

SID



سرویس های
ویژه



سرویس ترجمه
تخصصی



کارگاه های
آموزشی



بلاگ
مرکز اطلاعات علمی



سامانه ویراستاری
STES



فیلم های
آموزشی

کارگاه های آموزشی مرکز اطلاعات علمی جهاد دانشگاهی

کارگاه آموزشی
سرویس ویژه ای متن (مقدماتی)

کارگاه آنلاین
بررسی مقابله ای متون (مقدماتی)

کارگاه آموزشی
پروپوزال نویسی و پایان نامه نویسی

کارگاه آنلاین
پروپوزال نویسی و پایان نامه نویسی

کارگاه آموزشی
آشنایی با پایگاه های اطلاعات علمی بین المللی و ترند های جستجو

کارگاه آنلاین آشنایی با پایگاه های اطلاعات علمی
بین المللی و
ترند های جستجو

Effect of Solder Fumes on Liver Serum Markers and Hepatic Vascular Elements in Rats

Mohammad Reza Arab, Ph.D.^{1*}, Ramezan Mirzaei, Ph.D.², Feridoon Sargolzaei Aval, Ph.D.¹, Ali Reza Nakhaei, Ph.D.³, Mehrbod Karimi, M.D.⁴, Rezvaneh Mashhadi, M.Sc.⁵

1. Cellular and Molecular Research Center, Faculty of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
2. Occupational Health Department, Faculty of Health, Zahedan University of Medical Sciences, Zahedan, Iran
3. Biochemistry Department, Zahedan University of Medical Sciences, Zahedan, Iran
4. Pathology Department, Zahedan University of Medical Sciences, Zahedan, Iran
5. Zahedan University of Medical Sciences, Zahedan, Iran

* Corresponding Address: P.O.Box: 98165-493, Cell and Molecular Biology Research Center, Faculty of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
Email: mr_arabz@yahoo.com

Received: 12/Oct/2008, Accepted: 19/May/2009

Abstract

Objective: This study was performed to determine the effects of solder fume on liver serum markers and vascular elements in rats

Materials and Methods: A total number of 48 rats were randomly divided into experimental (n=30) and control (n=18) groups. Based on exposure time, each group was further divided into 2, 4 and 6 weeks of exposure subgroups. Rats in the experimental subgroups were placed in an exposure chamber and exposed to solder fume for one hour per day. The concentration of metal fumes and gases in the exposure chamber were measured daily by atomic absorption spectrophotometry. Blood and liver samples were collected from all rats in the experimental and control subgroups to determine the concentration of alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, as well as total and conjugated bilirubin levels. Histological examinations of specimens were performed under a stage-micrometer calibrated microscope.

Results: Despite some alterations in enzyme and bilirubin levels between control and experimental groups, the differences were not statistically significant. However, histopathological examinations of liver tissues revealed significant differences in the diameters of cross sectioned sinusoids of rats in the 4-week experimental and control subgroups ($p<0.001$). Furthermore, there were significant differences in the diameters of cross-sectioned central venules of all experimental and control subgroup members ($p<0.001$).

Conclusion: The results of this study suggest that although solder fume in the acute phase of exposure of up to 4 weeks does not significantly change liver serum marker enzymes, it can greatly increase the diameters of cross-sectioned hepatic sinusoids and the central venule.

Keywords: Fumes, Central Vein, Liver, Rat

Yakhteh Medical Journal, Vol 12, No 1, Spring 2010, Pages: 33-38

Introduction

Soft soldering is a widespread industrial activity, most typically performed manually using a flux cored solder wire commonly known as colophony (1). Welders and solderers use heat to permanently join pieces of metal (2). The soldering process, if not properly controlled (3), produces various contaminants at concentrations sufficient to cause both short-term and long-term health effects. Activated rosin core soldering wires contain stannum (Sn),

lead (Pb) and formaldehyde. The metal composition of the generated fumes during welding of metals is mostly derived from the welding electrode or wire, which is consumed during the process (4, 5).

