J. Biosci., Vol. 10, Number 2, June 1986, pp. 227-234. © Printed in India.

Effect of mandur bhasma on lipolytic activities of liver, kidney and adipose tissue of albino rat during CCl_4 induced hepatic injury

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MS received 26 December 1984; revised 16 December 1985

Abstract. 'Mandur bhasma', an ayurvedic preparation of iron is used in traditional medicine against hepatitis. In the present study the hepatoprotective property of this drug was tested in albino rats during $CC1_4$ induced hepatic injury. The effect of mandur bhasma on the activities of the lipolytic enzymes of rat liver, kidney and adipose tissue were studied during hepatitis induced by CCl_4. The activities of acid lipase, alkaline lipase, lipoprotein lipase and hormone sensitive lipase exhibited significant alterations during CCl_4 induced hepatic injury, indicating a role for these enzymes in the mobilization of fat from adipose tissue and accumulation of fat in liver and kidney. Simultaneous treatment with mandur bhasma prevented the paraffin mediated and $CC1_4$ mediated changes in the enzyme activities. These results suggest the hepatoprotective role of mandur bhasma during $CC1_4$ induced hepatic injury.

Keywords. Acid lipase; alkaline lipase; hormone sensitive lipase; lipoprotein lipase; mandur bhasma; liver; kidney; adipose tissue; CCl_4.

Introduction

Lipolytic enzymes play a very important role in the biological turnover of lipids and various forms of lipases have been reported (Brockerhoff and Jensen, 1974). Lipoprotein lipases have been detected in many tissues such as adipose tissue, mammary tissue, muscle, heart, aorta, liver, kidney, lung, spleen, medulla, diaphragm and fluids (plasma and milk) (Desnuelle, 1972; Fredrickson and Levy, 1972).

Hepatic triglyceride lipases have been assayed in liver homogenates (Varinkova and Mosinger, 1965), plasma membrane, cytosol, microsomes and lysosomes (Hayashi and Tappel, 1970; Assmann *et al*., 1973; Teng and Kaplan, 1974; Debeer *et al*., 1979). The cellular fractions show alkaline pH optima, except the lysosomal preparation which has an optimum pH of 4–6.

Mahadevan and Tappel (1968) reported the lysosomal and microsomal lipases of rat kidney. Similarly, Matsumura et al. (1976) reported 3 different forms of lipases in rat adipose tissue *viz*. lipoprotein lipase, hormone sensitive lipase and triglyceride lipase with alkaline pH optima. In our laboratory we have detected the lipolytic activity in rat adipose tissue having an acidic pH optimum of 4·2 (unpublished data). It is well known that treatment of CCl_4 to rats causes centrolobular hepatic necrosis leading to the accumulation of fat in liver and kidney. It was suggested that fats from the peripheral

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adipose tissue are translocated to the liver and kidney leading to accumulation during toxicity (Roullier, 1963).

Mandur bhasma, an ayurvedic preparation of iron (prepared using complex ayurvedic processes like Shodhana, Marana etc.) has long been used in the treatment of liver diseases (Sharma, 1977), but detailed biochemical studies are not available. Therefore, in the present investigation attempts have been made to find out the effect of mandur bhasma on lipolytic enzymes of liver, kidney and adipose tissue of albino rat during hepatitis induced by CCl_4.

Materials and methods

Swiss Norwegian male albino rats reared in the animal house ofthe department, were used for these experiments. The rats weighing 125–150 *g* were fed with standard laboratory diet (Hindustan Lever Ltd., Bombay) and water *ad libitum*.

Experimental protocol

Experiments were run in 5 sets and 5 rats were used in each group. To the first set, mandur bhasma (1 mg/100 g body wt.) was given orally for 11 days. To the second set paraffin (0·1 ml/100 g body wt.) was injected subcutaneously for 11 days. To the third set, paraffin (0·1 ml/100 g body wt.) was administered subcutaneously with the simultaneous oral administration of mandur bhasma (1 mg/100 g body wt.) for 11 days. To the fourth set 0·3 ml CCl_4 in liquid paraffin (3:1, v/v) per 100 g body wt. was given subcutaneously for 11 days. To the fifth set 0·3 ml CCl_4 in liquid paraffin (3:1, v/v) per 100 g body wt. was given subcutaneously concomitant with the oral administration of mandur bhasma (1 mg/100 g body wt.) for 11 days. The dose of mandur bhasma (1 mg/100 g body wt.) was found to be significantly protective in preliminary experiments, A group of 5 untreated rats was designated as normal.

