Antioxidant and anti-inflammatory efficacy of curcumin on lung tissue in rats with sepsis

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Abstract

OBJECTIVE: To detect antioxidant and anti-inflammatory efficacy of Curcumin (Cur) on lung tissue in rats with sepsis.

METHODS: Totally 32 rats were divided into 4 groups; the rats in Group 1 (control group) had abdominal incision under sterile conditions following anesthesia and the abdomen was sutured. Abdominal incision was performed in the rats in Group 2 (Cur group) under sterile conditions following anesthesia and the abdomen was closed. Cur was given to this group after dissolving within dimethylsulphoxide as 100 mg/kg through oral gavage and started for 3 d before surgical procedure. Group 3 (CLP group) had caecal ligation and puncture (CLP) under sterile conditions to create sepsis following anesthesia and the abdomen was sutured. CLP was performed in the rats in Group 4 (CLP + Cur group) under sterile conditions following anesthesia to create a sepsis model and the abdomen was closed. Cur was also given to this group after dissolving within dimethylsulphoxide as 100 mg/kg through oral gavage and started for 3 d before surgical procedure. All the rats were sacrificed through blood aspiration from the heart under sterile conditions following anesthesia and lung tissues were removed after 24 h following the surgical procedures. The tissue samples were homogenized for biochemical analyses; and malondialdehyde (MDA), nitric oxide (NO), myeloperoxidase (MPO), superoxide dismutase (SOD) and catalase (CAT) were analyzed through spectrophotometric method, immunohistochemical iNOS staining was performed to assess the inflammation; and histopathological differences between the groups were evaluated.

RESULTS: A statistically significant decrease was detected in the CLP + Cur group when compared with the CLP group of which Cur was not given in terms of MDA, MPO and NO levels (P < 0.05) whereas a statistically significant elevation was found in the CLP + Cur group when compared with the CLP group in terms of SOD and CAT levels (P < 0.05).

CONCLUSION: The study outcomes revealed that supplementation of Cur presents an antioxidant effect by reducing the free radical level and increasing the antioxidant enzyme levels; and an anti-inflammatory effect by reducing iNOS level.

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Keywords: Curcumin; Sepsis; Anti-inflammatory agents; Antioxidants; Nitric Oxide Synthase Type II

INTRODUCTION

Many diseases have been tried to be treated by the herbs throughout the history of humanity. World Health Organization assumes that more than 80% of the world population trust traditional medicine for ba-
The present study was conducted in Research Laboratory efficacy of Cur in the rats with sepsis created through caecal ligation and puncture (CLP). Studies have shown that many plants used in Traditional Chinese Medicine, especially containing complex antioxidants, have been used for the prevention and treatment of many diseases. Turmeric derived from the root of the Curcuma longa plant has been used in Ayurveda and Traditional Chinese Medicine for thousands of years to treat different inflammatory diseases. Curcumin (Cur) \([1,7\text{-bis-(4-hydroxy-3-methoxyphenyl)}-1,6\text{-hepadiene},3,5\text{-dione}]\) is a yellow substance obtained from rhizome of turmeric and commonly used in Indian cuisine. Cur is considered as a potential antioxidant and antiinflammatory agent and has been used in treatment of wounds, tumors and inflammatory conditions in Asian traditional medicine for over 4000 years. Cur was reported as a bi-functional antioxidant because of directly reacting with reactive species and providing increase of different cytoprotective and antioxidant proteins; it is accepted that antioxidant efficacy plays an important role in relieve of cellular inflammation. Use of Cur is safe and not toxic to human; and turmeric is classified as an additive substance in E100 category. Sepsis affects millions of people every year by an increasing incidence. However, it is one of the most common cause of death in coronary intensive care units. Sepsis is a systemic response of the host against microbial pathogens and originated from the injury of tissues and organs caused by the body itself; sepsis may be caused by bacterial, fungal, viral and parasitic infections stimulating the cellular dysfunction in the host and results with morbidity and mortality. Excessive systemic production of reactive oxygen species (ROS) both in rodents and humans as well as hyperinflammatory state defined by numerous pro-inflammatory mediators detected on the plasma are common findings in sepsis. Cur is known to have different antimicrobial, antiviral, antifungal, anticancer and wound healing pharmacological characteristics; and the anlogs are a strong candidate for current therapies for sepsis due to antioxidant and antiinflammatory efficacy. Preliminary exposure of the rats with Cur and the finding that Cur suppress the hepatic microvascular inflammatory response and endotoxin-originated hepatic blood supply all indicate Cur as a potential substance for treatment of sepsis and septic shock. The aim of the present study was to detect antioxidant and antiinflammatory efficacy of Cur in the rats with sepsis created through caecal ligation and puncture (CLP).

