**INTRODUCTION**

Diclofenac sodium was introduced in late 70’s as a potent anti-inflammatory and analgesic preparation, which on long-term use has shown hepatotoxic effects, which presented in the form of hepatic injury ranging from mild to fatal liver injury. Liver being an active organ for maintenance and regulation of the internal milieu is involved for the structural alterations of the administered drugs. It is the target organ, which gets exposed to the drugs in higher concentration than other organs of the body, where they are orally administered. Hence, it is the most vulnerable organ to be injured by the chemicals and the drugs, which leads to hepatic dysfunction. Generally, any drug in excess could be a burden on the liver causing toxic effects, but sometimes, even the drugs introduced in therapeutic ranges may also injure the liver. Some of the commonly hepatotoxic drugs, include, antineoplastic drugs such as isotosin, trimiprin, pimozamine, which contribute to hepatotoxicity, with the toxicity ranging between 2% to 23% (Singh & Hong 1986). More than 90% drugs are known to be hepatotoxic. For example, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) such as Aspirin, Naproxen, Diclofenac, Ibuprofen, which are very commonly used in the treatment of rheumatic conditions and apart from which they are the most commonly used analgesics and antiarthritics. They also make the most important group of drugs used over-the-counter as OTC preparations and contribute to adverse drug reactions (ADRs) (7). Concurrent administration of Aspirin and other NSAIDs is usually seen in many clinical situations. Drug-induced liver injury (DILI) according to the recent estimates show the incidence of 14-19 cases per 100,000 (8). Hence, the study was taken up to evaluate the most commonly used preparations in today’s practice, i.e. Diclofenac sodium, forits hepatotoxic effect.

**MATERIALS AND METHODS**

The study was conducted after obtaining the approval from the Institutional Animal Ethics Committee (IAEC) of SRK’s M.I. & R.C., Sumandeep Vidyapeeth Deemed to be University, Piparia, Vadodara, considering the rules and regulations of Committees of the purpose of Control and Supervision of Experiments on Animals ( CPCSEA).

Albino rats of either sex weighing between 100 - 400g were used. Each animal was used only once. The animals were housed separately in poly-ethylene rat-cages under controlled environmental conditions temperature 24 ± 2°C and 55% ± 5% relative humidity, in a 12-hour light-dark cycle throughout the experiment, which were kept fasting for 24 hours, before administering the drug.

The drugs and chemicals used were Diclofenac sodium from Aurobindo Instr. Chem. Vadodara. The chemicals included 10% Formalin. Xylene, Hematoxylin and Eosin stains.

To evaluate the levels of liver enzymes, serum glutamic-pyruvic Transaminase (SGPT), Serum Glutamic Oxaloacetic Aminotransferase (SGOT), Serum Alkaline Phosphatase, Serum bilirubin – Direct and Indirect bilirubin, Total Bilirubin – Serum Gamma-Glutaryl Transferase (GGT) and the diagnostic kit reagents (Era Diagnostics, Mumbai) was used.

All the drug solutions were freshly prepared before use and were administered orally with the volume of 10 mL. The animals were divided in four groups, with each group containing 6 rats. The dose of Diclofenac sodium was selected based on the LD50 dose in rats, when administered orally (9).

The 24-hour fasted rats were administered orally with Distilled Water for the control group while the remaining three groups were administered with Diclofenac sodium in the doses of 72, 36 and 240 mg/kg respectively and were re-housed in the individual polypropylene cages.

Following 24 hours of post-treatment, under light ether anaesthesia, 3 mL of blood sample was collected from retro-orbital plexus by capillary method technique in heparinized tube, which was centrifuged at 3000 rpm for 10 minutes to separate serum that was subjected to analyse the Liver Function tests (LFTs) so as to evaluate its hepatotoxic effect.

Liver from each animal was immediately dissected and cleaned with normal saline and was preserved in the specimen collection jar that contained 10% formalin. The liver samples were fixed in 10% formalin and embedded in paraffin. Sections of about 4-6 μm were stained with haematoxylin for 5 minutes at room temperature, 15 minutes later was counterstained with eosin for 2 minutes, washed with xylene and blotted dry. The histopathological studies and were observed under photomicroscope.

