ABSTRACT

Aim: This study was designed to evaluate the effects of curcumin supplementation on different biochemical parameters in thioacetamide induced cirrhotic rats. For this purpose 24 male Albino wistar rats were divided into four groups (n=6). Group I, remained healthy control rats, Group II, received thioacetamide (at a dose of 200mg/kg b.w, twice a week i.p, for 12 weeks) in first phase and saline in second phase, Group III, received thioacetamide (200mg/kg b.w, i.p for 12 weeks, twice a week) in first phase and curcumin (50 mg/kg b.w/day, i.p for 12 weeks ) in second phase and Group IV, received curcumin (50 mg/kg b.w/day, i.p for 12 weeks) in first phase and saline in second phase. Main methods: Biochemical analysis was evaluated by total and direct bilirubin (Sherlock, 1951), plasma and intraerythrocyte sodium and potassium (Tabssum et al., 1996), liver specific enzymes (Retiman and Franhel, 1957), and antioxidant enzymes [SOD (Kono et al., 1978), Catalase (Sinha et al., 1979) ,Glutathione reductase (Calberg and Mannervik, 1985) and MDA (Okhawa et al., 1979)]. Key findings: Marked increase in total and direct bilirubin and ALT activity was the indicative markers of liver cirrhosis while reduced antioxidant activity (SOD and GSH) and increased MDA and Catalase levels and disturbed electrolyte homeostasis were observed in cirrhotic group. Curcumin supplementation markedly reduced total bilirubin and ALT activity and restored the antioxidant enzymes (SOD and GSH) and MDA and catalase activity and electrolyte homeostasis. Significance: These results indicate that curcumin successively attenuates the thioacetamide induced liver cirrhosis.
KEYWORDS: Liver cirrhosis, Curcumin, thioacetamide, liver enzymes, Superoxide dismutase, GSH, Catalase, Malondialdehyde. Plasma sodium and potassium, Intraerythrocyte sodium and potassium

INTRODUCTION

Curcumin, obtained from a plant of ginger family, rhizome of turmeric (Curcuma longa), is a yellow coloring principal ingredient of curry powder. Curcumin (diferuloylmethane) is the major active ingredient of turmeric and has been used for years in indo-chinese medicines for the treatment of wound healing, skin problems, digestive disorders and liver diseases (Grant and Schneider., 2000). Curcumin possesses anti-inflammatory, antioxidant, anticarcinogenic, antimitogenic and nuclear factor–κβ inhibiting properties (Araujo and Leon. 2001) (Surh et al., 2001). Curcumin activates HSC and in this way inhibits the synthesis of collagen type I ( Kang et al.,2002) and used in steatohepatitis rodent models for attenuating inflammation and hepatic fibrosis (Leclercq et al., 2004). Okada reported prevention of lipidperoxidation by curcumin and Rukkumani reported amelioration of oxidative stress (Okada et al., 2001) (Rukkamani et al., 2004). Iqbal et al., 2003 reported the property of curcumin to enhance the expression of enzymes involved in xenobiotic detoxification reactions in the kidney and liver of mice such as glutathione reductase, glutathione S-transferase and NADPH (Iqbal et al., 2003).

Curcumin is also known to upregulate heme-oxygenase I, an enzyme involves in stress response, in endothelia cells, astrocytes and in renal epithelia cells (Hill-Kapturczak et al., 2002). Activities of many kinases are down regulated by curcumin. Curcumin inhibits many transcription factors such as activator and signal transducers of transcription proteins, β-Catenin, activated receptor-γ (Shishodia et al., 2007). Administration of curcumin increases the activities of antioxidant enzymes and thus decreases the lipidperoxidation in rats with iron induced hepatic toxicity. It also inhibits formation of hydroxyl radicals by inhibiting the oxidation of iron (Fe^{2+}) by H_{2}O_{2}. They reported a marked reduction in iron induced lipid peroxidation in wistar rats by the administration of 300mg/Kg of curcumin for 10 days (Reedy and Lokesh., 1994). Rajakrishnan et al., 1999 reported the reversal of biochemical and histopathological changes in the kidney, liver and brain in ethanol intoxicated rats (Rajakrishnan et al., 1999).

