ABSTRACT:

Mufarreh Yaqooti Motadil was investigated for its toxicological activity in human dose, in rats. The drug was found to be non-toxic and well tolerated even if treated for a long period of time. The biochemical studies revealed that the drug decreased the serum level of cholesterol, triglycerides, glucose and bilirubin non-significantly (P>0.05). On liver the drug showed very good affects as caused a significant decrease (P<0.05) in GGT, SGPT and SGOT.

INTRODUCTION

Since time immemorial, man has made use of plants in the treatment of diseases. The pharmacopoeias of many countries of the world include even today a large number of drugs of plant origin. While it is true that purely synthetic compounds are being employed in increasing measure, in clinical practice, interest in the examinations of plants as potential source of new drug has never waned.

The task of revival of the old system of medicine however, is not an easy one at the present time. Advances in knowledge are so fast in every time that an investigator is overwhelmed by the application of new matter with which is confronted. There comes a time, however, when we feel like going back to the ancient page and leave where secrets remain to be revealed and unfold. We are fortunately endowed with a very rich flora, because of the size of our country and varieties of climatic and soil conditions, obtained in the different parts and as such there is wonderful opportunity for working on plant products (Jain, 1990).

Another fortunate factor is that herbal medicines do not produce many side effects commonly seen after long-term administration of synthetic drugs, resulting in a revival of interest in their use all over the world in both developing and developed countries (Bateman et al., 1998). In recent survey it has been seen that 25-30% prescriptions, even in some developed countries contain plant ingredients. With the fast growing demand for herbal drugs in the last two decades in every branch of medical care, it was considered expedient if not imperative to explore the therapeutic claims with least side effects of reported herbal drugs in reference monograph to serve the clinicians and scientists alike of both modern and herbal system of medicine (Behl, 1993).

Now a days most of the individuals are preferring to take herbal medicine to control their health, not only in prevention of diseases but also to treat them because natural remedies are some how safer and more efficacious than remedies that are pharmaceutically derived (Bateman et al., 1998; Murphy, 1999). Hamdard Laboratories (Waqf) Pakistan has been manufacturing and practicing herbal drugs since long time. These of herbal drugs are widely prescribed for the treatment of various illnesses because many people cannot afford the use of expensive modern medicine.
One of such medicine is Mufarreh Yaqooti Motadil. It is indicated traditionally as general tonic, cardiac stimulant, cephalic tonic, antiarrhythmic. Now it has become imperative to conduct research on herbs to find out the toxicity and effectiveness of drugs for the benefit of man and animals and discard the ineffective, toxic and worthless drugs.

Therefore, the present study was conducted in determining the toxicity of the drug Mufarreh Yaqooti Motadil being manufactured and marketed by Hamdard Laboratories (Waqf) Pakistan and to validate the claim that herbal drugs are safe. With this perspective the present study has planned to evaluate the toxicity by using rats.

**MATERIALS AND METHODS**

**Drug:**
- MYM was used in the present study that was obtained from Hamdard laboratories (Waqf) Pakistan in semi solid dosage form. The Human dose of MYM is 2-tea spoon per day or 10g/70kg/day.

<table>
<thead>
<tr>
<th>70kg</th>
<th>10g</th>
</tr>
</thead>
<tbody>
<tr>
<td>1kg</td>
<td>0.142</td>
</tr>
<tr>
<td>350g</td>
<td>0.049g</td>
</tr>
</tbody>
</table>

**Animals:**
Sprague-Dawley rats weighing between 250-350g were obtained from animal house of Dr. HMI Institute of Pharmacology & Herbal Sciences and housed in separate cages for seven days prior to experimentation with free access to food and tap water ad libitum.

**Experimental Design:**
- **Toxicological studies in Rats:**
  - For rats human dose of MYM (10g/70kg) were administered for experimental use.
  - Saline (0.9% NaCl) was used as control.

Each group was containing 12 animals (6 males and 6 females). They were treated orally for six weeks and body weight was recorded every day. (Mohamed, 2002) Group I served as Control and Group II served as Treated. At the end of 6th week Animals were anaesthetized with Pentothal sodium 40mg/kg i.p. (Ulicna et al., 2003) 24 hours after the last dose of treatment. All animals were autopsied and their kidneys, heart and liver were dissected out and changes were observed.

**RESULTS**

**Toxicological studies in Rats:**
Male and female rats treated with MYM (10g/70kg) orally for six weeks, none of these animals showed any sign of toxicity except but some physical behavioral changes were
observed in first 2 hour after dosing like, corner sitting and palpable ptosis. Non significant decrease was observed in the weight of treated rats when compared with control i.e., 8% (p>0.05) as shown in Fig. 1 and Table 1.

Autopsy: Autopsy revealed that no gross changes were observed in organs like liver, spleen, heart and kidney. Non-significant decrease was observed in weight of heart, kidney, spleen and liver.

