CLINICAL STUDY REGARDING THE EFFECT OF NUTRICEUTICAL FOODS WITH ISOFLAVONES IN HYPERCHOLESTEROLEMIA AND METABOLIC DISORDERS

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Abstract. The aim of this study was to estimate the effect of the nutriceutical foods with isoflavones in hypercholesterolemic conditions and metabolic disorders. A daily intake of 250g nutriceutical foods, offers 40-50mg isoflavones/d that correspond with the literature reports about the hypocholesterolemic effect of isoflavones.

Nutriceutical foods have been obtained in two National Research Programs: • BIOTECH 408/2002 - „Obtaining of some nutriceutical foods from vegetal proteins” and • BIOTECH 503/2002 - „Methods for obtaining some vegetal foods for the persons with metabolic disorders” that happen in the 2002-2006 period.

This study has been performed at the Clinical Center of Diabetes, Nutrition and Metabolic Diseases Cluj-Napoca and the study group included 24 persons with following conditions: 95,8% were dislipidemic, 66,6% were overweight, 58,3% had diabetes mellitus or an alteration of the glucose tolerance.

The results of this study showed a statistically significant decrease of MCI and body weight (p<0,01) by 8,6% and 5%, respectively. There was also a statistically significant decrease of basal glicemic levels at the entire group of the study, by 13,4% (p=0,000), the most important decrease being registrate at the persons with diabetes mellitus by 27,5% (p=0,0006). Lipid indicators, in special total cholesterol, as major cardiovascular risk factor, didn’t demonstrate a significant variation, except the HDL cholesterol(„good cholesterol”) that demonstrate an important increase with 3,4% (p=0,01), after three month of study.

The conclusion of the study is that the nutriceutical foods with isoflavones obtained from soy protein can be used as an alternative solution in order to prevent obesity, diabetes mellitus and into the diets that endorse the reducing of cardiovascular risk factors.

INTRODUCTION

Cholesterol and other serum lipids are strongly associated with the various manifestations of atherosclerosis. Thus, the lowering by 1% of serum cholesterol entails 2-3% changes in the incidence of ischemic heart disease (1).

It is currently accepted that dyslipidemia and atherosclerosis are correlated with diet and may be partially influenced by adequate dietary measures (2).

The identification of the role of diet components, either combined or in isolation, in the pathogenesis of atherosclerosis is very difficult because of the interference with other factors such as: life style, genetic and environmental factors etc.

Studies of dietary intervention provide variable long-term results. The compliance of such studies is often reduced, especially when major changes in the diet are indicated (2).
The diet therapy usually indicated in hypercholesterolemia and metabolic diseases are low-calories and low fat. A major characteristic is the fact that such a diet should be observed for a long period of time, theoretically throughout the patient’s life. Practically, this is difficult, especially if dietary habits are drastically changed. The differences are usually in relation to meat, meat preparations and carbohydrates. Moreover, in time some restrictive diets may result in nutritional deficits.

At present there is a new trend in human nutrition, especially in the case of diseases requiring diet therapy, which consists of introducing functional aliments, easier to administer, less restrictive and with good therapeutic effects.

This trend originates in the acknowledgement of the fact that human diet contains besides micro- and macronutrients, a wide range of bioactive non-nutritional components called fitochemicals, incorporated into the diet either in natural form or as supplements which have long term health benefits.

Among the non-nutritional compounds, fitochemicals are compounds derived from plants (3), and the growing number of these biologically active substances is subject to a high number of epidemiological studies. Among these substances there is a large class of non-steroid estrogens called fitoestrogens. In the last 10 years the interest for them has been increasing due to the favourable effects reported in a number of conditions, especially in cardiovascular diseases (4, 5).

The aim of this study was to estimate the effect of the nutriceutical foods with isoflavones in hipercholesterolemic conditions and methabolic disorders. A daily intake of 250g nutriceutical foods, offers 40-50 mg isoflavones/d that corespond with the literature reports about the hypocholesterolemic effect of isoflavones (6, 7).

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This study has been performed at the CLINICAL CENTER OF DIABETES, NUTRITION AND METHABOLIC DISEASES CLUJ-NAPOCA “IULIU HATIEGÂNÚ” UNIVERSITY OF MEDICINE AND PHARMACY.

OBJECTIVES

♦ Short-term evaluation (3 month) of dietary isoflavones from nutriceutical foods on the lipid and metabolic parameters that represent risk factors in cardiovascular diseases.
♦ Evaluation of the possibilities regarding utilization of the new products (nutriceutical foods) in the diets that are recommended in the case of hypercholesterolemia and obesity.