Livers of the experimental animals were tested by routine biopsy methods on the 5th and 11th day to check for hepatic necrosis. Acute necrosis was observed on the 11th day in the livers of CCl_4 treated rats. All the animals were sacrificed on the 12th day by a sharp occipital blow. Liver, kidney and adipose tissue were dissected out and used for the assay of lipolytic activities. Hormone sensitive lipase, lipoprotein lipase and alkaline lipase were assayed according to Matsumura *et al*. (1976) using triolein as substrate, while the acid lipase activity was determined by the method of Mahadevan and Tappel (1968). At the end of incubation the enzyme activities were arrested and the liberated free fatty acids were estimated as described earlier (Patil *et al*., 1983). Protein estimations were carried out in kidney and liver (Lowry *et al*., 1951) and adipose tissue (Tornqvist and Belfrage, 1976) and lipid peroxidation was studied by the thiobarbituric acid method (Buege and Aust, 1978).

Results

Table 1 shows the changes in wet weights of liver, adipose tissue and kidney of normal, mandur bhasma, paraffin, paraffin + mandur bhasma, CCl_4 and CCl_4 + mandur

Table 1. Alterations in fresh weights of different tissues of rats treated with mandur bhasma, paraffin, paraffin + mandur bhasma, CCl_4 and CCl_4 + mandur bhasma.

Treatment	Liver	Adipose tissue	Kidney
Normal	3·836 ± 0·145	0·675 ± 0·036	0·634 ± 0·043
Mandur bhasma	3·460 ± 0·155[b]	0·397 ± 0·026[a]	0·525 ± 0·029[d]
Paraffin	3·462 ± 0·160[b]	0·637 ± 0·035[b]	0·693 ± 0·033[a]
Paraffin + mandur bhasma	3·325 ± 0·146[b]	0·358 ± 0·021[a]	0·471 ± 0·035[a]
CCl_4	4·224 ± 0·233[a]	0·510 ± 0·027[a]	0·707 ± 0.037[a]
CCl_4 + mandur bhasma	3·842 ± 0·187[b]	0·670 ± 0·037[b]	0·658 ± 0·031[d]

Values are expressed as g/100 g body wt.

[a]$P < 0·05$; [b]$P > 0·05$ compared to the control group.

bhasma treated rats. Treatment of mandur bhasma, paraffin and paraffin + mandur bhasma reduced the weights of liver, kidney and adipose tissue, paraffin treated rat kidney being the exception. A marked fall in the wet weights of kidney and adipose tissue of mandur bhasma treated rats was noticed as compared to that of normal rats, while the treatment with CCl_4 caused an increase in the wet weights of liver and kidney with a decrease in the wet weight of adipose tissue. Simultaneous treatment of CCl_4 and mandur bhasma did not exhibit the marked changes observed in the wet weights of these tissues.

Histologically the liver of mandur bhasma treated rats showed absolutely normal appearance having very rare binucleated cells. Paraffin treatment caused an increase in the size of hepatic cells which were stained intensely with eosin and the nuclei did not show staining with hematoxylin although they showed positive Feulgen reaction. Treatment of mandur bhasma concomitant with paraffin exhibited the normal histological picture of the liver. The blood in the blood vessels of the liver, which was vacuolated in paraffin treated rat became normal by treatment of mandur bhasma along with paraffin. CCl_4 treatment showed hepatic necrosis which was evidenced by the detection of highly vacuolated cells. Though the simultaneous treatment of mandur bhasma and CCl_4 did not alter the histological picture of the liver significantly, it showed an increased number of binucleated cells and mitotic figures.

The kidney of mandur bhasma treated rats displayed the normal histological picture. On the contrary paraffin treatment showed foggy patches of tubules mainly in the cortex region with the vacuolar appearance of blood in blood vessels, but treatment of mandur bhasma along with paraffin demonstrated the normal appearance of the kidney with a conspicuous decrease in the fogginess of tubules. The appearance of the blood in blood vessels was normal. Similarly the conspicuous foggy necrosis of proximal tubules observed in the kidney of CCl_4 treated rats was significantly reduced in CCl_4 + mandur bhasma treated rats (data not presented).

