

THE EFFECTS OF DIET ENRICHMENT WITH A HULL-LESS OAT CULTIVAR ON GLUCOSE, LIPID, LIPOPROTEIN, FIBRINOGEN, AND ESTRADIOL CONTENTS IN THE BLOOD OF POST-MASTECTOMY WOMEN

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The aim of the present study was to evaluate the effects of enriching the uncorrected diet of post-mastectomy women with a hull-less oat cultivar on the subjects' blood glucose, triacylglycerol, total cholesterol, HDL- and LDL-cholesterol, fibrinogen, and estradiol levels. The cholesterol levels were assayed in a closed system, with Roche reagents in an Integra biochemical analyser. The fibrinogen level was determined, following clotting, with a Behring BCT DADE, while estradiol was assayed by chemoluminescence in a DPC Immulite instrument. The subjects consumed oat grains 3 times a week, for 4 months, in amounts constituting 10–15% of the diet energy value. Whenever consumed, oats replaced a carbohydrate product usually served for a meal (e.g. bread for breakfast, lunch or dinner, or potatoes, grits, rice, pasta etc. for lunch or dinner). The oat enrichment was found to produce a statistically significant ($P < 0.01$) reduction in the glucose (from 98 to 90 mg/dL) and HDL-cholesterol (from 59.3 to 55.9 mg/dL) levels as well as a significant ($P < 0.01$) increase in the fibrinogen concentration (from 280 to 361 mg/dL). The post-hysterectomy women showed a significant ($P < 0.05$) increase in the blood estradiol level (from 10.0 to 19.5 pg/mL). Changes in triacylglycerol (from 126 to 130 mg/dL), total cholesterol (from 206 to 202 mg/dL), and LDL-cholesterol (from 122 to 115 mg/dL) levels as well as those of estradiol (from 62 to 290 pg/mL) in those subjects with intact ovaries were not significant.

INTRODUCTION

Long-term studies carried out by the author on post-mastectomy women have supplied data demonstrating frequent carbohydrate-lipid metabolism disorders in the subjects [Friedrich, 1998 b, 2000]. For this reason, in addition to comprehensive nutrition-related education and advice, such women concerned are recommended to enrich their diet with components that make it possible to maintain their metabolism at a correct level, without any special dietary regime or additional supplementation. Such components include dietary fibre present in various foods. The hypolipoemic effects of dietary fibre, including beta-glucans, on blood lipids and lipoproteins have already been well documented [Gerhardt & Gallo, 1998; Nicolosi *et al.*, 1999; Olson & Schneeman, 1998].

In 1997, a new hull-less oat cultivar (*Avena sativa* var. *nuda*), known under the name of Akt, was begun to be grown in Poland. Its grain, intended for consumption, does not require hull removal. Its dietary fibre content (40% of the dry weight) is twice that of the regular hulled oats (19.3% of the dry weight) and oat bran (20.3% of the dry weight) [Górecka *et al.*, 1998], with beta-glucans making up most of the dietary fibre. The very promising results with respect to the hypolipoemic effects of the Akt oats, obtained in an experiment involving male and female rats [Friedrich & Piech, 2000] prompted the author to carry out a study involving post-mastectomy women.

The aim of the present study was to evaluate effects of enriching the corrected in no other way diet, of post-mastectomy women with the hull-less oat on the subjects' blood glucose, lipid, lipoprotein, estrogen, and fibrinogen levels.

