# THE LONG TERM EFFECTS OF SOME COMMON VOLATILE SUBSTANCES (ACETONE, BENZENE AND KOLLA) ON BRAIN, LIVER AND KIDNEY: A STUDY ON ALBINO RATS AND HUMAN

BY

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## ABSTRACT

*This work was done to study the chronic toxicity of some common volatile substances on kidney, liver, and brain. The present study was divided into experimental and human parts. In the experimental part, 120 adult albino rats of both sexes weighing 200 ± 20 gm were divided into four groups each contained 30 rats: groups I, II and III received chronic doses of acetone,benzene, and kolla (its major component is toluene) respectively, and group IV was control group. After twelve weeks urea, creatinine, SGPT, and SGOT were done for control group and twenty rats of the other three groups, then these rats were sacrificed and histopathological studies were done for kidneys, livers, and brains.The other ten rats of the first three groups were left without any substance inhalation, and after two weeks the biochemical and histopathological studies were done for these withdrawal groups. The human study was done on sixty volunteers grouped into four groups, each included 15 persons: acetone group (from furniture varnishes workers), benzene group (from gasoline stations workers), kolla group (from kolla addicts), and control group . Biochemical studies were done for all volunteers. The results revealed that, rats experienced hyperactivity then became calm in all groups. Biochemical analysis revealed: significant increase in urea and creatinine in kolla group and significant increase in SGPT and SGOT in acetone, benzene and kolla groups. After withdrawal, the results revealed significant decrease in urea and creatinine in kolla group, and significant decrease in SGPT and SGOT in benzene and kolla groups, but still high than normal in acetone. Abnormal histopathological findings were shown in brain in the three groups which partially improved after withdrawal. Abnormal histopathological findings of the kidney specimens were recorded but improved after withdrawal .Also abnormal histopatholgical findings of the liver specimens were recorded in the three groups, which partially improved after withdrawal. As regards human part, the persons were complaining from drowsiness and mild anxiety in acetone group and chronic cough in benzene group. There were slurred speech, lack of attention, talkativeness, and euphoria in kolla addicts. Biochemical analysis revealed: significant increase in urea, creatinine, SGPT and SGOT in kolla group, and insignificant difference in urea and creatinine and insignificant increase in SGPT and SGOT in acetone and benzene groups. It is concluded that, these substances have dangerous effects on brain, kidney and liver and*

*it is recommended to limit the wide spread exposure of persons to these substances at work and persons who are addicted to these substances and doing periodic investigations for these persons to detect any early affection to these organs.*

## *INTRODUCTION*

The inhalation of volatile substances first emerged as a form of substance abuse in the early 1960s with the inhalation of model aeroplane glues. The practice has diversified to include the use of adhesive cements, aerosol paints, lacquer thinners, typewriter correction fluids, and fuels. These products contain a number of volatile substances including toluene, n-hexane, methyl ketones, chlorohydrocarbons, and benzene (Crowe et al., 2000).

Solvent abuse is the deliberate inhalation of volatile organic compounds to produce alterations in the conscious state and perception for recreational purposes. Solvent inhalation can rapidly produce euphoria, delusions, and sedation as well as visual and auditory hallucinations. Solvents can be addicting and often abused in combination with other drugs. Various solvents are present in a wide variety of household and commercial products including glue, model cement, paint thinner and stripper, aerosols, typewriter correction fluid, dry cleaning fluid, and gasoline. These products are relatively inexpensive and readily available to children and adolescents (Marelich, 1997).

Acetone belongs to ketones which are group of compounds in which 2 aliphatic or aromatic groups are joined by a carbon that is double-bonded to an oxygen molecule. Acetone is the best example of this group which could be obtained easily and legally in the form of nail polish remover and other solvents for varnishes, gums and adhesives (Gummin and Hryhorozuk, 2002).

Benzene is found in petroleum products such as gasoline, and diesel fuels. The chronic effects of benzene exposure depend on the level of exposure, and the symptoms are typically vague such as loss of appetite, diarrhea, pallor, pain in bones, fever, and hemorrhage. The most important toxic effect of benzene is hematopoietic toxicity as it can lead to bone marrow damage which may be manifested as anemia, leucopenia, thrombocytopenia, or a combination of these (Philip, 1998).

The aim of this work was to study the chronic toxicity of some common volatile substances (acetone, benzene, and kolla) on kidney, liver, and brain biochemically and histopathologically.

## *MATERIAL AND METHODS*

This work was done in Forensic Medicine and Toxicology Department, Faculty

of Medicine, El-Minia University.This study was divided into two parts, human part and experimental part.

**I- Experimental Part :**

**Material :**

***A- Volatile Substances:***

Acetone and Benzene bottles (each containing 1 liter and its concentration is 99%) were obtained from El-Nasr Company for chemicals. Kolla is composed mainly of toluene, and other solvents in small fractions. The boxes were obtained from El-Masria Company for adhesive materials and chemicals.

***B- Animals:***

**Species:**

One hundred and twenty adult albino rats of both sexes were employed in this experimental study. They were obtained from El-Minia animal house and their average weight were 200±20 gm. Acclimatization period was two weeks for all groups to exclude any possible stress effect secondary to sudden environmental modification as recommended by Poole and Lesile (1989). Animals were housed in animal cages made of galvanized iron containing 15 animals per cage (males and females were separated to avoid matting). Food and water were equally offered twice daily to all groups of rats.

**Grouping of animals:**

They were grouped into four groups each 30 rats and exposed daily to inhalation of the chronic toxic dose of studied substances.

**Group I :** exposed to acetone inhalation in a dose of 2500 parts per million (ppm) for each rat. each 1ppm=2.374 mg /$m^3$, so the toxic dose was 2500x2.374=5935 mg/$m^3$= 5.935g/$m^3$.Acetone density = 0.792g/ml, so the toxic dose for each rat was 5.935÷0.972 = 7.5ml, Dietz et al. (1991).

**Group II :** exposed to benzene inhalation in a dose of 100 ppm for each rat each 1ppm=3.25 mg /$m^3$, so the toxic dose was 100x3.25=325 mg/$m^3$= 0.325 g/$m^3$. Benzene density = 0.894 g/ml, so the toxic dose for each rat was0.325 ÷ 0.894 = 0.4ml, Nayeli et al. (2003).

**Group III :** exposed to kolla inhalation in a dose of 100 ppm for each rat each 1ppm = 3.75 mg /$m^3$, so the toxic dose was 100x3.75 = 375 mg/$m^3$= 0.375 g/$m^3$. Kolla density = 0.866 g/ml, so the toxic dose for each rat was 0.375÷0.866 = 0.4.ml, Raymond et al. (1994).

**Group IV:** a control group which live in completely normal conditions without any substance exposure.

The control group and twenty rats of each group of the other groups were sacrificed by decapitation, but the other ten rats were left without any substance exposure for two weeks and

they considered the withdrawal groups (Iw, IIw and IIIw).

**Substance inhalation:**

Inhalation was done in a special inhalation box.It was 0.32 cm thick aluminium sheets with outside dimensions of 61 cm long by 32 cm high by 34 cm deep, two stainless steel open mesh cages, separated by a barrier can be stacked within the central portion of the box. The duration of inhalation was: 5.5 minutes for acetone, 1.5 minutes for benzene, 3-5 minutes for kolla for each rat.

**II- HUMAN PART:**

*(A) Grouping:*

Sixty male persons aging between 18-46 years shared in this study. They were divided into four groups each 15 persons. Group I (Acetone group): persons were chosen from furniture varnishes workshops as they were exposed daily to acetone for more than 18 years. Group II (Benzene group): persons were chosen from gasoline stations, as they were exposed daily to benzene for more than 13 years. Group III (Kolla group): persons were kolla addicts for more than 6 years. Group IV (healthy control group) as they were not exposed to any volatile substances, they were volunteers. All sixty persons had no history of any neuropsychatric or organic disease. We got an informed written consent from all of them.

*(B) History:*

Persons of acetone group were asked about drowsiness, irritability and short memory deficit. Persons of benzene group were asked about cough, manifestations of anemia, petechia, headache, fatigue and anorexia and Kolla (Toluene) group was examined for any speech problems, lack of attention, talkativeness, euphoria, ataxia, spasticity, dysarthria, and dementia.

**METHODS:**

*I- Biochemical studies:*

After twelve weeks of inhalation of these substances, blood samples of about 5 cms were obtained from the venous plexus which localized in the orbit behind the eye ball using capillary pipette from control group and twenty rats of the other groups, then from groups Iw, IIw and IIIw, after two weeks of the inhalation withdrawal. In human, venous blood samples of about 5 cm were obtained from brachial veins. Biochemical analysis were done for all groups.

Blood urea was done according to Pollon and Crouch (1977). Serum creatinine according to Fabiny and Ertingshausen, (1971) and SGOT and SGPT were done according to Reitmans and Frankel ( 1957).

*II- Histopathological study:*

The control group and twenty rats of each group were sacrificed after twelve

weeks of substances inhalation, and then the remaining rats were sacrificed after two weeks from the inhalation withdrawal .All rats were sacrificed by decapitation. After sacrification, kidneys, livers, and brains were carefully dissected from each rat and were prepared for histopathological examination according to Carleton et al. (1980).

