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RESEARCH ARTICLE

BIOLOGICAL MONITORING OF EXPOSURE TO CHROMIUM AND TOLUENE AMONGST LEATHER WORKERS

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ABSTRACT

Although sophisticated processes have been developed to prepare the leather goods, handcrafts methods still remains an industry giving the high quality products. The job is performed by cutting, gluing, sewing, dyeing and buffing or polishing various leather products. Entire process involves the occupational exposure to toxic chemicals like benzene, toluene, styrene, n-hexane and metallic compounds like chromium and certain organic dyes. There exists a health risk of neuro-psychiatric disorders and behavioral changes after chronic toluene intoxication in these workers. Present investigation describes the magnitude of exposure to chromium and toluene in workers engaged in leather cottage industry, around Meerut, India. Urine samples were collected from a selected group of leather workers. The urine samples were examined for the metabolites of toluene and urinary chromium by spectrophotometer. These results show that excretion of hippuric acid, a metabolite of toluene was influenced by certain confounding factors i.e. cigarette smoke and food habits. It was also influenced by age and work experience. Presence of chromium in the urine samples denominates chromium toxicity in selected population of workers. It may lead to different health problems including lung cancer. Chromium concentration was found to be high in smokers, alcoholics and in non-vegetarians. With the current situation of industrial hygiene, exposure of leather dust, glues and chromium like metals amongst these workers needs continuous monitoring.

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INTRODUCTION

Leather industry which is the fifth single foreign exchange earner in India is mainly concentrated in a few states like Tamilnadu, Uttar Pradesh, West Bengal, Rajasthan, Maharashtra, Karnataka, Punjab, Andhra Pradesh and Bihar. About 1.2 million people are employed in leather and related industries in India (Ministry of Home Affairs, Govt. of India, 1971). More than 90% of this population belongs to socially and economically weaker sections. India has the highest livestock population of over 300 million which is about 13% of the world's livestock population. India produces about 100 million pieces of hides and skins which form 12% of the total world's output. Leather and leather goods industry is one of the biggest small scale industries in India. It is estimated that there are at present 2 lakh cottage sector units employing 1 to 4 persons in each, 3000 small scale units employing 20 to 50 persons in each and 150 large scale units employing 50 persons in each unit.

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With the emphasis on export of more and more finished leather and leather goods, a few units in the small and medium scale sectors have already diversified their activities and taking up the production of finished leather. It is expected that a number of existing tanning units will diversify their production activities in future and take up the manufacture of finished leather.

Most of the tanneries in the small and medium range are at present employing manual operations in these processes. But with the change of policy of the Government of India to export more finished leather and leather products, the tanning industry is gradually switching over to mechanization. There are nearly 56 tanneries in Utter Pradesh, India of which 48 are located in Kanpur (UP's bir boost for leather industry, 1978), four at Agra and one each at Etawa, Fatehpur, Bakshika-Talab and Unnao region of India. Out of the 48 tanneries in Kanpur, 32 tanneries process each 500 kg or less of hides. 60-70% of these tanneries carry out vegetable tanning. Most of the tanneries in Kanpur are located at Jajmou which is about 13 km. downstream of Kanpur on river Ganges. In Kanpur city there are some tanneries and these, in general are larger in capacity than those situated at Jajmou, and of the tanneries in Kanpur, the tanneries of TAFCO, Government of India (Tannery and Footwear Corporation) is the biggest. Harness and Saddlery tannery is the next biggest. Agra has four tanneries located in the city and suburbs.

Tannery effluents contain vegetable and non-vegetable tanning which cause chemical oxygen demand. They also contain high amounts of proteins, especially when a hair pulping-unhearing system is used. These proteins are biologically degradable and exert high BOD. Estimation of defined group of components present in the settled and filtered tannery waste water has shown that total protein constituted about 45.65%, volatile fatty acids 9.64%, ether soluble 3.46%, tannins 20.80% and inorganic volatile solids about 20.54% of the total dissolved volatile solids (Chakraborthy, 1972). In other words, about 79.80% of the total dissolved volatile solids in the settled and filtered composite tannery wastes are composed of organic matter present in the form of proteins, fatty acids, ether solubles and tannins 20-21% composed of other organic compounds.

Chlorides, trivalent chromium, nitrogen, phosphorous, sulphate, ammonium salts, lime etc, are the inorganic pollutants present in significant quantities. These pollutants are of more permanent nature, unless they are in suspended state or precipitated from solution and settled down. Using normal tanning techniques, chromium is present in the trivalent form which will be precipitated in the mixed effluent. The generally reported toxic effects of chromium refer to the hexavalent chromium. Such hexavalent chromium is likely to be encountered in practice in effluents “two bath chrome” tanning process. Toluene is highly soluble in blood and fat. The major route of absorption is through inhalation and skin absorption. Mainly paint, paint strippers, glues and some house hold cleaners contain toluene. 15-20% of the dose is excreted unchanged in the expired air. Complete clearance of toluene from the lung occurs in 24 hours. Urinary excretion of unchanged toluene is negligible. The remaining 80% of toluene is metabolized primarily to benzoic acid and excreted in the urine as the glycine conjugate i.e. hippuric acid. The half life time of hippuric acid ranges from 1 to 2 hours, it is completely eliminated after 24 hours.