Curcumin exerts protective effects against liver damage induced by aflalotoxins, erythromycin estolate, CCL_4, ethanol, iron overdose and thioacetamide (Yadira and Pablo. 2004). Curcumin
is known to have beneficial systemic and hepatic effects as it has safe ingestion and sufficient bioavailability in humans (Sharma et al., 2004). Thus, the present study is designed to examine the hepatoprotective role of curcumin in thioacetamide induced liver cirrhosis in experimental rats.

**MATERIALS AND METHODS**

24 male Albino Wistar rats weighing 200-250gm were purchased from the animal house of ICCCBS (International center for chemical and biological sciences, Karachi, Pakistan) for the study. Animals were acclimatized to the laboratory conditions before the start of experiment and caged in a quiet temperature controlled animal room (23±4°C). Rats had free access to water and standard rat diet.

**Ethical guidelines**

The experiments were conducted with ethical guidelines of institutional ERB (Ethical Review Board) and internationally accepted principles for laboratory use and care in animal research (Health research extension Act of 1985).

**Study design**

The rats were randomly divided into four groups, each of six rats. The duration of the study was 24 weeks, divided into two phases. Thioacetamide and curcumin were administered in either phase. Thioacetamide and curcumin were purchased from Merck and the other chemicals used in present study were purchased from BDH laboratory supplies, Fisher Scientific UK limited and Fluka AG.

- **Group I:** the control (remained untreated).
- **Group II:** TAA-treated
- **Group III:** TAA+ Curcumin treated
- **Group IV:** Curcumin treated

In Phase I, TAA-treated and TAA + Curcumin groups received TAA, dissolved in 0.9% NaCl and were injected intraperitoneally at a dosage of 200mg/kg b.w, twice a week for 12 weeks. Curcumin group received curcumin (orally at a dosage of 50 mg/kg b.w/ day for 12 weeks).

In phase II, TAA-treated group received saline, TAA + curcumin group received curcumin (orally at a dosage of 50mg/kg b.w/ day starting from 13th week for 12 weeks) after TAA in first phase. Curcumin group received saline in second phase. At the end of experimental period, rats from all the groups were decapitated. The blood was collected from the neck
wound in the lithium heparin coated tubes and centrifuged to collect plasma. Liver was excised, trimmed of connective tissues, rinsed with saline to eliminate blood contamination, dried by blotting with filter paper and weighed. The tissues then kept in freezer at –70°C until analysis.

**Estimation of ALT and total and direct bilirubin**
Plasma ALT (Retiman and Franhel, 1957) and total and direct bilirubin (Sherlock, 1951) were analyzed using commercially prepared reagent kits from Randox.

**Preparation of post mitochondrial supernatant**
Liver homogenate was prepared by taking 1g of liver tissue in 10ml of 5mM potassium phosphate buffer (pH 7.8) by using a homogenizer. The homogenates were centrifuged at 800g for five minutes at 4°C to separate the nuclear debris. The supernatant so obtained was centrifuged at 10,500g for 20 minutes at 4°C to get post mitochondrial supernatant which was used to assay SOD, Catalase, MDA, and glutathione reductase activity.

**Estimation of thiobarbituric acid substances**
The malonyldialdehyde (MDA) content, a measure of lipid peroxidation, was assayed in the form of thio-barbituric acid reacting substances (TBARS) by the lipid peroxidation method (Okhawa et al., 1979). Briefly, the reaction mixture consisted of 0.2 ml of 8.1% sodium dodecyle sulphate, 1.5 ml of 20% acetic acid solution adjusted to pH 3.5 with sodium hydroxide and 1.5 ml of 0.8% aqueous solution of thiobarbituric acid was added to 0.2 ml of 10%(w/v) of PMS. The mixture was brought up to 4.0 ml with distilled water and heated at 95°C for 60 minutes. After cooling with tap water, 1.0 ml distilled water and 5.0 ml of the mixture of n-butanol and pyridine (15:1 v/v) was added and centrifuged. The organic layer was taken out and its absorbance was measured at 532 nm and compared with those obtained from MDA standards. The concentration values were calculated from absorption measurements as standard absorption.