**III- Statistical analysis:**

Data were expressed as mean (M) ± standard deviation (SD). For comparison in the same group the paired student's (t) test was employed. For comparison between two groups, probabilities (p) were employed. Statistical significance was assumed when (p) was less than or equal 0.05.

## *RESULTS*

**Physical characters of the rats:**

*Acetone group :* the animals experienced anxiety within five minutes after acetone inhalation as shown by hyperactivity, then the rate of respiration was decreased and they experienced severe weakness as they became completely calm after 3-4 minutes of inhalation.

*Benzene group :* the rate of respiration of the rats was increased and the animals showed imbalance with mild anxiety within one and half minutes of inhalation, then they developed severe weakness and tremors.

*Kolla group :* the rats showed severe anxiety and increased rate of respiration within three minutes after kolla inhalation, then, the rate of respiration was decreased and they developed tremors and became calm after one minute. During the day, there were episodes of anxiety among the rats and they hurt themselves and others (Fig. 1). During the inhalation weeks, two swellings were appeared in one rat: one on the side of the neck and the other on the front of left fore limb (Fig. 2), but subsided after withdrawal. Hair fall was developed in most rats (Fig. 3).

*After withdrawal :* the rats of all groups experienced episodes of anxiety and intensive craving to smell and then these signs subsided gradually.

**Results of the biochemical study:**

The results of blood urea, serum creatinine, SGPT and SGOT concentrations are presented in tables (1-3). Acetone (I) and benzene (II) groups were within the normal average in urea and creatinine concentrations with no significant difference in comparison with the control group and consequently showed no significant differences after withdrawal.

SGPT and SGOT concentrations of acetone and benzene groups were signifi-

cantly higher than the control group, but in withdrawal groups they showed significant decrease in comparison with acetone and benzene groups at the end of the inhalation period.

Kolla (III) group (toluene) showed significant increase in blood urea, serum creatinine, SGPT and SGOT concentrations in comparison with the control group. As regards the withdrawal group of olla (III w) urea, creatinine, SGPT and SGOT concentrations showed significant decrease in comparison with kolla group at the end of the inhalation period.

**Histopathological study:**

Light microscopic examination (LME) of the brain sections of the control group showed normal histological picture, they composed of grey matter and white matter and both matters contained neurological cells and nerve cell processes (Fig. 4). In acetone group, it showed oedema in 50% of rats (Fig. 5), necrosis in 40% of rats (Fig. 6) while acetone withdrawal group showed necrosis in 20% of rats. In benzene group, it showed haemorrhage in 40% of rats (Fig. 7), cellular atypia in 25 % of rats (Fig. 8) and both persisted in 10% of rats after withdrawal. In Kolla group, it showed gliosis in 25% of rats (Fig.9), necrosis and gliosis in 50% of rats while withdrawal of kolla group showed necrosis in 20% of rats, gliosis and necrosis in 30% of rats.

LME of kidney sections of control group showed normal histological picture, they consisted of two main regions, an outer cortex and inner medulla. The renal cortex contained the renal corpuscles which consisted of a glomerulus covered by Bowman's capsule. The renal corpuscles were surrounded by proximal and distal convoluted tubules (Fig.10). In acetone group, it showed inflammatory cellular infiltration in 10% and cloudy swelling of renal tissues in 5% (Fig. 11). In benzene group, it showed inflammatory cellular infiltration in 10% (Fig. 12) and hyper cellularity in 10% (Fig. 13). Kolla group showed inflammatory cellular infiltration in 10%, hyper cellularity in 35%, cloudy swelling and hyper lobulated glomeruli in 20% (Fig. 14), withdrawal groups of acetone, kolla and benzene showed no abnormal histopathological changes.

LME of liver sections of control group showed normal histological picture, they contained a large number of hepatic lobules which are spherical in shape with a venous channel and a cortical vein (Fig. 15). Cloudy swelling of liver tissues was revealed in 90% of acetone group and decreased to 50% after withdrawal . Benzene group showed cloudy swelling in 30% and decreased to 10% after withdrawal. Also, it showed fatty changes and lymphocytic infiltration in 15% which improved after withdrawal (Fig. 16).

Kolla group showed cloudy swelling in 15% and decreased to 10% after withdrawal, lymphocytic infiltration in 20% (Fig. 17) and both in 30%. Withdrawal groups showed cloudy swelling in 50% of acetone withdrawal group, and 10% of benzene and kolla withdrawal groups. Dissection of swellings of kolla group oozed pus and LME of sections of these swellings showed central necrosis surrounded by inflammatory cells mainly neutrophils (Fig.18).

**Results of human study:**

***History:***

Acetone group complained of drowsiness on opening varnishes boxes and suffered from mild anxiety during the work. Workers in benzene group had chronic cough. Toluene group had slurred speech, lack of attention and euphoria. They were talkative.

***Biochemical study:***

The results presented in table (3). Blood urea, serum creatinine of acetone and benzene groups showed no significant differences in comparison with the control group. SGPT and SGOT were increased but with no significant difference in comparison with the control group. Kolla group showed significant increase in blood urea, serum creatinine, SGPT and SGOT concentrations in comparison with the control group.

## *DISCUSSION*

The term solvent refers to a class of liquid organic chemicals of variable lipophilicity and volatility (Bruckner and Alan, 2001).

Solvent abuse is the deliberate inhalation of volatile organic compounds to produce alterations in the conscious state and perception for recreational purposes. Solvents can be addicted and often abused in combination with other drugs. Various solvents are present in a wide variety of household and commercial products including glue, model cement, paint thinner and stripper, aerosols, typewriter correction fluid, dry cleaning fluid, and gasoline. These products are relatively inexpensive and readily available to children and adolescents (Marelich, 1997).

In acetone group, as regard the physical characters, the animals experienced anxiety followed by respiratory depression and weakness. These findings are in accordance with Kathleen et al. (1998) who found that simple lipophilic compounds as acetone cause excitation then depression of the CNS. They explained that these symptoms of acetone are often attributed to alterations in brain cell membrane structure and function.

Light microscopic examination of the brain of acetone group showed brain ede-

ma in 70% of specimens and necrosis in 20% (partially improved after withdrawal of acetone inhalation) these are in agreement with DeRoos (1998) who found that chronic acetone exposure caused brain lesions in the form of edema, gliosis, vaculation and necrosis and explained these findings by acetone's effect on the high lipid contents of the brain which may slowly dissolves it and the reversibility of acetone induced histopathological changes become less likely on prolonged abuse of about 3 months.

The present study demonstrated no significant differences in blood urea and serum creatinine levels of acetone group in comparison with the control group before and after withdrawal of acetone inhalation. The histopathological findings of the kidney showed kidney lesions (inflammatory cellular infiltration mainly lymphocytes in 10% and cloudy swelling in 5% of the specimens (improved after withdrawal of acetone inhalation). This is in agreement with Dietz et al. (1991) who stated that the pathogenesis for acetone mediated kidney affection could involve format, a metabolite of acetone with nephrotoxic effects. Formic acid vapors induced depressions in kidney glutathione content, P450 levels, and microsomal enzyme activity (ethoxycoumarin deethylase) in rats.

SGPT and SGOT of acetone group were significantly increased in comparison with the control group and they partially corrected after withdrawal of acetone inhalation. These results were confirmed by the histopathological findings of the liver which showed liver lesions (cloudy swelling) in 90% of specimens (persisted after withdrawal of acetone inhalation in 50%). These results were in accordance with Armutcu et al. (2005) who said that acetone is toxic to the liver, the mechanism of which is related to decrease of cellular detoxification capacity or increase of generation of reactive intermediates.

In benzene group, as regard the physical characters, the animals experienced anxiety, increased respiratory rate, and imbalance followed by severe weakness and tremors. These are consistent with Kathleen et al. (1998) who explained these phenomena by benzene neurotoxicity, which manifested by excitation then depression. This neurotoxicity might be related to the alterations of certain neurochemicals in certain brain regions. Benzene increased the contents of norepinephrine and dopamine in brain and other internal organs such as spleen, liver, and kidney, and also increased both 5-hydroxytryptamine and its metabolite, in the hypothalamus and corpus striatum.

As regard light microscopic examination of the brain of benzene group, there were hemorrhage in 40% and cellular atypia in 25% (persisted after withdrawal of

benzene inhalation), that coincide with Harada et al. (1999) who found brain lesions in the form of mild hemorrhage around arterioles and venules in the brain cortex with benzene exposure suggesting hyperpermeability of the vessels.

There were no significant differences in blood urea and serum creatinine before and after withdrawal of benzene inhalation. On the other hand, the histopathological findings of the kidney showed minimal kidney lesions in the form of inflammatory cellular infiltration mainly lymphocytes in 10% and hypercellularity in 10% of the specimens which improved after withdrawal of benzene inhalation. Gondi et al. (1988) found that the metabolites of benzene caused a moderate degree of glomerular change, desquamation and degeneration of tubular epithelium along with tubular casts, especially in the cortical region of the kidney.