Epidemiologic studies have shown higher rates of liver disease in certain occupations (6). Toxic gases, vapors and particles emitted during the soldering process are part of occupational and environmental substances associated with liver injury

(7). Soldering, welding, farming, chemistry and dry cleaning are examples of occupations with high risk of inhalation exposure to fumes (8). Exposure to welding fumes has been considered potentially carcinogenic by the International Agency for Research on Cancer (8). Epidemiological studies have shown that exposure to welding fumes is associated with metal-fume fever, increased prevalence of lung disease, and increased risk of mortality from ischemic heart disease(2). Previous studies demonstrated that 22% of solderers or persons working near solder were found to be suffering from occupational asthma and other lung diseases. While the adverse toxic effects of welding fumes on pulmonary function have been well documented, knowledge of toxic effects of these fumes on the liver is limited (1).

Liver is an important internal organ with many crucial functions on health maintenance; therefore, any level of liver dysfunction could be problematic (9). Extent of hepatotoxicity is usually determined by the measurement of certain enzymes in plasma. These include liver serum markers such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and bilirubin and are used to diagnose and evaluate liver disease (5, 9). Any increase in liver enzyme levels reflects acute liver damage (10, 11). Furthermore, any increase in the concentration of conjugated bilirubin is a result of hepatic cell dysfunction and an increase in the concentration of nonconjugated bilirubin is due to biliary tree problems (12).

Based on epidemiologic data, more than two million workers worldwide perform welding as part of their work duties (5). One of the main limitations in studying the adverse health effects of welding fumes is the variability of work-place environmental conditions. This includes different ventilation qualities as well as additional exposure to other toxic materials such as asbestos, silica and solvents (3).

Despite the wide use of soldering in small industries, the toxicity of inhalation of vapors produced during soft soldering is poorly understood. The aim of this study was to examine the potential toxic effects of manual soldering fume using flux cored (rosin based) solder wire on the rat liver.

Materials and Methods

A total number of 48 Sprague Dawley adult male rats weighing 125 ± 15 g were divided into experimental (n=30) and control (n=18) groups. After adaptation to standard laboratory conditions, each group was equally subdivided into 2, 4 and 6-week subgroups. Experimental groups were ex-

posed to colophony solder flux fume for 1 hour/day (13:00-14:00), directed into the plexyglass exposure chamber. The chamber had an internal volume of 0.83 m^3 , was connected to a 200 cm long hood inlet and outlet duct, and was ventilated 5-6 times per hour. The feeding rate of manual solder wire was 5m/min. The chamber temperature was maintained at $22 \pm 3 \text{ }^\circ\text{C}$. This experiment design was approved by Zahedan University of Medical Sciences' Ethics Committee.

The exposure chamber's fume concentrations of stannum (Sn), lead (Pb) and formaldehyde during the experiment were 0.35 mg/m^3 , 3 mg/m^3 and 0.193 mg/m^3 respectively. Air samples from the exposure chamber were collected daily using a SKC personal pump (SKC 224-EE, UK) and were analyzed for their formaldehyde, stannum and lead concentrations. These measurements were obtained in accordance with methods described by the National Institute of Occupational Safety and Health (ASTMD4185-90, NIOSH 3500, OSHA206) using a visible absorption spectrophotometer (Spetronic, 20D, Milton Ray, Belgium), and an atomic absorption spectrophotometer (ATI/Unicam, 929, USA). The commercially available soldering wire (Alloy 63/67, 0.8 mm diameter, Iran) was purchased from Jarfe Company, Iran. (13-15). The rats in both experimental and control groups were kept under deep anesthesia and at the designated time points their blood samples were collected directly from the heart. Their livers were also weighed (A&D). Liver samples from the right lobe were then collected, fixed in 10% formalin saline and processed for routine histopathological examination. The prepared sections (5-6 micrometer in thickness and stained with hematoxylin & eosin) were blind measured for the diameters of their cross sectioned sinusoids and central venule by two observers using a stage-micrometer calibrated Zeiss microscope. These histological measurements were performed on at least two sections of each animal's liver sample, and at least five microscopic fields in each section were studied. The mean number of measured central venule (CV) and sinusoid (Sin) samples for each experimental and control rat was 10 CVs and 20 Sins. Reliability of technique was ascertained when repeating the measurements in a number of randomly selected sections from control and experimental subgroups produced the same results. Measurements of serum alkaline phosphatase (ALP) and aminotransferase (ALT & AST) concentrations were carried out using commercially available kits (Pars Azmun) and in accordance with their