Thus hippuric acid in urine is most widely used biological exposure index for toluene and is recommended when toluene exposure exceeded to 50ppm and group of workers are to be monitored. Sample collected at the end of the work shift are most useful. The pre shift samples of urine are useful to provide baseline information on hippuric acid. In those cases where a timed urine samples can be obtained over the last 4 hours of the work shift the rate of excretion of hippuric acid in urine correlated much better with toluene uptake. Toluene in venous blood has been recommended where the toluene exposure is less than 50 ppm. The biological exposure index is specific and sensitive.

The most important health concern for man from exposure to toluene is harmful effect on nervous system. The effects of toluene are dependent on both the amount and length of exposure. Forms of exposure to moderate of toluene like work place exposure can produce confusion, general weakness, loss of memory, nausea and loss of aptitude. Long term exposure of toluene has been linked with permanent damage to the brain. Effect such as problems with speech, vision, and hearing, loss of mensural control and loss of memory have also been observed. According to “National Toxicological Program” toluene has been found to cause cancer also.

There are chances that a large section of people engaged in leather industry is exposed to chromium and toluene. Chromium is a toxic metal. Exposure to chromium may cause skin, liver & kidney damage. Therefore, health risk assessment of these workers is important from public health point of view. In this study, two villages located in Meerut (Sobha Pur) & Hapur (Ambedkar Nagar) famous for the preparation of skins/hides for leather industries were identified. After a primary survey of the population, public health problems were noticed. Therefore, an epidemiological study on biological monitoring of exposure to chromium and toluene in these workers was proposed.

MATERIALS AND METHODS

A significant number of people were found employed in leather & leather goods industry in Meerut and Hapur region. A primary survey reveals that the leather industry employs people of different age and different habits. However, female workers were not found to be engaged in leather industry. Leather workers from different areas of Meerut & Hapur region of India were registered and information like age, work experience, smoking habit, alcohol consumption, food habit, overall health conditions was sought after personal interviews.
Healthy persons who had never been occupationally exposed to chromium and toluene, living in clean surroundings were selected as controls.

The survey was made in months of July-August 2008. Urine samples were collected in white sterile bottles, from all subjects at the end of the work shift. These samples were transported in an ice box to the laboratory and stored frozen till analysis. The samples were processed for the determination of specific gravity, creatinine, hippuric acid and chromium, applying following methods:-

Determination of specific gravity urine

Specific gravity of urine samples was determined by a urinometer (Atago Company Ltd. Tokyo, Japan). Urine samples having values of specific gravity between 1.010-1.030 were selected for further analysis.

Determination of creatinine in urine

Creatinine was determined by alkaline picrate method (Toro & Ackerman, 1975), using a commercial kit supplied by Span Diagnostics Ltd. India. The absorbance was recorded at 520 nm using spectrophotometer.

Determination of Hippuric acid in urine

Hippuric acid in urine samples was determined by applying the method of Ogata and Hobara (1979), using paradimethyl aminobenzaldehyde in pyridine as the extraction medium. The absorbance was recorded at 440 nm using spectrophotometer.

Determination of Chromium in urine

Urine samples were acidified with a drop of nitric acid and stored into deep freezer till analysis. Standards of different concentrations were made using metallic chromium. The chromium was estimated using Atomic Absorption Spectrophotometer (AAS). The chromium concentration was determined at wavelength of 357.9 nm with 0.2 nm as the slit. The final observations were made by putting the absorbance in the standard graph.

Statistics

Data was analyzed using student's "t"- test (Fisher, 1950).

RESULTS

The target population in this study belonged to the village's viz. Ambedkar Nagar (Hapur) and Sobha Pur (Meerut). The results, obtained on specific gravity, creatinine, hippuric acid and chromium amongst workers of leather industry are described as below-

Specific gravity

The first observation made after the collection of urine samples was to determine specific gravity. Specific gravity of the urine samples of smokers was higher than those of non-smokers (Table 1; Figure 1). Similarly the alcoholic population among the leather workers exhibited higher specific gravity than the non-alcoholic population (Table 2; Figure 2).

The specific gravity of urine samples of non-vegetarians was higher than those of vegetarians (Table 3; Figure 3). The effect of age on the specific gravity was also examined. Those engaged in this industry for 10-20 years show highest specific gravity whereas the lowest values were observed for 51-60 years (Table 4; Figure 4). Work experience also influenced the specific gravity. It was found higher in workers engaged in this industry for 1-5 years, whereas lowest values were observed in the people having the work experience 21-25 years (Table 5; Figure 5).

Specific gravity of urine samples of leather industry workers with reference to smoking habit

Table 1.

S. No.	Group	Specific gravity
1.	Smokers	1.021 ± 0.004
2.	Non-smokers	1.019 ± 0.001
3.	Controls	1.012 ± 0.006

Results are expressed as mean ± SE (n = 5)

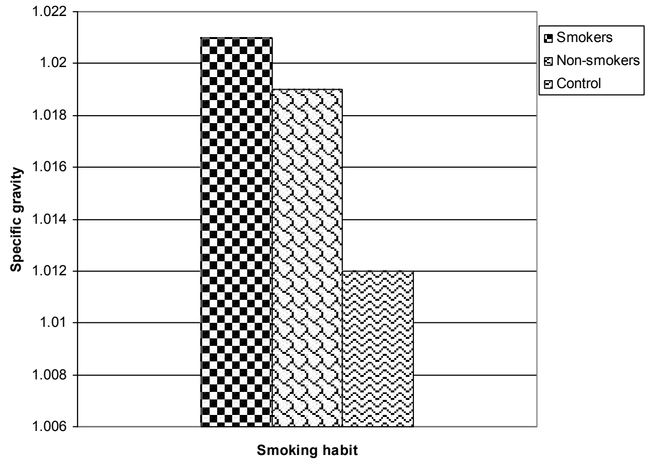

Fig.1.