SGPT and SGOT of benzene group showed significant increase in comparison with the control group but returned nearly to normal levels after withdrawal. These results were confirmed by the histopathological findings of the liver which showed liver lesions (cloudy swelling in 30% and fatty change in 15%) of the specimens (improved after withdrawal of benzene inhalation). These results are supported by Gondi et al. (1988) who reported that the histopathological examination of the liver showed loss of cytoplasmic details of hepatocytes as well as focal fatty change and necrosis with benzene.

Kolla (Toluene) group, the animals experienced severe anxiety, imbalance and increased rate of respiration followed by weakness. The mechanism of toluene toxicity is due to its effect on the neurotransmitters: increases dopamine and norepinephrine levels, reduces extracellular acetylcholine in striatum and hippocampus, and alters brain concentration of 5-hydroxy-tryptamine (Christophe et., 2004).

Brain lesions in the form of gliosis and necrosis appeared in 50% in kolla group this is in consistence with Uzun and Kendirli (2005) who found that chronic toluene (kolla) exposure caused slowly progressive central nervous system damage.

In kolla group, the brain lesions were irreversible, which are in consistence with Klaassen (2001) who found that MRI has revealed permanent changes in brain structure, and Gunter and Irene (1999) who told that with the exception of morphological damage, a recovery is mostly possible after a few months of withdrawal. Also Kathleen et al. (1998) said that chronic toluene exposure was associated with permanent neuropathy and encephalopathy and multifocal brain injury.

Kolla group in comparison with the control group revealed significant increase in blood urea and serum creatinine but returned nearly to normal levels after withdrawal. These results were confirmed by the histopathological findings of the kidney which showed kidney lesions in the form of inflammatory cellular infiltration mainly lymphocytes in 10%, hyperlobulation, hypercellularity in 35%, and cloudy swelling in 20% of the specimens (improved after withdrawal of kolla inhalation). These results are consistent with Goldfrank et al. (2002) who reported that chronic toluene abuse might result in damage to the kidney; glomerulonephrities, that is because of damage to glomerular capillary basement membranes which then become antigenic giving rise to antibodies with deposition, or in situ formation of immune complexes initiating glomerulonephrities.

Also these results are in agreement with Crowe et al. (2000) who said that renal toxicity due to toluene abuse is generally one of two types: glomerulonephrities or distal renal tubular acidosis. The mechanism of distal renal tubular acidosis is due to permeability changes in the nephron allowing backwards leakage of secreted acid, so chronic acid retention causes titration of alkaline bone salts leading to calcium mobilization, hypercalciuria and hence urinary calculi.

But these results are against Raymond et al. (1994) who did not find any renal dysfunction related to chronic toluene exposure at the level of 50 ppm, and against Mizutani et al. (1989) who found that no histopathological changes in the kidneys of toluene snifters.

In the present study, the kidney changes of kolla group are reversible, these are in accordance with Haddad et al. (1998) who found that toluene cause reversible renal tubular acidosis and glomerulonephrities. But in difference with Marjot and Mcleod (1989) who reported that chronic toluene abuse might result in permanent damage to the kidney.

SGPT and SGOT of kolla group were significantly increased in comparison with the control group but returned nearly to normal levels after withdrawal, these results were confirmed by the histopathological findings of the liver which showed liver lesions (inflammatory cellular infiltration mainly lymphocytes in 20% and cloudy swelling in 15% (improved after withdrawal of kolla inhalation).

These results of kolla group are in consistence with Kathleen et al. (1998) who reported that toluene raised the activities of SGOT, SGPT which indicate liver parenchymal injury.

The liver changes of kolla group are re-

versible, these are in agreement with Goldfrank et al. (2002) who said that liver injury of toluene exposure, manifested as amino-transferase elevation is usually reversible, except in massive overexposures. But in difference with Marjot and Mcleod (1989) who reported that chronic toluene abuse might result in permanent damage to the liver.

The appearance of abscess swellings in kolla group (which subsided after withdrawal of kolla inhalation) may be due to microbial infection of the injuries resulted from hurting themselves or due to skin contact as said by Ahaghotu et al.( 2005) who found that skin contact with toluene associated with granulocyte infiltration, swelling of the epidermis, and extensive disruption.

There were hair fall in kolla group that is in accordance with Ahaghotu et al. (2005) who found that toluene may cause damage of stratum corneum.

In acetone group (workers in furniture varnishes), as regard the history, the persons had drowsiness on exposure that is in accordance with Philip (1998). Also, they had anxiety that is in consistence with Baker and Fine (1986) who said that long-term daily exposure to acetone was accompanied with neuropsychiatric disorders in the form of mood changes such as irritability, depression, and short memory deficit.

Acetone group revealed no significant differences in blood urea and serum creatinine in comparison with control group. Literatures concerned these matters are rare.

SGPT and SGOT of acetone group were increased but in comparison with the control group, there was insignificant increase. Armutcu et al. (2005) found that acetone is moderately toxic to the liver, the mechanism of which is related to decrease of cellular detoxification capacity or increase of generation of reactive intermediates. These results also are in consistence with Morgott (1993) who found that hepatotoxicity was induced by acetone.

Studying benzene group (workers in gasoline stations), as regard the history, the persons had chronic cough which is in consistence with Harbison (1998) who found that cough, respiratory irritation and bronchitis occurred with benzene.

Regarding benzene group in comparison with the control group, there were no significant differences in blood urea and serum creatinine, these results are against Churchill et al. (1983) who summarized cases exposed to gasoline suffering from glomerulonephritis, he explained that the mechanism of this renal disorder may be related to a solvent-induced disruption of

the structural and functional integrity of the limited membranes of the kidney cells.

SGPT and SGOT of benzene group were increased but with no significant difference in comparison with the control group. Michailova et al. (1998) found that the liver function in workers in the petroleum industry showed increase because benzene is hepatotoxic (this occurs via phase I activation to a reactive intermediate).

As regard toluene group (kolla addicts for 6-12 years), as regard the physical characters, the persons had slurred speech, lack of attention, talkativeness, and euphoria that are in agreement with Uzun and Kendirli (2005) who reported that chronic toluene exposure associated with deterioration of cognitive function, orientation, attention, learning, calculation and memory function.

Gummin and Hryhorozuk (2002) reported that chronic occupational exposure or toluene abuse for five years or more may lead to chronic neurobehavioral syndrome (painter's syndrome) which includes ataxia, spasticity, dysarthria, and dementia.

Kolla group in comparison with the control group revealed significant increase in blood urea and serum creatinine that are in accordance with Goldfrank et al. (2002).

Also these results are in agreement with Crowe et al. (2000) who reported that the nephrotoxicity was caused by toluene, and various renal lesions had been associated with its abuse. But these results were in contrast with the results of Stengel et al. (1998) who did not find any renal dysfunction related to chronic toluene exposure at level of 50 ppm.

There were significant increase in SGPT and SGOT of toluene group in comparison with the control group which are in consistence with Goldfrank et al. (2002 ) who told that toluene raised the activities of SGOT and SGPT which indicate liver parenchymal injury. In contrast, these results are in difference with Seiji et al. (1987) who suggested that exposure to low dose toluene (30 ppm) showed no abnormalities in liver function tests.

Finally, from this study we conclude the dangerous effects of these substances especially due to their wide spread: in persons who directly exposed to these substances at work chronically, and also in persons who are addicted to these substances. So, in persons exposed to these substances, it is recommended to increase the attention about the dangerous effects of these substances on brain, kidney and

liver and explain the precautions which must be done during the exposure to these substances. Trials must be done to decrease the addictive spread of these substances. Periodic investigations of the kidney and liver functions should be done to workers who deal with toluene, acetone and benzene. Also persons who deal with benzene or toluene must do periodic imaging of the brain to detect early any pathological changes.

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**Table (1): Comparison of blood urea, serum creatinine, SGPT and SGOT concentrations of control group of rats versus tested groups of study (before withdrawal).**

| Variables | Groups | M | SD | t | P |
|---|---|---|---|---|---|
| **Blood urea (mg %)** | I | 20.84 | 6.14 | 0.28 | 0.78 |
| | II | 20.16 | 2.26 | 0.75 | 0.46 |
| | III | 30.31 | 4.6 | 3.55 | 0.002* |
| | IV | 21.63 | 5.01 | | |
| **Serum creatinine (mg %)** | I | 0.83 | 0.31 | 0.2 | 0.84 |
| | II | 0.78 | 0.23 | 0.26 | 0.79 |
| | III | 0.92 | 0.28 | 1042 | 0.003* |
| | IV | 0.8 | 0.15 | | |
| **SGPT (IU)** | I | 45.55 | 14.43 | 4.19 | 0.0009* |
| | II | 43.14 | 8.53 | 5.50 | 0.00005* |
| | III | 30.11 | 10.18 | 3.44 | 0.04* |
| | IV | 22.88 | 5.11 | | |
| **SGOT (IU)** | I | 59.46 | 17.05 | 5.92 | 0.00003* |
| | II | 37.15 | 17.65 | 2.36 | 0.03* |
| | III | 30.8 | 9.86 | 2.18 | 0.05* |
| | IV | 21.60 | 6.04 | | |

M= Mean; SD= Standard Deviation; $P \leq 0.05$ is significant; $P > 0.05$ is non significant
I: Acetone group; II: Benzene group; III: Kolla group; IV: Control group.

