Nutrición Hospitalaria

Nutr Hosp. 2015;32(4):1636-1644
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original/*Investigación animal*

The effect of dietary wheat bran on sucrose-induced changes of serum glucose and lipids in rats

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Abstract

Introduction: **wheat bran has been known for many health benefits, but its glucose- and lipid-lowering activity still remains unresolved.**

Objective: **to investigate effects of varying amounts of wheat bran and feeding period on serum glucose and lipids in sucrose-fed rats.**

Methods: **eighty male Sprague–Dawley rats were assigned into 4 sucrose-based diets containing either 0, 5, 10 or 20% wheat bran (WB) and given *ad libitum* to rats for 4, 8, 12 or 16 weeks. Serum glucose, total cholesterol (TC), low- and high-density lipoprotein cholesterol (LDL-C and HDL-C), triglycerides (TG), phospholipids (PL) and total lipids (TL) were quantified at end of each feeding period and other biological parameters were assessed.**

Results: **in all feeding periods, food intake showed ascending linear trend ($p < 0.05$), whereas body weight did not respond to WB. Compared to 0%, 10 or 20% WB induced decrease ($p < 0.05$) in TC (16 weeks) and HDL-C (12 or 16 weeks), whereas 5, 10 or 20% WB induced similar decrease in PL (4 or 12 weeks), TL (all periods) and glucose (4 or 8 weeks). This glucose- and lipid- lowering effect was substantiated by descending linear responses ($p < 0.05$) to WB. PL and TL descending responses to WB were seen in all feeding periods. TG exhibited no change with WB, but linearly responded (4 or 8 weeks). Differences in glucose or lipid variables of rats fed WB diets for all feeding periods were less evident.**

Conclusions: **results suggest that wheat bran reduces serum glucose and lipids mainly phospholipids in sucrose fed rats in an interaction that is likely to have clinical implications in cardiometabolic conditions.**

(*Nutr Hosp*. 2015;32:1636-1644)

DOI:10.3305/nh.2015.32.4.9457

Key words: *Wheat bran. Phospholipids. Total lipids. Serum glucose. Cardiometabolic risks. Sucrose.*

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Recibido: 15-VI-2015.
Aceptado: 26-VII-2015.

EL EFECTO DEL SALVADO DE TRIGO EN LA DIETA SOBRE LOS CAMBIOS INDUCIDOS POR LA SACAROSA DE GLUCOSA Y LOS LÍPIDOS EN SUERO EN RATAS

Resumen

Introducción: **son conocidos los muchos beneficios del salvado de trigo para la salud, pero su glucosa y la actividad hipolipemiante aún sigue sin resolverse.**

Objetivos: **investigar los efectos de cantidades variables de salvado de trigo en la alimentación sobre la glucosa en suero y los lípidos en ratas alimentadas con sacarosa.**

Métodos: **se asignaron a ochenta ratas Sprague-Dawley macho cuatro dietas a base de sacarosa que contenían 0, 5, 10 o 20% de salvado de trigo (WB) dadas *ad libitum* a las ratas durante 4, 8, 12 o 16 semanas. Glucosa sérica, colesterol total (CT), colesterol de baja y alta densidad de lipoproteínas (LDL -C y HDL -C), los triglicéridos (TG), fosfolípidos (PL) y lípidos totales (TL) se cuantificaron al final de cada período de alimentación y otros parámetros biológicos se evaluaron.**

Resultados: **en todos los períodos de alimentación, la ingesta de alimentos mostró una tendencia lineal ascendente ($p < 0,05$), mientras que el peso corporal no respondió a WB. En comparación con 0%, 10% o 20 inducida WB disminución ($p < 0.05$) en TC (16 semanas) y HDL-C (12 o 16 semanas), mientras que 5, 10 o 20% WB inducida disminución similar en PL (4 o 12 semanas), TL (todos los períodos) y glucosa (4 u 8 semanas). Este efecto de glucosa y lípidos bajar se justificó descendiendo respuestas lineales ($p < 0.05$) a WB. PL y TL descendente respuestas a WB se observaron en todos los períodos de alimentación. TG exhibió ningún cambio con WB, pero respondió linealmente (4 u 8 semanas). Las diferencias en la glucosa o lípidos variables de ratas alimentadas con dietas WB para todos los períodos de alimentación fueron menos evidentes.**