Specific gravity of urine samples of leather industry workers with reference to alcohol intake

Table 2.

S. No.	Group	Specific gravity
1.	Alcoholics	1.021 ± 0.001
2.	Non-alcoholics	1.019 ± 0.001
3.	Controls	1.012 ± 0.006

Results are expressed as mean ± SE (n = 5)

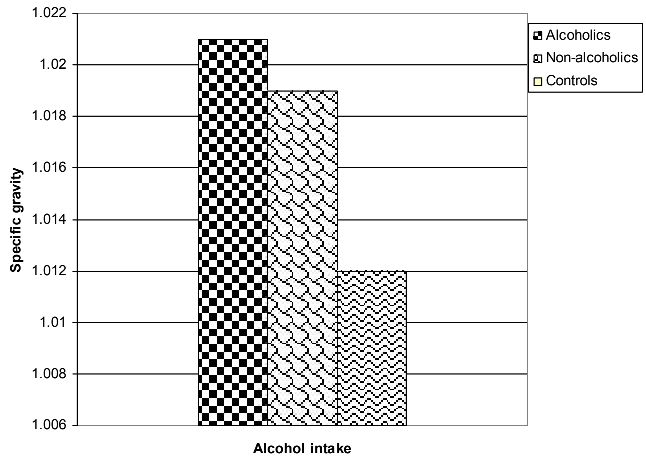

Fig.2.

Specific gravity of urine samples of leather industry workers with reference to food habit

Table 3.

S. No.	Group	Specific gravity
1.	Vegetarians	1.020 ± 0.006
2.	Non-vegetarians	1.022 ± 0.001
3.	Controls	1.012 ± 0.006

Results are expressed as mean ± SE (n = 5)

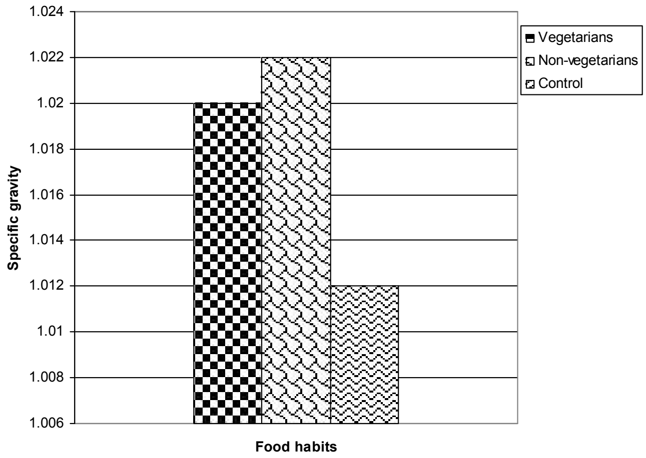

Fig. 3.

Specific gravity of urine samples of leather industry workers with reference to age

Table 4.

S. No.	Age group (years)	Specific gravity
1.	10-20	1.024 ± 0.0006
2.	21-30	1.017 ± 0.001
3.	31-40	1.019 ± 0.001
4.	41-50	1.018 ± 0.001
5.	51-60	1.014 ± 0.001
6.	61-70	1.018 ± 0.001
7.	Control	1.012 ± 0.0006

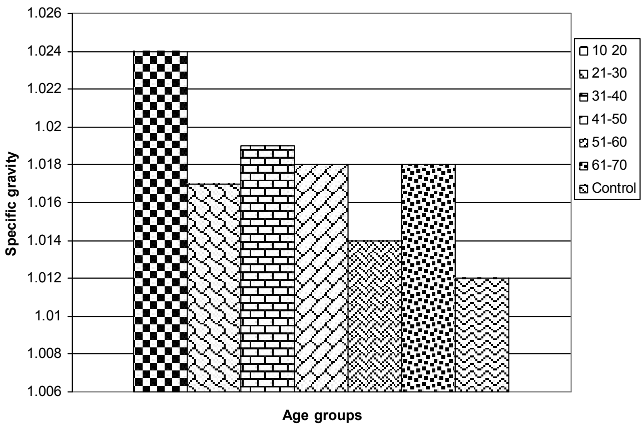

Fig. 4.

Specific gravity of urine samples of leather industry workers with reference to work experience

Table 5.