**Estimation of catalase**
Catalase activity was assayed by the method of Sinha (Sinha et al., 1979). Briefly, the assay mixture was consisted of 1.96 ml phosphate buffer (0.01M,pH 7.0), 1.0 ml hydrogen peroxide (0.2 M) and 0.04 ml PMS (10%w/v) in a final volume of 3.0 ml. 2 ml dichromate acetic acid reagent was added in 1 ml of reaction mixture, boiled for 10 minutes, cooled. Changes in absorbance were recorded at 570 nm.
Estimation of SOD
Superoxide dismutase levels in the cell free supernatant were measured by the method of (Kono et al., 1978). Briefly 1.3ml of solution A (0.1 m EDTA containing 50 mM Na₂CO₃, pH 10.0), 0.5 ml of solution B (90µmNBTnitro blue tetra zolium dye) and 0.1 ml of solution C (0.6%Triton X-100 in solution A), 0.1 ml of solution D (20 mM Hydroxyl amine hydrochloride, pH 6.0) were mixed and the rate of NBT reduction was recorded for one minute at 560 nm. 0.1 ml of the supernatant was added to the test cuvette as well as reference cuvette, which do not contain solution D. Finally, the percentage inhibition in the rate of reduction of NBT was recorded as described above. One enzyme unit was expressed as inverse of the amount of protein (mg) require in one minute.

Estimations of glutathione reductase
GSH activity was determined by continuous spectrophotometric rate determination (Calberg and Mannervik, 1985). In a clean glass test tube, 0.3 mL of 10% BSA, 1.5mL of 50mM potassium phosphate buffer (pH 7.6), 0.35mL of 0.8mM β-NADPH and 0.1mL of 30mM oxidized glutathione was taken and finally added 0.1mL of homogenate, mixed well by inversion. Absorbance was recorded at 340nm at 25°C for 5 minutes on kinetic spectrophotometer PRIM 500 (Germany) with automatic aspiration and thermostat. The activity was calculated using the molar coefficient for NADPH of 6.22 µmol cm⁻¹ and expressed in unit/gram tissue.

Estimation of intraerythrocyte sodium and potassium
Heparinized blood was centrifuged and plasma was separated. Buffy coat was aspirated and discarded. Erythrocytes were washed three times at room temperature by suspension in the magnesium chloride( 112mmol/L), centrifugation at 450g at 4°C for 5 minutes and aspiration of the supernatant was done(Fortes and Starkey, 1977). Final supernatant was retained for the estimation of intraerythrocyte sodium and potassium concentration. Neither electrolyte zwas detectable in the final wash. Washed erythrocytes were then used for the estimation of intraerythrocytes sodium and potassium.

RESULTS
Effect of thioacetamide and Curcumin treatment on body weight in control and treated rats
Decreased body weight was observed after chronic administration of TAA in TAA and TAA+curcumin groups. Rats of TAA + curcumin group regained their body weight after
curcumin treatment in second phase. Rats of TAA group continuously lost their body weights. Rats of curcumin group and control group gained their body weights throughout the treatment (fig1).

Figure 1. Effect of thioacetamide and Curcumin treatment on body weight in control and treated rats

Effect of thioacetamide and Curcumin treatment on liver weight and liver to body weight ratio in control and treated rats

Increased liver weight and liver-body weight ratio was observed in TAA group after 12 week administration of TAA as Compare to control (6.33±1.31 P<0.01) (0.028±0.003 P<0.01) (Table-1) whereas reduction in the liver weight and liver to body weight ratio was observed in TAA + curcumin group as compare to control (5.534±0.45 P<0.01) (0.03±0.004 P<0.01) respectively. Curcumin treated group had reduced liver weight and liver to body weight ratio (5.15±0.54 P<0.01) (0.026±0.002 P<0.05).

