INTRODUCTION
Liver plays a vital role in clearing and transforming the chemicals but some medicinal agents can damage the organ if given in therapeutic or high dose. Non-medicinal agents including industrial and environmental chemicals can also lead to hepatotoxicity, and are called as hepatotoxins. Liver metabolizes the xenobiotics by the reduction in fat solubility and alters the biological activity after chemical transformation. Some biochemical markers such as bilirubin, alanine transferase and alkaline phosphatase indicate the normal function of hepatocytes or liver damage. Liver injury is present when bilirubin and alkaline phosphatase is more than twice of upper limit of normal or alanine transferase is more than three times of upper limit of normal. Liver normal function can be changed by the action of some toxins or due to infections. Some agents such as carbon tetrachloride and paracetamol elevate the level of alkaline phosphatase and induce the liver injuries. Damage to liver is identified with the help of the level of aspartate aminotransferase and alanine transaminase. Traditional herbal drugs have a great demand in under developed countries due to their efficacy, low cost and lesser adverse effects, and are considered to be “natural”. Aloe vera at the dose of 500 mg body weight per oral was studied for the gross toxicities and hepatoprotective effect and observed the level of liver biochemical parameters in rabbits. Aloe vera showed highly significant (p<0.001) hepatoprotective effect by lowering the serum levels of serum glutamic oxaloacetate transaminase (SGOT), serum glutamic pyruvates transaminase (SGPT) and direct bilirubin. The overall experimental results suggest that Aloe vera protects the liver from oxidative stress and inhibits the excessive free radicals accumulation and possessing many hepatoprotective phytoconstituents which are biologically active such as flavonoids, alkaloids, they may be responsible for the significant hepatoprotective activity and the results justify the use of Aloe vera as a hepatoprotective agent.

Keywords: Aloe vera, gross toxicities, liver profile, rabbits.

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Traditional herbal drugs have a great demand in under developed countries due to their efficacy, low cost and lesser adverse effects, and are considered to be “natural. Aloe vera at the dose of 500 mg body weight per oral was studied for the gross toxicities and hepatoprotective effect and observed the level of liver biochemical parameters in rabbits. Aloe vera showed highly significant (p<0.001) hepatoprotective effect by lowering the serum levels of serum glutamic oxaloacetate transaminase (SGOT), serum glutamic pyruvates transaminase (SGPT) and direct bilirubin. The overall experimental results suggest that Aloe vera protects the liver from oxidative stress and inhibits the excessive free radicals accumulation and possessing many hepatoprotective phytoconstituents which are biologically active such as flavonoids, alkaloids, they may be responsible for the significant hepatoprotective activity and the results justify the use of Aloe vera as a hepatoprotective agent.

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**Experimental Protocol**

*Aloe vera* was purchased from the market in the form of capsules and was used for experiment. The daily dosing of *Aloe vera* for the determination of liver function parameters was done for a period of 30 days in the dose of 500 mg / 70 kg orally according to the body weight of animal. This dose is in accordance to control adult dose of *Aloe vera* capsule of 500 mg.

**Assessment of Gross Toxicities**

The gross toxicities of rabbits were assessed on weekly basis for 30 days and observing righting reflex, skin ulceration, anxiety, hematuria, passivity, loss of hair, loss of activity, tremor, salivation, vomiting, diarrhea, change in pupil size, edema and aggressive behavior.

**Mortality Rate**

Mortality Rate was observed in animals receiving *Aloe vera* and note the number of animals died during the total period of experiment.

**Assessment of liver function**

Blood samples were collected after 7, 15 and 30 day of dosing of *Aloe vera* in vacuum blood collection tubes. Centrifuging blood samples at 3000 rpm for 15 minutes immediately separated serum out. The serum was used for estimation of biochemical parameters to determine the functional state of the liver within 3 hours of sample collection and analyzed on Humalyzer 3000, Semi-automatic chemistry analyzer, Model # 16700 (Human Germany), using standard kits supplied by Human (HUMALYZER 3000).

