PHARMACOKINETIC PROFILE OF WHEAT BRAN ON HYPERLIPIDEMIC WISTAR STRAIN RATS

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ABSTRACT

The milling by product of wheat is bran its constituents are cellulose, pectin, polysaccharides and proteins the oral ingestion of bran the undigested portion of the bran interact with the bile acids and excretes, this effect enhance cholesterol degradation in the liver. Total cholesterol (TC), triglycerides (TG), phospholipids, low density lipoprotein (LDL), very low density lipoprotein (VLDL), high density lipoprotein (HDL), in normal and wheat bran treated rats were evaluated. When comparing the values of the wheat bran treated group with those of the control diabetic group, we found that the wheat bran significantly decreased the elevated blood cholesterol, triglycerides, phospholipids, LDL, VLDL. It showed a significant increase in liver glycogen and HDL level. These results clearly indicated that wheat bran shows anti-hyperlipidemic activity in rats, on the basis of this activity anti hyperlipidamic (synthetic drugs) are replaced with bran in case of hyperlipidamic patients with hypertension to avoid the drug - drug interaction.

Keywords: Wheat bran, Total cholesterol, Triglycerides, LDL, VLDL, HDL, Simvastatin.

INTRODUCTION

Interaction between the drug and drug or food and drug can have profound influence on the success of drug treatment and on the side effect profile of many drugs, the interactions not always detrimental to therapy. Multiple-drug therapy is common for patients hospitalized for infections and other disorders. Furthermore, a patient may be suffering from more than one unrelated disorder which demands simultaneous treatment with two or more drugs. Drugs are sometimes administered concurrently and deliberately to make use of expected interactions. A drug may affect the response to another drug in a quantitative way. On the other hand, the intensity of either the therapeutic effect or side effect may be augmented or suppressed. A drug may not necessarily affect either the quality or partial intensity or effect of another-drug but may cause significant to profound changes in the duration of action. Recent scientific developments— Particularly in the area of cytochrome P450 drug metabolizing enzymes have revolutionized the study of drug interactions. The result has been a deluge of polished drug interactions research that has overwhelmed most health care practitioners. While it is not possible for an individual health care practitioner to recognize all clinically significant drug interactions. It is possible to understand the important scientific principles and mechanisms that pertain to this topic. When discussing drug interactions, the drug affected by the interaction is called the “Object drug”, and the drug, causing the interaction is called the “Precipitant drug”.

Concurrently use of anti hypertensive drugs and anti lipidamic drugs shows profound drug - drug interactions or adverse drug reactions in patient suffering with the hypertension and hyperlipidamic disorder (Anonymous 1-6; Remington, 2000).

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Object of this study is to minimize the drug-drug interaction or adverse reactions by avoiding the concurrently administration of two drug formulations. The milling by product of wheat is bran its constituents are cellulose, pectin, polysaccharides and protein’s the oral ingestion of bran the undigested portion of the bran interact with the bile acids and excretes, this effect enhance cholesterol degradation in the liver and lowers the LDL-levels in the plasma on the basis of this activity anti-hyperlipidamias are replaced with bran in case of hyperlipidemic patients with hypertension to avoid the drug - drug interaction.

Experimental Animals
Male wistar rats (weighing 200-220 grams) were selected from our animal house Jyothismathi institute of pharmaceutical sciences, Karimnagar. Animals were randomly divided into three groups each group contains six animals. Each rat was maintained under controlled lab environment atmosphere humidity of 50% each rat was fed with standard pellet diet and water ad libitum. The protocol of animal study was approved by the institutional animal ethical committee. Before induction of hyperlipidemia in animals, the weight of the individual animal and plasma cholesterol levels were observed. Then standard cholesterol rich diet was administered up to 20 days.

In addition, butter was been fed twice a day (0.5ml) to each rat for three groups till 20 days. During which period the animal weight changes, food consumption, water consumption are checked periodically. At the end of the one month cholesterol rich diet feeding, the blood was pooled from tail vein. The Plasma samples were analyzed for baseline reading to determine induction of total cholesterol, triglycerides, high density lipoprotein (HDL-C) and (LDL-C) low density lipoprotein- cholesterol. Plasma triglycerides and total cholesterol, HDL-C were estimated by enzymatic method and using spectrophotometer (Dheni S et al., 1999; Van Geijn HP et al., 2005; Basile J, 2004; Martine Dale, 1999).

Study Design
As above described, the elevated hyperlipidemic animals were divided into three groups. One more normal animal group was kept as non hyperlipidemic and each group consists of six animals. Open labeled parallel study design was followed.

The rats were grouped as follows
Group I : Hyperlipidemic rats.
Group II : Simvastatin alone in single dose / day in hyperlipidemic rats.
Group III : Wheat bran administration as a single dose 200mg/kg/day.

Preparation of Simvastatin
10mg of pure Simvastatin was suspended in 10ml of carboxy methyl cellulose (0.5%) to a final concentration of 8mg /ml immediately before use.

Preparation of wheat bran and rice bran
5kg of wheat were milling in Flore mill and sieved it, the by product were separated almost 500 mg bran obtained from 5 kg of wheat, the wheat bran suspended in carboxy methyl cellulose (0.5%) the final concentration of 200mg/kg /day three divided doses

Collection of Blood Samples
After administration of the drugs, blood samples of 0.5 ml were drawn through retro orbital sinus into heparinized effendorff tubes at 0,0.5, 1,2,4,6 8 and 24 hrs. Equal amount of saline were administered to replace blood volume at every blood withdrawal time. Centrifugation was performed by using REMI ULTRA cooling centrifuge at 3000 rpm for 5 minutes. All samples were stored at 4°C until analysis of pharmacokinetic parameters. As described above all the procedures were followed on day 10 and 20.