**Table (2): Comparison of blood urea, serum creatinine, SGPT and SGOT concentrations of tested groups of rats versus withdrawal groups.**

| Variables | Groups | t | P |
|---|---|---|---|
| **Blood urea (mg %)** | I versus I w | 0.42 | 0.68 |
| | II versus II w | 0.08 | 0.94 |
| | III versus III w | 3.61 | 0.03* |
| **Serum creatinine (mg %)** | I versus I w | 0.33 | 0.77 |
| | II versus II w | 0.75 | 0.47 |
| | III versus III w | 2.42 | 0.002* |
| **SGPT (IU)** | I versus I w | 2.70 | 0.0305* |
| | II versus II w | 3.07 | 0.008* |
| | III versus III w | 2.5 | 0.049* |
| **SGOT (IU)** | I versus I w | 4.35 | 0.007* |
| | II versus II w | 3.85 | 0.04* |
| | III versus III w | 3.3 | 0.02* |

M= Mean; SD= Standard Deviation; $P \leq 0.05$ is significant; $P > 0.05$ is non significant
I: Acetone group; II: Benzene group; III: Kolla group; IV: Control group.

**Table (3): Comparison of blood urea, serum creatinine, SGPT and SGOT concentrations of control human group versus other study groups.**

| Variables | Groups | M | SD | t | P |
|---|---|---|---|---|---|
| **Blood urea (mg %)** | I | 36.24 | 6.58 | 0.07 | 0.94 |
| | II | 34.02 | 7.64 | 0.51 | 0.62 |
| | III | 45.76 | 11.31 | 2.12 | 0.04* |
| | IV | 36.58 | 9.57 | | |
| **Serum creatinine (mg %)** | I | 0.86 | 0.22 | 0.06 | 0.95 |
| | II | 0.88 | 0.25 | 0.16 | 0.88 |
| | III | 1.96 | 0.32 | 0.74 | 0.02* |
| | IV | 0.85 | 0.40 | | |
| **SGPT (IU)** | I | 39.45 | 18.42 | 1.84 | 0.095 |
| | II | 32.90 | 19.66 | 1.04 | 0.32 |
| | III | 42.80 | 15.06 | 2.55 | 0.03* |
| | IV | 23.33 | 11.06 | | |
| **SGOT (IU)** | I | 30.03 | 14.06 | 0.19 | 0.86 |
| | II | 29.75 | 7.53 | 0.17 | 0.87 |
| | III | 39.62 | 7.51 | 2.18 | 0.03* |
| | IV | 29.04 | 7.24 | | |

M= Mean; SD= Standard Deviation; $P \leq 0.05$ is significant; $P > 0.05$ is non significant
I: Acetone group; II: Benzene group; III: Kolla group;