Conclusiones: **los resultados sugieren que el salvado de trigo reduce la glucosa y los lípidos en suero, principalmente fosfolípidos, en ratas alimentadas con sacarosa en una interacción que puede tener implicaciones clínicas en condiciones cardiometabólicas.**

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DOI:10.3305/nh.2015.32.4.9457

Palabras clave: *Salvado de trigo. Fosfolípidos. Lípidos totales. Glucosa sérica. Riesgos cardiometabólicos. Sacarosa.*

Abbreviations

WB: wheat bran.
TG: triglycerides.
TC: total cholesterol.
HDL-C: high-density lipoprotein cholesterol.
LDL-D: low-density lipoprotein cholesterol.
PL: phospholipids.
TL: total lipids.

Introduction

Wheat bran is a by-product of conventional milling of wheat grains and is a concentrated dietary source of insoluble fiber[1]. The importance of wheat products such as wheat bran has become more appreciated over the past few years with advances in our understanding of its role in human physiology[2]. Many physiological effects associated with wheat bran intake have been documented and have been linked with several pathological conditions[3,4].

A considerable amount work has been devoted to the effects of wheat bran on serum glucose or lipid concentrations searching primarily for a dietary means of possibly reducing chronic disease risk, yet findings produced are rather inconsistent. Several studies have shown that grain products rich in insoluble fiber, such as wheat bran, do not or variably affect serum glucose or lipid profile in humans[5,6] and animals[7,8]; nevertheless, other studies failed to support this[9,10]. Furthermore, consumption of whole grains including wheat bran has been reported to be inversely correlated with insulin resistance and thus diabetes risk[11], and to have a strong favorable influence on obesity and cardiovascular disease risk[12], although their exact role in reducing disease risk is not yet fully elucidated.

During the past six decades, most of the nutritional studies concerning atherosclerosis and cardiovascular disease have ignored serum phospholipids as a biomarker for the disease risk prediction. It is well known that phospholipids constitute the major structural components of biological membranes and affects a number of their physical and biochemical properties and thus cellular functions, particularly their fluidity and permeability, activities of membrane-bound enzymes, transport systems, bioenergetics, and cell growth, viability, proliferation, recognition, signal transduction and apoptosis[13]. Phospholipids are also the source of polyunsaturated fatty acids which serve as precursors of eicosanoids[14]. Alterations in the metabolism of phospholipids have been reported in a number of disorders, such as obesity and type 2 diabetes mellitus[15,16]. Early investigations in this regard have shown that increased serum phospholipids as well as cholesterol and triglycerides are important predictors of the cardiovascular events[17]. This is especially important in conditions with increased cardiovascular disease risk such as clinical or experimentally-induced diabetes mellitus and obesity[18]. Increased serum phospholipids have also been known to be associated with sucrose or fructose[19]. It is widely cited that sucrose or fructose feeding is associated with increased diabetes and cardiometabolic risk in humans and animals[18,20]. In spite of these facts, controlled long-term studies that link the consumption of wheat bran and sucrose with serum glucose and phospholipids in particular are generally lacking.

Objectives

In view of the apparent advantages of wheat bran in reducing diabetes and cardiovascular disease risk and the lack of an obvious mechanism in acute or short term studies, we investigated whether the consumption of high-sucrose diets with varying amounts of wheat bran had any effect on serum concentrations of glucose, total cholesterol, low- and high-density lipoprotein cholesterol and triglycerides in rats fed such a dietary regimen for periods of 4, 8, 12 and 16 weeks. We determined also serum concentrations of phospholipids and total lipids which have not previously been measured in studies of this field. We included different feeding periods so that possible adaptation of the animals for the bulking effects of wheat bran could be evaluated.

Methods

Diets

One batch (20 kg) of the wheat bran (*Triticum durum*) with 500 microns particle size was obtained from Al-Jowaidah Mills, Jordan Ministry of Supply. The protein and fat content of the wheat bran as determined by the Weende method[21] was 16% and 6% respectively. The wheat bran was found to contain 44% dietary fiber as given elsewhere[4].