Total and Direct bilirubin were estimated by photometric test.

Serum glutamic pyruvic transaminase (SGPT) was estimated by kinetic method with reference to the International Federation of Clinical Chemistry.

Alkaline phosphatase (ALP) was estimated by method described by Mac Comb and Bowers.

γ-GT was estimated by colorimetric method.

Serum glutamic oxalo-acetic transaminase (SGOT) or Aspartate amino-transferase (ASAT) was estimated by a UV kinetic method based on the reference method of International federation of Clinical Chemistry.

**Statistical Analysis**

All results were expressed as average value ± standard deviation (St.Dev). The significance of difference between averages was determined and the data obtained from present study was analyzed for P-value. P-value < 0.01 was considered significant and P-value < 0.001 was considered highly significant, following the one way ANOVA.

**RESULTS**

**Assessment of Gross Toxicities**

The gross toxicity was observed in animals receiving *Aloe vera* and no significant change was observed in animals during the total period of experiment.

**Mortality Rate**

Mortality Rate was observed in animals receiving *Aloe vera* and no death occurred during the total period of experiment.

**Assessment of liver function**

Figures 1, 2, 3, 4, 5 and 6 show the statistical analysis of total bilirubin, direct bilirubin, SGPT, alkaline phosphatase, γ-GT, SGOT after 07, 15 and 30 day of dosing of *Aloe vera* and data analyzed by One Way ANOVA show a significant effect of drug *Aloe vera*.

**Effect on Total Bilirubin**

In Figure 1, Post-hoc analysis by Newman–Keuls test shows that after 15 and 30 days of dosing of *Aloe vera* there was significant increase in total bilirubin, i.e. 0.22±0.02 and 0.19±0.005 (mg/dl) respectively and after 07 day of dosing of *Aloe vera* showed non-significant rise in total bilirubin, i.e. 0.12±0.03 (mg/dl) in comparison to control animals group, i.e. 0.08±0.03 (mg/dl). Results showed that the total bilirubin level of *Aloe vera* animals group after 15 and 30 day was increased much significantly than after 7 day of dosing.

**Effect on Direct Bilirubin**

In Figure 2, Post-hoc analysis by Newman–Keuls test shows that animals at 07, 15 and 30 day of dosing of *Aloe vera* showed highly significant decrease in direct bilirubin, i.e. 0.01±0.004, 0.01±0.005 and 0.03±0.005 (mg/dl) respectively in comparison to control animals group, i.e. 0.06±0.004 (mg/dl). Results showed that the direct bilirubin level of *Aloe vera* animals group after 7, 15 and 30 day was decreased much significantly.

**Effect on SGPT**

In Figure 3, Post-hoc analysis by Newman–Keuls test shows that after 07 day of dosing of *Aloe vera* showed there was significant decrease in SGPT, i.e. 39±1.5 U/l and after 15 and 30 days of dosing showed non-significant rise in SGPT, i.e. 136±37U/l and 144±88.5 U/l respectively in comparison to control animals group, i.e. 100±0.4 U/l. Results showed that the SGPT level of *Aloe vera* animals group after 7 day was decreased much significantly than after 15 and 30 days of dosing.

**Effect on Alkaline Phosphatase**

In Figure 4, Post-hoc analysis by Newman–Keuls test shows that animals after 07 and 15 day of dosing of *Aloe vera* showed significant rise in alkaline phosphatase (ALP), i.e. 27±14.6 U/l and 24±5.5 U/l and after 30 day of dosing of *Aloe vera* showed decrease in levels of Alkaline Phosphatase, i.e. 9±1.0 U/l in comparison to control animals group, i.e. 9±0.5 U/l. Results showed that the alkaline phosphatase level of *Aloe vera* treated animals group was decreased much significantly after 30 days of dosing.