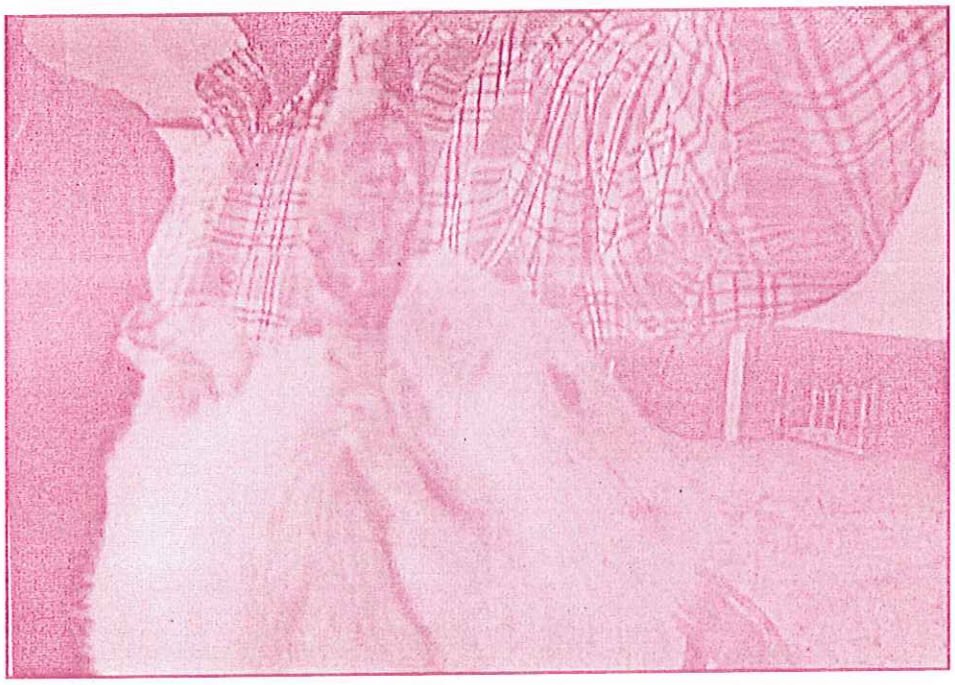

**Fig. (1) :** Showing lesion in a limb of a rat caused by anxiety of animals that lead to hurting themselves.

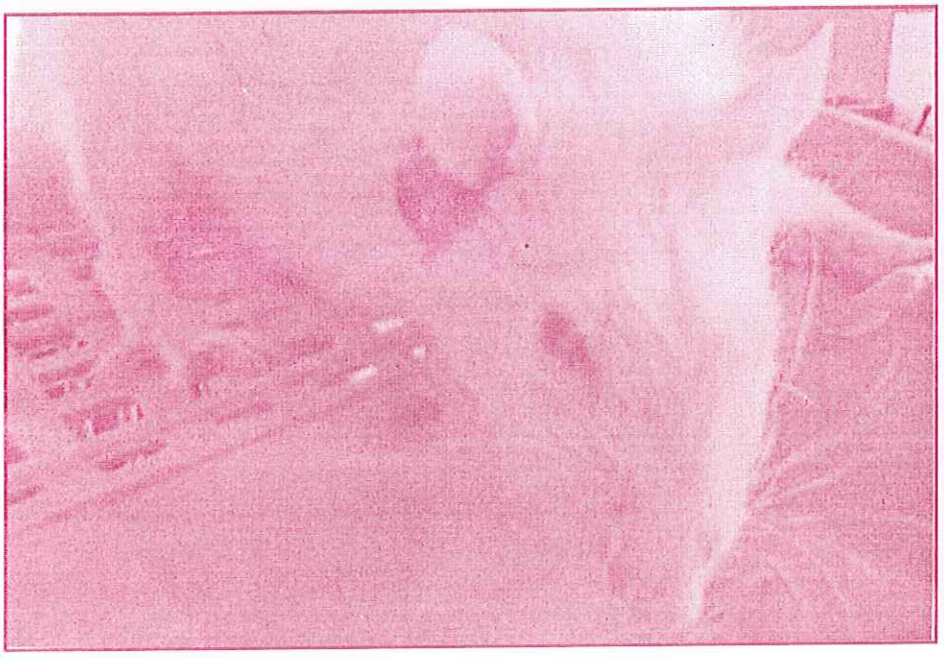

**Fig. (2):** Showing swelling in a neck of a rat of the kolla group.

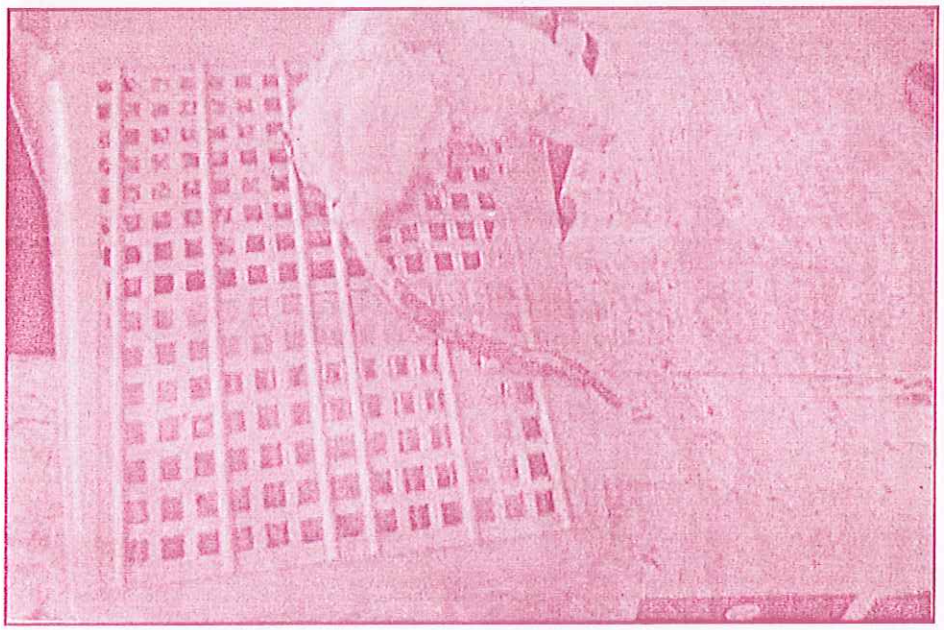

**Fig. (3):** Showing hair fall in a rat of the kolla group.

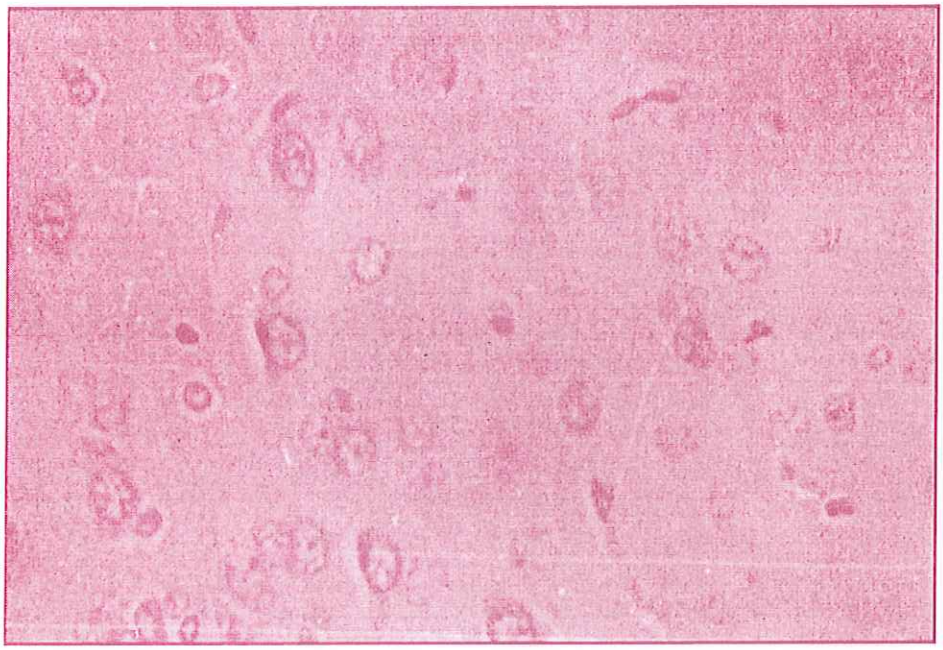

**Fig. (4):** A photomicrograph of the control group showing normal brain. (H&E x 200)

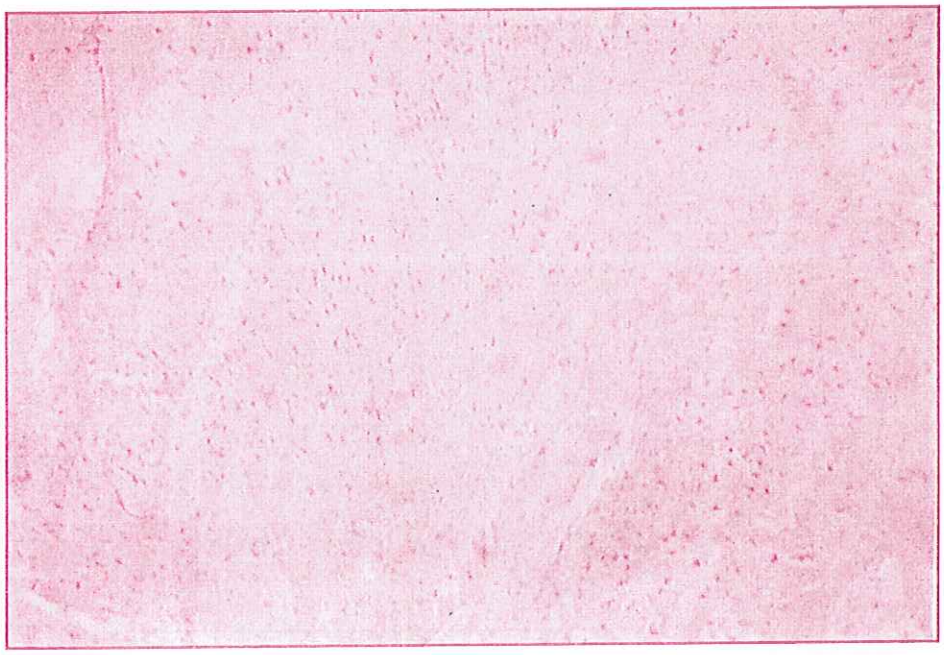

**Fig. (5):** A photomicrograph of the brain showing edema in acetone group. (H & E x 200)

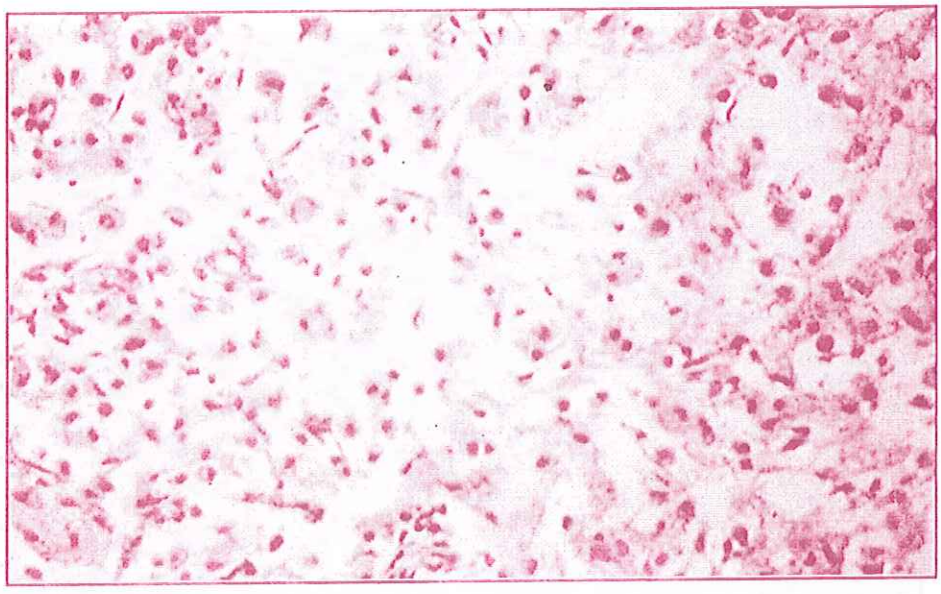

**Fig. (6):** A photomicrograph of the brain showing necrosis in acetone group. (H & E x 200)

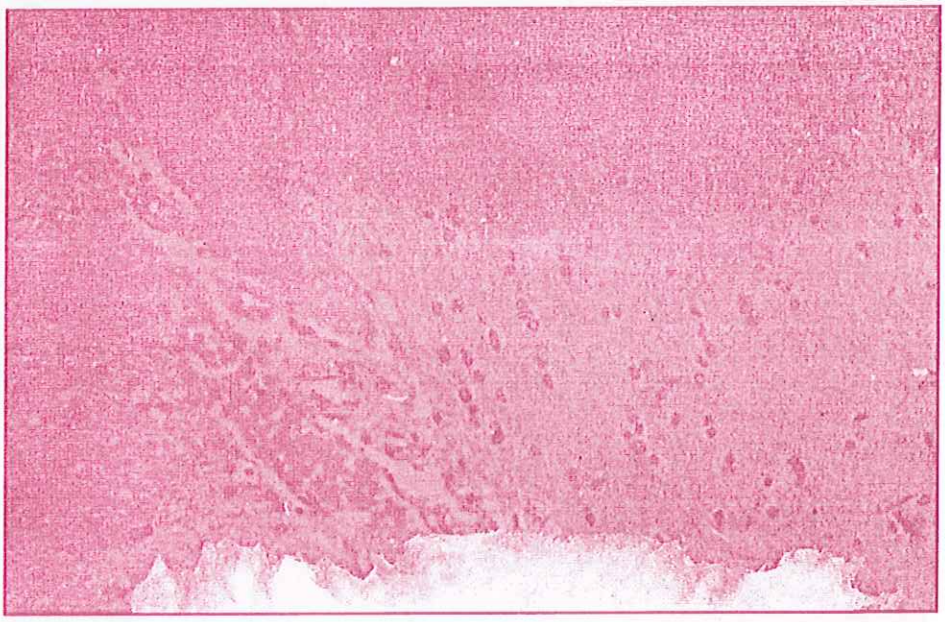