**MATERIALS AND METHODS**

The present study was conducted in Research Laboratory of Medical Biochemistry department of Medical Faculty of Namık Kemal University to analyze antiinflammatory and antioxidant efficacy of Cur against the injury of the pulmonary tissue in the sepsis model created on 32 Wistar Albino rats through CLP method. Approval was obtained from Animal Experiments Local Ethics Committee of Namık Kemal University with resolution number of 2016/03 on 03/03/2016. The researcher carrying out the laboratory part of the research has been awarded with Certificate of Experimental Animals Implementation and Ethics from Gazi University, Laboratory Animals Growing and Experimental Research Center.

**Procurement and care of the animals of the study**

Totally 32 Wistar Albino male rats with an average age of 2.5 to 3 months and weight average of 250 to 300 g were obtained from Animal Experiments Center of Trakya University. All animals were kept in a temperature-controlled room (20-24 °C, 45%-50% humidity) in stainless steel cages following a 12-h light/12-h dark cycle. Access of the animals to pellet feed diet and tap water was provided as ad libitum.

**Creation of research groups**

Totally 32 male rats were used within 4 groups including 8 rats in each group. The rats were divided into 4 groups as the control, Cur, CLP and CLP + Cur. Group 1 (Control) \((n = 8)\): abdominal incision was performed only in the rats in this group under sterile conditions following anesthesia and the abdomen was closed.

Group 2 (Cur) \((n = 8)\): abdominal incision was performed only in the rats in this group under sterile conditions following anesthesia and the abdomen was closed. Cur was also given to this group after dissolving within dimethylsulphoxide as 100 mg/kg through oral gavage and started for 3 d before surgical procedure.

Group 3 (CLP) \((n = 8)\): CLP was performed in the rats in this group under sterile conditions following anesthesia and the abdomen was closed.

Group 4 (CLP + Cur) \((n = 8)\): CLP was performed in the rats in this group under sterile conditions following anesthesia and the abdomen was closed. Furthermore, Cur was also given to this group after dissolving within dimethylsulphoxide as 100 mg/kg through oral gavage and started for 3 d before surgical procedure.

All the rats were sacrificed through blood aspiration from the heart under sterile conditions following anesthesia and lung tissues were removed after 24 h following the surgical procedures.

**Light microscope examination**

The lung tissues were processed in Light Microscope Laboratory of Histology and Embryology Department of Medical Faculty of Namık Kemal University for microscopic examinations. The pulmonary injury grade was assessed according to the technique developed by Murakami et al. in the histopathological examination.
Alveolar wall thickness, inflammation and edema were reviewed on 10 zones randomly selected from the pulmonary parenchyma on each slide and scored between 0 and 4 as follows: 0; no injury and normal appearance, 1: mild injury, 2: moderate injury, 3: severe injury, 4: very severe injury). As a result of the scores obtained, average value of each group was obtained.

**Immunohistochemical examination**

Slices of 5 μm were obtained from the pulmonary tissue for immunohistochemical examination and positive cells under large magnification (× 400) were counted on randomly selected five zones. The data obtained were determined as iNOS-positive cell counts in average.

**Biochemical Examination**

The tissues were immediately washed by cold isotonic water and kept in the deep freezer after wrapping to aluminum foil at −85 °C until biochemical tests. The homogenates obtained were centrifuged at 3220 rpm at +6 °C cooling centrifuge device for 30 min and a supernatant was obtained. Malondialdehyde (MDA), myeloperoxidase (MPO), nitric oxide (NO), superoxide dismutase (SOD) and catalase (CAT) analyses were performed.

**Statistical data evaluation**

SPSS 18.0 (SPSS Inc. Released 2009. SPSS Statistics for Windows, Version 18.0, Chicago, IL, USA) was used for data analysis. The findings were provided in mean ± standard deviation (x ± s). The differences measured between four groups were analyzed by Kruskal-wallis non-parametric test. The binary comparisons between the groups providing significant values were assessed by Mann-Whitney U test. The P value < 0.05 was accepted as statistically significant.

