AT A GLANCE

MEGASPOREBIOTIC AND HEPATOTOXICITY STUDY

PROBIOTIC BACILLUS SPORES PROTECT AGAINST ACETAMINOPHEN INDUCED ACUTE LIVER INJURY IN RATS.

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RESEARCH SUMMARY

High doses of acetaminophen (APAP) may lead to acute liver failure. APAP overuse is the main cause of acute liver toxicity in the US and Europe. Under normal circumstances, APAP is detoxified in phase II reactions in the liver. In excess, the liver cannot keep up with the detoxification process and begins to deplete hepatic glutathione storage. This results in increased oxidative stress and mitochondrial dysfunction. This study was performed to evaluate the possible protective effect of Bacillus sp. spores on acute hepatic injury induced by APAP. Researchers found that MSB had a protective effect on acute hepatic injury induced by APAP overdose in rats. Pretreatment with MSB resulted in a significant reduction in liver enzymes, inflammatory markers, ZO-1 release, improved total antioxidant capacity, and liver cell death.

GOALS

This study was performed to evaluate the possible protective effect of Bacillus sp. spores on acute hepatic injury induced by APAP.

KEY TERMINOLOGY

SILYMARIN
A flavonolignans extracted from milk thistle. Silymarin has been shown to possess various pharmacological properties like hepatoprotective, antioxidant, anti-inflammatory, anticancer, and cardioprotective activities.

ZONULA OCCLUDENS (ZO-1)
A tight junction protein found in intestinal epithelial cells that functions as a scaffold protein and anchors tight junctions. It is released in the bloodstream in the presence of leaky gut.

SUBJECTS

White male rats (n=35)

MATERIALS AND METHODS

Rats were randomly divided into 7 groups (n=5 per group)

- Group 1: control receiving 1% CMC
- Group 2: Silymarin (100mg/kg/day)
- Group 3: MegaSpore Biotic (1 x 109 CFU/day)
- Group 4: APAP (2g/kg) (this is a model for hepatotoxicity)
- Group 5: APAP (2g/kg) and Silymarin (100mg/kg/day)
- Group 6: APAP (2g/kg) and MSB (1 x 109 CFU/day)
- Group 7: APAP (2g/kg) and Silymarin (100mg/kg/day) and MSB (1 x 109 CFU/day)

MATERIALS AND METHODS (CONTINUED)

CMC, Silymarin, MSB were administered orally through a feeding tube daily for 12 days.

Groups 4-7 received a single dose of APAP on day 11 through a feeding tube.

Blood was collected and analyzed after the experiment. Markers analyzed:
- Aspartate aminotransferase (AST) and alanine aminotransferase (ALT)
- Total antioxidant capacity (TAC)
- TNF-a, IL-1B, and zonula occludens (ZO-1)

After being euthanized, the liver of each animal was removed and analyzed.

RESULTS

LIVER FUNCTION TESTS:
- APAP caused a significant elevation in ALT & AST (group 1 vs group 4)
- Pretreating with silymarin or MSB or both significantly alleviated the hepatotoxic effect of APAP.
    - The impact of silymarin or MSB on ALT & AST levels were similar.

INFLAMMATORY MARKERS:
- APAP significantly increased TNF-a and IL-1B compared to the control group
- MSB and silymarin significantly decreased inflammation markers

TOTAL ANTIOXIDANT CAPACITY (TAC):
- APAP significantly decreased TAC compared to the control group
- MSB and silymarin significantly increased TAC

HISTOPATHOLOGY:
- Groups 1, 2, 3 revealed normal liver tissue
- Group 4 showed several abnormalities such as focal hepatocellular necrosis, proto-central necrotic bridges, and diffuse and circumferential pericentral hepatitis.
- Group 5: 11 of 33 central veins presented with adjacent hepatitis, minimal hepatocyte dystrophy, low immune cell involvement and low inflammatory infiltrates.
- Group 6: 2 of the 46 central veins showed mild hepatitis. Low immune cell involvement. Hepatocyte dystrophy was absent.
- Group 7: half of the central veins presented with immune cell infiltration and inflammatory infiltration associated with hepatitis. Hepatocyte dystrophy was observed in 20% of the sectional area and 70% of the portal spaces.

ZONULA OCCLUDENS (ZO-1):
- Increased significantly after APAP administration
- Silymarin and MSB significantly reduced ZO-1 levels

CONCLUSIONS

- MSB pretreatment ameliorated APAP-induced acute liver injury.
- Hepatic injury was improved by pre-administration of MSB or silymarin versus administering APAP alone.
- When MSB or Silymarin were administered in conjunction with APAP (groups 5-7, liver enzyme markers were significantly reduced compared APAP treatment alone (group 4).
- Liver necrosis was observed in group 4.
- Pretreatment with MSB had the best hepatic protection.
- APAP overdose causes TAC of glutathione to slowly decrease compared to the control group but pretreatment of silymarin and MSB increased TAC.
- Group 4 had an elevated level of ZO-1 indicating increases in intestinal permeability.
- MSB reduced the ZO-1 levels through strengthening the intestinal barrier and decreasing the translocation of toxins into the bloodstream.
- The combination of MSB and silymarin decreased proinflammatory cytokines to normal levels.