**RESULTS**

**Statistical analysis:**

All the observations were subjected for statistical analysis and the results were expressed as Mean ± SEM. All calculations were
Observations and results:

Albino rats (n=6) that were administered Distilled Water (10 ml/kg) were considered as control (Group I). Diclofenac sodium administered as a single oral dose in each group (n=6). Group I (Diclofenac sodium 72 mg/kg), Group II (Diclofenac sodium 96 mg/kg) and group IV (Diclofenac sodium 240 mg/kg), respectively, when compared to the control group showed statistically significant rise (p < 0.05) in the serum SGPT and Serum SGOT levels as indicated in the Table 1 below, and as depicted in the Figure 1 and Figure 2, respectively.

Table 1: Shows changes in the levels of liver enzymes, following administration of Diclofenac sodium (72 mg/kg, 96 mg/kg and 240 mg/kg).

<table>
<thead>
<tr>
<th>No.</th>
<th>Liver Function Tests</th>
<th>Group (mg/kg)</th>
<th>Mean ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>SGPT (IU)</td>
<td>Control (72 mg/kg)</td>
<td>32.62 ± 7.91</td>
</tr>
<tr>
<td></td>
<td>Diclofenac 72 mg/kg</td>
<td>85.67 ± 7.37***</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diclofenac 96 mg/kg</td>
<td>17.67 ± 13.72***</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diclofenac 240 mg/kg</td>
<td>24.03 ± 24.03***</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>SGOT (IU)</td>
<td>Control (72 mg/kg)</td>
<td>12.00 ± 15.07</td>
</tr>
<tr>
<td></td>
<td>Diclofenac 72 mg/kg</td>
<td>52.63 ± 85.00***</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diclofenac 96 mg/kg</td>
<td>12.00 ± 30.30***</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diclofenac 240 mg/kg</td>
<td>240 ± 240***</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Total Serum Bilirubin (mg/dL)</td>
<td>Control (72 mg/kg)</td>
<td>0.70 ± 0.09</td>
</tr>
<tr>
<td></td>
<td>Diclofenac 72 mg/kg</td>
<td>0.11 ± 0.11</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diclofenac 96 mg/kg</td>
<td>1.17 ± 0.12</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diclofenac 240 mg/kg</td>
<td>1.17 ± 0.12</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Serum ALP (IU)</td>
<td>Control (72 mg/kg)</td>
<td>166.17 ± 23.51</td>
</tr>
<tr>
<td></td>
<td>Diclofenac 72 mg/kg</td>
<td>120.17 ± 23.51</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diclofenac 96 mg/kg</td>
<td>113.01 ± 52.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diclofenac 240 mg/kg</td>
<td>229.00 ± 32.06</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Serum GGTP (IU)</td>
<td>Control (72 mg/kg)</td>
<td>2.23 ± 0.56</td>
</tr>
<tr>
<td></td>
<td>Diclofenac 72 mg/kg</td>
<td>12.01 ± 7.43</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diclofenac 96 mg/kg</td>
<td>3.39 ± 3.40</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diclofenac 240 mg/kg</td>
<td>1.10 ± 0.25</td>
<td></td>
</tr>
</tbody>
</table>

Note:
* p<0.05 = Significant, values are represented as Mean ± SEM

Serum Glutamic-Pyruvic Transaminase (SGPT), Serum Glutamic-Oxaloacetic Aminotransferase (SGOT), Total serum bilirubin, Alkaline Phosphatase (ALP) and Gamma Glutamyl Transpeptidase (GGTP) or γ-Glutaryl Transferase (GGT), DW = Distilled Water.

However, there was no statistically significant rise in the serum levels of total serum bilirubin, alkaline phosphatase and γ-Glutamyl Transpeptidase, as shown in Figure 3 and 4 above.

Figure 1: Changes in the Serum Glutamic-Pyruvic Transaminase (SGPT) levels

Figure 2: Changes in the Serum Glutamic-Oxaloacetic Aminotransferase (SGOT) levels

Figure 3: Changes in the Total Serum Bilirubin levels.

Figure 4: Changes in the serum Alkaline Phosphatase (ALP) levels.

Figure 5: Changes in the Serum Gamma Glutamyl Transpeptidase (GGTP) levels.