S. No.	Work experience (years)	Specific gravity
1.	1-5	1.022 ± 0.001
2.	6-10	1.017 ± 0.001
3.	11-15	1.022 ± 0.001
4.	16-20	1.016 ± 0.001
5.	21-25	1.011 ± 0.0006
6.	26-30	1.014 ± 0.001
7.	31-35	1.018 ± 0.001
8.	36-40	1.016 ± 0.001
9.	Controls	1.012 ± 0.0006

Results are expressed as mean ± SE (n = 5)

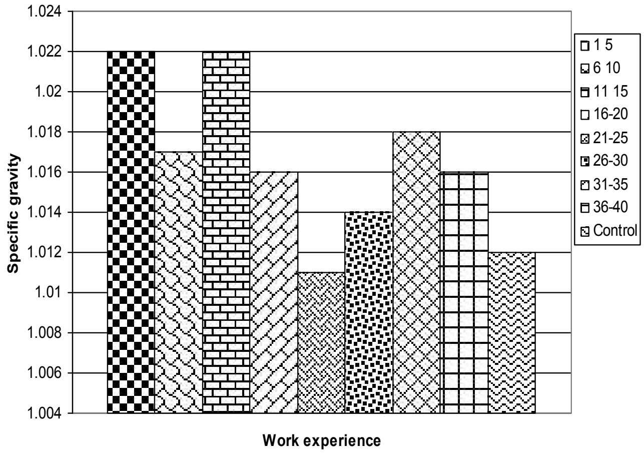

Fig. 5.

Creatinine

To study the affect of different chemicals/organic solvents on renal function, creatinine in the urine samples is treated as a reliable test. It was higher in non-smokers in comparison to smokers. However, it was higher in alcoholics in comparison to non-alcoholics. Again the non-vegetarians excreted more creatinine in comparison to vegetarians (Table 6-8; Figure 6-8). Effect of age on creatinine values showed interesting results. It was highest in the age group of 31-40 followed by those having the age of 61-70 years (Table 9; Figure 9). Effect of job experience showed that creatinine values were highest in the subjects having the work experience of 16-20 years, followed by those having the job experience of 11-15 years (Table 10; Figure 10).

Hippuric acid

Another study was made on the excretion of hippuric acid, a metabolite of toluene. It showed significant difference in different groups. It was higher in non-smokers in comparison to smokers. It was higher in alcoholics in comparison to non-alcoholics. Non-vegetarian excreted more hippuric acid than the vegetarian population. Age also affected the urinary content of hippuric acid. It was found to be highest in the population comprising subjects of 61-70 years. The population of people having the job experience of 11-15 years excreted highest amount of hippuric acid followed by those having the job experience of 6-10 years (Table 5-10; Figure 5-10).

Creatinine and hippuric acid in urine samples of leather industry workers with reference to smoking habit

Table 6.

S. No.	Groups	Creatinine (mg/L)	Hippuric acid (mg/L)
1.	Smokers	506 ± 134.6*	117 ± 2.7*
2.	Non-smokers	817 ± 331.7**[a]	120 ± 2.5**
3.	Controls	225 ± 1.5	88 ± 3.6

Results are expressed as mean ± SE (n = 5). * P<0.05 compared to control; ** p<0.02 compared to control; a p<0.05 compare to non smokers

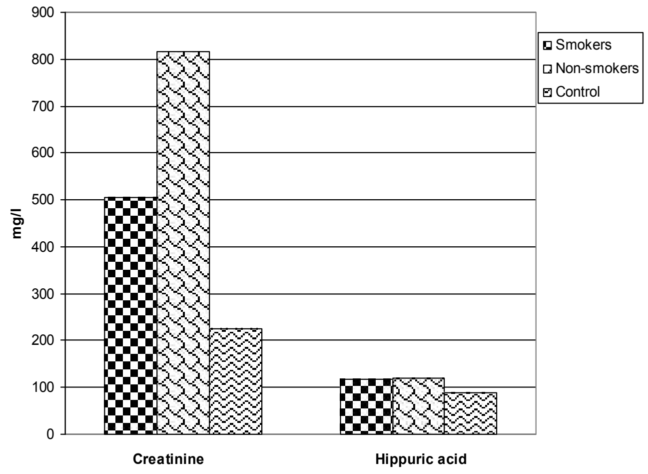

Fig. 6.

Creatinine and hippuric acid in urine samples of leather industry workers with reference to alcohol intake

Table 7.

S. No.	Group	Creatinine (mg/l)	Hippuric acid (mg/l)
1.	Alcoholics	1008 ± 255.8**[a]	123 ± 1.2*
2.	Non-alcoholics	247 ± 20.8	98 ± 6.9
3.	Controls	225 ± 1.5	88 ± 3.6

Results are expressed as mean ± SE (n = 5). * P<0.05 compared to control; ** p<0.02 compared to control; a p<0.05 compare to non alcoholic

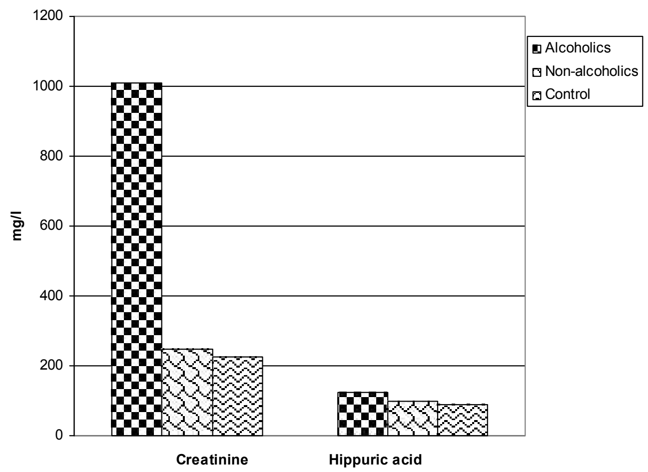

Fig. 7.

Creatinine and hippuric acid in urine samples of leather industry workers with reference to food habit

Table 8.