**Fig. (7):** A photomicrograph of the brain showing hemorrhage in benzene group. (H&E x 200)

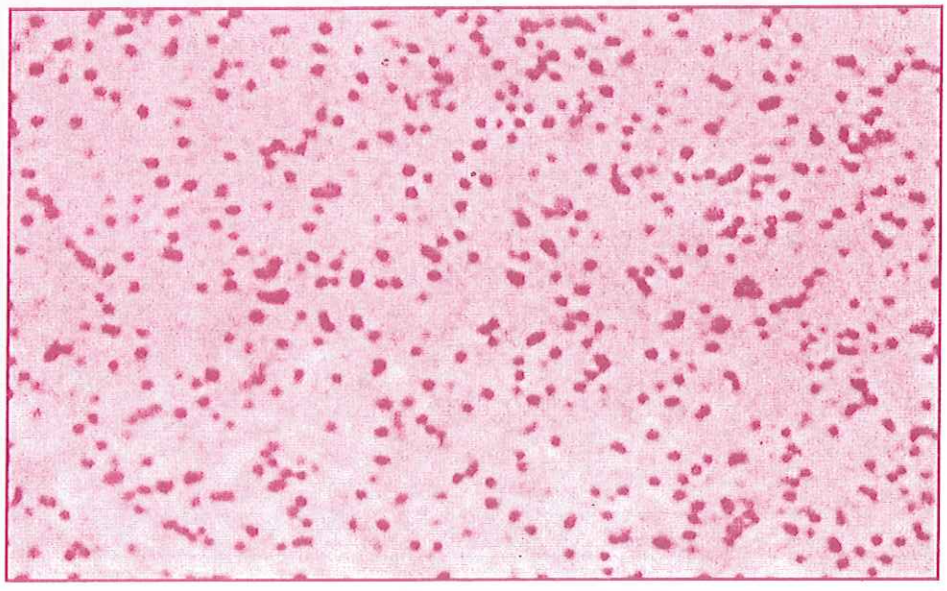

**Fig. (8):** A photomicrograph of the brain showing cellular atypia in benzene group. (H & E x 200)

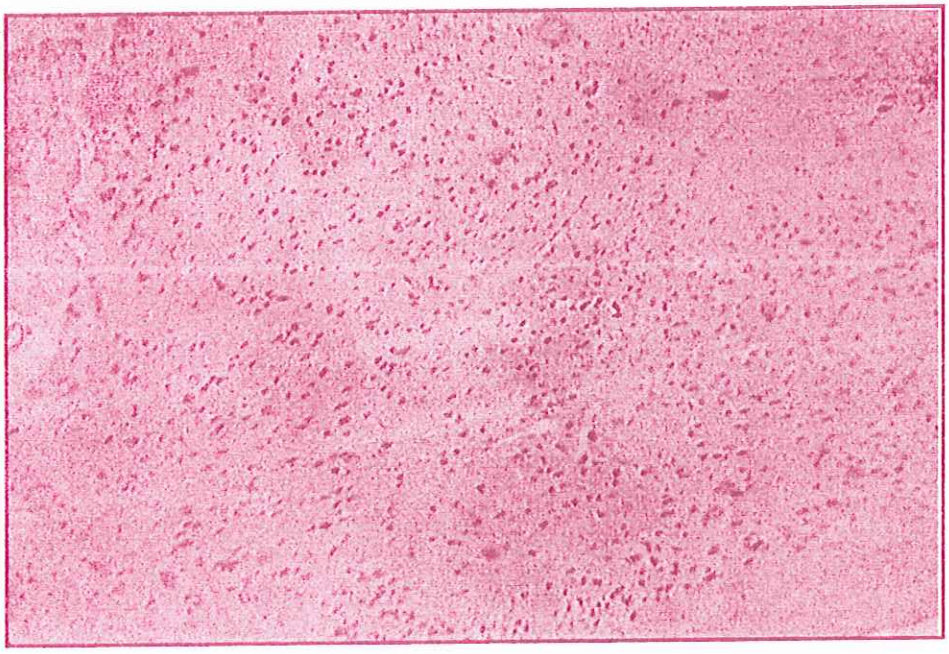

**Fig. (9):** A photomicrograph of the brain showing gliosis in kolla group. (H & E x 200)

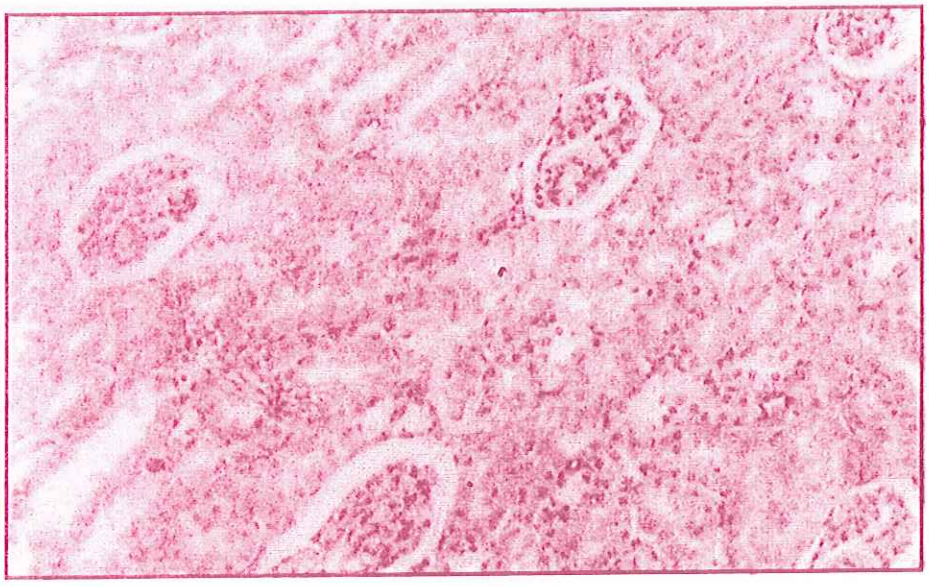

**Fig. (10):** A photomicrograph of the control group showing normal kidney. (H & E x 200)

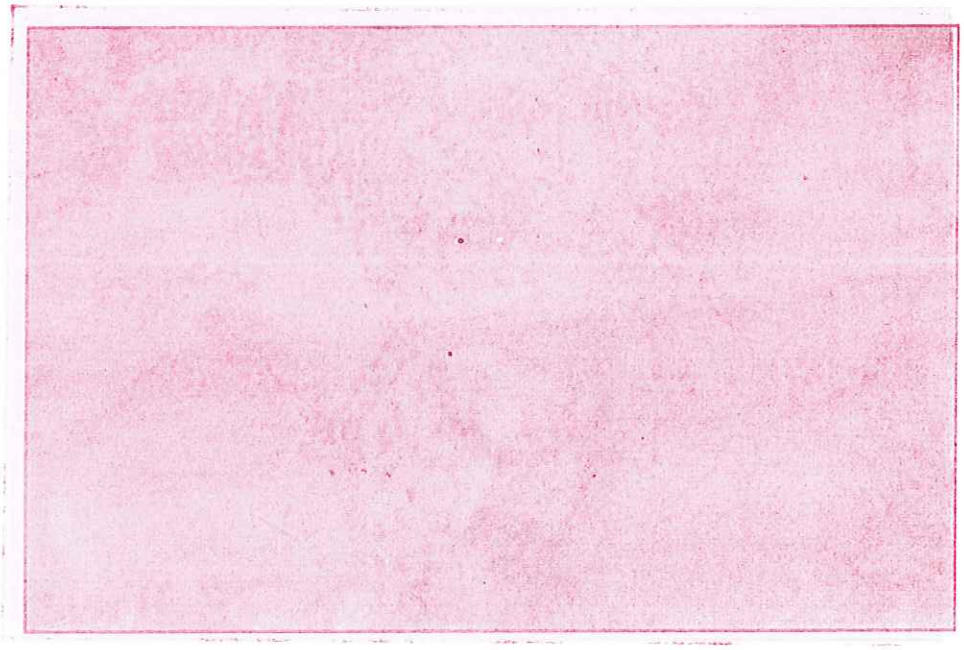

**Fig. (11):** A photomicrograph of the kidney showing inflammatory cellular infiltration and cloudy swelling in acetone group. (H & E x 200)

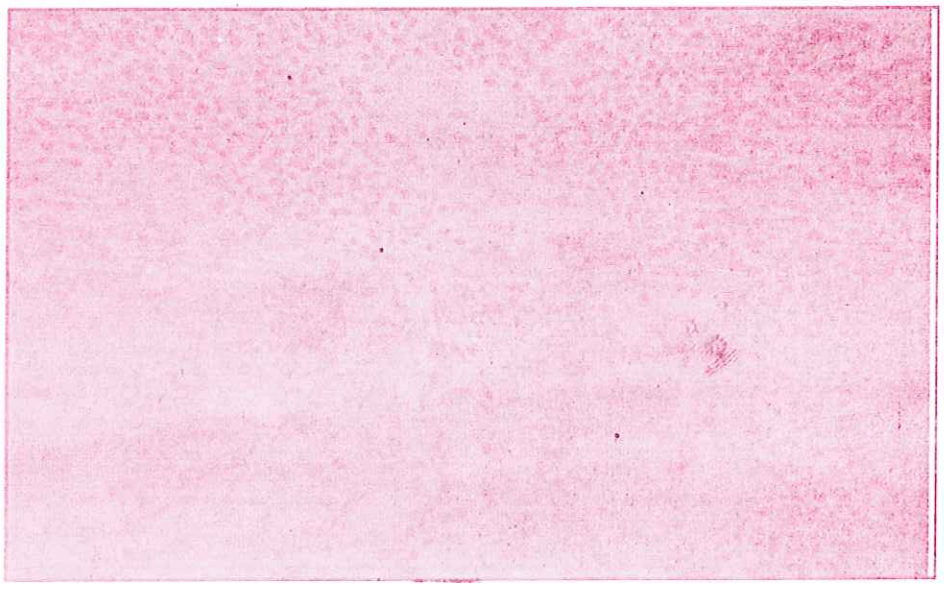

**Fig. (12):** A photomicrograph of the kidney showing inflammatory cellular infiltration in benzene group. (H & E x 200)