Alterations in the lipolytic activities of the liver of normal rats and the rats treated with mandur bhasma, paraffin, paraffin + mandur bhasma, CCl_4 and CCl_4 + mandur bhasma are represented in table 2. Mandur bhasma, paraffin and paraffin + mandur bhasma treatments caused an increase in alkaline and lipoprotein lipase activities, while

Table 2. Effect of administration of mandur bhasma, paraffin, paraffin + mandur bhasma, CCl_4 and CCl_4 + mandur bhasma on the lipolytic activities of rat liver.

Treatment	Lipolytic activities					
	Acid lipase		Alkaline lipase		Lipoprotein lipase	
	K units/g wet wt.	Units/mg protein	K units/g wet wt.	Units/mg protein	K units/g wet wt.	Units/mg protein
Normal	$10{\cdot}00 \pm 0{\cdot}59$	$33{\cdot}33 \pm 2{\cdot}33$	$2{\cdot}00 \pm 0{\cdot}11$	$6{\cdot}67 \pm 0{\cdot}31$	$6{\cdot}00 \pm 0{\cdot}26$	$20{\cdot}00 \pm 0{\cdot}86$
Mandur bhasma	$1{\cdot}40 \pm 0{\cdot}06^{c}$	$5{\cdot}28 \pm 0{\cdot}21^{c}$	$6{\cdot}40 \pm 0{\cdot}28^{b}$	$24{\cdot}15 \pm 1{\cdot}13^{c}$	$7{\cdot}00 \pm 0{\cdot}09^{d}$	$26{\cdot}41 \pm 0{\cdot}99^{b}$
Paraffin	$7{\cdot}20 \pm 0{\cdot}48^{a}$	$31{\cdot}30 \pm 1{\cdot}59^{b}$	$7{\cdot}86 \pm 0{\cdot}41^{b}$	$34{\cdot}17 \pm 1{\cdot}48^{c}$	$7{\cdot}80 \pm 0{\cdot}47^{a}$	$33{\cdot}91 \pm 1{\cdot}30^{b}$
Paraffin + mandur bhasma	$23{\cdot}60 \pm 0{\cdot}91^{c}$	$118{\cdot}00 \pm 3{\cdot}75^{c}$	$7{\cdot}80 \pm 0{\cdot}41^{b}$	$39{\cdot}00 \pm 1{\cdot}33^{c}$	$6{\cdot}20 \pm 0{\cdot}46^{d}$	$31{\cdot}00 \pm 1{\cdot}52^{b}$
CCl_4	$3{\cdot}84 \pm 0{\cdot}18^{c}$	$16{\cdot}70 \pm 0{\cdot}61^{b}$	$12{\cdot}50 \pm 0{\cdot}46^{c}$	$54{\cdot}35 \pm 2{\cdot}75^{a}$	$2{\cdot}98 \pm 0{\cdot}12^{b}$	$12{\cdot}78 \pm 0{\cdot}44^{a}$
CCl_4 + mandur bhasma	$7{\cdot}20 \pm 0{\cdot}56^{a}$	$38{\cdot}91 \pm 1{\cdot}88^{a}$	$15{\cdot}60 \pm 0{\cdot}91^{c}$	$84{\cdot}31 \pm 3{\cdot}16^{b}$	$9{\cdot}46 \pm 0{\cdot}85^{a}$	$51{\cdot}13 \pm 2{\cdot}03^{c}$

Values are mean ± S. E. of 5 animals.
$^{a}P < 0{\cdot}05$; $^{b}P < 0{\cdot}01$; $^{c}P < 0{\cdot}001$; $^{d}P > 0{\cdot}05$ compared to the control group.

these treatments lowered the acid lipase activity but with a significant increase in acid lipase activity of paraffin + mandur bhasma treated rat liver. Lysosomal and lipoprotein lipase activities of CCl_4 treated rat liver showed a decrease, while the alkaline lipase activity of CCl_4 treated rats showed an increase compared to normal rats. The enzyme specific activities expressed per mg protein paralleled the changes in the activities expressed per gram wet weight of liver indicating the alterations in enzyme proteins *per se*. Mandur bhasma treatment along with CCl_4 resulted in an increase in the activities of all the enzymes compared to the levels obtained with CCl_4 or mandur bhasma treatment only. Concomitant treatment of mandur bhasma and paraffin did not alter the enzyme activities, except the lysosomal lipase which showed an increase compared to the levels of mandur bhasma and paraffin treated rats.