S. No.	Group	Creatinine (mg/l)	Hippuric acid (mg/l)
1.	Vegetarians	310 ± 3.1	93 ± 0.6
2.	Non-vegetarians	1011 ± 254.5*[a]	123 ± 1.2*
3.	Controls	225 ± 1.5	88 ± 3.6

Results are expressed as mean ± SE (n = 5). * P<0.05 compared to control; ** p<0.02 compared to control; a p<0.05 compare to vegetarian

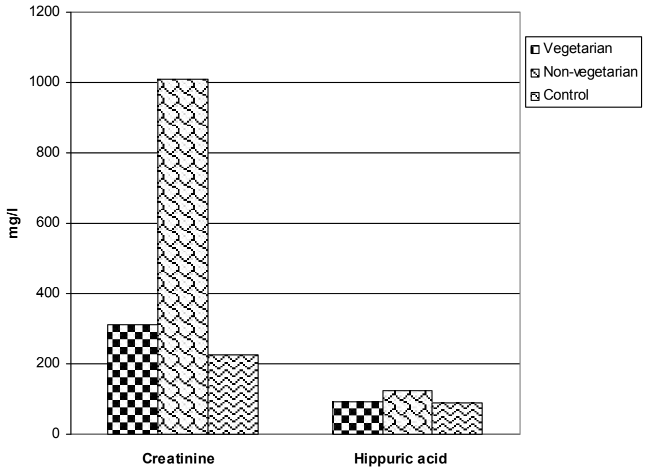

Fig. 8.

Creatinine and hippuric acid in urine samples of leather industry workers with reference to age

Table 9.

S. No.	Age group (years)	Creatinine (mg/l)	Hippuric acid (mg/l)
1.	10-20	- - -	9 ± 0.3
2.	21-30	287 ± 22.1	79.8 ± 17.4
3.	31-40	948 ± 285.2	106 ± 9.8
4.	41-50	264 ± 12.1	95.2 ± 7.4
5.	51-60	332 ± 11.0	69.4 ± 21.3
6.	61-70	367 ± 26.7	115 ± 6.3
7.	Control	225 ± 1.5	88.8 ± 3.6

Results are expressed as mean ± SE (n = 5)

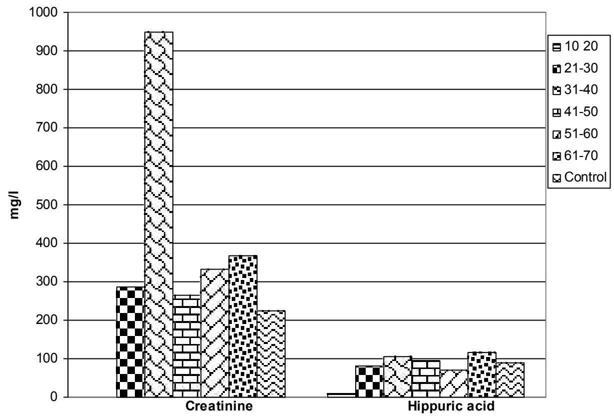

Fig. 9.

Creatinine and hippuric acid in urine samples of leather industry workers with reference to work experience

Table 10.

S. No.	Work experience (years)	Creatinine (mg/l)	Hippuric acid (mg/l)
1.	1-5	225 ± 4.4	8 ± 0.9
2.	6-10	270 ± 17.7	98 ± 6.8
3.	11-15	562 ± 160.9	118 ± 7.2
4.	16-20	615 ± 285.3	77 ± 17.7
5.	21-25	243 ± 7.3	4 ± 0.6
6.	26-30	461 ± 144.8	59 ± 20.4
7.	31-35	255 ± 4.1	59 ± 28
8.	36-40	318 ± 26.1	85 ± 19.5
9.	Controls	225 ± 1.5	88 ± 3.6

Results are expressed as mean ± SE (n = 5)

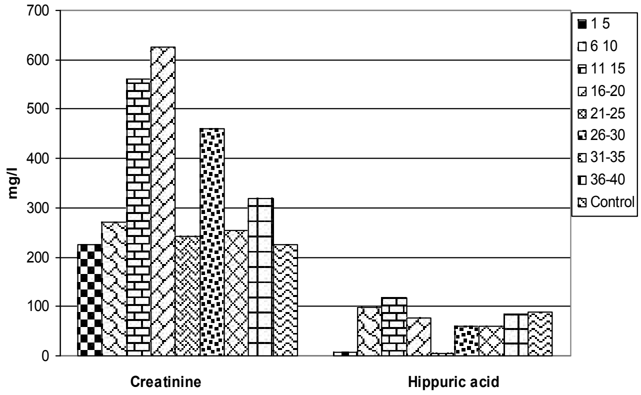

Fig. 10.

Chromium

To examine the exposure fo chromium amongst the workers of this cottage industry, urine concentration of chromium was determined. It was found to be higher in smokers, alcoholics & non-vegetarians (Table 11-13; Figure 11-13). Effect of age and work experience was also studied. Chromium concentration was highest in the population of the age group 51-60 years whereas those people having the job experience of 21-25 years exhibited highest concentration of urinary chromium (Table 14-15; Figure 14-15).

Chromium in urine samples of leather industry workers with reference to smoking habit

Table 11.