included instructions. Conjugated and non-conjugated bilirubin was also measured (Pars Azmun Kinetic method). Normal distribution of the data was confirmed using the Kolmogorov-Smirnov test for all obtained data. Analysis of the collected data was performed using Statistical Package for Social Sciences (SPSS v.12), and differences between the means were compared using ANOVA [with Least Significant Difference (LSD) as post-hoc test and 0.05 significance level].

Results

After measuring the serum levels of liver markers [alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), as well as conjugated and non-conjugated bilirubin], analysis of variance revealed that despite the existence of some degree of marker concentration differences between the control and experimental groups, there was no statistically significant difference among them (experimental and control groups of 2, 4 and 6 weeks of exposure time). There was also no significant liver weight difference between the control and experimental groups (Table 1).

The comparison of diameters of the cross sectioned sinusoids and cross sectioned central

venules of the experimental and control group specimens (using ANOVA and LSD as post-hoc test) demonstrated a significant difference in cross sectioned sinusoidal diameters of only the 4-weeks of exposure-time group ($p < 0.001$).

Furthermore, similar data analysis for the cross-sectioned central venule diameters revealed a significant difference among all exposure-time categories in the control and experimental groups ($p < 0.001$) (Table 2).

Histopathological examination of control specimens showed branched hepatic cell cords with intervening sinusoids in a radial arrangement directed from periphery of the lobule to the central venule at its center. In the experimental group, dilatation of the sinusoids (with an elongated endothelium nucleus) was prominent especially in the 4-week exposure-time subgroup. There were also signs of inflammatory process and congestion of the central vein in its periphery (infiltration of lymphocyte) in the experimental group, especially in the 4- and 6-week exposure-time subgroups (Fig 1).

In contrast to the control group, in the experimental group, the diameters of sinusoids and central venules were increased in a time-dependent manner.

Table 1: Effect of solder fume on liver serum markers in rats

| Groups | Two-week group | | Four-week group | | Six-week group | |
|---------------------------|-------------------|--------------------|-------------------|-------------------|-------------------|------------------|
| | Mean \pm SD | | Mean \pm SD | | Mean \pm SD | |
| Variants | Control | Experimental | Control | Experimental | Control | Experimental |
| ALP IU/L | 768.6 \pm 130.3 | 892.9 \pm 232.22 | 739.8 \pm 168.7 | 777.8 \pm 189.7 | 366.6 \pm 45.3 | 495.7 \pm 71.2 |
| AST IU/L | 129.3 \pm 36.78 | 120.3 \pm 31.54 | 144.5 \pm 17.05 | 140.3 \pm 23.41 | 119.6 \pm 18.37 | 139.8 \pm 38.2 |
| ALT IU/L | 49.2 \pm 16.9 | 70.3 \pm 13.43 | 48.66 \pm 5.18 | 47.3 \pm 8.49 | 39.6 \pm 6.08 | 45.2 \pm 6.79 |
| AST/ALT | 2.62 | 1.71 | 2.96 | 2.96 | 3.02 | 3.09 |
| Direct Billirubin (mg/dl) | 0.086 \pm 0.001 | 0.076 \pm 0.026 | 0.166 \pm 0.09 | 0.2 \pm 0.07 | 0.2 \pm 0.09 | 0.19 \pm 0.08 |
| Total bilirubin (mg/dl) | 0.382 \pm 0.07 | 0.315 \pm 0.05 | 0.866 \pm 0.17 | 0.849 \pm 0.067 | 0.862 \pm 0.06 | 0.856 \pm 0.1 |
| Weight of Liver (g) | 9.85 \pm .17 | 9.58 \pm 1.64 | 9.5 \pm 1.65 | 10.2 \pm 0.94 | 9.05 \pm 0.48 | 10.55 \pm 1.31 |

