INTRODUCTION
Liver fibrosis is the accumulation of collagen following chronic inflammation. The cascade of events leading to its formation begins with inflammatory stimuli, which further proceeds to the activation of quiescent stellate cells in the space of Disse to myofibroblast like cells, that secrete collagen. A range of inflammatory diseases can cause liver fibrosis including viral hepatitis, immune injury, and alcoholic and non-alcoholic steatohepatitis (NASH). TAA is well established model of experiment liver fibrosis in rodents. TAA is bioactivated in the liver via oxidative process leading to its S-oxidative and the highly reactive S,S-oxidative, which is presumably responsible for TAA hepatotoxicity. Use of TAA model is showing direct effect of liver fibrosis which is not through down regulation of steatosis and inflammation. While therapies for the underlying diseases leading to fibrosis have advanced, for example those for viral hepatitis, there are currently no approved therapies for fibrosis. Non-viral liver fibrosis is a major cause of chronic liver disease and one of the leading causes of death in many industrialized countries. Liver fibrosis which is not through down regulation of steatosis and inflammation.

AIM
The aim of this study was to investigate the anti fibrotic effect of Aramchol™ using the Thioacetamide (TAA) rat model of fibrosis.

METHOD
Liver fibrosis was induced by intraperitoneal injections of TAA (100mg/ml) at A dose of 20mg/100g body weight twice weekly for up to 10 weeks. Rats were treated orally by gavage with Aramchol™ (1 and 5 mg/kg/day) or vehicle. Control TAA induced fibrosis were also treated with vehicle for the same duration. At the end of the experiment, liver samples were obtained. A histological assessment of the livers was performed after staining with hematoxylin-eosin (H&E) and Mason trichrome staining. Evaluation of fibrosis was based on the Ludwig and Batts staining system using the following parameters: portal fibrosis (stage 1) characterized by mild fibrous expansion of portal tracts; periporal fibrosis (stage 2) showing fine strands of connective tissue in Zone 1 with only rare portal-portal septa; septal fibrosis (stage 3) manifested by connective tissue bridges that link portal tracts with other portal tracts and central veins but not regenerative nodules; and cirrhosis (stage 4) showing bridging and nodular regeneration.

RESULTS

Effect of Aramchol™ on Liver Cirrhosis – Macrosopic Evaluation

Treatment with ARAMCHOL™ significantly prevents TAA induced cirrhosis.

<table>
<thead>
<tr>
<th>Saline Control</th>
<th>TAA</th>
<th>TAA + Aramchol™ 1 mg/Kg</th>
<th>TAA + Aramchol™ 5 mg/Kg</th>
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<tr>
<td>[Image of liver samples]</td>
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Effect of Aramchol™ on Liver Fibrosis – Microscopic Evaluation / Masson Goldner Staining

Treatment with ARAMCHOL™ significantly prevents TAA induced fibrosis in a dose dependent manner.

Effect of Aramchol™ on Liver Fibrosis – Microscopic Evaluation Score 0-4

<table>
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<tr>
<th>TAA No Treatment</th>
<th>TAA + ARAMCHOL™ 1mg/kg</th>
<th>TAA + ARAMCHOL™ 5mg/kg</th>
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<tbody>
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REFERENCES

ACKNOWLEDGEMENTS
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