ALD is a major cause of morbidity and mortality especially in developing countries like India. Prevention of ALD is a therapeutic challenge and identifying inexpensive natural agents which can achieve the goal is further a higher challenge in correcting the fundamental cellular disturbances from excessive alcohol consumption. According to the World Health Organization report of 2005, approximately 2 billion people worldwide consume alcohol, and about 76 million of them have been estimated to be suffering from ALD, which is one of the major causes of illness and death worldwide (Liu et al., 2010). If alcohol consumption is continued, hepatic steatosis are vulnerable to progress, to the advanced targets of ALD, such as steatohepatitis, fibrosis, cirrhosis, and even hepatocellular carcinoma. Susceptibility to alcoholic hepatitis and cirrhosis appear to be influenced by heredity, gender, diet, and co-occurring liver illness. Most of the ALD is attributed to alcohol metabolism. Liver injury may be caused by direct toxicity of metabolic by-products of alcohol as well as by inflammation induced by these by-products.

The pathogenesis of the damage involves in all the cell types present in the liver via apoptosis, necrosis, ischemia and regeneration, all processes leading to altered gene expression. Oxidative stress, resulting from an imbalance between the generation of free radicals and the antioxidant defense, affects biologically significant macromolecules causing their structural alterations that lead to the cell damage and its death. This phenomenon is considered to be a major factor in the pathogenesis of numerous diseases, including a variety of liver diseases. In addition, reactive oxygen as well as nitrogen species can promote pathogenesis through cell signaling, and in this way modulate gene expression, cell adhesion, cell metabolism, cell cycle, and cell death, thereby contributing to the damages.

Treatment strategies for ALD (lifestyle changes, pharmacological therapy, nutrition therapy and liver transplantation) are expensive and often beyond the
reach of the common man. Several studies have been conducted toward finding protective agents for ALD. In recent times, the search for alternative and affordable therapy has been the focus of researchers and of public health. Currently, the active principles from natural products have gain attention for the treatment of various ailments due to safe and lesser side effects than synthetic one. Liver protective plants contain a variety of chemical constituents like phenols, coumarins, and flavanoids etc., Among the natural products, phenolic compounds are attracting the interest because of their beneficial effects in human health. In particular morin, a natural polyphenol, has potent antioxidant capacity to reduce the production of ROS and suppression of lipid peroxidation. Medicinal plants containing morin have been used in folk medicine before it was known, whose constituents are responsible for their therapeutic effectiveness.

Morin was reported to produce a wide variety of pharmacological properties including anti-inflammatory, antioxidant and antitumor. Hence, in the present study, we have made an attempt to evaluate the protective effect of morin and possible mechanism of action on ethanol-induced toxicity in terms of cytokines response.

SPECIFIC OBJECTIVES

The study was planned to unreveal the effects of morin on ethanol mediated abnormalities in circulation, liver, kidney and brain. In particular we focused their effect, upon ethanol mediated oxidative stress, antioxidants system, hyperlipidemia, changes in mRNA expression, changes in protein expression of cytokines and histological alterations. Thus, the objectives were

1. To find out the *in vitro* free radical scavenging effect of morin.

2. To fix the optimum/effective dose of morin by assaying the hepatic markers, nephritic marks, lipid profiles, oxidative stress markers and antioxidant status in plasma and erythrocytes.

3. To find out the effect of morin on the serum proteins.
4. To explore the role of morin on the levels of lipids in the liver, kidney and brain.

5. To evaluate the effect of morin on lipid metabolizing enzymes in the plasma.

6. To investigate the effect of morin on oxidative stress.

7. To explore the role of morin on plasma nitrite and iron in the liver.

8. To determine the effect of morin on the liver alcohol metabolizing enzymes.

9. To investigate the effect of morin on xenobiotic metabolising enzymes.

10. To investigate the effect of morin on membrane bound adenosine triphosphatase (ATPase) in the liver, kidney and brain.

11. To determine the effect of morin on structural and functional alterations in the liver by Fourier Transform Infared (FTIR) spectroscopic study.

12. To evaluate the effect of morin on inflammatory markers’ mRNA (CD14, NF-κB, and IL-6) and proteins (TNF-α, TGF-β, COX-2 and iNOS) expression in the liver of experimental rats.

13. To explore the role of morin on DNA damage in the lymphocytes of experimental rats.

14. To reveal the effect of morin on ALD by doing immunoblotting investigations of apoptotic and antiapoptotic markers (Bax and Bcl-2).

15. To evaluate the histopathological changes in the liver, kidney and brain of rats upon morin administration to ALD rats.

This study would be useful to get a comprehensive insight into the biochemical activities of morin which may pave way to desire a conclusion on its suitability to treat ethanol toxicity.