Histopathological Observations:

I. Gross appearance of the liver sample:

The gross appearance of liver of albino rats administered with Distilled Water did not show any abnormal changes in texture, shape, size or colour. It was reddish brown and showed typical lobular architecture, whereas, those treated with Diclofenac sodium were pale yellow to pale brown colour.

II. Microscopic examination of liver:

The evidence of changes in the liver cells of Diclofenac sodium at 72 mg/kg, 96 mg/kg & 240 mg/kg p.o. showed dose-dependent changes in the liver section.
The histopathological changes observed in the liver tissue sections show mainly hepatocellular changes along with the changes in the portal area which also revealed microvascularization, that is diffuse hepatic vacuolation (degeneration) seen which was dose-dependent and marked congestion. Whereas, irreversible changes in the tissue such as severe hepatic degeneration or centrilobular focal necrosis was not seen.

**CONCLUSION**

With observations made by the authors, Diclofenac in the doses of 72 mg/kg, 56 mg/kg 62.40 mg/kg as a single oral dose has shown toxic hepatotoxicity in albino rats.

**ACKNOWLEDGEMENT**

Authors are grateful to Mr. Bhikchand Kanabhai Shah Medical Institute & Research Centre, Saurashtra, that they are a University, Bhavnagar, for permitting us to conduct the study.

We are also grateful to Dr. Swapan Goswami, Professor, Department of Pathology for his valuable contribution and guidance pertaining to the histopathological examinations in the present study.

We are also grateful to Mr. Devendra Waghasia, Statistician, Department of Community Medicine for his valuable guidance pertaining to the statistical analysis in the present study.

**DECLARATIONS**

Funding: Nil

Conflicts of Interest: Nil

Ethical approval: The present study was approved and approved by the Institutional Animal Ethics Committee (IAEC), which is registered under Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) of S.L.K.S.M.L. & R.C., Saurashtra, Deemed University, Bhavnagar.

**REFERENCES**


**DISCUSSION**

The NSAIDs are considered as the major groups to cause hepatotoxicity, since they are used as both preservative and OTC preparations. Of the currently used NSAIDs, the most common drugs associated with liver disease include Diclofenac, Sulindac, and Aspirin.

Diclofenac sodium being widely used Non steroidal anti-inflammatory and an analgesic compound, we have observed for the hepatotoxic effect of single dose of Diclofenac sodium in dose-dependent manner, in the albino rats.

Diclofenac had shown statistically significant rise (p < 0.001) in the levels of serum SGOT and serum SGPT, when compared with the control group, which was evident for the hepatotoxic effect of the diclofenac sodium at the dose dose 72 mg/kg, 56 mg/kg and 62.40 mg/kg as a single oral dose. The observation of our coincides with the observations made by D. Schapera et al. (1999). Along with the rise in the serum levels, the histopathological studies have demonstrated the toxic effects of diclofenac sodium in the form of amorphous dilatation, cytoplasmic vacuolation and mild portal congestion.

We are also grateful to Mr. Devendra Waghasia, Statistician, Department of Community Medicine for his valuable guidance pertaining to the statistical analysis in the present study.
Original Research Article

Hepatoprotective effect of DL-methionine on diclofenac-induced hepatotoxicity in albino rats: an experimental study

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Abstract

Background: Liver is the main detoxifying organ, which is affected by most of the drugs and xenobiotic agents that could result in liver damage. The present study was designed to evaluate the hepatoprotective effect of DL-Methionine against experimentally induced liver injury in albino rats.

Methods: Hepatotoxicity was induced by administering high doses of positive control drug Diclofenac sodium in albino rats, which was confirmed by estimating Liver Function Tests. Hepatoprotective effect was determined by administering DL-Methionine concurrently with positive control drug. Albino rats were administered with DL-Methionine (700 mg/kg and 1400 mg/kg) respectively as a single oral dose, concurrently with positive control drug Diclofenac sodium (96 mg/kg and 240 mg/kg) respectively. After 24-hours of post-treatment, serum levels of the liver enzymes were evaluated to demonstrate the hepatoprotective effect of DL-Methionine on drug-induced hepatotoxicity, and all the liver samples were examined for the histopathological study.