Four isocaloric and isonitrogenous semipurified diets were prepared; they were sucrose-based and differed in the content of wheat bran: 0% or wheat bran-free (control diet), 5%, 10% or 20% w/w (experimental diets). Sucrose was the sole carbohydrate source in these diets. The wheat bran was added at the expense of sucrose. The casein and corn oil were adjusted according to the protein and fat, respectively, provided by the wheat bran. The composition of experimental diets is described in table I. All diets contained the same amount of calories, protein, carbohydrate, fat, vitamins and minerals. Dietary supplies of nutrients were in accordance with the dietary recommended allowances for rats from the American Institute of Nutrition[22]. The experimental diets were freshly prepared once a week, placed desiccated in sealed polythene bags and stored refrigerated at 4 °C.

Animals

Young male Sprague- Dawley rats (n= 80) were obtained from the Experimental Animal Unit of the De-

partment of Nutrition and Food Technology, The University of Jordan, Amman, Jordan. The animals were acclimatized for one week before the experiment, during which they were fed on chow diet with free access to tap water. They were individually housed in plastic cages with stainless steel wire-mesh bottom (North Kent Plastic Cages, Ltd, Dartford, England) under controlled temperature (22 ± 2ºC) and hygienic conditions with 12- hour light, 12- hour dark cycle. All the experiments involving animals were approved by the Institutional Animal Ethics Committee and carried out according to the recommended guidelines for animal use.

Experimental protocol

At the beginning of the experiment, animals weighed 134±2 g and they were randomly divided into four groups and fed one of the four semipurified diets described above. The experimental design was devised to include four different periods: 4, 8, 12 and 16 weeks. Therefore, at the end of each feeding period, five animals from each of the above four groups were randomly taken and tested. All animals had free access to tap water and special diets. Body weight and food intake were monitored weekly. Food efficiency ratio as body weight gain per 100 g food intake was also calculated. On the termination day and after an overnight fast, animals were anesthetized using chloroform. Blood was collected by performing cardiac puncture and serum was isolated and stored frozen at −20 °C until chemical analysis.

Chemical analysis

Concentrations of serum glucose and lipids and lipoproteins were determined by using commercial kits and in accordance to the manufacturer's instructions (Boehringer Mannheim GmBH, Germany). The lipid variables included total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, phospholipids and total lipids Analysis was performed at the Islamic Hospital Medical Laboratories, Amman, Jordan, using a pre-calibrated automated clinical chemistry analyzer (Roche/Hitachi 912 chemistry analyzer). Ratios of total cholesterol/triglycerides and low-density lipoprotein cholesterol/high-density lipoprotein cholesterol were calculated. The protein and fat content of the wheat bran was determined by the Weende method[21].

Statistical analysis

Data analysis was performed using statistical analysis software (SAS version 9, USA). Statistical significance was assessed by two-way ANOVA followed by the Duncan's multiple range tests, and the significance was set at $p < 0.05$. Data were expressed as means ± standard errors of the mean (SEM). Orthogonal polynomial comparisons were used to identify statistically significant trends. This test determines the nature of the response of the studied variables to increasing levels (%0, 5%, 10% and 20%) of the wheat bran. Linear trends were given as coefficient of determination (r^2) at $p < 0.05$.

Results

Table II presents body weight, food intake and food efficiency ratio of rats fed sucrose-based diets with increasing wheat bran content for 4, 8, 12 and

Table I
Composition of semipurified sucrose-based diets with increasing wheat bran (g·kg^{-1})

Ingredient	*Wheat bran (%)*			
	0.0	*5.0*	*10.0*	*20.0*
Wheat bran	0.0	50.0	100.0	200.0
Sucrose	657.0	618.0	579.0	501.0
Casein	180.0	172.0	164.0	148.0
Maize oil	100.0	97.0	94.0	88.0
Mineral mix (AIN-93)[#]	40.0	40.0	40.0	40.0
Vitamin mix (AIN-93)[#]	20.0	20.0	20.0	20.0
DL-Methionine	3.0	3.0	3.0	3.0
Carbohydrate (%)	65.7	65.7	65.7	65.7
Protein (%)	18.0	18.0	18.0	18.0
Fat (%)	10.0	10.0	10.0	10.0
Fiber (%)	0.0	2.2	4.4	8.8
Energy (kcal. 100g^{-1})	424.8	424.8	424.8	424.8

[#]AIN: American Institute of Nutrition.[22]