**RESULTS**

When haematoxylin and eosine (HE) stained slices of the control and Cur groups were examined, bronchi, bronchioli, alveols and interstitial areas were observed as normal. Examination of HE stained slices of the CLP group revealed a diffuse pulmonary injury when compared with the control and Cur groups. Alveolar septal thickening as well as heorrhage and edema were observed in the pulmonary interstitium. Furthermore, desquamation on bronchi and bronchioli, and inflammatory cell infiltration both around the bronchi and bronchioli and on interstitial area were detected. Less injury was detected in the CLP + Cur group when compared with the CLP group in terms of alveolar and interstitial areas. Moreover, inflammatory cell infiltration, edema and alveolar septal thickening scores were considerably higher in the CLP group when compared with the control and Cur groups; and were significantly lower in the CLP + Cur group when compared with CLP group (Figure 1).

In the present study, examination of the lung slides of the rats in the control and Cur groups under light microscope revealed very less iNOS-positive cells on the alveolar and interstitial areas. Number of iNOS-positive cells was observed quite higher in the alveolar and interstitial areas; and iNOS-positive cells created accumulations on some areas. Immunostaining of iNOS in the lung tissue of all groups is shown in the Figure 2. Number of iNOS-positive cells were found significantly higher in the CLP + Cur group when compared with CLP group (P < 0.05). There was not any statistically significant difference detected between the Control and Cur groups (P > 0.05).

In the present study, analyses of MDA, MPO, NO, SOD and CAT in lung tissues of the rats in the control, Cur, CLP and CLP + Cur groups revealed that a statistically significant elevation was detected in the pulmonary MDA (P < 0.05; P < 0.01), MPO (P < 0.001; P < 0.001) and NO (P < 0.001; P < 0.001) levels in CLP group when compared with the control and Cur groups. A statistically significant decrease was detected in MDA (P < 0.05), MPO (P < 0.001) and NO (P < 0.001) levels of CLP + Cur group when compared with the CLP group of which Cur was not given.

![Figure 1](image-url)

**Figure 1** Inflammation, edema and alveolar wall thickness scores in lung tissue of control and experimental groups

A: inflammation; B: edema; C: alveolar wall thickness. Rats were randomly divided into four groups. Control group was performed only abdominal incision. Curcumin group was performed abdominal incision and curcumin (100 mg/kg) was given through oral gavage and started for 3 d before surgical procedure. CLP group was performed CLP. CLP + Cur group was performed CLP and curcumin (100 mg/kg) was given through oral gavage and started for 3 d before surgical procedure. CLP: caecal ligation and punction. P < 0.001; as compared to the control and curcumin groups; P < 0.001; as compared to the control, curcumin and CLP groups)
There was not any statistically significant difference detected between the Control and Cur groups. Evaluation of SOD (\(P < 0.001\), \(P < 0.01\)) and CAT (\(P < 0.001\), \(P < 0.001\)) levels presented a statistically significant decrease in CLP group when compared with the control and Cur groups. A statistically significant decrease was detected in SOD (\(P < 0.05\)) and CAT (\(P < 0.05\)) levels of CLP + Cur group when compared with the CLP group of which Cur was not given. There was not any statistically significant difference detected between the Control and Cur groups (\(P > 0.05\)) (Table 1).