S. No.	Group	Chromium (µg/l)
1.	Smokers	10.6 ± 0.9* **
2.	Non-smokers	8.6 ± 1.9* [a]
3.	Controls	4 .0± 0.7

Results are expressed as mean ± SE (n = 5). * P<0.05 compared to control; ** p<0.02 compared to control; a p<0.05 compare to smokers

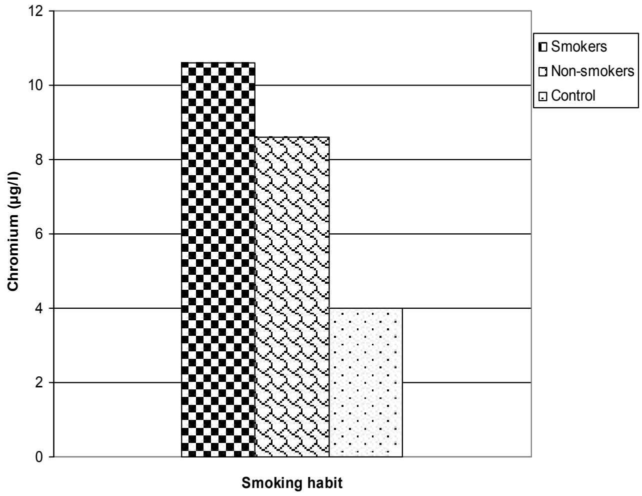

Fig. 11.

Chromium in urine samples of leather industry workers with reference to alcohol intake

Table 12.

S. No.	Group	Chromium (µg/l)
1.	Alcoholics	9.8 ± 1.3**
2.	Non-alcoholics	6.2 ± 1.1*[a]
3.	Controls	4.0 ± 0.7

Results are expressed as mean ± SE (n = 5). * P<0.05 compared to control; ** p<0.02 compared to control; a p<0.05 compare to alcoholics

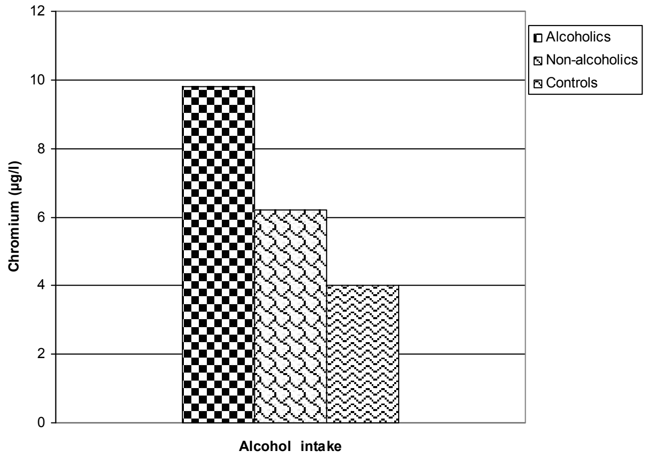

Fig. 12.

Chromium in urine samples of leather industry workers with reference to food habit

Table 13.

S. No.	Group	Chromium (µg/l)
1.	Vegetarians	7.9 ± 0.1*
2.	Non-vegetarians	11.4 ± 0.7**[a]
3.	Controls	4.0 ± 0.7

Results are expressed as mean ± SE (n = 5). * P<0.05 compared to control; ** p<0.02 compared to control; a p<0.05 compare to vegetarian

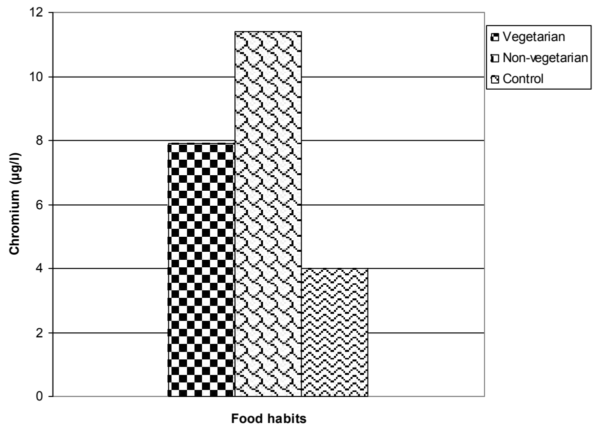

Fig. 13.

Chromium in urine samples of leather industry workers with reference to age

Table 14.

S. No.	Age group (years)	Chromium (µg/l)
1.	10-20	6.0± 0.3
2.	21-30	6.2 ± 1.3
3.	31-40	8.6 ± 1.9
4.	41-50	6.8 ± 1.4
5.	51-60	9.8 ± 1.2
6.	61-70	7.6 ± 0.4
7.	Control	4.0 ± 0.7

Results are expressed as mean ± SE (n = 5)

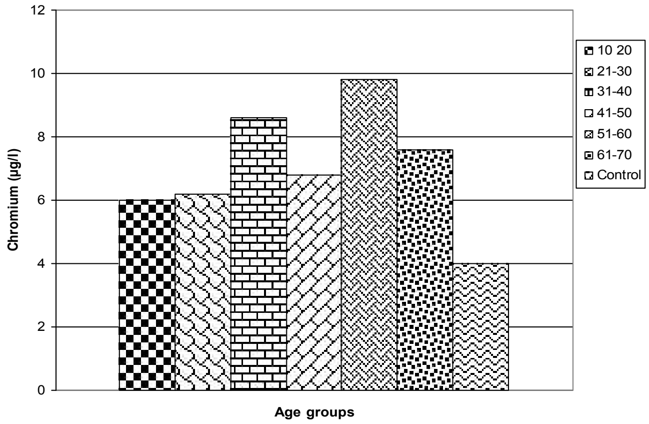

Fig. 14.