Table.1. Effect of thioacetamide and curcumin treatment on liver weight, liver to body weight ratio in control, thioacetamide-treated, thioacetamide+curcumin-treated and curcumin- treated rats

<table>
<thead>
<tr>
<th>Groups</th>
<th>Liver Weights</th>
<th>Relative Liver Weights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>6.33±1.31*</td>
<td>0.028±0.003*</td>
</tr>
<tr>
<td>TAA-treated</td>
<td>6.82±0.71*</td>
<td>0.39±0.002*</td>
</tr>
<tr>
<td>TAA+curcumin</td>
<td>5.534±0.45*</td>
<td>0.03±0.004*</td>
</tr>
<tr>
<td>curcumin-treated</td>
<td>5.15±0.54*</td>
<td>0.026±0.002**</td>
</tr>
</tbody>
</table>

n=6

Values are mean ± SD. Significant difference among control, TAA-treated, TAA+curcumin and curcumin treated groups by t-test **P<0.05, *P<0.01.
Effect of thioacetamide and Curcumin treatment on plasma total and direct bilirubin and plasma ALT activity in control and treated rats

Table 2 shows a marked increase in total bilirubin level in TAA-treated group as compare to control (3.6±0.1P<0.01) whereas, in TAA + curcumin treated group, curcumin supplementation brought those increased levels to the normal concentrations as compare to control (0.72±0.01P<0.01). Curcumin treated group showed normal range of total bilirubin as compare to control (0.61±0.03 P<0.05). Increased levels of direct bilirubin was shown by TAA-treated group as compare to control (3.8±0.03 P<0.01) whereas curcumin supplementation in TAA + curcumin group brought those higher levels to normal levels as compare to control (1.40±0.01 P<0.05). Alone curcumin had no effect on direct bilirubin level (table 2).

Plasma alanine aminotransferase level was markedly increased in TAA-treated group as compare to control (960.3±30.19 P<0.01). Alanineaminotransferase level was decreased in TAA + curcumin group as compare to control (280±11.6 P<0.01). Alone curcumin had no effect on plasma ALT level as compare to control (210±9.6 P<0.01) (table 2).

Table 2. Effect of thioacetamide and curcumin treatment on total and direct bilirubin and ALT activity in control, thioacetamide-treated, thioacetamide+curcumin-treated and curcumin-treated rats.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>TAA-treated</th>
<th>TAA+curcumin treated</th>
<th>curcumin-treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bilirubin (unit/L)</td>
<td>0.60±0.04*</td>
<td>3.6±0.2*</td>
<td>0.75±0.01*</td>
<td>0.61±0.03**</td>
</tr>
<tr>
<td>Direct bilirubin (unit/L)</td>
<td>1.35±0.03*</td>
<td>3.8±0.03*</td>
<td>1.40±0.01**</td>
<td>1.34±0.01**</td>
</tr>
<tr>
<td>Alanin-amino transferase(unit/L)</td>
<td>210±9.6*</td>
<td>960.3±30.19*</td>
<td>280±11.6*</td>
<td>210±8.5*</td>
</tr>
</tbody>
</table>

n=6

Values are mean ± SD. Significant difference among control, TAA-treated ,TAA+curcumin treated and curcumin treated groups by t-test **P<0.05, *P<0.01.

Effect of thioacetamide and curcumin treatment on hepatic concentration of Glutathione reductase in control and treated rats:

Hepatic concentration of glutathione reductase was significantly reduced in TAA-treated
group as compare to control (0.052±0.001 P<0.01). TAA + curcumin group, after curcumin supplementation, showed increased level of glutathione reductase as compare to control (0.80±0.01 P<0.01) (table 3). Glutathione reductase was almost normal in curcumin group as compare to control (0.89±0.02 P<0.01).

