

# Hepatoprotective Evaluation of *Butea monosperma* against Liver damage by Paracetamol in Rabbits

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Traditional Medicines derived from medicinal plants are used by about 60% of the world's population.

**Objective:** To evaluate the hepto-protective effect of *Butea monosperma* (Dhaak) flowers in the rabbits in whom hepatotoxicity was produced.

**Material and Methods:** Flowers of *Butea monosperma* (BM) were collected, air dried and ground to powder. Hepatotoxicity was induced by oral administration of Paracetamol suspension (2000 mg/kg body weight). Twenty four rabbits were divided into 4 groups such as group A, B, C and D (n=6). Group A and B served as Normal and Paracetamol treated respectively while rabbits in group C were drug treated and received (100 mg/kg body weight) crude powder of dried flowers of *Butea monosperma*. Group D rabbits were given paracetamol (2000mg/Kg) and *Butea* Powder (100mg/Kg). Serum transaminases and alkaline phosphates (ALP) were monitored after 7 days and 14 days in Groups B,C and D.

**Results:** Oral administration of BM flowers powder (100 mg/kg) effectively inhibited paracetamol induced changes in the serum marker enzymes in rabbits. Increase in transaminases Aspartate transaminase (AST), Alanine transaminase (ALT) and Alkaline phosphatase (ALP) was observed with paracetamol treated group. These values significantly decreased when paracetamol along with BM powder were given at a time and monitored after seven and fourteen days ( $p < 0.001$ ). However no significant difference was observed in BM powder treated group of rabbits ( $p > 0.05$ ). The results suggest that the BM flowers powder possessed significant potential as hepatoprotective agent.

**Conclusion:** These results indicate that *Butea monosperma* flowers contain some active constituent(s) responsible for its hepatoprotective activity in paracetamol treated rabbits.

**Key words:** *Butea monosperma*, hepatotoxicity, paracetamol.

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## Introduction

Herbs are the natural drugs used to regain the alterations made in normal physiological system by foreign organisms or by any malfunctioning of the body. Herbal medicines (now widely known as Natural Products and Nutraceuticals) had been the oldest form of healthcare. For centuries, natural products have been a major source of new drugs and drug leads. By the middle of the 19th century at least 80 % of all medicines were derived from herbs. In every ethnic group there exists a traditional health care system, which is culturally patterned. The WHO has already recognized the contribution of traditional health care in tribal communities.<sup>1</sup>

*Butea monosperma* (B.M) is a species of *Butea* native to tropical southern Asia, from Pakistan, India, Bangladesh, Nepal, Sri Lanka, Myanmar, Thailand, Laos, Cambodia, Vietnam, Malaysia, and western Indonesia. It is a good anti-inflammatory agent. It improves digestion and stimulates liver for adequate functioning. Its flowers are astringent, hemostatic and diuretic.

Few studies were found revealing the hepatoprotective effects of *Butea monosperma* and virtually very few studies was available on the efficacy of BM flowers as hepatoprotective. A study conducted in 1999 revealed antihepatotoxic effects of BM flowers against liver damage induced by

rifampicin and paracetamol in chicks where pretreatment with BM extracts and Hepatochron DS prevented the rifampicin induced rise of serum ALT, ALP and bilirubin. Plant extract and the control drug efficiently inhibited the rise in ALT, ALP and bilirubin due to Paracetamol. However aqueous and methanolic extracts of BM and control drug Hepatochron DS were not found to significantly affect the liver function tests.<sup>2</sup> In another study, an aqueous extract of BM offered protection against experimentally induced liver injury by CCl<sub>4</sub> in albino rats as shown by biochemical and histopathological studies. It was observed that BM. had a definite role in preventing the increase of alkaline phosphatase activity induced by CCl<sub>4</sub>. However, in animals treated with CCl<sub>4</sub> alone, the ALT values showed a tremendous increase ( $P < 0.001$ ) and in animals treated with CCl<sub>4</sub> + BM. Such a significant increase was not observed.<sup>3</sup>