**DISCUSSION**

Curcumin presents a radical sweeping and anti-inflammatory efficacy along with antimicrobial, antiviral, antifungal, and wound healing pharmacological characteristics.\(^2\)\(^3\)\(^4\) Curcumin has a double-functioned antioxidant characteristics as ROS sweepier and antioxidant response inducer.\(^5\) It was reported that Curcumin inhibits lipid peroxidation and efficiently clears superoxide anion and hydroxyl radicals.\(^6\) The aim of the present study was to detect antioxidant and anti-inflammatory efficacy of Curcumin on the lung tissue of the rats of which sepsis was created. At the end of the study, a statistically significant elevation was detected in the CLP group for pulmonary MDA, MPO and NO levels, when compared with the control and Cur groups. A statistically significant decrease was detected in MDA, MPO and NO levels of CLP + Cur group when compared with the CLP group of which Cur was not given. However, evaluation of SOD and CAT levels presented a statistically significant decrease in LP group when compared with the control and Cur groups. A statistically significant decrease was detected in SOD and CAT levels of CLP + Cur group when compared with the CLP group of which Cur was not given. Same Cur dose (100 mg/dL) was used in another study where antioxidant effect was searched on the rats of which acute pulmonary injury was created by stimulating the intestines through ischemia/reperfusion (I/R). The rats were divided into 3 groups (\(n = 10\) as sham, I/R and I/R + Cur (100 mg/kg)). Cur was started 3 d before I/R and given by gastric gavage. At the end of the study, it was reported that the SOD level of the pulmonary tissue reduced by I/R significantly increased by Cur therapy and the increased MDS level was detected significantly reduced.\(^7\) The outcomes of the present study are similar to the present study.

A review on methods of different rat studies planned to examine potential antioxidant efficacy of Curcumin notices existence of different study designs. The Curcumin administration time especially differs in the studies. In a study where antioxidant effect of Curcumin is reviewed, Curcumin was given through gastric tract for 14 d following the surgical procedure to analyze protective effect against oxidative stress parameters in the livers and kidneys of the rats. The rats were divided into 3 groups (\(n = 8\)) as sham, biliary duct ligation (BDL) and biliary duct ligation (BDL) and gallbladder ligation (BDL) and biliary duct ligation (BDL). The rats were divided into 3 groups (\(n = 8\)) as sham, biliary duct ligation (BDL) and biliary duct ligation (BDL). The rats were divided into 3 groups (\(n = 8\)) as sham, biliary duct ligation (BDL) and biliary duct ligation (BDL).

**Figure 2** INOS immunostaining in the lung tissue (immunoperoxidase, hematoxylin counterstaining, \(\times 100\)) A: control group; B: curcumin group; C: CLP group; D: CLP + curcumin group. Arrow: INOS positive cells. Rats were randomly divided into four groups. Control group was performed only abdominal incision. Curcumin group was performed abdominal incision and curcumin (100 mg/kg) was given through oral gavage and started for 3 d before surgical procedure. CLP group was performed CLP. CLP + Cur group was performed CLP and curcumin (100 mg/kg) was given through oral gavage and started for 3 d before surgical procedure. CLP: caecal ligation and puncture. CLP: caecal ligation and puncture; INOS: inducible nitric oxide synthase.

**Table 1** Mean and standard deviation of biochemical data from all groups (\(\bar{x} \pm s\))

<table>
<thead>
<tr>
<th>Biochemical finding</th>
<th>Control ((n = 8))</th>
<th>Cur ((n = 8))</th>
<th>CLP ((n = 8))</th>
<th>CLP + Cur ((n = 8))</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA (nmol/g protein)</td>
<td>2.5940±0.4191</td>
<td>2.4304±0.8292</td>
<td>3.6431±0.8615(^a)</td>
<td>2.6998±0.3654(^a)</td>
</tr>
<tr>
<td>MPO (U/g protein)</td>
<td>0.0098±0.0016</td>
<td>0.0120±0.0311</td>
<td>0.0311±0.0048(^d)</td>
<td>0.0197±0.0042(^d)</td>
</tr>
<tr>
<td>NO (mmol/g protein)</td>
<td>75.5825±16.0593</td>
<td>98.1725±28.2628</td>
<td>190.0525±31.8740(^d)</td>
<td>116.5313±10.4552(^d)</td>
</tr>
<tr>
<td>SOD (U/mg protein)</td>
<td>0.4791±0.0909</td>
<td>0.4540±0.0714</td>
<td>0.2919±0.0733(^d)</td>
<td>0.4120±0.0747(^d)</td>
</tr>
<tr>
<td>CAT (k/g protein)</td>
<td>12.1874±3.5252</td>
<td>12.7761±2.5301</td>
<td>5.1051±1.5119(^a)</td>
<td>8.7933±1.2204(^a)</td>
</tr>
</tbody>
</table>