MATERIALS AND METHODS

The study involved 14 post-mastectomy, non-smoking women (7 post-ovariectomy subjects with the so-called negative estrogen receptors and 7 with intact ovaries, positive receptors, menstruating, and taking Tamoxifen, a non-steroid estrogen receptor blocker), aged 35–50 years, with BMI and value ranging within 19.8–23.0 and WHR of 0.80 ± 0.02 . All the subjects volunteered to participate in the study and supplied their written consent to the procedures to be applied. All the women had undergone mastectomy 4 years before. Over the experimental period (4 months: October–January), the subjects consumed 70-g oat portions (equivalent to 15–20% of the diet energy content) 3 times a week. They received their oat portions during weekly meetings with the author. The oat grains were consumed cooked, with any meal and any dish (e.g. served with milk or yogurt, as a component of soups or second dishes, breakfast muesli or salads eaten for dinner, or in casseroles with fruits, vegetables, or meat). Whenever consumed, the oats replaced a carbohydrate product usually eaten during a meal (e.g. bread for breakfast, lunch or dinner or potatoes,

grits, rice, pasta *etc.* for lunch or dinner). With the exception of oats, the energy content of which was equivalent to that of the products replaced, the subjects' dietary habits of the remained unchanged.

As no subject volunteering to participate in the experiment (of the 42 Agata Club members as few as 14 volunteered) wanted to be included in the control group, the experiment was open-ended.

Dietary information was collected, with a semi-quantitative food-frequency questionnaire developed by Willett *et al.* [1985], for 5 randomly chosen days of the week in November and December. The portion size was assessed using the "Album of Products and Meal Portions" [Szczygłowa *et al.*, 1991]. The nutrient content was derived from a database-containing software "Dietetyk"® v.2.5.

The subjects' physical activity was regarded as higher than average because all the women were professionally active, managed the household, meticulously observed the post-mastectomy rehabilitation regime (exercises, biking, swimming, marching, *etc.*), attended Club meetings, and formed a support group for women who had just undergone surgery, which involved, *i.e.*, visiting the hospital.

The oat grains used in the experiment were analysed for their protein (Kjeldahl technique, in a 2100 Kjeltec apparatus) and fat (Soxhlet technique, in a Foss Tecator Soxtec instrument) contents. The dry matter content was determined by drying oat samples at 100–105°C to constant weight and the amount of ash was determined by combustion at 550° for about 6 h. The carbohydrate level was calculated as a difference between dry weight and the sum of protein, fat, and ash contents. In addition, the insoluble dietary fibre fraction content was determined using the Van Soest detergent technique in an Ankom 220 analyser.

The blood for assays was collected, before and after the experiment, from the fasted subjects, at the Szczecin Central Public Hospital's laboratory and the assays were performed immediately. The blood serum was used for the following assays: (i) glucose, determined with the enzymatic colorimetric technique of Tietz [1995]; (ii) triacylglycerols, determined with the enzymatic colorimetric technique of Stein [1987]; (iii) HDL-cholesterol, determined by elimination, a technique involving a HDL-dissolving detergent which blocks enzymatic activity of esterase and cholesterol oxidase towards VLDL- and LDL-cholesterols [Morrison, 1997].

The assays were run with Roche reagents in an Integra biochemical analyser, in a closed system. The analyser automatically calculated the LDL-cholesterol content.

The fibrinogen content was determined by clotting the blood in a Behring BCT DADE instrument. Estradiol was assayed with an Immulite analyser (DPC).

Data for individual blood components were processed statistically by comparing the means using the paired observations – paired t-test [Steel & Torrie, 1981].

RESULTS

Analysis of the subjects' daily menus showed that the mean energy content of the daily food rations consumed on each of the 5 randomly chosen days of the week was considerably lower than the recommended levels of 2300±10%

kcal/day for women having a correct body weight and being moderately physically active [Ziemlański *et al.*, 1994] (Table 1). Although the total protein uptake was correct, the proportion of animal protein in the diet was too high. Carbohydrate consumption was close to the lower limit of the recommended range, while the total lipid consumption exceeded the recommended levels. In addition, the consumption of dietary fibre was found to be too low; similarly, uptakes of beta-carotene, vitamin B₆ as well as calcium, magnesium, and zinc were lower than required. The incorrect uptake of the basic nutrients was reflected in the per cent break-down of the diet's energy content into contributions supplied by proteins, carbohydrates, and lipids (Table 2).

TABLE 1. Contents of energy and basic nutrients in daily food rations of post-mastectomy women (no oat addition; n = 140 daily menus).

