$^3$ paraquat aerosol (PQ), and groups exposed to PQ and treated with 150 and 600 mg/kg/day C. longa or 30 and 120 mg/kg/day curcumin (Cl-L, Cl-H, Cu-L and Cu-H respectively), (in each group, n=5). **p<0.01 and ***p<0.001 compared to the control group; ++p<0.05, compared to the PQ group; $$p<0.01 comparison between two doses of C. longa, and curcumin; #p<0.05, comparison between C. longa and curcumin. The results are shown as mean±SEM. One-way ANOVA and Tukey’s test was applied for comparisons among different groups.

Figure 4. Total white blood cells (WBC), neutrophil and lymphocyte counts in the bronchoalveolar lavage fluid (BALF) of control group (C), group exposed to 54 mg/m$^3$ paraquat aerosol (PQ), and groups exposed to PQ and treated with 150 and 600 mg/kg/day C. longa or 30 and 120 mg/kg/day curcumin (Cl-L, Cl-H, Cu-L and Cu-H respectively), (in each group, n=5). *p<0.05, **p<0.01, and ***p<0.001 compared to the control group; +p<0.05, +++p<0.001 compared to the PQ group; $p<0.05, $$p<0.01 comparison between two doses of C. longa, and curcumin; #p<0.05, ## p<0.01, and ### p<0.001 comparison between C. longa and curcumin. The results are shown as mean±SEM. One-way ANOVA and Tukey’s test was applied for comparisons among different groups.
Curcuma longa and curcumin influenced lung toxicity and inflammation

The effects of curcumin treatment

Total WBC and neutrophil counts both in the blood and the BALF as well as eosinophil count in the BALF were significantly reduced in groups treated with both doses of curcumin (p<0.05- p<0.001). Lymphocyte counts both in the BALF and the blood, and eosinophil count in the blood were also significantly reduced in the group treated with high dose of the curcumin (p<0.05 for all cases). Monocyte counts were also significantly reduced in the groups treated with high dose of the curcumin and C. longa in the blood (p<0.01, Figures 2-5). The effects of high dose of curcumin on differential counts of all WBC subtypes (both in the blood and in the BALF) were significantly higher than those of low dose, except monocyte count in the BALF (p<0.05- p<0.01, Figures 2-5).

The results of oxidative stress markers

The effects of paraquat

The level of MDA was significantly increased, but those of CAT, SOD and thiol were decreased due to exposure of rats to PQ inhalation (p<0.001 for cases, Figures 6-9).

The effects of C. longa extract treatment

Both doses of the extract decreased the level of MDA and increased the thiol level. In contrast, CAT increased in treating animals with high dose of extract both in the serum and BALF, as well as SOD activities were increased in the high dose of serum and the BALF (p<0.05-p<0.001, Figures 6-9). The effects of high dose of the extract on all oxidative stress markers both in the blood and in the BALF were significantly higher than those of low dose (p<0.05-p<0.001, Figures 6-9).

The effects of curcumin treatment

Treatment with both doses of the curcumin decreased the levels of MDA, while increased CAT both in the serum and the BALF (p<0.05 for CAT in the BALF and p<0.001 for other cases). The effects of high dose of curcumin on all oxidative stress markers, both in the serum and in the BALF were markedly higher than those of low dose (p<0.01-p<0.001, Figures 6-9).
Figure 6. Malondialdehyde (MDA) level in the serum and the BALF of the control group (C), group exposed to 54 mg/m$^3$ paraquat aerosol (PQ), and groups exposed to PQ and treated with 150 and 600 mg/kg/day C. longa or 30 and 120 mg/kg/day curcumin (Cl-L, Cl-H, Cu-L and Cu-H respectively), (in each group, n=5). ***p<0.001 compared to the control group; ++p<0.01 and +++p<0.001 compared to the PQ group; $$ p<0.01 and $$$, comparison between two doses of C. longa, and curcumin; # p<0.05, ## p<0.01, and ### p<0.001, comparison between C. longa and curcumin. The results are shown as mean±SEM. One-way ANOVA and Tukey’s test was applied for comparisons among different groups.