16 weeks**.** Body weights of the groups of animals assigned for different diets were essentially similar ($p \geq 0.05$) at the start of each experimental feeding period. In neither animal group did the level of wheat bran in the diet affect significantly ($p \geq 0.05$) body weight gain. Rats fed the wheat bran-containing diets in the order of 5%, 10, or 20% for periods of 8, 12 or 16 weeks had significantly ($p<0.05$) higher food intake compared to those fed the wheat bran-free diet. Differences in this variable of rats fed the wheat bran-containing diets for the same periods were less noticeable. The wheat bran-containing diets had some increasing effects on food intake, but this did not reach statistical significance in rats fed such diet for 4 weeks. Food efficiency ratio was not significantly ($p \geq 0.05$) affected in rats fed different diets for 4, 8 and 12 weeks. A significant ($p<0.05$) decrease in this variable was observed between rats fed diets with and without wheat bran for a period of 16 weeks. The drop in food efficiency ratio was more pronounced in rats fed the 10% wheat bran diet compared to other groups (Table II).

Serum concentrations of lipids and lipoproteins and their indices of rats fed sucrose-based diets with increasing wheat bran content for 4, 8, 12 and 16 weeks are shown in table III. Compared to control, wheat bran feeding in the order of 5%, 10% or 20% for periods of 4, 8 or 12 weeks did not significantly influence ($p \geq 0.05$) serum concentration of total cholesterol. A significant ($p<0.05$) decrease in this variable was noticed between control rats and those fed diets with 10% or 20% wheat bran for 16 weeks. Noteworthy, serum concentration of HDL-cholesterol exhibited a pattern of change almost similar to that of total cholesterol, but its decrease was noticed after 12 and 16 weeks of wheat bran feeding. In neither animal group did wheat bran feeding affect serum concentrations of LDL-cholesterol and triglycerides. Differences in concentrations of serum lipid variables and ratios of HDL-cholesterol/LDL-cholesterol and total cholesterol/triglycerides of rats fed the wheat bran-containing diets for periods of 4, 8, 12 or 16 weeks were less noticeable (Table III).

Table II

Body weight and food intake of rats fed sucrose-based diets with increasing wheat bran for 4, 8, 12 and 16 weeks.

Period (weeks)	*Variable*	*Wheat bran (%)**			
		0.0	*5.0*	*10.0*	*20.0*
4	Initial body weight (g)	126 ± 6[a]	139 ± 9[a]	126 ± 9[a]	133 ± 5[a]
	Final body weight (g)	244 ± 14[a]	249 ± 11[a]	238 ± 17[a]	247 ± 13[a]
	Weight gain (g. day^{-1})	4.2 ± 0.4[a]	3.9 ± 0.6[a]	4.0 ± 0.4[a]	4.1 ± 0.4[a]
	Food intake (g. day^{-1})	13.7 ± 0.6[a]	13.4 ± 1.0[a]	14.8 ± 0.5[a]	15.8 ± 0.9[a]
	Food efficiency ratio[#]	30.7 ± 2.4[a]	28.9 ± 2.4[a]	27.0 ± 2.6[a]	25.7 ± 1.8[a]
8	Initial body weight (g)	150 ± 6[a]	149 ± 6[a]	133 ± 9[a]	139 ± 11[a]
	Final body weight (g)	363 ± 21[a]	369 ± 31[a]	360 ± 19[a]	367 ± 29[a]
	Weight gain (g. day^{-1})	3.8 ± 0.7[a]	3.9 ± 0.5[a]	4.0 ± 0.2[a]	4.1 ± 0.5[a]
	Food intake (g. day^{-1})	16.3 ± 0.6[b]	16.2 ± 0.4[b]	18.8 ± 0.4[a]	17.8 ± 0.6[a]
	Food efficiency ratio[#]	23.3 ± 1.6[a]	24.0 ± 2.4[a]	21.5 ± 0.9[a]	22.7 ± 2.5[a]
12	Initial body weight (g)	136 ± 7[a]	140 ± 8[a]	124 ± 4[a]	124 ± 10[a]
	Final body weight (g)	400 ± 19[a]	463 ±22[a]	402 ± 27[a]	424 ± 14[a]
	Weight gain (g. day^{-1})	3.1 ± 0.2[a]	3.8 ± 0.2[a]	3.3 ± 0.3[a]	3.6± 0.2[a]
	Food intake (g. day^{-1})	13.3 ± 0.3[c]	17.8 ± 0.3[a]	17.2 ± 0.5[b]	17.8 ± 0.3[a]
	Food efficiency ratio[#]	22.3 ± 1.1[a]	21.6 ± 0.7[a]	19.9 ± 1.6[a]	19.9 ± 1.7[a]
16	Initial body weight (g)	126 ± 7[a]	122 ± 8[a]	143 ± 10[a]	143 ± 8[a]
	Final body weight (g)	436 ± 6[a]	452 ± 9[a]	451 ± 14[a]	458 ± 13[a]
	Weight gain (g. day^{-1})	2.8 ± 0.1[a]	2.8 ± 0.1[a]	2.8 ± 0.2[a]	2.8 ± 0.1[a]
	Food intake (g. day^{-1})	14.7 ± 0.2[c]	16.6 ± 0.3[b]	18.5 ± 0.5[a]	17.2 ± 0.4[b]
	Food efficiency ratio[#]	18.8 ± 0.7[a]	17.8 ± 0.4[ab]	14.9 ± 1.0[c]	16.4 ± 0.4[b]