**Effect on γ-GT**

In Figure 5, Post-hoc analysis by Newman–Keuls test shows that animals after 07 and 15 day of dosing of *Aloe vera* showed highly significant increase in γ-GT i.e. 8±0.5 and 24±4.5 U/l respectively and after 30 day of dosing showed significant increase in γ-GT i.e. 9±2.5 U/l in comparison to control animals group, i.e. 5±0.5 U/l. Results showed that the γ-GT level of *Aloe vera* animals group after 7 and 15 days was increased much significantly than after 30 day of dosing.

**Effect on SGOT**

In Figure 6, Post-hoc analysis by Newman–Keuls test shows that animals after 07 and 15 days of dosing of *Aloe vera* showed highly significant decrease in SGOT, i.e. 27±1.0 and 28±1.0 U/l respectively and after 30 day of dosing showed significant rise in SGOT, i.e. 143±90.6 U/l in comparison to control animals group, i.e. 42±0.4 U/l. Results showed that the SGOT level of *Aloe vera* animals group after 7 and 15 days was decreased much significantly than after 30 day of dosing.

**DISCUSSION**

Direct bilirubin is water soluble and is a constituent of bile. Bile duct open into the small intestine and then bile is released into the intestine after the action of GI bacteria, bilirubin then metabolizes to urobilinogen and ultimately into stercobilin. This stercobilin provides the brown color of the feces. In urine some of urobilinogen is excreted out with urobilin, which is oxidized state of urobilinogen. Elevated direct bilirubin indicates the liver injury but in current
In current study Aloe vera slightly decreases the level of direct bilirubin. In the blood plasma total bilirubin is measured with the direct bilirubin. Elevated bilirubin indicates the liver disease. In present study Aloe vera slightly increases the level of total bilirubin as compared to control group animals but it is within the reference range. Increase level of total bilirubin may be damaging of plasma membrane of hepatocytes or due to the liver cell cytosis.

Due to the structural damage of liver, the level of liver enzymes are increased in serum because liver enzymes are located in cell cytoplasm after damaging or injury they are released into the blood circulation and raises the level of enzymes in serum. Alanine transaminase (ALT) or Serum glutamic pyruvic transaminase (SGPT) is only present in hepatocytes and in blood. Hepatocellular injury produces some health problems such as congestive heart failure, diabetes, bile duct problems and viral hepatitis.

Aloe vera possesses hepatoprotective activity and reduces the level of SGPT. In current study Aloe vera also decreases the level of Alanine transaminase (ALT) or Serum glutamic pyruvic transaminase (SGPT) after 7day administration. For the detection of liver damage ALT is a biomarker to evaluate the liver disease. Reduction of SGPT indicates the restoration of normal functioning of liver.

Aloe vera protects the liver from oxidative stress and inhibits the excessive free radicals accumulation. In conclusion Aloe vera has hepatoprotective and antioxidative property through oxidative stress suppression. Aloe vera has liver protective effect against hepatotoxic agent by restoration of glutathione, glucose-6-phosphate, lipid peroxidation, amidopyrine N-demethylation and microsomal aniline hydroxylase, and showing the normal histopathology of liver tissues. Acute liver toxicity strongly blocked by the use of Aloe vera and it reduces the liver enzymes.

Some bioactive compounds of Aloe vera are very effective such as tannins, steroids and alkaloids. Specific steroids and flavonoids are responsible to protect the liver from oxidative stress and play a key role as hepatoprotective agent. Aloe vera has several microsomal enzymes that reduce the level of SGPT and SGOT, but also found in skeletal, cardiac muscles and blood cells.

REFERENCES


Figure 1: Effect of *Aloe vera* on Total Bilirubin

Figure 2: Effect of *Aloe vera* on Direct Bilirubin

Figure 3: Effect of *Aloe vera* on SGPT

Figure 4: Effect of *Aloe vera* on ALP

Figure 5: Effect of *Aloe vera* on γ GT

Figure 6: Effect of *Aloe vera* on SGOT

n = 10, Average value ± St.Dev, Significant difference by Newman keuls test, **p < 0.001 as compared to control rabbits, following one way ANOVA

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