Components	Mean±SD
Energy [kJ]	7815.2±1252.0
Total protein [g]	52.8±21.44
Animal protein [g]	40.0±18.06
Plant protein [g]	22.8±8.35
Total carbohydrates [g]	244.8±47.27
Starch [g]	142.6±46.65
Sucrose [g]	48.5±8.48
Lactose [g]	8.5±8.48
Dietary fibre [g]	20.9±8.93
Total fat [g]	70.5±23.67
Saturated fatty acids [g]	50.1±12.6
Unsaturated fatty acids [g]	20.4±12.3
Cholesterol [mg]	273.7±217.4
Beta-carotene [mg]	3.72±3.12
Vitamin E [mg]	10.1±5.0
Ascorbic acid [mg]	85.6± 51.1
Piridoxine [mg]	1.41±0.41
Nicotinamide [mg]	11.25±3.87
Calcium [mg]	560.0±350.0
Magnesium [mg]	226.45±77.54
Zinc [mg]	8.98±3.24

TABLE 2. The share of protein, carbohydrates, and lipids in the total energy content of daily food rations of post-mastectomy women (no oat addition; n = 140 daily menus).

Components	[%]
Protein	13.5
Carbohydrates	52.5
Lipids	34.0
Saturated	24.0
Unsaturated	10.0

The analysis of the Akt oat grain chemical composition (Table 3) allowed assuming that a 70-g dose administered 3 times a week resulted in a mean increase in the daily lipid uptake of 6.44 g (about 9%), reduced by the amount of lipids present in the products replaced by the oats (average of 0.3–0.6 g). The dietary fibre consumption increased as well. The dietary fibre content, calculated as 40% of the grains' dry weight [Górecka *et al.*, 1998] (only the insoluble

fraction content was determined in this work), resulted in an increase of consumption averaging about 50% (10.5 g/day, including 1.7 g of the insoluble fraction), reduced by the amount of dietary fibre present in the products replaced by the oats (verge of 1.2–3.5 g). The uptake of protein and carbohydrates provided with oats was shown to be comparable to that resulting from consumption of the products being replaced.

The Akt oat enrichment of the post-mastectomy women's uncorrected diet was found to result in a significant ($P < 0.01$) reduction in glucose and HDL-cholesterol contents and a significant ($P < 0.01$) increase in the blood serum fibrinogen content (Table 4). The post-hysterectomy subjects showed a significant ($P < 0.05$) increase in the estradiol content (Table 5).

TABLE 3. Chemical composition of the hull-less Akt oat grains

Components	[%]	[% d.m.]
Dry matter	87.4	100
Proteins	10.1	11.6
Fats	9.2	10.5
Ash	1.7	1.9
Carbohydrates	67.4	77.1
Insoluble fibre fraction	2.4	2.6

Changes in the contents of the remaining blood components assayed were not statistically significant. However, noteworthy is the high increase in the estradiol content in the women with intact ovaries (shaded rows in Table 5), the lack of significance resulting from a high individual variability (coefficient of variation 96%). Interesting is also a tendency towards an increase in the triacylglycerol (TG) content and a reduction in total and LDL-cholesterol.

Increased TG contents were observed in 64% of the subjects. An identical percentage of the women (64%) showed total cholesterol levels to be reduced, while the

TABLE 5. Blood estradiol II content (a) and its increase (+) or reduction (-) after a 4-month period on a diet enriched with hull-less Akt oat cultivar (n=14).

No.	Estradiol II (E2II) [pg/mL]	
	a	+/-
1	10.8	+4.6
2	9.0	+13.1
3	16.6	+3.8
4	9.0	+5.8
5	9.0	+4.3
6	9.0	+21.3
7	12.6	+7.7
\bar{x}	10.9	+8.6*
SD	2.9	5.8
8	56.1	+593.9
9	19.1	+708.6
10	53.4	+20.8
11	51.5	+30.8
12	97.9	+81.1
13	82.1	+97.3
14	73.2	+60.7
\bar{x}	61.9	+227.6
SD	25.4	276.8

* – difference statistically significant at $P < 0.05$; shaded rows concern subject with intact ovaries.