Table 3: Effects of thioacetamide and curcumin treatment on hepatic concentration of Glutathione Reductase, superoxide dismutase, Malondialdehyde and catalase in control, thioacetamide, thioacetamide+curcumin and curcumin-treated rats:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>TAA-treated</th>
<th>TAA+curcumin treated</th>
<th>curcumin-treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glutathione Reductase (unit/gm of tissue)</td>
<td>0.91±0.02</td>
<td>0.052±0.01*</td>
<td>0.80±0.01*</td>
<td>0.89±0.02*</td>
</tr>
<tr>
<td>Superoxide dismutase unit/gm of tissue.</td>
<td>890±2.0</td>
<td>500±2.3*</td>
<td>760±4.5*</td>
<td>890±3.2*</td>
</tr>
<tr>
<td>Malondialdehyde nmol/gm of tissue.</td>
<td>58.1±3.4</td>
<td>130.2±2.1*</td>
<td>60±1.5*</td>
<td>58.4±1.5*</td>
</tr>
<tr>
<td>Catalase nmol/gm of tissue.</td>
<td>7.2±0.01</td>
<td>42.3±0.01*</td>
<td>7.5±0.16*</td>
<td>7.2±0.01*</td>
</tr>
</tbody>
</table>

n=6
Values are mean ± SD. Significant difference among control, TAA-treated, TAA+curcumin treated and curcumin-treated groups by student’s t-test **P<0.05, *P<0.01.

Effect of thioacetamide and curcumin treatment on hepatic concentration of MDA in control and treated rats
Level of MDA was markedly increased in TAA group as compare to control (130±2.1 P<0.01). Curcumin administration in TAA + curcumin group decreased the concentration of MDA as compare to control (60.1±1.5 P<0.01) while rats of curcumin group showed normal range of MDA level as compare to control (58.4±1.5 P<0.01) (table-3).

Effect of thioacetamide and curcumin treatment on hepatic concentration of superoxide dismutase in control and treated rats
Table-3 showed a significant decrease in SOD activity in TAA group as compare to control (500±2.3 P<0.01). TAA + curcumin group, after curcumin supplementation, showed a significant reduction in SOD activity (760±4.5 P<0.01) as compare to control. SOD activity was almost normal in curcumin group (890±3.2 P<0.01) as compare to control.
Effect of thioacetamide and curcumin treatment on hepatic concentration of catalase in control and treated rats

Concentration of catalase was significantly increased in TAA group (42.3±0.01 P<0.01) as compare to control. Administration of curcumin in second phase in TAA + curcumin group brought these higher levels to normal limits (7.5±0.16 P<0.01) as compare to control. Activity of catalase was normal (7.2±0.01 P<0.01) in curcumin group as compare to control (table 3).

Effect of thioacetamide and curcumin treatment on intra-erythrocytes sodium and potassium in control and treated rats

Decreased levels of intraerythrocyte sodium was observed in TAA group (2.9±0.01 P<0.01), whereas curcumin supplementation significantly increased intraerythrocyte sodium in TAA+curcumin group (3.5±0.01 P<0.01) as compare to control. Curcumin group showed almost normal level of intraerythrocyte sodium as compare to control (3.68±0.03 P<0.01) (table 4).

Decreased intraerythrocyte potassium level was observed in TAA group as compare to control (42.33±1.5 P<0.01). Whereas increased intra-erythrocyte potassium level was observed in TAA+curcumin group (50.2±2.3 P<0.01) as compare to control. Alone curcumin supplementation had no effect on intraerythrocyte potassium (53.37±3.1 P<0.05) (table 4).