Results: Significant increase in serum transaminase enzymes were observed by the positive control drug Diclofenac sodium. There was significant reduction in the serum transaminases on concomitant administration of DL-Methionine with Diclofenac sodium. Liver injury induced by positive control drug, and its protection with DL-Methionine was revealed by histopathological study. The combination of Diclofenac sodium and DL-Methionine showed no significant histopathological difference when compared to the normal liver section.

Conclusions: The results reveal that, DL-Methionine significantly prevented the rise in transaminase levels produced by hepatotoxic doses of the positive control drug.

Keywords: Diclofenac, Drug-induced hepatotoxicity, Liver injury, NSAIDs, Serum markers

Introduction

Liver as a major organ involved in drug metabolism is susceptible to the injury when exposed to drugs, chemicals, and xenobiotics, which is generally indicated by the elevated levels of serum enzymes in the liver. Chemicals that cause liver injury are called hepatotoxins. Hepatotoxicity could be idiosyncratic or non-idiosyncratic. However, the drug-induced liver toxicity has been a major concern with the hepatotoxic drugs such as antitubercular drugs (Isoniazid, Rifampicin, Pyrazinamide), Non-Steroidal Anti-inflammatory Drugs (NSAIDs) such as Ibuprofen, Diclofenac, Salicylic acid, Asprin, Paracetamol which are commonly used as, anti-inflammatory and analgesics anti-infective preparations. The major concern with the group of NSAIDs is they belong to the class of non-prescription and commonly used Over-the-Counter (OTC) preparations. The toxicity induced by these drugs have been the major concern since most of these are used for the long-term treatment, which has been a cause of withdrawal of the preparations.
from the market or their termination during the clinical trials.

Hepaticocytes death is a characteristic presentation that occurs in case of liver injury, mainly due to the fibrosis and necrosis, which are generally prevented by N-Acetyl-L-cysteine, particularly in case of Acetaminophen toxicity.

Similarly, the essential amino acid Methionine has also found to be a beneficial hepatoprotective agent which is also been proposed for the treatment of certain disease condition. Thus, the present study was taken up to demonstrate its hepatoprotective effect on Diethofenate-induced hepatotoxicity.

METHODS

Albino rats of either sex weighing between 100-140gm were used. Each animal was used only once. The animals were housed separately in poly-ethylene rat cages under controlled environmental conditions temperature 24±4°C and 55±5%, relative humidity, in a 12-hour light-dark cycle throughout the experiment, which were kept fasting for 24 hours, before administering the drug.

The drugs and chemicals used were Diethofenate sodium and DL-Methionine from Astra Intra Chem, Vadodara. The chemicals included 10% Formalin, Xylene, Hematoxylin and Eosin stains. To evaluate the levels of liver enzymes, serum Glutamic-Pyruvic Transaminase (SGPT), Serum Glutamic-Oxaloacetic Aminotransferases (SGOT), Serum Alkaline Phosphatase, Serum bilirubin-Direct and Indirect Euthion, Total Euthion; Serum Gamma-Glutamyl Transpeptidase (GGTP) by diagnostic kit reagents (Eiba Diagnostics, Manehim) was used.

Diethofenate sodium in the dose of 66mg/kg and 240mg/kg are used as positive control drug for their hepatotoxic effects and DL-Methionine 700mg/kg and 1400mg/kg are used as the test drugs to evaluate their hepatoprotective action on toxicity induced by Diethofenate sodium; by evaluating the liver enzymes and histopathological studies of liver.

The animals were grouped into seven groups (n=6). Group I (Control) was treated with Distilled Water 10ml/kg, while Group II, and III were treated with Diethofenate 96mg/kg and 240mg/kg respectively, which were considered as positive control group to demonstrate their hepatotoxic action.

Group IV was treated with DL-Methionine 700mg/kg and Diethofenate 96mg/kg concomitantly. Group V was treated with DL-Methionine 700mg/kg and Diethofenate 240mg/kg concomitantly, Group VI was treated with DL-Methionine 1400mg/kg and Diethofenate 96mg/kg concomitantly and Group VII was treated with DL-Methionine 1400mg/kg and Diethofenate 240mg/kg concomitantly.