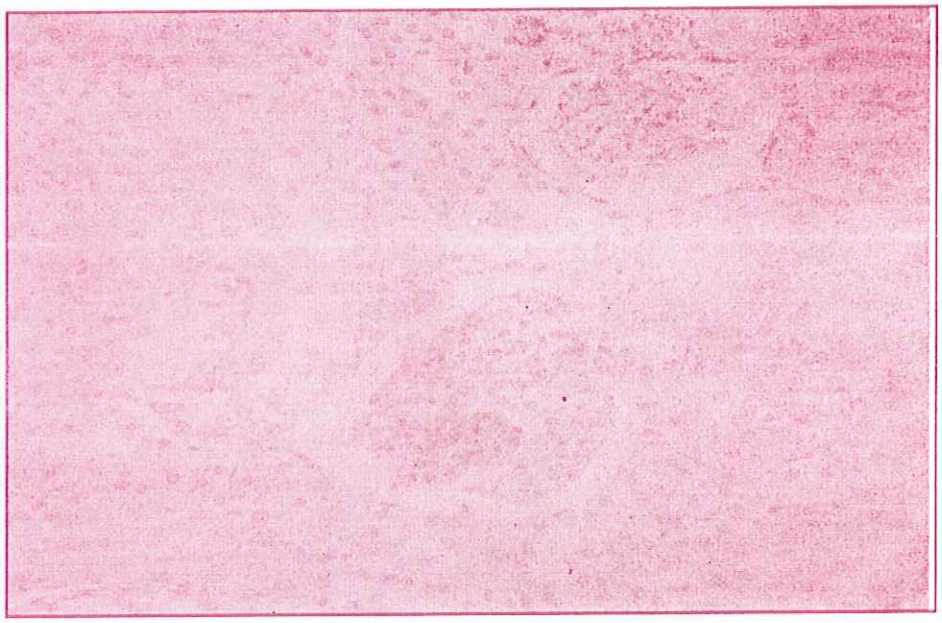

**Fig. (13):** A photomicrograph of the kidney showing hypercellularity in benzene group. (H & E x 200)

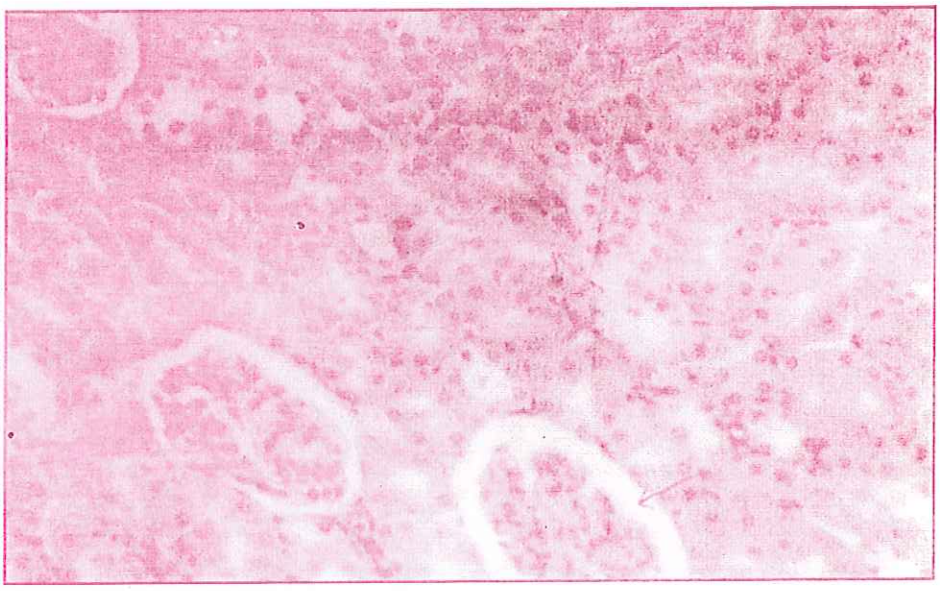

**Fig. (14):** A photomicrograph of the kidney showing hyperlobulation of the glomeruli and cloudy swelling in kolla group. (H & E x 200)

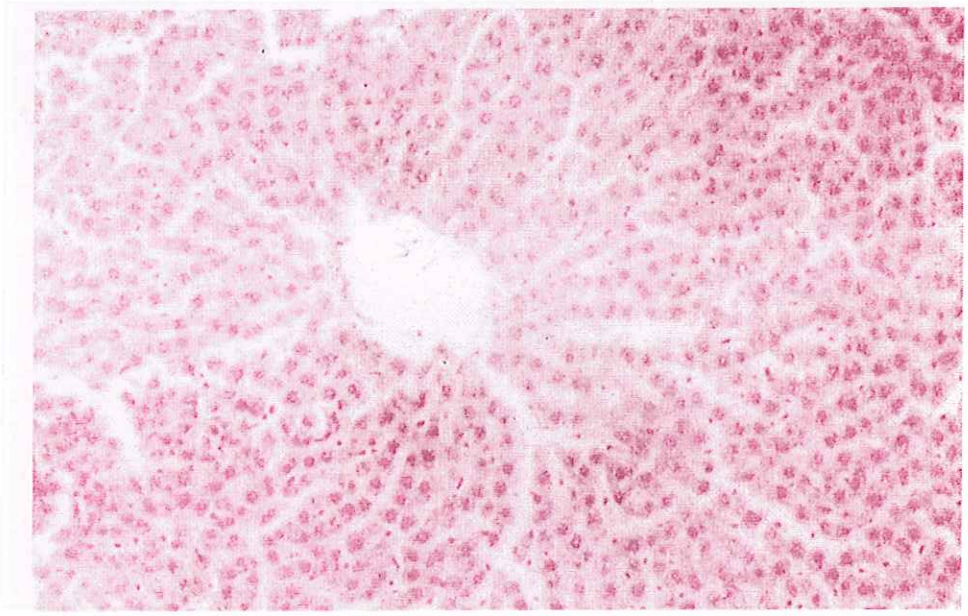

**Fig. (15):** A photomicrograph of the control group showing normal liver. (H &E x 200)

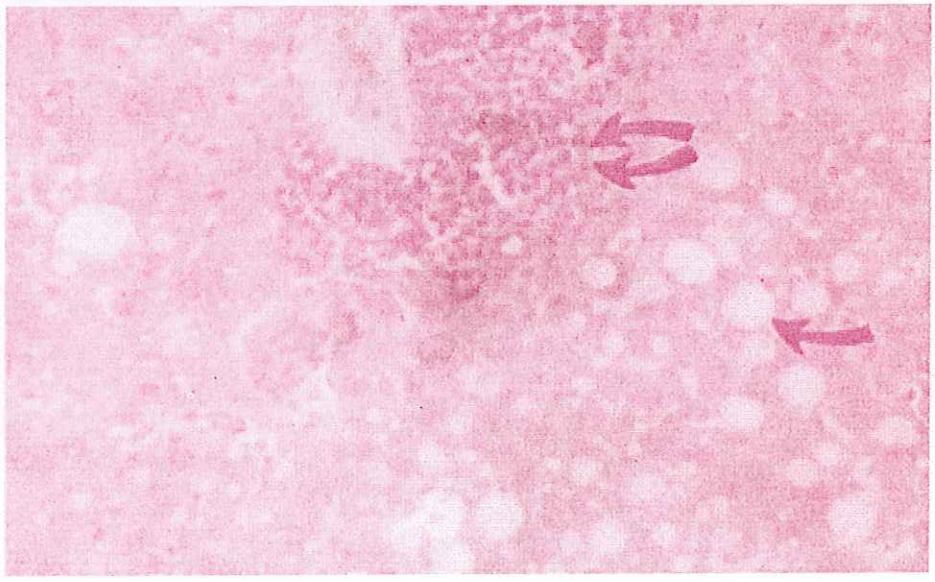

**Fig. (16):** A photomicrograph of the liver showing fatty change and inflammatory cellular infiltration in benzene group. (H & E x 200)