Data are given as mean ± SEM.

[*]Means with different superscripts within the same row are significantly different ($P < 0.05$).

[#]Body weight gain (g)/100g food intake.

Table III
Serum concentrations of glucose, lipids and lipoproteins of rats fed sucrose-based diets with increasing wheat bran for 4, 8, 12 and 16 weeks

Period (weeks)	*Variable*[#]	*Wheat bran (%)*[*]			
		0.0	*5.0*	*10.0*	*20.0*
4	TC (mg.dl^{-1})	112 ± 12^{a}	115 ± 8^{a}	97 ± 10^{a}	106 ± 3^{a}
	HDL-C (mg.dl^{-1})	103 ± 11^{a}	105 ± 9^{a}	88 ± 10^{a}	94 ± 4^{a}
	LDL-C (mg.dl^{-1})	9.8 ± 1.4^{a}	9.8 ± 2.4^{a}	8.8 ± 1.0^{a}	12.6 ± 1.9^{a}
	Triglycerides (mg.dl^{-1})	109 ± 8^{a}	83 ± 7^{a}	82 ± 12^{a}	98 ± 9^{a}
	Phospholipids (mg.dl^{-1})	450 ± 33^{a}	475 ± 38^{a}	344 ± 33^{b}	341± 18^{b}
	Total lipids (mg.dl^{-1})	672 ± 31^{a}	673 ± 35^{a}	522 ± 34^{b}	545 ± 25^{b}
	HDL-C/LDL-C	11.3 ± 1.8^{a}	15.2 ± 5.1^{a}	10.7 ± 1.8^{a}	8.2 ± 1.4^{a}
	TC/Triglycerides	2.4 ± 0.3^{a}	3.2 ± 0.2^{a}	3.0 ± 0.6^{a}	2.6 ± 0.2^{a}
	Glucose (mg.dl^{-1})	152 ± 14^{a}	69 ± 7^{b}	66 ± 8^{b}	79 ± 13^{b}
8	TC (mg.dl^{-1})	103 ± 6^{a}	120 ± 12^{a}	104 ± 7^{a}	114 ± 8^{a}
	HDL-C (mg.dl^{-1})	85 ± 6^{a}	103 ± 9^{a}	86 ± 11^{a}	101 ± 6^{a}
	LDL-C (mg.dl^{-1})	17.4 ± 2.8^{a}	17.2 ± 4.3^{a}	18.0 ± 4.0^{a}	14.0 ± 2.7^{a}
	Triglycerides (mg.dl^{-1})	140 ± 12^{a}	115 ± 16^{a}	101 ± 7^{a}	92 ± 15^{a}
	Phospholipids (mg.dl^{-1})	362 ± 40^{a}	361± 25^{a}	285 ± 14^{a}	310 ± 20^{a}
	Total lipids (mg.dl^{-1})	604 ± 36^{a}	596 ± 30^{a}	490 ± 18^{b}	517 ± 31^{ab}
	HDL-C/LDL-C	5.5 ± 1.1^{a}	6.8 ± 1.0^{a}	7.1 ± 2.9^{a}	8.0 ± 1.3^{a}
	TC/Triglycerides	1.8 ± 0.2^{a}	2.6 ± 0.2^{b}	2.5 ± 0.3^{ab}	3.0 ± 0.3^{b}
	Glucose (mg.dl^{-1})	132 ± 14^{a}	87 ± 5^{b}	80 ± 6^{b}	113 ± 14^{ab}
12	TC (mg.dl^{-1})	123 ± 3^{a}	94 ± 11^{a}	104 ± 8^{a}	122 ± 10^{a}
	HDL-C (mg.dl^{-1})	99 ± 2^{a}	66 ± 7^{b}	77 ± 6^{bc}	86 ± 6^{ac}
	LDL-C (mg.dl^{-1})	24.6 ± 1.4^{a}	27.8 ± 4.1^{a}	26.6 ± 3.5^{a}	36.2± 5.1^{a}
	Triglycerides (mg.dl^{-1})	112 ± 7^{a}	117 ± 15^{a}	124 ± 17^{a}	120 ± 11^{a}