Table 3 shows the changes in the lipolytic activities of adipose tissue under the given experimental conditions. Mandur bhasma treatment resulted in the sharp fall in the activities of hormone sensitive, alkaline and lipoprotein lipases. The treatment of paraffin caused the conspicuous rise in the activities of all the 4 lipases. Mandur bhasma given concomitant with paraffin resulted in the marked decrease in enzyme activities compared to normal rats, but resembled the enzyme activities of mandur bhasma treated rat adipose tissue. Treatment of mandur bhasma alone did not alter the acid lipase activity significantly. Similarly, treatment of mandur bhasma along with paraffin showed full protection to acid lipase activity. A significant increase in the activities of all lipolytic enzymes was observed in CCl_4 treated rats, except in the case of lipoprotein lipase, which showed a decrease. Mandur bhasma treatment prevented the CCl_4 mediated increase in acid and hormone sensitive lipase activities. It also counteracted the decrease in lipoprotein lipase activity. Mandur bhasma had a marginal effect on the CCl_4 mediated increase in alkaline lipase activity. The alkaline lipase activity of CCl_4 + mandur bhasma treated rat adipose tissue exhibited a marginal increase when expressed per mg protein, but exhibited a marginal decrease when expressed per gram fresh tissue. Simultaneous treatment of mandur bhasma and CCl_4 resulted in the sharp increase in the activities of all lipases. Parallel variations were noticed when activities were expressed per gram fresh weight and per mg protein.

Variations in the lipolytic activities of the kidney of normal rats and the rats treated with mandur bhasma, paraffin, paraffin + mandur bhasma, CCl_4 and CCl_4 + mandur bhasma are given in table 4. The enzyme activities declined in the paraffin treated rats as well as CCl_4 treated groups compared to normal animals; but the reductions were more in the paraffin treated rats than in the CCl_4 treated rats. Treatment of only mandur bhasma and paraffin + mandur bhasma exhibited a conspicuous fall in all the enzyme activities compared to normal rats except in the case of lysosomal lipase activity in paraffin + mandur bhasma treated rats. Lysosomal and lipoprotein lipase activities of paraffin + mandur bhasma treated rats were significantly higher than in mandur bhasma treated rats, but alkaline lipase did not exhibit a significant change in its activity. Mandur bhasma counteracted the CCl_4 mediated decrease in the enzyme activities. The activities of all the enzymes of CCl_4 + mandur bhasma treated rats were conspicuously higher than in mandur bhasma or CCl_4 treated rats. Similar to liver and adipose tissue lipases, the enzymes of kidney also exhibited the parallel alterations in enzyme activities when expressed per gram fresh weight and per mg protein indicating changes in enzyme proteins *per se*.

Table 3. Effect of administration of mandur bhasma, paraffin, paraffin + mandur bhasma, CCl_4 and CCl_4 + mandur bhasma on the lipolytic activities of rat adipose tissue.