Table 1
Weight of rats during six weeks

<table>
<thead>
<tr>
<th>Dose</th>
<th>Weeks</th>
<th>% Fall in weight</th>
<th>Mortality</th>
<th>Toxic effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (saline)</td>
<td>6</td>
<td>-15.7067±14.21</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Treated 10 g/70kg</td>
<td>6</td>
<td>5.88±0.625</td>
<td>Nil</td>
<td>Nil</td>
</tr>
</tbody>
</table>

The value indicate the mean ± S.E.M

Table 2
Effect of MYM(10 mg/70kg) on Biochemical Parameters after six weeks treatment

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>MYM</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bili. Direct</td>
<td>2.37 ± 0.41</td>
<td>0.81 ± 0.035</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Bili Total</td>
<td>0.81 ± 0.014</td>
<td>0.281 ± 0.004</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>116.7 ± 0.14</td>
<td>116.3 ± 0.28</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>157.74 ± 3.64</td>
<td>157.79 ± 5.03</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>HDL</td>
<td>0.281 ± 0.009</td>
<td>0.258 ± 0.005</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>GGT</td>
<td>1.07 ± 0.14</td>
<td>0.705 ± 0.02</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>ALAT</td>
<td>1.75 ± 0.014</td>
<td>1.13 ± 0.12</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>ASAT</td>
<td>15.25 ± 0.63</td>
<td>2.7 ± 0.07</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>26.06 ± 7.26</td>
<td>52.82 ± 7.07</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>CK</td>
<td>266.73 ± 2.14</td>
<td>225.5 ± 2.08</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.67 ± 0.098</td>
<td>3.63 ±</td>
<td>P&gt;0.05</td>
</tr>
</tbody>
</table>

The value indicate the mean ± S.E.M

Fig. 1: Average weight of control and treated rats after six weeks treatment
Effect of MYM on different Biochemical parameters:

The alterations in the lipid profile like cholesterol, HDL, Triglycerides, in concentration of Glucose, in concentration of different enzymes, Alkaline Phosphatase, Bilirubin, SGOT, GGT, CK, and SGPT is shown in Table 2.

The dose of MYM (10g/70kg) had decreased the serum level of Cholesterol, HDL, and glucose the decrease was non-significant (P>0.05). No change was observed in Triglycerides (Fig. 2). Bilirubin and HDL were decreased non significantly (P>0.05) (Fig. 3). Liver enzymes GGT, SGPT and SGOT were decrease significantly (P<0.05)
Drug caused a highly significant decrease in CK (P<0.05). A non-significant increase was observed in Alkaline Phosphatase (Fig. 5). While albumin was decreased non-significantly (Fig. 6). These changes were observed in rats as compared to their respective control.

**Histopathological Studies:**

*Examination of Heart:*

**Control:**

![Histological Examination](image1)

Fig. 7(10X) Histological Examination suggested that cardiac muscles (CM) are showing cross-striations (CS) and each muscle fiber showing a central nucleus (N). A distinguishing and characteristic feature of the intercalated disks (ID).

**Treated:**

![Histological Examination](image2)

Fig. 9: (10X) The myofibrils (MY) within each cell are well displayed. Histological pictures of cardiac muscle, demonstrating that the fiber dividing, then recombining and then spreading again. Each muscle cell possesses centrally located oval nuclei (N). Occasionally muscle cell possesses two nuclei. Intercalated disc (ID) indicating intracellular junction between two cardiac muscle cells. The intercellular areas are richly supplied by capillaries (CA). (Gartner L. P. 2000). This is comparable with its control.

*Examination of Kidney:*

**Control:**

![Histological Examination](image3)

Fig. 10: (10X) Kidney cortex components were observed. The Renal corpuscles (RC) in the center display a slight shrinkage artifact and...
Toxicological Studies of a Poly Herbal Drug

thus clearly demonstrate Bowman’s space (BS). The renal corpuscles are surrounded by cross sections of proximal convulated tubules (PT). Distal convulated tubule (DT) and macula densa (MD). (Eroschenko, 1996; Gartner, 2000).

Treated:

Examination of Liver:

The liver cells are arranged into lobules in both control and treated slides. Liver cells (hepatocytes) (H) are flat and arranged. A discontinuous layer of cells lines the sinusoids. Central vein (CV) is lined by epithelial cells (EP) and filled with biconcave Red Blood cells. Hepatic sinusoids appear to radiate from central vein. Necrotic lesions were not seen in MYM treated animals and hepatocytes were comparable with the control as shown in Figures 12 and 13 (Gartner, 2000).

Examination of Spleen:

Spleen is subdivided into red pulp (RP) and white pulp (WP). White pulp is arranged as a cylindrical sheath of lymphocytes i.e., periarterial lymphatic sheath (PALS) it surrounds a blood vessel known as central artery (CA) as shown in both control and treated spleen (Figs. 14 and 15). Red pulp consists of sinusoids. While treated spleen contains an area of germinal center (GC). The marginal zone also present around lymphatic nodules present in MYM treated spleen (Fig. 15) (Gartner, 2000).
CONCLUSION

Mufarreh Yaqooti Motadil (MYM) was administered to rats in human doses and it is concluded that MYM is non-toxic herbal drug and well tolerated even if treated for a long period of time. The Biochemical studies also suggest that MYM did not produce any significant alteration rather it was proved to be beneficial for the liver and heart muscles. Histopathological examination also suggests that the drug if used in human doses for a longer period of time (6 weeks) did not produce any pathological changes.

REFERENCE