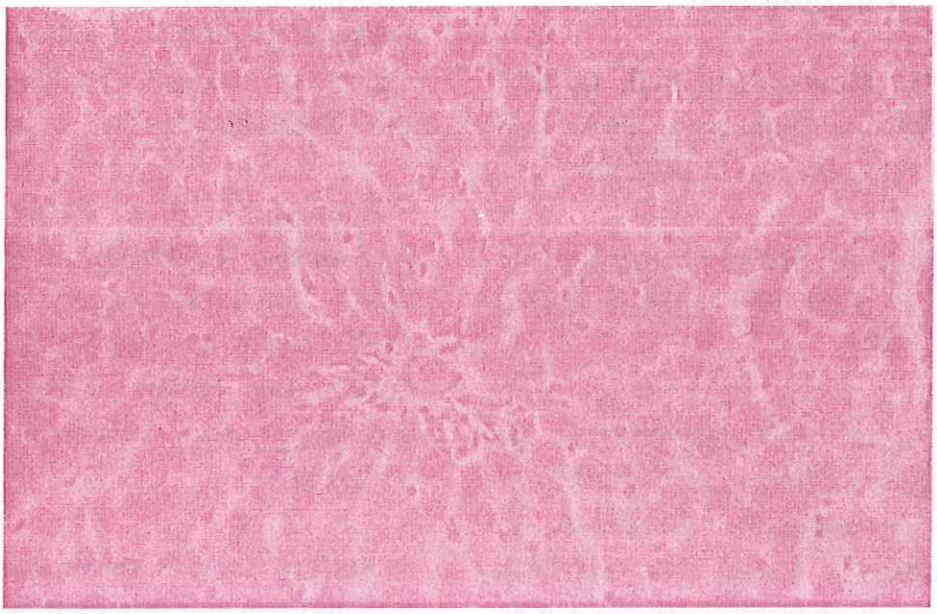

**Fig. (17):** A photomicrograph of the liver showing inflammatory cellular infiltration in kolla group. (H & E x 200)

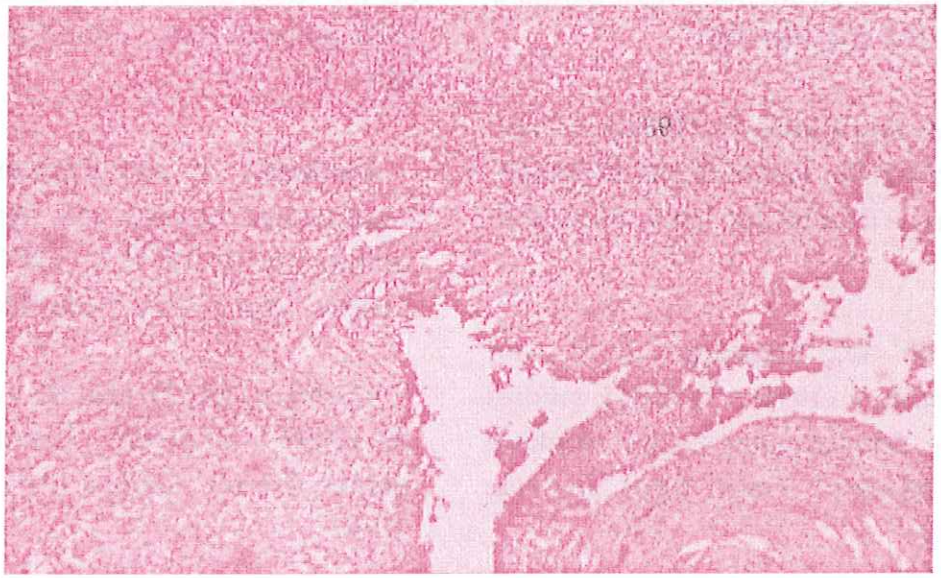

**Fig. (18):** A photomicrograph of the swelling showing central necrosis surrounded by inflammatory cellular infiltration in kolla group. (H & E x 200)

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# التأثير الطويل لبعض المواد المتطايرة الشائعة الاستخدام (الأسيتون والبنزين والكوله) على المخ والكبد والكلى دراسة على الجرذان البيضاء والآدميين

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أجريت هذه الدراسة لمعرفة التأثير السمى المزمن لبعض المواد المتطايرة الشائعة الاستخدام على المخ والكبد والكلى وقسمت الدراسة إلى جزئين، الجزء الأول أجرى على ١٢٠ من الجرذان البيضاء بمتوسط وزن ٢٠٠ ± ٢٠ تم تقسيمهم إلى أربعة مجموعات كل مجموعة تحتوى على ٣٠ جرذ بحسب نوع المادة المستنشقة لكل مجموعة، مجموعة الأسيتون والبنزين والكلة وأخيراً المجموعة الضابطة التى لم تستنشق شيئاً لكن عاشت فى نفس الظروف البيئية لباقى الجرذان.

وبعد مرور ١٢ إسبوع من استنشاق الجرعة المزمنة لهذه المواد، تم أخذ عينات دم من كل جرذ من المجموعة الضابطة و٢٠ جرذاً من كل مجموعة من الثلاث الأخرى لقياس نسبة اليوريا والكرياتينين وأنزيمات الكبد ثم ذبحت هذه الجرذان وتم أخذ الكلى والكبد والمخ وتجهيزها للفحص الميكروسكوبى، أما العشر جرذان المتبقية من الثلاث مجموعات فقد تركوا بدون استنشاق لأى مادة لمدة إسبوعين ثم تم أخذ عينات دم منهم لإجراء نفس التحاليل المعملية السابقة ثم ذبحت هذه الجرذان وتم أخذ الكلى والكبد والمخ وتجهيزها للفحص الميكروسكوبى.

أما بالنسبة للجزء الثانى من الدراسة (الجانب الآدمى) فقد أجرى على ٦٠ شخص متطوع بعد أخذ موافقة مكتوبة منهم لإجراء البحث وقسموا إلى ٤ مجموعات : مجموعة تعرضت لاستنشاق الأسيتون فى ورش تلميع الأثاث، مجموعة تعرضت لاستنشاق البنزين فى محطات الجازولين، مجموعة تعرضت لاستنشاق التولوين (المتعاطين الكولة)، المجموعة الضابطة التى لم تتعرض لاستنشاق أى من المواد المراد دراستها، وقد تم أخذ التاريخ المرضى لكل منهم بالإضافة إلى عينة دم من كل فرد من كل مجموعة.

وقد لوحظ على الجرذان عند استنشاقهم هذه المواد الاضطراب ثم الخمول، أما التحاليل الكيميائية الحيوية لهم قبل سحب المواد فقد أظهرت

: وجود زيادة ذات دلالة إحصائية فى مستوى اليوريا والكرياتينين فى مجموعة الكولة (تناقصت بعد سحب المواد)، كما وجد زيادة ذات دلالة إحصائية فى أنزيمات الكبد فى مجموعة الأسيتون والبنزين والكولة (تناقصت بعد سحب المواد ولكن الأنزيمات مازالت مرتفعة عن الطبيعى فى مجموعة الأسيتون).

وأظهرت الفحوصات المجهرية لمخ الجرذان قبل سحب المواد وجود أوديما ونخر فى مجموعة الأسيتون وتليف ونخر فى مجموعة الكولة، ونزيف وخلايا شاذة فى مجموعة البنزين، أما بعد سحب المواد فقد استمر تواجد النخر في مجموعة الأسيتون والنخر والتليف فى مجموعة الكولة والخلايا الشاذة فى مجموعة البنزين.

كما أظهرت الفحوصات المجهرية لكلى الجرذان قبل سحب المواد وجود رشح خلوى التهابى فى مجموعات الأسيتون والبنزين والكلة، تكاثر خلوى فى مجموعتى البنزين والكولة، تزايد فصيصى فى التكببات الكلوية فى مجموعة الكولة، فساد غيمى فى مجموعة الأسيتون، أما بعد سحب المواد فقد كانت الكلى لاتحتوى على تغيرات مرضية فى أنسجتها.

أما الفحوصات المجهرية لكبد الجرذان قبل سحب المواد فقد أظهرت وجود رشح خلوى إلتهابى فى مجموعة الكولة وفساد غيمى فى مجموعات الأسيتون والبنزين والكولة، فساد دهنى فى مجموعة البنزين، أما بعد سحب المواد فقد استمر تواجد الفساد الغيمى فى مجموعات الأسيتون والبنزين والكولة.

وقد لوحظ من التاريخ المرضى للأشخاص وجود قلق بسيط ووسن فى الأشخاص العرضى لاستنشاق الأسيتون فى ورش تلميع الأثاث، أما الذين تعرضوا لاستنشاق البنزين فى محطات الجازولين فكانت شكواهم من السعال، أما الذين تعرضوا لاستنشاق التولوين (المتعاطين للكولة) فقد لوحظ عليهم نقص الانتباه والثرثرة والتلعثم فى الكلام والانبساط المصاحب للإدمان، أما التحاليل الكيميائية الحيوية لهؤلاء الأشخاص فقد أظهرت وجود زيادة ذات دلالة إحصائية فى مستوى اليوريا والكرياتينين وانزيمات الكبد فى مجموعة التولوين، أما فى مجموعتى الأسيتون والبنزين فلم يوجد فرق ذو دلالة إحصائية فى مستوى اليوريا والكرياتينين ووجدت زيادة ليست لها دلالة إحصائية فى انزيمات الكبد.

نستخلص من هذه الدراسة حجم خطورة مضاعفات التعرض لهذه المواد على المخ والكبد والكلى مع الأخذ بالاعتبار انتشارها الواسع وخاصة لدى الأشخاص الذين يعملون بالصناعات المرتبطة بهذه المواد ويتعرضون مباشرة لها بصفة مزمنة وكذلك المتعاطين لها نظراً لرخص أسعارها. وعلى ضوء هذه النتائج فإنه يجب متابعة وظائف الكلى والكبد للأشخاص العرضى للتولوين، كما يجب متابعة وظائف الكبد للأشخاص العرضى للأسيتون والبنزين، وأيضاً الاكتشاف المبكر ومتابعة أى تغيرات فى المخ للأشخاص العرضى للثلاثة مواد، كما يلزم العمل على زيادة الوعى لدى المتعرضين لها وضرورة أخذ الاحتياطات اللازمة عند التعرض لها والعمل على الحد من إنتشار التعاطى لهذه المواد.