	Acid lipase		Hormone sensitive lipase		Alkaline lipase		Lipoprotein lipase	
Treatment	K units/g wet wt.	Units/mg protein	K units/g wet wt.	Units/mg protein	K units/g wet wt.	Units/mg protein	K units/g wet wt.	Units/mg protein
Normal	$1{\cdot}96 \pm 0{\cdot}08$	$9{\cdot}80 \pm 0{\cdot}46$	$8{\cdot}99 \pm 0{\cdot}32$	$44{\cdot}95 \pm 1{\cdot}94$	$16{\cdot}18 \pm 0{\cdot}70$	$80{\cdot}90 \pm 3{\cdot}85$	$8{\cdot}34 \pm 0{\cdot}67$	$41{\cdot}70 \pm 2{\cdot}34$
Mandur bhasma	$2{\cdot}17 \pm 0{\cdot}13^{d}$	$42{\cdot}35 \pm 3{\cdot}23^{c}$	$0{\cdot}16 \pm 0{\cdot}01^{c}$	$3{\cdot}26 \pm 0{\cdot}13^{c}$	$0{\cdot}31 \pm 0{\cdot}06^{c}$	$6{\cdot}13 \pm 0{\cdot}21^{c}$	$0{\cdot}66 \pm 0{\cdot}03^{c}$	$13{\cdot}02 \pm 0{\cdot}85^{b}$
Paraffin	$27{\cdot}57 \pm 1{\cdot}19^{c}$	$119{\cdot}87 \pm 4{\cdot}43^{c}$	$27{\cdot}51 \pm 2{\cdot}30^{c}$	$119{\cdot}61 \pm 5{\cdot}11^{c}$	$17{\cdot}81 \pm 0{\cdot}93^{d}$	$77{\cdot}39 \pm 4{\cdot}07^{d}$	$17{\cdot}82 \pm 1{\cdot}22^{b}$	$77{\cdot}48 \pm 3{\cdot}62^{b}$
Paraffin + mandur bhasma	$2{\cdot}25 \pm 0{\cdot}09^{d}$	$48{\cdot}14 \pm 3{\cdot}11^{c}$	$0{\cdot}24 \pm 0{\cdot}02^{c}$	$5{\cdot}26 \pm 0{\cdot}22^{c}$	$0{\cdot}12 \pm 0{\cdot}02^{c}$	$2{\cdot}63 \pm 0{\cdot}11^{c}$	$0{\cdot}37 \pm 0{\cdot}02^{c}$	$7{\cdot}90 \pm 0{\cdot}36^{c}$
CCl_4	$60{\cdot}82 \pm 2{\cdot}43^{c}$	$202{\cdot}73 \pm 6{\cdot}53^{c}$	$47{\cdot}96 \pm 3{\cdot}22^{c}$	$159{\cdot}87 \pm 6{\cdot}14^{c}$	$31{\cdot}76 \pm 1{\cdot}84^{b}$	$105{\cdot}67 \pm 4{\cdot}82^{a}$	$1{\cdot}05 \pm 0{\cdot}02^{c}$	$3{\cdot}50 \pm 0{\cdot}31^{c}$
CCl_4 + mandur bhasma	$7{\cdot}13 \pm 0{\cdot}37^{c}$	$31{\cdot}01 \pm 5{\cdot}71^{c}$	$15{\cdot}95 \pm 0{\cdot}83^{b}$	$69{\cdot}31 \pm 2{\cdot}77^{a}$	$28{\cdot}22 \pm 0{\cdot}05^{b}$	$127{\cdot}70 \pm 5{\cdot}92^{b}$	$13{\cdot}10 \pm 1{\cdot}06^{a}$	$56{\cdot}44 \pm 2{\cdot}86^{a}$

Values are mean ± S.E. of 5 animals. *P* values are as in table 2.

Table 4. Effect of administration of mandur bhasma, paraffin, paraffin + mandur bhasma, CCl_4 and CCl_4 + mandur bhasma on the lipolytic activities of rat kidney.

	Lipolytic activities					
	Acid lipase		Alkaline lipase		Lipoprotein lipase	
Treatment	K units/g wet wt.	Units/mg protein	K units/g wet wt.	Units/mg protein	K units/g wet wt.	Units/mg protein
Normal	$13{\cdot}60 \pm 0{\cdot}57$	$68{\cdot}00 \pm 4{\cdot}50$	$13{\cdot}60 \pm 0{\cdot}78$	$68{\cdot}00 \pm 4{\cdot}13$	$12{\cdot}00 \pm 0{\cdot}76$	$60{\cdot}00 \pm 3{\cdot}82$
Mandur bhasma	$4{\cdot}44 \pm 0{\cdot}21^{c}$	$33{\cdot}85 \pm 1{\cdot}20^{b}$	$1{\cdot}60 \pm 0{\cdot}06^{c}$	$12{\cdot}31 \pm 0{\cdot}55^{c}$	$1{\cdot}24 \pm 0{\cdot}05^{c}$	$9{\cdot}54 \pm 0{\cdot}38^{c}$
Paraffin	$3{\cdot}76 \pm 0{\cdot}13^{c}$	$18{\cdot}80 \pm 0{\cdot}75^{c}$	$10{\cdot}20 \pm 0{\cdot}52^{a}$	$51{\cdot}00 \pm 2{\cdot}05^{a}$	$0{\cdot}90 \pm 0{\cdot}06^{c}$	$4{\cdot}50 \pm 0{\cdot}22^{c}$
Paraffin + mandur bhasma	$21{\cdot}00 \pm 0{\cdot}75^{b}$	$91{\cdot}30 \pm 3{\cdot}68^{b}$	$1{\cdot}65 \pm 0{\cdot}06^{c}$	$7{\cdot}17 \pm 0{\cdot}19^{c}$	$4{\cdot}40 \pm 0{\cdot}17^{b}$	$19{\cdot}13 \pm 0{\cdot}73^{b}$
CCl_4 treated	$5{\cdot}40 \pm 0{\cdot}21^{c}$	$29{\cdot}19 \pm 1{\cdot}61^{b}$	$10{\cdot}40 \pm 0{\cdot}66^{a}$	$56{\cdot}22 \pm 3{\cdot}14^{a}$	$1{\cdot}80 \pm 0{\cdot}08^{c}$	$9{\cdot}73 \pm 0{\cdot}51^{c}$
CCl_4 + mandur bhasma	$14{\cdot}46 \pm 0{\cdot}81^{d}$	$72{\cdot}30 \pm 4{\cdot}90^{a}$	$34{\cdot}80 \pm 1{\cdot}83^{c}$	$174{\cdot}00 \pm 5{\cdot}53^{c}$	$6{\cdot}40 \pm 0{\cdot}35^{b}$	$32{\cdot}00 \pm 1{\cdot}27^{b}$