Preparation of Plasma Samples for HPLC Analysis
Rat plasma (0.5 ml) samples were prepared for chromatography by precipitating proteins with 2.5 ml of ice-cold absolute ethanol for each 0.5 ml of plasma. After centrifugation the ethanol was transferred into a clean tube. The precipitate was resuspended with 1 ml of acetonitrile by vortexing for 1 min. After centrifugation (5000 – 6000 rpm for 10 min), the acetonitrile was added to the ethanol and the organic mixture was taken to near dryness by a steam of nitrogen at room temperature. Samples were reconstituted in 200 µl of 70 % of acetonitrile and 30% water was injected for HPLC analysis (The Merk Index, 1999; Mary J. Mycek, 2000).

Estimation of parameters
1. Triglycerides (TG):
Comprise the largest proportion of fats in the diet, in adipose tissue, and in the blood in the liver, TG is packaged into very low-density lipoprotein (VLDL) particles.

2. High-Density Lipoprotein Cholesterol (HDL-C):
A lipoprotein synthesized in the liver and intestine which carries cholesterol from the peripheral tissues (including arterial wall) to the liver in a process termed “reverse cholesterol transport”.

3. Low-Density Lipoprotein Cholesterol (LDL-C):
The major cholesterol transport lipoprotein in human plasma which transports cholesterol from the liver to the peripheral tissues. LDL-C = TC - (TG/5 + HDL-C) = mg / dl.

4. Total Cholesterol (TC):
Total cholesterol present in the body (Lise A Eliot and fakhreddin Jamali, 1999;
Statistical comparison was carried out with student’s paired T-Test; a value of P<0.05 was considered to be statistically significant. Data were reported as mean ± S.E.M. Linear regressions were used to determine the parameters.

RESULTS & DISCUSSION

The triglyceride level in the wheat bran treated group was significantly reduced than that in the vehicle treated group and Simvastatin treated group (P<0.001). Simvastatin also showed significant reduction in the triglyceride levels (P<0.001) as compared to the vehicle treated group. Comparison of results obtained from control rats and bran treated rats revealed that there was a significant decrease of TC in serum, liver and kidney. (Table 2). However the control rats treated with wheat bran shows a significant decrease (p<0.05) in liver TC levels. A significant decrease (p<0.001) in LDL, VLDL levels were observed in the serum of rats compared to control rats, whereas the HDL level was increased significantly (p<0.01).

### Table 1. Mean triglyceride levels ± SEM (mg/dl)

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Mean triglyceride levels at day 10 (mg/dl)</th>
<th>Mean triglyceride levels at day 20 (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vehicle</td>
<td>60 ± 3.2</td>
<td>75 ± 4.8</td>
</tr>
<tr>
<td>2</td>
<td>Simvastatin</td>
<td>45 ± 5.4</td>
<td>52 ± 2.9</td>
</tr>
<tr>
<td>3</td>
<td>Wheat bran</td>
<td>48 ± 3.6</td>
<td>50 ± 4.5</td>
</tr>
</tbody>
</table>

### Table 2. Total cholesterol levels ± SEM (mg/dl)

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Total cholesterol level at day 10 (mg/dl)</th>
<th>Total cholesterol levels at day 20 (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vehicle</td>
<td>107 ± 3.9</td>
<td>125 ± 4.7</td>
</tr>
<tr>
<td>2</td>
<td>Simvastatin</td>
<td>65 ± 3.4</td>
<td>69 ± 4.8</td>
</tr>
<tr>
<td>3</td>
<td>Wheat bran</td>
<td>58 ± 5.7</td>
<td>61 ± 6.9</td>
</tr>
</tbody>
</table>

### Table 3. Concentration of serum HDL, LDL and VLDL Effect of Wheat bran on at day 10

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>HDL (mg/dl)</th>
<th>LDL (mg/dl)</th>
<th>VLDL (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vehicle</td>
<td>41.49 ± 1.78</td>
<td>82.54 ± 0.91</td>
<td>13.93 ± 0.79</td>
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<tr>
<td>2</td>
<td>Simvastatin</td>
<td>39.92 ± 0.79</td>
<td>54.59 ± 1.53</td>
<td>12.53 ± 1.15</td>
</tr>
<tr>
<td>3</td>
<td>Wheat bran</td>
<td>40.24 ± 0.20</td>
<td>52.71 ± 1.51</td>
<td>11.35 ± 0.62</td>
</tr>
</tbody>
</table>

Values are mean ± S.E.M (n = 6). Statistical Comparison: 1 vs. 2; 2 vs. 3; ***P<0.001, **P <0.01, *P <0.05.

### Table 4. Effect of Wheat bran on concentration of serum HDL, LDL and VLDL at day 20

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>HDL (mg/dl)</th>
<th>LDL (mg/dl)</th>
<th>VLDL (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vehicle</td>
<td>36.0.9 ± 1.20</td>
<td>80.54 ± 0.67</td>
<td>14.53 ± 0.45</td>
</tr>
<tr>
<td>2</td>
<td>Simvastatin</td>
<td>40.69 ± 0.70</td>
<td>48.51 ± 1.33</td>
<td>10.43 ± 1.24</td>
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<tr>
<td>3</td>
<td>Wheat bran</td>
<td>47.13 ± 0.10</td>
<td>52.71 ± 1.51</td>
<td>09.25 ± 0.43</td>
</tr>
</tbody>
</table>

Values are mean ± S.E.M (n = 6); Statistical Comparison: 1 vs. 2; 2 vs. 3; ***P<0.001, **P <0.01, *P <0.05.
**REFERENCE**