Figure 7. Thiol level in the serum and the BALF of the control group (C), group exposed to 54 mg/m$^3$ paraquat aerosol (PQ), and groups exposed to PQ and treated with 150 and 600 mg/kg/day C. longa or 30 and 120 mg/kg/day curcumin (Cl-L, Cl-H, Cu-L and Cu-H respectively), (in each group, n=5). ***p<0.001 compared to the control group; ++p<0.01 and +++p<0.001 compared to the PQ group; $$ p<0.01 and $$$ p<0.001, comparison between two doses of C. longa, and curcumin; # p<0.05 and ## p<0.01, comparison between C. longa and curcumin. The results are shown as mean±SEM. One-way ANOVA and Tukey’s test was applied for comparisons among different groups.

**Comparison between the effects of C. longa and curcumin**

The effects of high dose of curcumin on total and differential WBC in the BALF and the blood except monocyte in the BALF were markedly higher than those of the high dose of the extract (p<0.05-p<0.001). The effects of low dose of curcumin on total WBC and neutrophil both in the blood and the BALF and on eosinophil in the BALF were also higher than those of low dose of the extract (p<0.05-p<0.001, Figures 2-5).

Treatment with high dose of curcumin improved MDA levels, both in the serum and the BALF, and the serum CAT activity was significantly higher than those of the C. longa extract (p<0.5- p<0.001). The effects of high dose of curcumin on the serum thiol content and SOD activity, and its low dose on the BALF thiol level were also significantly higher than corresponding doses of the extract (p<0.05-p<0.001, Figures 5-9).
Curcuma longa and curcumin influenced lung toxicity and inflammation

Discussion
In this study, the effects of the C. longa ethanolic extract and curcumin as the main constituent of the plant, on the total and differential WBC as well as oxidant markers (MDA, thiol, SOD, and CAT) on a rat model of PQ-induced lung and systemic toxic changes were investigated.

Sixteen days exposure of rats to PQ aerosol (54 mg/m³) inhalation significantly increased the total and differential WBC counts as well as MDA level, but CAT, SOD and thiol levels were significantly decreased both in the blood and the BALF which were in line with previous findings (Amin et al., 2021). However, treatment with the extract of the plant and curcumin, improved WBC (total and differential) counts as well as oxidant markers (MDA, thiol, SOD, and CAT) both in the blood and the BALF.
Experimental models of PQ toxicity have been proposed as an oxidant-initiated lung and systemic degenerative and inflammatory lesions (Amin et al., 2021; Bus & Gibson, 1984). PQ generates the superoxide anion that resulted in production of more reactive oxygen and toxic oxidative stress biomarkers, which confirmed the present study findings as lung and systemic elevation of MDA and decrease in thiol, SOD, and CAT. Therefore, antioxidant therapy has been considered as a beneficial strategy in the healing and prevention of the toxic effects of PQ (Suntres, 2002). The antioxidant properties of C. longa and curcumin against asthma model induced systemic and lung oxidative stress were indicated (Shakeri et al., 2017). In addition, several antioxidant effects including reduction of MDA, CK-MB, LDH activities, and NO metabolites and elevation of SOD, CAT, GSH, GPX and GR have been suggested for C. longa in various toxic and inflammatory experimental models and clinical trials (Memarzia et al., 2021). The findings of inflammation and oxidative stress may show a cause and effect relationship. Elevation of ROS might cause lung and systemic inflammation, which increase and activate eosinophils, neutrophils, monocytes, and macrophages for generation of more ROS (Biswas, 2016; Shakeri et al., 2017). In this study, PQ-induced oxidative stress was in line with total and differential WBC changes.