$p > 0.05$: Not significant in all of experimental and control subgroups

Table 2: Effect of solder fume on sinusoid and central venule diameters of the rat liver

| Groups | Two-week group | | Four-week group | | Six-week group | |
|--|-------------------|-------------------|-------------------|------------------|-------------------|-------------------|
| | Mean \pm SD | | Mean \pm SD | | Mean \pm SD | |
| Variants | Control | Experimental | Control | Experimental | Control | Experimental |
| Diameter of sinusoid (μm) | 9.8 \pm 2.06 | 10.13 \pm 2.26 | 8.66 \pm 1.7 | 10.25 \pm 2.16 | 8.4 \pm 1.97 | 8.45 \pm 1.87 |
| Diameter of central venule (μm) | 44.66 \pm 14.99 | 65.12 \pm 23.24 | 55.77 \pm 21.59 | 65.88 \pm 22.4 | 49.43 \pm 17.05 | 60.44 \pm 21.24 |

$p < 0.001$ between control and experimental 4-week groups

$p < 0.001$ between control and experimental categories of all subgroups

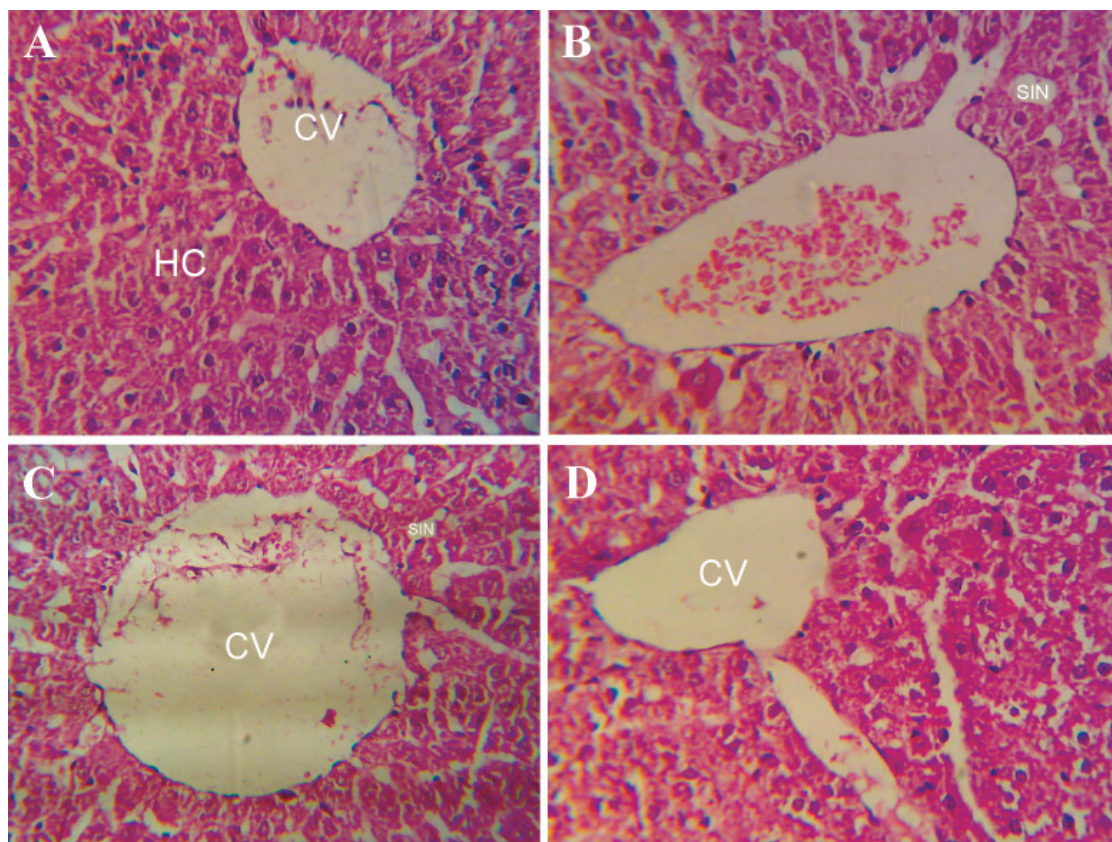


Fig 1: Normal appearance of a hepatic cell cord (HC), hepatocytes, central venule and sinusoid (Sin) in the control group (A); disorganized architecture of hepatic cell cords and dilatation of sinusoids and central venule (CV) in experimental groups after inhalation exposure to soldering fume in the 2-week (B), 4-week (C), and 6-week subgroups (D). H-E \times 400.