Notes: rats were randomly divided into four groups. Control group was performed only abdominal incision. Curcumin group was performed abdominal incision and curcumin (100 mg/kg) was given through oral gavage and started for 3 d before surgical procedure. CLP group was performed CLP. CLP + Cur group was performed CLP and curcumin (100 mg/kg) was given through oral gavage and started for 3 d before surgical procedure. CLP: caecal ligation and puncture; MDA: Malondialdehyde; MPO: Myeloperoxidase; NO: Nitric Oxide; SOD: Superoxide Dismutase; CAT: Catalase; \(P < 0.05\) as compared to the control group; \(P < 0.001\) as compared to the Cur group; \(P < 0.01\) as compared to the control group; \(P < 0.001\) as compared to the cur group; \(P < 0.05\) as compared to the CLP group; \(P < 0.001\) as compared to the CLP group.
tion 4 Cur (BDL + Cur, 50 mg·kg⁻¹·d⁻¹). The results obtained are in line with the present study. Hepatic and renal MDA and MO levels were found significantly lower in the BDL group when compared with the SHAM group. However, MDA level was found significantly lower in the BDL + Cur group than BDL group. Furthermore, renal SOD and CAT enzyme activities were found significantly lower in the BDL group when compared with the SHAM group whereas significantly higher in the BDL + Cur group than BDL group.²⁵

Another study compared the post-treatment efficiency of Cur. In this study aiming to analyze protective effect of Cur against isoprenaline-originated myocardial ischemia, animals were divided into 6 groups (n = 6) including Salin Control, Cur Control, isoprenaline (ISO), Cur (15 mg/kg) + ISO (pre-treatment (PRT)), Cur (15 mg/kg) + ISO + Control Cur (15 mg/kg) (pre-and post treatment (PPT)) vs ISO + Cur (15 mg/kg) (post-treatment (POT)). Cur was administrated orally for 30 min before (PRT) and after (POT) ISO administration. The study concluded that PPT increased SOD and CAT enzyme activities by 90% and 35%, respectively whereas there is not any significant increase in enzymatic antioxidant enzyme levels in PRT and POT groups.²⁶ Significant results are obtained by pre-treatment of Cur of 100 mg/kg in the present study; however, lack of significant results by pre-treatment of 15 mg/kg Cur; and significant results with pre-and post-treatment at same doses indicate that post-treatment along with pre-treatment would be more effective.

Another important aspect is comparison of different doses of Cur. In a such study, sepsis and hepatic failure were created by lipopolysaccharide (LPS) implementation in the mice and they have started LPS administration 4 weeks before Cur administration.²⁷ Five (n = 10) groups including the control, LPS, LPS + Cur (20 mg/kg), LPS + Cur (40 mg/kg) ve LPS + Cur (80 mg/kg) were created in the study. The study outcomes revealed that despite the significant recovery at all Cur doses in SOD activity, the significant decrease in CAT level was only detected in doses of 40 and 80 mg/kg. However, NO level evades in the mica induced by LPS whereas a significant decrease was found in 40 and 80 mg/kg dose groups. Post-treatment efficacy at different Cur dose administrations was analyzed in another study. In another study, Wistar Albino rats were grouped as sham, CLP, CLP + Cur (50 mg/kg) ve CLP + Cur (100 mg/kg) (n = 6); and effect of Cur against chronic lung injury was examined and Cur was administrated orally for 45 minutes. As a result, MPO enzyme activity and MDA content significantly increased in CLP group whereas Cur treatment reduced MPO enzyme activity by 26.32% (50 mg/kg cur) and 63.16% (100 mg/kg cur) as well as lipid peroxidation by 25% and 39.28%, respectively. However, SOD activity in the CLP group significantly decrease whereas SOD activity as well as Cur treatment increased by 34.48% and 110%, respectively.²⁸ Although lower doses of Cur were used in those two studies when compared with the present study (100 mg/kg), similar results may be associated with longer use of Cur.