MATERIAL AND METHOD

Group selection

The study group included 24 persons selected at the Clinical Center of Diabetes, Nutrition and Metabolic Diseases Cluj-Napoca “Iuliu Hatieganu” University of Medicine and Pharmacy in aug-oct. 2003, by the following criteria:
dislipidemia: total cholesterol (TC) and LDL cholesterol ("bad cholesterol") moderate elevated (TC >190mg/dl, LDL chol >115mg/dl);
- HDL cholesterol ("good cholesterol") and triglycerides (TGL) normal or moderate elevated (HDL >30mg/dl, TGL <300mg/dl);
- normal blood pressure;
- normal anthropometric indicators (corporal mass indicator, abdominal circumference)
- Framingham cardiovascular risk <10%;
- no hipolipemiant therapy before the study.

All of them had a daily intake of 250g nutriceutical foods that offered 40-50mg isoflavones/d. The study duration was 3 month.

Group characteristics:

- Average was 47.79±1.95 years;
- Women: man ratio was 3.8:1;
- Overweight, characterised by corporal mass indices (CMI) (kg/m²) between 25-30, was presented at 5 persons from 24 (20.8%);
- Obesity, characterised by CMI (kg/m²) more than 30, was presented at 11 persons from 24 (45.8%);
- The body weight was 93.54±18.40 Kg;
- The abdominal circumference was 113.6±20.15 cm.

Hypercholesterolemia (plasma cholesterol ≥ 190 mg/dl) was presented at 23 persons from 24 (95.8%). There have been registered other lipid parameters and there mean values are presented in label I.

Table 1

<table>
<thead>
<tr>
<th>Lipid parameter</th>
<th>Mean value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>210.5±47 mg/dl</td>
</tr>
<tr>
<td>LDL-cholesterol</td>
<td>139.72±11.87 mg/dl</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>44.83±7.26</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>212.94±95.85 mg/dl</td>
</tr>
</tbody>
</table>

Reduced glucose tolerance characterised by basal glicemia between 110-125 mg/dl, was presented at 9 persons (37.5%) and diabetes mellitus characterised by basal glicemia between >126 mg/dl, was presented at 5 persons (20.8%); the mean value of basal glicemia was 128.36±36.9mg/dl.

An important characteristic of the study group was an overlap of major parameters. So:
- all of normoponderal persons had hypercholesterolemia with normoglicemia;
- just 3 of them had reduced glucose tolerance;
- all of the overweight persons had hypercholesterolemia with normoglicemia except 1 person that had all lipid and glicemic parameters in normal range
- all of the persons with obesity had hypercholesterolemia; 6 of them had associated reduced glucose tolerance and 5 of them had diabetes mellitus.

RESULTS AND DISSCUTIONS
Considering the entire study group, the evolution of the biochemical and anthropometrical parameters is presented in label II:

### Table 2: Evolution of the biochemical and anthropometrical parameters at the study group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Initial</th>
<th>Final</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>210.70 ± 21.99</td>
<td>202.08 ± 20.50</td>
<td>NS</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dl)</td>
<td>139.75 ± 16.20</td>
<td>133.33 ± 16.20</td>
<td>NS</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>44.83 ± 7.26</td>
<td>46.37 ± 5.57</td>
<td>0.01</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>212.95 ± 84.34</td>
<td>202.41 ± 1.91</td>
<td>NS</td>
</tr>
<tr>
<td>Basal glucose (mg/dl)</td>
<td>128.36 ± 36.9</td>
<td>111.11 ± 38.06</td>
<td>0.0001</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>93.54 ± 18.40</td>
<td>88.87 ± 17.04</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Corporal mass indices (kg/m²)</td>
<td>36.2 ± 3.1</td>
<td>33.1 ± 2.7</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Abdominal circumferences (cm)</td>
<td>113.6 ± 20.15</td>
<td>111 ± 14.7</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>133.54 ± 12.80</td>
<td>130.41 ± 11.12</td>
<td>0.05</td>
</tr>
</tbody>
</table>

**Lipid parameters**, including total cholesterol, as a major cardiovascular risk factor, didn’t register a statistical significant decrease, except HDL-cholesterol which had a significant increase by 3.4% (p=0.01) (fig. 1).

![Decrease of the lipid parameters](image)

* statistical significance, p=0.01

**Basal glicemia** had a statistical significant decrease at the entire group (p=0.0001) most important being registered at the persons with diabetes mellitus (p=0.0006); modification of the basal glicemia was non significant at the persons with reduced glucose tolerance (fig 2).
Decrease of the basal glycemia (%)

Entire group Reduced glucose tolerance Diabetes mellitus

* statistical significance, $p<0.01$

Fig 2. The effect of the isoflavones from nutriceutical foods on basal glycemia (250g nutriceutical foods/d with 20mg izoflavones/100g).