LDL-cholesterol reduction was recorded in 57% of the subjects.

Over the experiment, several women reported various positive effects of hull-less oat consumption. The most important effects included an exceptional defecation improvement, a long-lasting sensation of a “nicely feeling” satiation.

TABLE 4. The levels of components in the blood of subjects (a) and their increase (+) or reduction (-) after a 4-month period on a diet enriched with the hull-less Akt oat cultivar (n = 14).

	Glucose [mg/dL]		Triacylglycerols [mg/dL]		Total cholesterol [mg/dL]		HDL- [mg/dL]		LDL- [mg/dL]		Fibrinogen [mg/dL]	
	a	+/-	a	+/-	a	+/-	a	+/-	a	+/-	a	+/-
1	109	-9	135	-28	168	+17	55.3	+1.7	86	+20	240	+38
2	95	-12	124	+23	254	-3	71.3	-9.1	158	+2	392	+131
3	96	-12	146	+1	176	-8	67.8	-3.4	99	-5	375	+59
4	99	-4	87	-2	206	-12	58.0	-11.1	131	-1	247	+79
5	101	-12	113	-20	207	-7	49.7	-4.2	135	+1	335	+84
6	130	-12	149	+64	178	+22	44.6	+3.2	104	+6	239	+120
7	115	-12	88	+1	216	-9	59.6	-4.6	139	-5	221	+28
8	88	+10	138	+6	151	-9	49.8	-10.7	74	-13	222	+71
9	96	-13	80	+20	114	+11	35.1	+6.8	63	0	234	+115
10	83	+4	140	+17	328	-44	101.0	-11.3	218	-93	316	+48
11	97	-3	117	-21	189	+26	62.1	-0.4	104	+30	260	+42
12	101	-14	168	-11	233	-32	64.4	-0.3	155	-22	226	+124
13	98	-7	134	+5	230	-10	59.8	-3.1	112	-8	320	+106
14	101	-10	141	+10	228	+12	52.1	-0.9	125	-4	290	+97
\bar{x}	98	-8**	126	+4	206	-4	59.3	-3.4**	122	-7	280	+81**
SD	16.6	16.2	25.9	36.5	51.1	41.3	15.3	12.8	39.7	28.0	58	73

* – difference statistically significant at $P < 0.05$; ** – 0.01

DISCUSSION

The analysis of the post-mastectomy women's menus revealed that they had not been haphazard. On the contrary, the women were convinced that they had very strictly adhered to their physicians' recommendations concerning, *i.a.* reduced consumption of fats and sugars as well as the body weight control. This explains the reduced energy content of the diets and the too low total carbohydrate uptake, including both simple and complex carbohydrates which are perceived as fattening. This also explains, in the context of women's fat consumption assessment [Friedrich, 1998 a], the almost correct lipid uptake, the amount of lipids consumed being, however, too high when compared to the reduced energy content of the diet.

The results obtained demonstrate the addition of the hull-less Akt oat grains to the uncorrected diet of post-mastectomy women to have been beneficial not only with respect to the blood glucose content, as the blood of some subject showed also positive effects with respect to triacylglycerol (TG) as well as to the total and LDL-cholesterol levels. On the other hand, unfavourable effects of oat addition were visible as increased levels of fibrinogen and estrogens in all the subjects as well as increased TG, total and LDL-cholesterol levels and reduced HDL-cholesterol content in some of the women.

The hypoglycaemic effect of oat-derived dietary fibre, beta-glucans in particular, has been known for a long time. The effect was described, by, *i.a.*, Anderson [1986] and Welch [1995]. Later on, the effect was observed in rats, particularly in females, by Piech and Friedrich [1999] in an experiment involving the Akt oats. The reduced blood glucose level observed in the present experiment involving post-mastectomy women lends support to the hypoglycaemic properties of the Akt oat cultivar.