Table-4: Effect of thioacetamide and curcumin treatment on plasma and intraerythrocyte sodium and potassium in control, thioacetamide-treated, thioacetamide+curcumin-treated and curcumin-treated treated rats

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>TAA-treated</th>
<th>TAA+curcumin</th>
<th>curcumin-treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraerythrocyte Na⁺ mmol/L</td>
<td>3.78±0.06</td>
<td>2.9±0.01*</td>
<td>3.5±0.01*</td>
<td>3.68±0.03*</td>
</tr>
<tr>
<td>Intraerythrocyte K⁺ mmol/L</td>
<td>53.28±1.1</td>
<td>42.33±1.5*</td>
<td>50.2±2.3*</td>
<td>53.37±3.1**</td>
</tr>
<tr>
<td>Plasma Na⁺mmol/L</td>
<td>140.8±1.2</td>
<td>122±1.0*</td>
<td>103±0.6*</td>
<td>105±0.8*</td>
</tr>
<tr>
<td>Plasma K⁺mmol/L</td>
<td>5.16±0.3</td>
<td>4.3±0.2*</td>
<td>5.72±0.1*</td>
<td>5.78±0.24*</td>
</tr>
</tbody>
</table>

n=6

Values are mean ± SD. Significant difference among control, thioacetamide, thioacetamide and curcumin and curcumin treated groups by t-test **P<0.05, *P<0.01
Effect of thioacetamide and curcumin treatment on plasma sodium and potassium in control and treated rats

Plasma sodium was decreased in TAA group (122.3±1.0 P<0.01) as compare to control whereas it was also decreased in TAA + curcumin group (103±0.6 P<0.01). Curcumin group also showed a significant reduction in plasma sodium (105±0.8 P<0.01) (table 4). Table 4 Showed decreased plasma potassium in TAA group (4.3±0.2 P<0.01) as compare to control whereas curcumin treatment in TAA + curcumin group significantly increased plasma potassium as compare to control (5.7±0.1 P<0.01). Curcumin group showed slightly increased concentration of plasma potassium (5.78±0.24 P<0.01) as compare to control.

Histology of liver in control and treated rats

After 12 week administration of thioacetamide in TAA-treated rats, histological examination showed last stage of liver cirrhosis, amount of fibrosis was (++++++) maximum. Supplementation of curcumin in TAA+curcumin group reduces the amount of fibrous tissue and the stage of nodule formation was (00) minimum (Figure 2)

Table 5. Histological examination of liver of thioacetamide and curcumin treatment on control, thioacetamide-treated, thioacetamide+curcumin treated and curcumin treated rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Amount of fibrosis</th>
<th>Disorganization of liver architecture</th>
<th>Stage of nodule formation and disorientation of vascular architecture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Thioacetamide</td>
<td>+++++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Thioacetamide+curcumin</td>
<td>++</td>
<td>+</td>
<td>00</td>
</tr>
</tbody>
</table>
DISCUSSION