Anthropometrical indicators: CMI and body weight had a significant decrease ($p<0.01$) by 8.6% and 5%, respectively; abdominal circumference hadn’t a significant modification (fig 3).

Fig 3. The effect of the isoflavones from nutriceutical foods on anthropometrical indicators (250g nutriceutical foods/d with 20mg izoflavones/100g).

All of the persons from the study group had a good tolerability of the nutriceutical food and there was no abandons. There were also no side effects.

DISCUSSIONS

The main objective of our clinical study was a short-term evaluation (3 month) of dietary isoflavones from nutriceutical foods on the lipid and metabolic parameters that represent risk factors in cardiovascular diseases. These foods represent a new alternative in treatment of hypercholesterolemia and obesity disorder because of the specific technology of fabrication from soy protein and because of the content of large amounts of isoflavones ($20\text{mg izoflavones/100g}$).

In the case of the lipid parameters, the results showed that even there was a reducing tendency of lipid parameters, their values hadn’t a statistical significance. A possible explanation can be the relative short period of evaluation (93 month). Another explanation can be that the initial levels of the plasmatic cholesterol were not very high ($<300\text{mg/dl}$). At
similar values James W. Anderson also demonstrated, in 1995, that the effect of soy protein with isoflavones was non significant (8).

In our study, the most important modification was registered in the case of HDL-cholesterol (3,4%). This evolution is very important because several studies demonstrated that an increase with 1 mg/dl of HDL-cholesterol is associated with a decrease by 2-3% of the cardiovascular risk especially in woman rows (1).

When we made a comparison between men and women evolution of the HDL-cholesterol, we saw that the increase was most important at the women group (at 15 women from 19) and just at a 1 man. The average of the women group was between 45-50 years. This is the perimenopausal period when important modification in estrogens levels appears and this is associated with a decrease of HDL cholesterol in many cases. Because this type of cholesterol is considered as “good” or a protection factor in cardiovascular diseases, we consider that nutriceutical foods can be a protection alternative against cardiovascular disease especially in the case of women at the perimenopausal period of life.

Interesting was the reducing effect of basal glicemia especially in the case of the persons with diabetes mellitus (27,5%, p=0,0006); this reducing was correlate with the body weight and MCI reducing. There was also a reducing of anthropometrical indicators (CMI and body weight) especially at the persons with overweight. These effects are very important because these foods can be used as an alternative to the traditional foods that contain animal protein and saturated fats and are rich in calories in metabolic disorders. In opposite with the traditional foods, nutriceutical foods have a low fats content and most of all are unsaturated. Also nutriceutical foods are low in calories (label IV)

<table>
<thead>
<tr>
<th>Food sources</th>
<th>Proteins (g/100g product)</th>
<th>Lipids (g/100g product)</th>
<th>Calories (Kcal/100g product)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal protein salami</td>
<td>17</td>
<td>34,6</td>
<td>391</td>
</tr>
<tr>
<td>Vegetal protein salami</td>
<td>14,38</td>
<td>12,48</td>
<td>176,8</td>
</tr>
<tr>
<td>Animal protein sausage</td>
<td>19,4</td>
<td>31,7</td>
<td>374</td>
</tr>
<tr>
<td>Vegetal protein sausage</td>
<td>21,11</td>
<td>6,66</td>
<td>150,7</td>
</tr>
<tr>
<td>Animal protein patė</td>
<td>12,5</td>
<td>25</td>
<td>287</td>
</tr>
<tr>
<td>Vegetal protein patė</td>
<td>12,5</td>
<td>12,5</td>
<td>166,5</td>
</tr>
</tbody>
</table>

CONCLUSIONS

1. Isoflavones from nutriceutical foods didn’t determine significant modification of the total cholesterol, LDL cholesterol and triglycerides, when the initial values were not very high (between 190-300mg/dl).
2. Isoflavones from nutriceutical foods determined a significant increase of HDL cholesterol (3,4%, p=0,01) especial at the women with an average between 45-50 years.
3. Nutriceutical foods with low content of calories had a very good effect in reducing of basal glicemia and anthropometric indicatorsat the persons with diabetes mellitus and overweight.
4. Nutriceutical foods can be used as an alternative for preventing metabolic disorders and cardiovascular diseases at these persons and for improving cardiovascular protection at the women in perimenopausal conditions.

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