A study conducted on Wistar rats also revealed that the methanolic extract of BM possessed hepatoprotective effects. The alcoholic extract of BM used in the study seemed to offer dose-dependent protection and maintained the structural integrity of hepatic cells and also it might suppress the promotion stage via inhibition of oxidative stress and polyamine biosynthetic pathway.<sup>4</sup> Butrin, isobutrin and butein present in BM extracts were found to be antihepatotoxic.<sup>5</sup>

At molecular level its powerful anti-inflammatory

effect had been detected in one study through its active ingredients. The results showed that butrin, isobutrin and butein significantly reduced the PMACI-induced inflammatory gene expression and production of TNF- $\alpha$ , IL-6 and IL-8 in HMC-1 cells by inhibiting the activation of NF- $\kappa$ B. Isobutrin was most potent in suppressing the NF- $\kappa$ B p65 activation by inhibiting I $\kappa$ B $\alpha$ -degradation, whereas butrin and butein were found relatively less effective.<sup>6</sup>

In another study the protective effect of ethanolic extract of BM leaves was evaluated in alloxan (ALXN)-induced diabetic male adult mice and significant anti-oxidant activity was found in *B. monosperma* leaves.<sup>7</sup> Its anti-oxidant effect was further supported by another study done on male albino rats in which free radical scavenging potential of the bark of BM extract was studied.<sup>8,9</sup> Antiperoxidative effect of BM was identified in different studies.<sup>10,11</sup> In a study conducted by Asif A.R. also supported the hepatoprotective role of *Butea monosperma*.<sup>12</sup>

Pakistan is enriched with medicinal herbs and many of them have been documented as effective therapies for various diseases. Need of the day is to explore these indigenous herbal wealth to at least minimize the agony of diseases in human beings.

**Materials and methods**

**Plant material:** *Butea monosperma* trees are identified in local yards in Lahore. In the flowering season, flowers were collected, washed under running water, dried between folds of filter papers then air dried, powdered using Chinese herbal grinder and were stored at -20°C in zipped plastic bags until used.

**Chemicals:** Paracetamol was gifted by Askari pharmaceuticals (Lahore, Pakistan).

**Biochemical Analysis:** AST and ALT and ALP levels were evaluated by enzymatic kits (Randox) using Micro-lab 200 (Merck).

**Animals:** Male rabbits of local strain (*Oryctolagus cuniculus*) with average weight 1.35 kg and a range of 1.0-1.5 kg were used.

**Treatment of Rabbit:** All animals were housed in iron cages under standard lab conditions green fodder and water were available ad libitum at the animal house. Animals received human care. The study protocol was approved by the local ethical committee.

**Table 1:** AST, ALT, and ALP levels of group A and B in rabbits after 7 days:

Control Group A	AST	ALT	ALP
	38.83 ± 6.26	32.58 ± 4.07	44.51 ± 3.71
Experimental Group B after 7 days	36.41 ± 6.37	30.20 ± 2.03	41.58 ± 2.26
p-Value	ns	ns	ns

**Table 2:** AST, ALT, and ALP levels of group A and B in rabbits after 14 days:

Control Group A	AST	ALT	ALP
	38.83 ± 6.26	32.58 ± 4.07	44.51 ± 3.71
Experimental Group B after 10 days	35.61 ± 6.40	29.50 ± 1.91	41.21 ± 2.27
p-Value	ns	ns	ns

**Table 3:** AST, ALT, and ALP levels of group C and D in rabbits after 7 days:

Control Group C	AST	ALT	ALP
	245.93 ± 16.40	312.23 ± 12.44	159.90 ± 11.66
Experimental Group D after 7 days	150.36 ± 10.15	182.63 ± 12.93	108.93 ± 13.89
p-Value	< 0.001	< 0.001	< 0.001