Discussion

The obtained data from this study relating to defined fume-exposure times (1 hour/day for 2, 4 and 6 weeks) and concentration (0.193 mg/m^3 for formaldehyde, 0.35 mg/m^3 for Stannum and 3 mg/m^3 for lead) revealed that despite some differences in liver function test (LFT) results, there was no statistically significant difference between control and experimental groups (LSD test) in all studied subgroups. This finding is in disagreement with the Uboh et al. report showing that 4 hours/day of kerosene and petroleum fume inhalation in a period of 2 weeks significantly increased the concentration of ALP and aminotransferase in an experimental rat group in comparison to the control group (10). In their study, Uboh et al. have proposed that increased activity of aminotransferase, especially of ALT, in the experimental group is caused by liver cell injury due to increased permeability of hepatocyte cell membranes or focal necrosis of hepatic cells. They documented that the increase in concentration of AST in the experimental group may be due to abnormal dynamic properties of cellular membranes following

exposure to inhaled fumes. In this regard, Uboh and colleagues introduced the ratio of AST/ALT as an important index of hepatic cell injury (10).

Our results demonstrated a moderate increase in the AST/ALT ratio in the experimental group in a time-dependent manner. They also showed a slight increase in the amount of bilirubin. Bilirubin, as a by-product of red blood cell (RBC) breakdown, could be increased following hepatic cell injury. The increased concentration of ALP in the experimental group reported in this study is in accord with the results of Jadhav et al. and Marques et al. (16, 17). It is probable that a lack of significant difference in the LFT marker in our study is attributable to the low duration of exposure time. Jadhav and colleagues' study showed that intoxication of rats by heavy metals induced an increase in the concentration of serum transferase, which is statistically significant only after 60 days of exposure (16).

Histopathological examination of specimens showed that a significant difference in sinusoidal diameters ($p < 0.001$) was detected in the ex-

perimental group compared to the control group of only the 4-week exposure-time subgroup. It seems that there was a tendency for time-dependent increase in the sinusoid diameters of the experimental groups. In accordance with our results, Kutlu and colleagues reported a sinusoidal dilatation and liver congestion in rats exposed to polychlorinated biphenyl mixture (18). The appearance of inflammatory cells in the liver as a sign of inflammation after exposure to solder fume is attributable to a general response of the organism to this toxic compound. The study of Kim and colleagues showed that acute exposure to welding fumes was associated with increased levels of systemic inflammatory markers in welders (2). Furthermore, statistical analysis demonstrated a significant difference in the central venule diameters among control and experimental groups of 2, 4 and 6-week exposure time. The study of Marroni and colleagues showed histopathological changes such as periportal fibrosis in the human liver (19). The study of Uboh et al. showed changes in the rat liver cell integrity after inhalation exposure to toxic fumes (10).

According to a study reported by Marques and colleagues on Pb treated mice, despite a reduction in the RBCs, hematocrit and mean corpuscular hemoglobin, an increase in aminotransferase did not show a statistically significant difference. Additionally, in another study on intoxication of mice with Pb, they proved that mice possess a remarkable poisoning resistance (17). The latter finding might also be true for similar resistance in the rats exposed to soldering fume in our study. It seems that reaction of the rat liver vascular elements to solder fume followed an adaptive pattern. It also revealed that there were no significant changes in the liver after the first two-weeks of fume inhalation. However, in animals in the six-week exposure subgroup, there was a new fume resistance due to animal adaptation; significant changes were also seen in the liver vascular elements.