On the other hand, the well-known hypolipoemic effect of the oat-derived dietary fibre was very weak in the women examined. The blood total cholesterol content decreased by an average of 2% and was accompanied by a 3% increase, on the average, in the blood TG content. A similar effect of the oat dietary fibre on TG contents was reported by Gerhardt & Gallo [1998]. Their study focusing on the effects of oat bran-enriched human diets revealed no changes in TG contents, but the subjects showed a 17% cholesterol content reduction. On the other hand, the hypolipoemic effects of the oat dietary fibre on both TG and total cholesterol were described by Gawlak [1994] and Hryniewiecki *et al.* [1994] who added oat bran to diets of subjects affected by lipid metabolism disorders. A similar effect of dietary fibre contained in the Akt oat cultivar added to rat diet was reported by Friedrich and Piech [2000] and by Kaira and Joad [2000].

The beneficial effect of oat addition on LDL-cholesterol was visible as a reduction, by 6% on the average, in the fraction's content in blood. On the other hand, HDL-cholesterol was unfavourably affected, as the fraction's content decreased in 79% of the women examined. Opinions on the effects of oats and their products on HDL-cholesterol blood contents vary. Thus, effects similar to those described here were reported from human subjects by Gould *et al.* [1980] and Davidson *et al.* [1991], and from experimental animals by Gerhard and Gallo [1998], Olson and

Schneeman [1998], and Friedrich and Piech [2000]. A reverse effect, *i.e.* enhancement of HDL-cholesterol by diet enrichment with oats, was described in humans affected by lipid metabolism disorders by Gawlak [1994] and Hryniewiecki *et al.* [1994], while Kaira and Joad [2002] observed such effect in experimental animals.

The experiment described in this paper showed an unexpected and unfavourable effect of the hull-less Akt oats on the blood fibrinogen level. The reason for running fibrinogen assays was a reduced blood coagulation observed during an earlier experiment on rats; that observation was, however, not backed by any assay. In the present experiment, the hull-less oat addition to diet resulted in an increase in the blood fibrinogen level of all the women by as much as 29%, on the average. Data on effects of oat grains and/or their products on the blood fibrinogen content are scant. When studying human subjects, Djouss'e *et al.* [1998] found increased consumption of dietary fibre to result in an increase (statistically insignificant) in the blood fibrinogen. That was accompanied by a significant ($P < 0.01$ in men and $P < 0.05$ in women) reduction in the plasminogen activator inhibitor type 1 (PAI-1). Similarly, a reduction in PAI-1 content, accompanying increased dietary fibre consumption, was reported by Sundell and Ranby [1993] who used oat bran in the diet they administered.

A similarly unexpected, and undesirable in post-mastectomy women, was the effect of the hull-less oat on the blood estradiol content. The content increased by an average of 79% in the post-hysterectomy women and by as much as 368% in those women with intact ovaries. The reasons for the increase can be sought in, *i.e.* the amount and type of fatty acids present in the hull-less Akt oat grains. Compared to hulled cultivars, the Akt was found to contain more lipids (9.4% *vs.* 4.6%), including palmitic acid (28.9 *vs.* 18.6%), and less unsaturated acids: linolic (17.9 *vs.* 27.0%), linolenic (0.63 *vs.* 1.96%), and eicosatrienic (0.14 *vs.* 0.61%) [Pisulewska *et al.*, 1998].

It seems that the magnitude and nature of changes recorded could have been also affected by the nature of lipid metabolism disorders and perhaps by the women's very specific individual organismic abilities of breast cancer patients to utilise diet components, including lipids. This is indicated by, *i.e.* the increase in the TG content accompanied by the reduction of glucose. As shown by numerous studies, a reduction in the blood glucose content, resulting from increased dietary fibre uptake, brings about flattening of insulin curve and a statistically significant reduction in the insulin content [Frantz, 1993; Friedrich, 1998 a]. Insulin is known to be central to adipose tissue metabolism control [Pelikanova & Kohout, 1980; Fanelli *et al.*, 1993] and may contribute to increased blood TG level [Pedersen *et al.*, 1993]. For this reason it was expected that observed reduction in the blood glucose content should have been accompanied by a TG reduction, or normalization on the TG level rather than the increase, observed in 50% of subjects.