Thioacetamide, by the action of hepatic cytochromes, is converted into effective hepatotoxins, although it is not toxic itself (Hunter et al., 1977). Such effective hepatotoxins generate strongly reactive compounds which become the cause of liver injury (Bruck et al., 2004). Fulminant hepatic failure and early death are resulted from high dose administration of thioacetamide (Bruck et al., 2002). Whereas liver cirrhosis resulted from a long term lower dose administration of thioacetamide (Pines et al., 1997). In our study, chronic administration of thioacetamide in a dose of 200mg/Kg b.w, twice a week resulted in the induction of definite cirrhotic changes in albino Wistar rats which was indicated by the increased levels of total bilirubin and ALT activity (table 2), showing the toxic effects of thioacetamide on bile ductular system (Yamada and Fausto, 1998). Our results are in agreement with the studies of Torres (Torres, 1996) and Strugill (Strugill and Lambert, 1997).
These increased activities can be attributed to the discharge of these enzymes from injured hepatic cells into blood streams due to altered permeability of liver membrane (Shohda et al., 2009). Supplementation with curcumin to thioacetamide treated rats resulted in normalization of level of bilirubin and ALT activity (table 2). Thioacetamide administration in animals resulted in induction of mechanisms which leads to the development of fulminant hepatic failure such as increased generation of reactive oxygen species and lipidperoxides by the liver (Sun et al., 2000). NF-κβ stimulation and the resultant formation of proinflammatory molecules (Rahman et al., 2003). Bruck et al reported development of liver cirrhosis in rats by the 12 weeks biweekly, i.p administration of thioacetamide indicated by gross macroscopic appearances, histopathology of liver, content of hepatic hydroxyproline and an increase in spleen weight, the activation of hepatic stellate cells was shown by the liver which was determined by enhanced expression of α-smooth muscle actin and expression of type I collagen gene (Bruck et al., 1977). In present study, the elevation of ALT and bilirubin was coupled with a significant increase in liver oxidative stress as indicated by a marked elevation in TBARS levels and a reduction in GSH and SOD levels in liver in thioacetamide treated rats. Antioxidant defense mechanism is affected by the reactive oxygen species (superoxide anion, H\textsubscript{2}O\textsubscript{2}, hydroxyl radical) generated in the process of lipidperoxidation, initiated by the administration of hepatotoxin which results in the reduction of reduced glutathione concentration and a decrease in the activity of SOD (Srilaxmi et al.,2010). Curcumin acts as a potent scavenger for a number of reactive oxygen species (Maheshwari et al., 2006). The mechanism of antioxidant action of curcumin is because of its specific conjugated structure, comprises of two methylated phenols and an enol form of β-diketone. The ability of curcumin to act as a chain breaking antioxidant and trapping of free radicals is due to this structure (Masuda et al., 2001). In present study, the antioxidant role of curcumin was confirmed by the reversal of the level of SOD, MDA, GSH and Catalase (table 3). Our results are in agreement with Oetari et al., 1996 who reported role of curcumin in reducing oxidative stress by preventing hepatic lipoperoxides formation which was indicated by decreased levels of TBARS in rats acutely intoxicated with thioacetamide (Oetari et al., 1996). Curcumin has the ability to scavenge free radicals because of which it prevents ROS formation and increases endogenous antioxidant activity. Many antioxidant enzymes of liver such as catalase, SOD and glutathione system are induced or activated by curcumin (Joe et al., 2004; Sharma et al., 2001: Iqbal et al., 2003). Bruck et al., 2007 found that anti-inflammatory and antioxidant properties of curcumin are involved in the protection of liver cirrhosis induced by chronic administration of thioacetamide (Bruck et al., 2007). Haim Shapiro reported that co-
administration of curcumin in a dose of 300mg/Kg/day for 12 weeks to thioacetamide treated rats appeared in a marked improvement of all the changes found in cirrhotic group. In present study, curcumin supplementation to thioacetamide treated rats resulted in the reversal of altered levels of bilirubin and ALT activity, in the level of antioxidant enzymes, in the level of MDA, in electrolyte homeostasis and in body weight indicates that curcumin successfully attenuates liver cirrhosis in rats.

REFERENCES


Comparative effects of curcumin on alcohol and PUFA induced oxidative stress.
J.Pharm.Sci, 7. 274-283


Molecular mechanisms underlying chemopreventive activities of anti-inflammatory
phytochemicals; down regulation of COX-2 and INOS through suppression of NF-Kβ
activation. Mutat.Res; 24

hydroperoxide, vitamin C and vitamin E during apoptosis and necrosis caused by
thioacetamide in rat liver. Biochem Biophys Acta. 1500:181-5.

nucleotides on liver structural recovery and hepatocyte binuclearity in cirrhosis induced

35. Yadira Rivera-Espinoza and Pablo Muriel.(2009). Pharmacological actions of curcumin in
liver diseases or damage. Liver international. 1478-3223.

36. Yamada and N.fausto(1998). Deficient liver regeneration after carbon tetrachloride in
mice lacking type 1 but not type 2 tumor necrosis factor receptor, American Journal of
pathology. 152:1577-1589.