Based on previous studies, the toxicity of organic Sn compounds is much higher than that of inorganic Sn compounds. Inhibition of adenosine triphosphate hydrolysis and uncoupling of oxidative phosphorylation taking place in the mitochondria have been suggested as the cellular mechanisms of tin toxicity (20). Aminotransferases include aspartate aminotransferase (AST) and alanine aminotransferase (ALT) which catalyze the transfer of amino groups from aspartic acid and pyruvic acid, respectively. ALT is a cytosolic enzyme, whereas AST is both a cytosolic and a mitochondrial enzyme (21). According to the obtained results, it seems that with this fume concentration and time exposure,

there was some potential for adaptation of the animals before any dramatic changes in liver serum markers appeared. In all the studied parameters, a degree of increase was seen in the experimental group when compared to the control group. ALT is specific to the liver, whereas AST is also found in the cardiac muscle, the kidneys and the brain (22). Alkaline phosphatase (AP) comprises a group of enzymes present in a variety of tissues including those of the liver and kidney. An increase of up to three times in AP levels is relatively non-specific. Redlich and colleagues reported that occupational liver diseases may occur more frequently in workers exposed to occupational fumes than in the general population, and stated that improvement in conditions with liver enzyme abnormalities were seen after modification of the workplace (23). Studies of Dossing and colleagues also demonstrated focal necrosis, portal tract enlargement and fibrosis in livers of workers exposed to organic solvents (24).

Conclusion

We can conclude that vascular structures of the liver respond to toxic fumes before the beginning of hepatic cell injury and before the appearance of significant elevation of serum transferase.

Acknowledgments

The authors thanks deputy for research of Zahedan University of Medical Sciences for financial support (grant number 748, awarded on 12/2/2005) of this study and Dr. S. J. Mowla for his encouragement and editing of this manuscript. There is no conflict of interest in this article.

References

1. Palmer K, Crane G. Respiratory disease in workers exposed to colophony solder flux fumes: Continuing health concerns. *Occ Med*. 1997; 47(8): 491-498.
2. Kim JY, Chen JC, Boyce PD, Christiani DC. Exposure to welding fumes is associated with acute systemic inflammatory responses. *Occup Environ Med*. 2005; 62(3): 157-163.
3. Antonini JM, Clarke RW, Krishna Murthy GG, Sreekanthan p, Jenkins N, Eagar TW, et al. Freshly generated stainless steel welding fumes induces greater lung inflammation in rats as compared to aged fume. *Toxicol Lett*. 1998; 98(1-2): 77-86.
4. Antonini JM, Lewis AB, Roberts JR, Whaley DA. Pulmonary effects of welding fumes: Review of worker and experimental animal studies. *Am J Indust Med*. 2003; 350-360.
5. Solano Lopez C, Zeidler-Erderly PC, Hubbs AF, Reynolds SH, Roberts JR, Taylor MD, et al. Welding fumes exposure and associated inflammatory and hyperplastic changes in the lungs of tumor associated A/J mice. *Toxicol Pathol*. 2006; 34(4): 364-372.