Chromium in urine samples of leather industry workers with reference to work experience

Table 15.

S. No.	Work experience (years)	Chromium (µg/l)
1.	1-5	6.2 ± 0.3
2.	6-10	7.6 ± 2
3.	11-15	3.6 ± 0.8
4.	16-20	5.8 ± 1.3
5.	21-25	12.8 ± 0.5
6.	26-30	9.0 ± 0.8
7.	31-35	9.8 ± 1.5
8.	36-40	7.2 ± 0.5
9.	Controls	4.0 ± 0.7

Results are expressed as mean ± SE (n = 5)

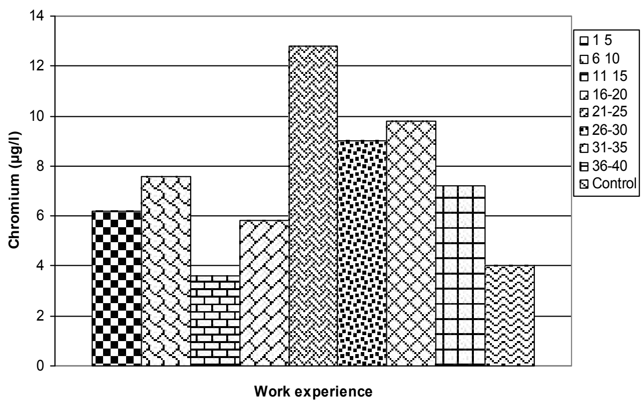

Fig. 15.

DISCUSSION

Present study deals with the biological monitoring of exposure to toluene and chromium in skin/hide workers of two cities of West U.P. i.e. Meerut and Hapur. Toluene is a general industrial solvent, which is used as a solvent for paints; lacquer, thinner, glues and coating agents. After inhalation, toluene is rapidly absorbed by various tissues /organs. It accumulates in soft or adipose tissue from which it is slowly eliminated after metabolism (Pyykko *et al.*, 1977). Toluene is metabolized via cytochrome P450 to benzyl alcohol which is further oxidized by alcohol and aldehyde dehydrogenase to benzaldehyde and benzoic acid respectively (Pyykko, 1983). Benzoic acid conjugates with glycine to form hippuric acid which is excreted in the urine. This metabolite serves as a reliable marker of exposure to toluene.

Presence of hippuric acid in the urine samples of skin/hide workers observed during present study confirms that they are exposed to toluene in their work environment. The excretion of toluene was influenced by confounding factors viz. cigarette smoke, alcohol and food habits. Further its metabolism was influenced by age and their work experience.

Toluene causes induction of microsomal liver enzymes at relatively low concentrations. Although it has no carcinogenic or mutagenic potency, it can cause serious kidney damage. Further toluene exposure is related to central nervous system depression including symptoms i.e. drowsiness, dizziness, headache and nausea. These symptoms are related with its ability to lipid interactions in neural membranes. Solvent molecules can bind to hydrophobic part in the membrane integral proteins which disturb ion balance in the membrane (Naskali *et al.*, 1993). Long term inhalation of toluene is known to cause multi focal neurological disorders characterized by ectesia, tremors, emotional labiality and brain stem atrophy (King *et al.*, 1985; Ikeda and Tsukagoshi, 1990). There is a risk of neuro-psychiatric disorders and behavioral changes after chronic toluene intoxication.

Epidemiological studies have demonstrated that nickel, chromium, arsenic, cadmium and beryllium compounds are human carcinogens. Lung cancer in workers, producing dichromate from the raw material, was reported in Germany in 1930s (Baetjer, 1950). In more then 50 epidemiological studies on chromium exposure and lung cancer, the major investigation have been performed on chromium leather workers, chromate paint makers and chrome platters (IARC, 1990). The over all relative risk of lung cancer in these studies have been estimated at 2.78 (95% confidence interval).

Animal models have also contributed to the precise identification of the carcinogens in the chromate production in industry, although, they confirmed the carcinogenic potential of the chromium in leather industry. No such epidemiological studies have so far been made especially in India. Leather stained either used by chromium salt or wetting which uses vegetable extracts. This process is believed to produce a carcinogen as leather dust. Reports from Florence in Italy (1963-1977) were reviewed to identify cases of primary cancer of the nasal cavity; seven out of 66 cases belonged to shoe makers (Cecchi, 1980). A similar study was performed in England. The author identified 266 cases of nasal cancer in leather workers (Acheson *et al*., 1981). The high risk population included those, who were exposed to leather dust and used vegetable tanned leather, however, no such cases were noted during tanning process. It is very likely that these leather workers may develop nasal polyps in due course of time. Therefore, present results suggest that leather workers may suffer from a number of illnesses. With the current situation of industrial hygiene in India, exposure of leather dust or toluene should be strictly limited and monitored.

Further epidemiological study on same population of workers will be important from occupational health point of view.

REFERENCES

"U. P's bir boost for leather industry" 1978. Leather processing, 7:11.

Abbritti, G. *et al*. 1976. Shoe-makers polyneuropay in Italy. The aetiological problem. *Br. J. Ind. Med.,* 33:92.