The 24-hour fasted albino rats were administered with Diethofenate sodium and DL-Methionine as mentioned above. Later, after 24-hours of post-treatment, 3ml of blood sample was collected from retro-orbital plexus by capillary method technique, under light ether anesthesia, that was centrifuged at 3000rpm for 10 minutes to obtain the serum that was subjected to analyse the levels of liver enzymes. Liver from each animal was immediately dissected out and cleaned with normal saline and was preserved into the specimen collection jars that contained 10% formalin. The liver samples were quickly fixed in 10% formalin and embedded in paraffin. Sections of about 4-5µm were stained with hematoxylin for 5 minutes at room temperature; 15 minutes later was counterstained with eosin for 3 minutes, washed with xylene and bloomed by eosin for histopathological studies and were observed under photomicroscope.

Statistical analysis

All the observed data were subjected for statistical analysis and the results were expressed as Mean±SEM. All calculations were performed using statistical software SSPS version 21.0 computer-based. Values were considered to be significant when P values were less than or equal to 0.05 (P ≤ 0.05).

RESULTS

The positive control drug Diethofenate sodium in the dose of 96mg/kg and 240mg/kg showed significant rise (P value ≤ 0.0001) of serum SGPT and SGOT level when compared to the control group.

On concomitant administration of DL-Methionine 700mg/kg with Diethofenate sodium 96mg/kg and 240mg/kg (Group IV and Group V) respectively, there occurred significant reduction (P ≤ 0.05) in the serum SGOT and SGPT levels as compared to control and positive control group. Similarly, a significant reduction in the serum SGPT as shown in Table 1 and Figure 1, and serum SGOT levels, as shown in Figure 2, was observed in Groups VI and VII, which were treated concomitantly with DL-Methionine 1400mg/kg and Diethofenate sodium 96mg/kg and 240mg/kg respectively.

However, in both the dose of DL-Methionine (700mg/kg and 1400mg/kg), with Diethofenate sodium 96mg/kg and 240mg/kg, these occurred no statistically significant changes in the other liver enzymes such as, Total Serum Bilirubin, serum Alkaline Phosphatase and serum Gamma-Glutamyl Transpeptidase (GGTP) levels as indicated in Table 1 and Figures 3, 4 and 5.

Histopathological examination

Gross appearance of liver

The gross appearance of liver of albino rats in control group showed reddish to brown colour. On administration
of positive control drug Diclofenac sodium, which were pale yellow, on concomitant administration of DL-Methionine with hepatotoxic drug Diclofenac sodium, showed near normal gross appearance of liver, of mild reddish-brown color.

Table 1: Hepatoprotective action of DL-Methionine, on concomitant administration of positive control drug Diclofenac sodium.

<table>
<thead>
<tr>
<th>Group (n = 4)</th>
<th>Biochemical parameters of LFTS Mean ± SEM values</th>
<th>SGPT (IU/L)</th>
<th>SGOT (IU/L)</th>
<th>Total serum bilirubin (μmol/L)</th>
<th>ALP (IU/L)</th>
<th>GGT (IU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control DW 10ml/kg</td>
<td>32.83±2.91</td>
<td>21.60±15.07</td>
<td>0.76±0.08</td>
<td>106.1±21.15</td>
<td>2.33±0.56</td>
<td></td>
</tr>
<tr>
<td>Diclofenac 95 mg/kg</td>
<td>147.67±13.78***</td>
<td>1220.83±130.50***</td>
<td>1.07±0.12</td>
<td>152.83±32.01</td>
<td>3.33±1.40</td>
<td></td>
</tr>
<tr>
<td>Diclofenac 230 mg/kg</td>
<td>236.30±20.01**</td>
<td>1490.00±168.88***</td>
<td>1.25±0.11</td>
<td>225.00±32.06</td>
<td>1.09±0.28</td>
<td></td>
</tr>
<tr>
<td>Diclofenac sodium 90mg/kg + DL-Methionine 700mg/kg</td>
<td>57.17±5.19**</td>
<td>205.00±22.87**</td>
<td>0.95±0.08</td>
<td>151.17±8.42</td>
<td>2.42±0.30</td>
<td></td>
</tr>
<tr>
<td>Diclofenac sodium 240mg/kg + DL-Methionine 700mg/kg</td>
<td>69.17±3.57***</td>
<td>395.83±20.95**</td>
<td>1.01±0.09</td>
<td>136.83±27.79</td>
<td>7.36±1.62</td>
<td></td>
</tr>
<tr>
<td>Diclofenac sodium 90mg/kg + DL-Methionine 140mg/kg</td>
<td>43.00±4.23***</td>
<td>225.17±9.27***</td>
<td>0.88±0.09</td>
<td>133.83±16.07</td>
<td>2.76±0.88</td>
<td></td>
</tr>
<tr>
<td>Diclofenac sodium 140mg/ml + DL-Methionine 140mg/kg</td>
<td>69.50±5.76***</td>
<td>301.83±22.76**</td>
<td>1.11±0.20</td>
<td>134.56±31.48</td>
<td>2.96±0.44</td>
<td></td>
</tr>
</tbody>
</table>