**Table 4:** AST, ALT, and ALP levels of group C and D in rabbits after 14 days:

Control Group C	AST	ALT	ALP
	246.40 ± 17.36	310.93 ± 8.89	159.61 ± 10.62
Experimental Group D after 14 days	118.66 ± 8.13	122.63 ± 10.15	70.85 ± 8.36
p-Value	< 0.001	< 0.001	< 0.001

**Induction of Hepatotoxicity and Experimental Design:**

Twenty four rabbits were divided randomly into 4 groups i.e A, B, C and D. Group A served as Normal Control group. Group B was given BM powder in a dose of 50 mg per Kg body weight. Group C was paracetamol treated receiving 2000 mg per Kg body weight. Paracetamol (2000mg/Kg) and BM powder (50 mg/Kg) was simultaneously given to Group D Rabbits. Two comparisons were made after 7 days and 14 days i.e. first between Group A and B. to observe the effects of BM on Normal liver enzymes and second between Group C and D to see the hepatoprotective role of B.M on liver enzymes affected by the toxic effects of Paracetamol.

**Statistical Analysis:** Unpaired ‘t’ Test was used to compare control and experimental groups with the help of SPSS

ver 13 and p-Value was calculated. Level of significance was set at p-value less than 0.05.

### Results

No significant difference ( $P > 0.05$ ) in AST, ALT and ALP was found in BM treated rabbits after 7 days (Table 1) and after 10 days (Table 2). While comparing Group D with Group C after 7 days, AST, ALT AND ALP levels of group D were significantly lower in Group D ( $p < 0.000$ ) (Table 3). Similarly significant difference was found after 14 days ( $p < 0.000$ ) (Table 4).

### Discussion

Liver is exposed to metabolites that may cause direct toxicity or there may be chance of immunological reaction either by drug itself or its active metabolite.<sup>13</sup> It has been reported that 62% of withdrawn drugs produce toxic metabolites when administered.<sup>14</sup>

Various reactive species like hydroxyl radicals, superoxide anions, hydrogen peroxide, single oxygen, nitric oxide and lipid oxides are generated in the body by external and internal factors.<sup>15-17</sup> These radicals, act with various cellular organelles. This can lead to many disorders like cancer, hepatic ailments, inflammation and process of aging.<sup>18</sup> Antioxidants are agents that can neutralize deleterious effects of free radicals. In order to keep balance between oxidants and antioxidants exogenous support is taken. Plants with antioxidant properties are becoming more and more popular all over the world.<sup>19</sup>

Flowers of *Butea monosperma* have been reported to be used in number of liver diseases as well. Effects of BM as hepatoprotective were demonstrated in the past through various studies. One study revealed its antihepatotoxic effects in rifampicin and paracetamol induced hepatotoxicity in chicks.<sup>3</sup> Another study on Wistar rats also showed hepatoprotective effects of BM.<sup>4</sup> In one study on male albino rats, antioxidant effect of BM was demonstrated.<sup>8,9</sup> All these findings were showing hepatoprotective role of BM. Present study results are found similar to the above mentioned studies carried out in past. In the present study, paracetamol caused the liver injury at higher doses. The elevation of AST, ALT and ALP were an indicative for the release of enzymes from disrupted cells. BM treatment (crude powder) significantly reduced the raised levels of AST, ALT and ALP in hepatotoxic rabbits. The decrease in the serum levels of these enzymes might possibly be due to the presence of such constituents in B.M that enhanced the regeneration ability of liver. Crude powder of dried flowers of BM was used first time to see its hepatoprotective effect.

### Conclusion

We concluded that BM contains active constituent(s) that attributed towards its hepatoprotective effect in paracetamol induces toxicity in rabbits. It may be one of the potential targets for the development of new therapies for the treatment of various hepatic diseases. Findings in this study give an

indication that *Butea monosperma* proved to be an effective hepatoprotective. This herb can be used for various hepatic disorders in human beings.

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