In addition to dose and duration differences, it is noted that similar doses of Cur by intraperitoneal or oral administration provide similar results.²⁹ Thirty similar to this study, another study focusing on effect of Cur on acute lung injury stimulated by sepsis administrated Cur intraperitoneally; however, effect of lower and higher Cur doses was investigated rather than single dose Cur. For that purpose, the rats were divided into 5 groups (n = 20) including sham, CLP, CLP + carrier solution, CLP + 50 mg/kg Cur (Low Dose Cur (L-Cur)) and CLP + 200 mg/kg Cur (High Dose Cur (H-Cur)). Cur was administrated intraperitoneally after 2 and 12 h following surgical procedure. In the sepsis group created by CLP, MDA and MPO activities were observed increased whereas MDA and MPO levels were found significantly lower in both Cur dose groups when compared with CLP group, and a significant recovery was observed in SOD activity which reduces with CLP procedure.²⁹ Another study conducted searched antiinflammatory and antioxidant efficacy of Cur on lung lesion at lower doses of Cur (1 and 5 mL/kg) from femoral vein; Cur was administrated 50 min after surgical occlusion. Although quite lower doses of Cur were administrated in such study, significant improvements were detected both in SOD and MPO levels and there was not any significant difference between the groups. When the aforesaid study was compared with the present study, higher doses of Cur were used orally; very less Cur quantity used for vein administration may be explained by lower bioavailability of Cur.²⁹-³⁰

iNOS is an enzyme stimulated by inflammation, expressed by many cell types and catalyzing NO production.³¹ iNOS, as a rate-limiting enzyme is closely associated with inflammatory diseases.³² Antinflammatory activity of Cur depends on cytokine-release inhibiting capability of proinflammatory cytokine by inhibiting the transcriptional activity of NF-κB, activated proprotein-1, COX-2 expression and TREM-1 basically in the macrophages.³³ Such characteristics of Cur provides a potential for recovery of inflammatory diseases.³⁴ Ca-macho-Barquero et al.³⁴ performed a study in 2007 and investigated expression of iNOS by Cur administration on an experimental chronic ulcerative model on the rats through trinitrobenzenesulphonic acid (TNBS). The rats were divided into groups including sham, TNBS, TNBS + Cur (50 mg/kg) and TNBS + Cur (100 mg/kg). Cur was started 24 h after TNBS and administrated through oral gavage for 2 weeks. At the end of the study, exposure to TNBS caused strong expression of iNOS whereas a significant decrease of iNOS expression was detected in the Cur treatment groups when compared with TNBS group. Another study conducted created the groups as (n = 6) fish oil + ethanol (FE),
fish oil + dextrose (FD), FE + Cur (75 mg/kg) and FD + Cur (75 mg/kg) in the rats with alcoholic liver disease through fish oil + ethanol (FE) diet. Cur was administered by intragastric infusion for 4 weeks. The hepatic lipoidosis necrosis and inflammation developed characterized by iNOS stimulation in the rats fed by FE. The analysis revealed that iNOS was detected in the FE group only and not observed in treatment groups. In the present study, examination of the lung slides of the rats in the control and Cur groups under light microscope revealed very less iNOS-positive cells on the alveolar and interstitial areas. Number of iNOS-positive cells was observed quite higher in the alveolar and interstitial areas; and iNOS-positive cells created accumulations on some areas. The number of iNOS-positive cells was found significantly higher in the CLP + Cur group when compared with CLP group. The findings support the outcomes obtained from the researches.

In conclusion, the outcomes of the present study showed that Cur supplements in the sepsis model rats have antioxidant efficacy by suppressing iNOS enzyme expression and increasing antioxidant enzyme levels and anti-inflammatory efficacy. We believe that dour findings indicate that Cur may be used as an efficient and reliable disease preventing and therapeutic agent.

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REFERENCES

1. Faydaoglu E, Surucuoglu, MS. Geçişten günümüze tıbbi ve aromatik bitkilerin kullanılabileceği ekonomik öne
8. Jain SK, Rains J, Jones K. Effect of curcumin on protein glycosylation, lipid peroxidation, and oxygen radical gener
ity of curcumin-loaded solid lipid nanoparticles in IL-1b transgenic mice subjected to the lipopolysaccharide-induced sepsis. Biomaterials 2015; (53): 475-483.
15. Sagy M, Al-Qaqaa Y, Kim P. Definitions and pathophysi
tory effect of curcumin in an experimental model of sepsis is mediated by up-regulation of peroxisome prolifera
22. Davery A, Agrawal SK. Curcumin alleviates oxidative stress and mitochondrial dysfunction in astrocytes. Neuro
science 2016; (333): 92-103.
24. Güzel A, Kanter M, Güzel A, Yücel AF, Erboğa M. Protective effect of curcumin on acute lung injury induced by in
cumin against oxidative stress parameters and DNA dam
age in the livers and kidneys of rats with biliary obstruc