The results of this study showed that the higher doses of C. longa and curcumin were more effective against PQ-induced elevation of WBC (total and differential) and MDA level, and also the reduction of thiol content and antioxidant enzymes in blood and BALF. In most of toxic and inflammatory experimental models the effective dose of C. longa or its extract was more than 200 mg/kg and the ethanolic extract was more effective than aqueous extract or C. longa powder (Memarzia et al., 2021), which confirmed the result of this study. Moreover, the dose dependent protective effects of both C. longa and curcumin on WBC and oxidative stress marker were indicated previously in ovalbumin-induced asthma rat model (Shakeri et al., 2017). The present study findings showed that the higher dose of curcumin (120 mg/kg) had more therapeutic potency than higher dose of C. long (600 mg/kg). Therefore, the antioxidant and anti-inflammatory effects of C. long might be attributed to curcumin, which is the main constituents of C. longa. In previous studies the comparative effects of Curcuma longa and curcumin with those of dexamethasone were shown (Shakeri et al., 2017, Boskabady MH et al., 2021) therefore, in the present study a positive group was not performed. Regarding to the safety of C. longa even at high dose and many document addressing its anti-inflammatory and antioxidant effects in clinical trials (Memarzia et al., 2021), thus the plant might be a good candidate to prevent PQ poisoning in clinics.

C. longa and curcumin as the main constituent of the plant improved inhaled PQ-induced lung and systemic oxidative stress and inflammation but the effect of curcumin was more prominent. These findings indicate a potential therapeutic effect of C. longa and specially curcumin in inhaled PQ-induced lung and systemic oxidative stress and inflammation.

Acknowledgment
Research Council of MUMS financially supported this work by a research grant (Code: 961810), Mashhad, Iran.

Conflicts of interest
The authors have declared that there is no conflict of interest.

References
Amin F, Roohbakhsh A, Memarzia A, Kazerani HR, Boskabady MH. 2021. Immediate and late systemic and lung...
Curcuma longa and curcumin influenced lung toxicity and inflammation

effects of inhaled paraquat in rats. J Hazard Mater, 415: 125633.
Biswa SK. 2016. Does the interdependence between oxidative stress and inflammation explain the antioxidant paradox? Oxidative Med Cell Longev, 2016: 1-9.
Boskabady MH, Amin F, Shakeri F. 2021. The effect of Curcuma longa on inflammatory mediators and immunological, oxidant, and antioxidant biomarkers in asthmatic rats. Evid Based Complement Alternat Med, 2021: 4234326.
Boskabady M, Marefati N, Farkhondeh T, Shakeri F, Farshbaf A, Boskabady MH. 2018. The effect of environmental lead exposure on human health and the contribution of inflammatory mechanisms, a review. Environ Int, 120: 404-420.
Bus JS, Gibson JE. 1984. Paraquat: model for oxidant-initiated toxicity. Environ Health Perspect, 55: 37-46.
Chainani-Wu N. 2003. Safety and anti-inflammatory activity of curcumin: a component of tumeric (Curcuma longa). J Altern Complement Med, 9: 161-168.
Chen ES, Melton GB, Wasserman RC, Rosenau PT, Howard DB, Sarkar IN. 2015. Mining and visualizing family history associations in the electronic health record: a case study for Pediatric Asthma. AMIA Annu Symp Proc, 2015: 396-405.
Chen KG, Valencia JC, Gillet JP, Hearing VJ, Gottesman MM. 2009. Involvement of ABC transporters in melanogenesis and the development of multidrug resistance of melanoma. Pigment Cell Melanoma Res, 22: 740-749.
De Maglia Botella J, Belenguer JT. 2000. Paraquat poisoning. A study of 29 cases and evaluation of the effectiveness of the" Caribbean scheme". Medicina clinica, 115: 530-533.
Debjit Bhowmik C, Kumar K, Chandira M, Jayakar B. 2009. Turmeric: a herbal and traditional medicine. Arch Appl Sci Res, 1: 86-108.
Dinis-Oliveira R, Duarte J, Sanchez-Navarro A, Remiao F, Bastos M, Carvalho F. 2008. Paraquat poisonings: mechanisms of lung toxicity, clinical features, and treatment. Crit Rev Toxicol, 38: 13-71.
Emami B, Shakeri F, Ghorani V, Boskabady MH. 2017. Relaxant effect of Curcuma longa on rat tracheal smooth muscle and its possible mechanisms. Pharm Biol, 55: 2248-2258.
Hu X, Liang Y, Zhao H, Zhao M. 2019. Effects of AT-RvD1 on paraquat-induced acute renal injury in mice. Int Immunopharmacol, 67: 231-238.
Jurenka JS. 2009. Anti-inflammatory properties of curcumin, a major constituent of Curcuma longa: a review of preclinical and clinical research. Altern Med Rev, 14: 141-153.
Kim Sj, Gil HW, Yang JO, Lee EY, Hong SY. 2008. The clinical features of acute kidney injury in patients with acute paraquat intoxication. Nephrol Dial Transplant, 24: 1226-1232.
Kocher A, Schiborr C, Behnam D, Frank J. 2015. The oral bioavailability of curcuminoids in healthy humans is markedly enhanced by micellar solubilisation but not further improved by simultaneous ingestion of sesamin, ferulic acid, naringenin and xanthohumol. J Funct Foods, 14: 183-191.
Koffler L, Roshong S, Kyu Park I, Cesen-Cummings K, Thompson DC, Dwyer-Nield LD, Ruch RJ. 2000. Growth inhibition in G1 and altered expression of cyclin D1 and p27kip-1 after forced connexin expression in lung and liver carcinoma cells. Mol Cell Biochem, 79: 347-354.
Kumar P, Mishra S, Malik A, Satya S. 2011. Insecticidal properties of Mentha species: a review. Ind Crops Prod, 34: 802-817.
Memarzia A, Khazdair MR, Behrouz S, Gholamnezhad Z, Jafarnezhad M, Saadat S, Boskabady MH. 2021. Experimental and clinical reports on anti-inflammatory, antioxidant, and immunomodulatory effects of Curcuma longa and curcumin, an updated and comprehensive review. Biofactors, 47: 311-350.
Memarzia A, Saadat S, Behrouz S, Boskabady MH. 2021. Curcuma longa and curcumin affect respiratory and allergic disorders, experimental and clinical evidence: A comprehensive and updated review. Biofactors, 21.
Morán J M, Ortiz-Ortiz MA, Ruiz-Mesa LM, Fuentes JM. 2010. Nitric oxide in paraquat-mediated toxicity: A review. J Biochem Mol Toxicol, 24: 402-409.
Saadat S, Beheshti F, Askari VR, Hosseini M, Roshan NM, Boskabady MH. 2019. Aminoguanidine affects systemic and lung inflammation induced by lipopolysaccharide in rats. Respir Res, 20: 1-3.