Acheson, E.D., Cowdell, R.H. and Rang E.H. 1981. Nasal cancer in England and Wales: An occupational survey. Br. J. Ind. Med., 38:218.

Aksoy, M., Erdem, S. and Dincol, K. 1974. Leukemia in shoe-workers exposed chronically to benzene. *Blood*, 44:837.

Baetjer, A.M. 1950. Pulmonary carcinoma in chromate workers. AMA Arch. *Ind. Hyg. Occup. Med*., Nov. 2(5), 487:504.

Cairns, R.J. and Calnon, C.D. 1966. Green tattoo reactions associated with cement dermatitis. *Brit. J. Dermatol*., 74:288.

Cecchi, F. *et al*. 1980. Adenocarcinoma of the nose and paranasal sinuses in shoe makers and wood workers in the province of Florence, Italy (1963-1977). *Br. J. Ind. Med*., 37:222.

Chakraborthy, R.N. 1972. "Some aspects of tannery waste treatment". Proc. Symp. Tannery wastes, CLRI, Madras, 1:4.

Dyro, F.M. 197). Methyl ethyl ketone polyneuropathy in shoe factory workers. *Clin. Toxicol*., 13:371.

Fisher, R.A. 1950. Statistical methods for research workers. 2nd edn, Oliver and Boyd, London.

Holz, H., Mappes, R., and Weidmann, G. 1961. Chromatalergie bei Bohrolekzem. *Berufs-Dermatoson*., 9:113.

Ikeda, M. and Tsukagoshi, H. 1990. Encephalopathy due to toluene sniffing. Report of a case with the magnetic resonance imaging. *Eu. Neurol*., 30, 347:349.

Infante, P.F. *et al*. 1977. Leukemia in benzene workers. Lancet, 2:766.

International Agency for Research on Cancer 1990. IARC Monographs on the Evaluation of the Carcinogenic risk to Humans: Chromium Nickel and Welding. Vol., 49, IARC Lyon France.

Karacic, V., Skender, L. and Prpic-Majic, D. 1987. Occupational exposure to benzene in the shoe industry. *Am. J. Ind. Med*., 12:531.

King, G.I., Jacobs, R.E. and White, S.H. 1985. Hexane dissolved in dioleoyllecithin bilayers has a partial molar volume of approximately zero. *Biochem*., 24, 4637:4645.

Kuttruff, J. T. DeHart, S.G. and O' Brien M.J. 1998. 7500 years of prehistoric footwear from Arnold Research Cave, Missouri. *Science*, 281:720.

Mallory, T. B., Gall, E.A. and Brickley, W.J. 1939. Chronic exposure to benzene (benzol) III. The pathologic results. *J. Ind. Hyg. Toxicol*., 21:355.

Naskali, L., Engelke, M., Tahti, H. and Dichl, H. 1993. The effects of selected organic solvents on rat synaptosomal membrane fluidity and integral enzyme activities. *Neurosei. Res. Commun*., 13, 27:35.

Ogata, M. and Hobara, T.A. 1979. Industrial Health, 17:61.

Parmeggiani, L. 1983. Footwear industry, In Encyclopedia of occupational Health and Safety, 3rd ed. Geneva, International Labour Organization.

Pyykko, K. 1983. Time course of effects of toluene on microsomal enzymes in rat liver, kidney and lung during and after inhalation exposure. *Chem. Biol. Interact*., 44, 299:310.

Pyykko, K., Tahti, H. and Uapaatalo, H. 1977. Toluene concentration in various tissues of rats after inhalation and oral administration. *Arch. Toxicol*., 38, 169:176.

Report of Census of India, 1971. Ministry of Home Affairs, Govt. of India.

Rinsky, R.A. *et al*. 1987. Benzene and leukemia, an epidemiologic risk assessment. *N. E. ngl. J. Med*., 316:1044.

Rizzuto, N., Terzian, H. and Galiazzo-Rizzuto, S. 1977. Toxic polyneuropathies in Italy due to leather cement poisoning in shoe industries. A light and electron-microscopic study. *J. Neurol. Sei*., 31:343.

Samitz, M. H. and Katz, S. 1964. A study of the chemical reactions between chromium and skin. *J. Invest. Dermatol*., 35:45.

Samitz, M.H. and Katz, S. 1963. Priliminary studies on the reduction and binding of chromium with skin. *Arch. Dermatol*., 88:816.

Scarpelli, A. *et al*. 1993. Exposure to solvents in the shoe and leather goods industries. *Int. J. Epidemiol*., 22 (suppl 2), 546.

Scheideggar, J.P., Schwarz-Speck, M., Schwarz, K. and Storck, H. 1967. Experimentalles Ekzem auf Kaliumbichromat im Tierversuch. *Dermatologica*., 135:382.

Schwarz, E. and Spier, H.W. 1960. Die percutane Resorption von 3- und 6-wertigem Chrom (Cr51). Zur pathogens des Kontaktekzems, *Arch. Klin. Exp. Derm*., 210:220.

Spiar, H.W. and Natzel, R. 1952. Zur Pathogenes des zementekzems. I. Zementekzem and Chromatallergic. *Arch. Dermatol., Syph*., 193:537.

Toro, G. and Ackerman, P.G. 1975. Practical Clinical Chemistry. Little Brown and company, Boston, p-154.

Vigliani, E.C. and Saita, G. 1964. Benzene and leukemia. *N. Engl. J. Med*., 271:872.

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