* p value < 0.05 = significant, **p < 0.01 = highly significant and ***p < 0.001 = very highly significant. Values are presented as Means ± SEM. Serum Glutamic-Pyruvic Transaminase (SGPT), Serum Glutamic-Oxaloacetic Aminotransferase (SGOT), Total serum bilirubin, Alkaline Phosphatase (ALP) and Gamma Glutamyl Transpeptidase (GGT) or γ-Glutamyl Transferase (GGT)). DW = Distilled Water

Figure 1: Changes in the Serum Glutamic-Pyruvic Transaminase (SGPT) levels on concomitant administration of DL-Methionine and the positive control drug.

Microscopic examination of liver

The histopathological changes observed in the liver sections in control group revealed normal liver architecture (Figure 6). Diclofenac treated rats, shows mainly hepatic cellular changes in the portal area, mainly microvascular vacuolation, that is diffuse hepatic vacuolation degeneration, cytoplasmic vacuolation and sinusoidal dilatation.

Portal congestion was markedly seen in the hepatotoxic drug Diclofenac sodium, compared to those concomitantly administered with DL-Methionine (Figure 7(a), 7(b) and 7(c)).

Figure 2: Changes in the Serum Glutamic-Oxaloacetic Aminotransferase (SGOT) levels on concomitant administration of DL-Methionine and the positive control drug.
Figure 3: Changes in the Total Serum Bilirubin levels on concomitant administration of DL-Methionine and the positive control drug.

Figure 4: Changes in the serum Alkaline Phosphatase (ALP) levels on concomitant administration of DL-Methionine and the positive control drug.

Figure 5: Changes in the Serum Gamma Glutamyl Transpeptidase (GGTP) levels on concomitant administration of DL-Methionine and the positive control drug.

Figure 6: Liver sections from control rats showing central vein.

Figure 7(a): Liver section from diclofenac sodium 72mg/kg.

Figure 7(b): Liver section from diclofenac sodium 56mg/kg.

Diffuse hepatic vacuolar degeneration was observed prominently in Diclofenac treated rats, which was reduced significantly in the DL-Methionine treated rats (Figure 8(a), 8(b), 8(c) and 8(d)).
positive control drug with DL-Methionine, it was observed that there occurred a significant reduction (P < 0.05) in serum levels of SGOT, SGPT in both the groups which received 90mg/kg and 240mg/kg of the hepatotoxic drug Diclofenac sodium.

This observation concurs with that of observations made by Dass E et al. It also proves DL-Methionine to be a good hepatoprotective agent as shown by Jast QM et al.

CONCLUSION

With the observations made in the present study, we conclude that DL-Methionine is a hepatoprotective agent as it has protected the hepatotoxicity induced by Diclofenac sodium, a known NSAID to cause hepatotoxicity. Although, N-Acetylcysteine is an established hepatoprotective agent for paracetamol-induced hepatotoxicity, from the present study, it is evident that Methionine also has been a hepatoprotective agent on Diclofenac sodium which belongs to the class of NSAIDs.

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Authors also grateful to Mr. Devesh Dave, Statistics, Department of Community Medicine for his valuable guidance pertaining to the statistical analysis in the present study. Authors are also grateful to Dr. Kiran Kumar, Tutor, Department of Pharmacology, for his valuable support.

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Ethical approval: The study was approved by the Institutional Ethics Committee.
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