Saadat S, Roshan NM, Aslani MR, Boskabady MH. 2020. Rosuvastatin suppresses cytokine production and lung inflammation in asthmatic, hyperlipidemic and asthmatic-hyperlipidemic rat models. Cytokine, 128: 1-3.

Shakeri F, Boskabady MH. 2017. Anti-inflammatoty, antioxidant, and immunomodulatory effects of curcumin in ovalbumin-sensitized rat. Biofactors, 43: 567-576.

Shakeri F, Soukhtanloo M, Boskabady MH. 2017. The effect of hydro-ethanolic extract of Curcuma longa rhizome and curcumin on total and differential WBC and serum oxidant, antioxidant biomarkers in rat model of asthma. Iran J Basic Med Sci, 20: 155-165.

Shin HS, See H, Jung SY, Choi D W, Kwon DA, Bae MJ, Shon DH. 2015. Turmeric (Curcuma longa) attenuates food allergy symptoms by regulating type 1/type 2 helper T cells (Th1/Th2) balance in a mouse model of food allergy. J Ethnopharmacol, 175: 21-29.

Srinivas L, Shalini V, Shylaja M. 1992. Turmerin: a water-soluble antioxidant peptide from turmeric [Curcuma longa]. Arch Biochem Biophys, 292: 617-623.

Suntres ZE. 2002. Role of antioxidants in paraquat toxicity. Toxicology, 180: 65-77.

Trujillo J, Chirino YI, Molina-Jijón E, Andérca-Romero AC, Tapia E, Pedraza-Chaverrí J. 2013. Renoprotective effect of the antioxidant curcumin: Recent findings. Redox Biol, 1: 448-456.