The exceptionally specific utilization, by the post-mastectomy women's systems, of a slightly increased amount of lipids consumed, containing, however, more saturated fatty acids, is indicated also by the increased estradiol contents, observed even in the post-ovariectomy women of normal body weight, as shown by their BMI's ranging within 19.8–3.0.

It has to be admitted that the effects of the hull-less Akt oats added to the uncorrected diets of post-mastectomy women were not entirely expected. Originally, enriching the diets with oat grains rich in dietary fibre, including beta-glucans, had been anticipated to result in beneficial changes more extensive than those actually observed as a consequence of hulled oat consumption, the effects of the latter being generally known. Except for beneficial effects on the general glucose content and, in individual cases, on total and LDL-cholesterol, the results obtained cannot support recommending permanent reliance on a hull-less oat-enriched human diet. Although the literature does contain descriptions of differences between oat product effects on blood lipid components [Kirby *et al.*, 1981; Djouss'e *et al.*, 1998], no published work has demonstrated such a strong enhancement of those blood components which, from the medical point of view, are regarded as unfavourable.

CONCLUSIONS

In spite of a beneficial effect of diet enrichment with hull-less Akt oat cultivar on the blood glucose content in general and on total and LDL-cholesterol in individual cases, such enrichment, is not recommended for post-mastectomy women on a day-to-day basis, due to its enhancing effect on the blood estradiol and fibrinogen contents.

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OCENA WPŁYWU DODATKU DO DIETY ODMIANY OWSA NIE OPLEWIONEGO AKT NA STĘŻENIE GLUKOZY, LIPIDÓW, LIPOPROTEIN, FIBRYNOGENU I ESTRADIOLU WE KRWI KOBIEC PO MASTEKTOMII

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W doświadczeniu badano wpływ dodatku do nie korygowanej diety kobiet po mastektomii ziarna owsa nie oplewionego odmiany Akt na stężenia glukozy, triacylogliceroli, cholesterolu całkowitego, jego frakcji HDL- i LDL- (oznaczanych na analizatorze biochemicznym Integra przy użyciu odczynników firmy Roche, w systemie zamkniętym), fibrynogenu (oznaczanego metodą wytworzenia skrzepu przy użyciu aparatu BCT DADE Behring'a) i estradiolu (oznaczanego metodą chemiluminiscencyjną przy użyciu aparatu Immulite firmy DPC).

Ziarno spożywane było w ilości stanowiącej 10–15% wartości energetycznej diety, 3 razy w tygodniu, przez okres 4-miesięcy. Owies wprowadzany był do posiłku zamiast produktu węglowodanowego, który miał być w nim spożyty (np. zamiast pieczywa na śniadanie, kolację lub zamiast ziemniaków, kaszy, ryżu, makaronu itp. na obiad).

Stwierdzono, że dodatek ten spowodował u kobiet statystycznie istotny $P < 0.01$ spadek stężenia glukozy (z 98 do 90 mg/dL) i frakcji HDL-cholesterolu (z 59,3 do 55,9) oraz statystycznie istotny $P < 0.01$ wzrost stężenia fibrynogenu (z 280 do 361 mg/dL), a u kobiet po owarietomii statystycznie istotny $P < 0.05$ wzrost stężenia estradiolu (z 10,0 do 19,5 pg/mL) we krwi (tab. 3 i 5). Zmiany stężenia triacylogliceroli (z 126 do 130 mg/dl), cholesterolu całkowitego (z 206 do 202 mg/dL) i jego frakcji LDL- (z 122 do 115 mg/dL) oraz estradiolu u kobiet z zachowanymi jajnikami (z 62 do 290 pg/mL) były statystycznie nieistotne (tab. 4).