6. Leikin JB, Davis A, Klodd DA, Thunder T, Kelafant GA, Paquette DL, et al. Selected topics related to occupational exposures. Part IV. Occupational liver disease. *Dis Mon.* 2000; 46(4): 295-310.
7. Heederik D, Sigsgaard T, Thorne PS, Kline JN, Avery R, Bonlokke JH, et al. Health effects of airborne exposures from concentrated animal feeding operations. *Environ Health Perspect.* 2007; 115(2): 298-302.
8. Gustavson P, Jakobson R, Nyberg F, Pershagen G, Jarup L, Scheele P. Occupational exposure and lung cancer risk: a population based case referent study in Sweden. *Am J Epidemiol.* 2000; 152(1): 32-40.
9. Kakar S, Batts KP, Poeterucha JJ, Burgart LJ. Histologic changes mimicking biliary disease in liver biopsies with venous outflow impairment. *Mod Pathol.* 2004; 17(7): 874-878.
10. Uboh FE, Akpanabiatu MI, Eyong EU, Ebong PE, Offiong O. Evaluation of toxicological implications of inhalation exposure to kerosene fumes and petrol fumes in rats. *Acta Biol Szegediensis.* 2005; 49(3-4): 19-22.
11. Sheweita SA, Abd El-Gabar M, Bastawy M. Carbon tetrachloride induced changes in activity of phase II drug metabolizing enzyme in the liver of male Rats: role of antioxidants. *Toxicol.* 2001; 165(2-3): 217-224.
12. Berk PD, Wolkff AW. Billirubin metabolism and the hyperbilirubinemias. In: Braunwald AS, Kasper DL, Hauser SL, Longo DL, Jamoson JL, editors. *Harrison principle of internal medicine.* 15th edition.; Mc Graw Hill Com; 2001; 3: 1715-1721.
13. American Society for Testing and Materials (ASTM), Annual book of ASTM standards: Atmospheric analysis and occupational health and safety; Standard practice for measurement of metals in work place atmosphere by atomic absorption spectrophotometer. Easton, USA: ASTM; 1996; Vol. 11.03, D 4185-90: 246-253.
14. <http://www.cdc.gov/niosh/docs/2003%2D154/pdf/3500.pdf>.
15. Occupational Safety and Health Administration. Analytical Methods Manual ICP Analysis of Metal/metalloid particulate from solder Operations. Method No ID 206. Osha, Salt Lake city, Utah 1991.
16. Jadhav SH, Sarkar SN, Patil RD, Tripathi HC. Effects of Subchronic exposure via drinking water to a mixture of eight water contaminating metals: a biochemical and histopathological study in male rats. *Arch Environ Contam Toxicol.* 2007; 53(4): 667-677.
17. Marques CC, Nunes AC, Pinheiro T, Lopes PA, Santos MC, Viegas AM, et al. An assessment of time dependent effects of lead exposure in Algerian mice (*Mus spretus*) using different methodological approaches. *Biol Trace Elem Res.* 2006; 109(1): 75-89.
18. Kutlu S, Colakoglu N, Halifeoglu I, Sandal S, Seyran AD, Aydin M, et al. Comparative evaluation of hepatotoxic and nephrotoxic effects of aroclors 1221 and 1254 in female rats. *Cell Biochem Funct.* 2007; 25(2): 167-172.
19. Maroni M, Mocchi F, Visentin S, Preti G, Fanetti AC. Periportal fibrosis and other liver ultrasonography finding in vinyl chloride workers. *Occup Environ Med.* 2003; 60(1): 60-65.
20. Dossing M. Occupational toxic liver damage. *J Hepatol.* 1986; 3(1): 131-135.
21. Amdur OM. *Toxicology the basic science of poisons.* Singapore: McGraw-Hill; 1992; 670-671.
22. Massaro JE. *Handbook of human toxicology.* New York: CRC Press; 1997; 56-59.
23. Redlich CA, Beckett WS, Sparer J, Barwick KW, Riley CA, Miller H, et al. Liver disease associated with occupational exposure to the solvent dimethylformamide. *Ann Intern Med.* 1988; 108(5): 680-686.
24. Dossing M, Soborg PA, Peterson LM, Ranek L. Liver damage associated with occupational exposure to organic solvents in house painters. *Eur J Clin Invest.* 1983; 13(2): 151-157.

SID



سرویس های ویژه



سرویس ترجمه تخصصی



کارگاه های آموزشی



بلاگ مرکز اطلاعات علمی



سامانه ویراستاری STES



فیلم های آموزشی

کارگاه های آموزشی مرکز اطلاعات علمی جهاد دانشگاهی



نوبت آزمون

بررسی مقاله ای متون (مقدماتی)

کارگاه آنلاین
بررسی مقابله ای متون (مقدماتی)



PROPOSAL

پروپوزال

نوبت آزمون

پروپوزال نویسی و پایان نامه نویسی

کارگاه آنلاین
پروپوزال نویسی و پایان نامه نویسی



نوبت آزمون

آشنایی با پایگاه های اطلاعات علمی بین المللی و ترند های جستجو

کارگاه آنلاین آشنایی با پایگاه های اطلاعات علمی بین المللی و ترند های جستجو