Values are mean ± S.E. of 5 animals. *P* values are as in table 2.

Discussion

The treatment of mandur bhasma resulted in a decrease in lysosomal lipase of liver with increase in lipoprotein lipase and alkaline lipases, which suggest the increased secretion of lipoproteins as well as release of fatty acids needed for the metabolic processes, because the histological architecture of liver was totally normal and there was no detectable lipid peroxidation. The lowered lipolytic activities of adipose tissue and kidney due to mandur bhasma treatment, except in the case of acid lipase of adipose tissue indicate the reduced uptake and mobilization of lipids. The mass of adipose tissue of mandur bhasma treated rats was decreased by about 41 % than normal rats, but the lipids of adipose tissue of mandur bhasma treated rats (877 mg/g fresh wt.) was not altered significantly compared to normal rats (918 mg/g fresh wt.). The reduction in the mass of adipose tissue without alteration in lipid content along with the increased acid lipase activity by mandur bhasma is a clear indication of adipose tissue lysis. These observations lend credence for the use of preparations of iron such as mandur bhasma, Louh bhasma in the treatment of obesity (Sharma, 1977).

Similar lines of argument can be advanced to suggest that the paraffin toxicity results in a high turnover of lipids in the adipose tissue and that mandur bhasma treatment counteracts this situation. In the liver, mandur bhasma may bring about the enhanced release of fatty acids to protect against paraffin toxicity. In the kidney, this protection may involve enhanced uptake of lipids and elevated lysosomal lipolysis.

Mandur bhasma in general counteracted the effects of CCl_4 on the levels of lipases. The higher liver lipoprotein lipase activity in CCl_4 + mandur bhasma treated rats than in CCl_4 treated rats suggests the increased secretion of liver lipoproteins and rapid uptake of fatty acids by adipose tissue. The acid and hormone sensitive lipolytic activities in the adipose tissue were significantly lowered in mandur bhasma + CCl_4 treated rats. From these observations it appears that the rate of lipolysis was less than the uptake of fatty acids by adipose tissue in CCl_4 + mandur bhasma treated rats. Mandur bhasma also counteracted the decrease in liver and kidney lysosomal lipase activities brought about by CCl_4 treatment. Surprisingly alkaline lipase activities of all the 3 tissues in CCl_4 + mandur bhasma treated rats were significantly higher than those observed in normal and only mandur bhasma or CCl_4 treated rats. When the liver homogenate of CCl_4 treated rats was incubated in the presence of mandur bhasma, the rate of lipid peroxidation was significantly lower (3·33 %) when compared with the lipid peroxidation in the absence of mandur bhasma (100 %). It is possible that the increased alkaline lipase in CCl_4 + mandur bhasma treated rats is responsible for the synthesis of complex lipids of membranes and other cellular components for the regeneration of new cells in these tissues. Histologically, the liver and kidneys were not damaged significantly and new regenerating hepatic regions were observed in the region of necrosis. Similarly lysosomal lipase activities of liver and kidney of CCl_4 + mandur bhasma treated rats were significantly higher than in rats treated with mandur bhasma only. This increase may be attributed to the enhanced release of fatty acids to meet the metabolic energy demand during the protection of the liver and kidney by mandur bhasma against CCl_4 induced toxicity.

Further studies are being carried out in this laboratory on the chemical nature of mandur bhasma and on the mechanism of its hepatoprotective action in hepatopathology.

Acknowledgement

One of the authors (P.D.) is grateful to University Grants Commission, New Delhi, for financial assistance.

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