	Phospholipids (mg.dl^{-1})	366 ± 8^{a}	337 ± 20^{a}	185 ± 11^{b}	215 ± 10^{b}
	Total lipids (mg.dl^{-1})	602 ± 13^{a}	547 ± 24^{a}	413 ± 25^{b}	457 ± 29^{b}
	HDL-C/LDL-C	4.1 ± 0.2^{a}	2.4 ± 0.2^{b}	3.1 ± 0.4^{b}	2.5 ± 0.3^{b}
	TC/Triglycerides	2.6 ± 0.3^{a}	1.9 ± 0.0^{b}	2.0 ± 0.1^{cb}	2.3 ± 0.1^{ac}
	Glucose (mg.dl^{-1})	143 ± 13^{a}	113 ± 12^{a}	108 ± 10^{a}	120 ± 13^{a}
16	TC (mg.dl^{-1})	139 ± 8^{a}	126 ± 9^{a}	104 ± 4^{b}	106 ± 6^{b}
	HDL-C (mg.dl^{-1})	103 ± 11^{a}	91 ± 6^{ab}	78 ± 3^{b}	76 ± 3^{b}
	LDL-C (mg.dl^{-1})	35.6 ± 5.2^{a}	35.4 ± 5.7^{a}	26.2 ± 2.2^{a}	30.4 ± 4.2^{a}
	Triglycerides (mg.dl^{-1})	122 ± 13^{a}	146 ± 16^{a}	113 ± 21^{a}	92 ± 11^{a}
	Phospholipids (mg.dl^{-1})	253 ± 14^{a}	257 ± 22^{a}	193 ± 15^{a}	203 ± 22^{a}
	Total lipids (mg.dl^{-1})	514 ± 27^{a}	529 ± 28^{a}	410 ± 23^{b}	408 ± 30^{b}
	HDL-C/LDL-C	3.2 ± 0.6^{a}	2.8 ± 0.4^{a}	3.1 ± 0.2^{a}	2.7 ± 0.3^{a}
	TC/Triglycerides	2.7 ± 0.3^{a}	2.0 ± 0.2^{a}	2.4± 0.4^{a}	2.5 ± 0.2^{a}
	Glucose (mg.dl^{-1})	131 ± 16^{a}	106 ± 14^{a}	117 ± 14^{a}	123 ± 13^{a}

Data are given as mean ± SEM.
[*]Means with different superscripts within the same row are significantly different ($P < 0.05$).
[#]Abbreviations: TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.

Interestingly, in contrast to control, wheat bran feeding for periods of 4, 8, 12 or 16 weeks resulted in a significant ($p<0.05$) decrease in serum concentration of total lipids (Table III). A similar pattern of decrease was also observed for serum concentration of phospholipids in rats fed wheat bran diets for periods of 4 or 12 weeks compared to control. The decrease in these lipid fractions was more evident in rats fed the 10% and 20% wheat bran diets compared to other groups. The wheat bran-containing diets (10% and 20%) had noticeable decreasing effects on serum concentration of phospholipids, but this did not reach statistical significance in rats fed such diets for 8 or16 weeks. Compared to control, feeding either 5%, 10%, or 20% wheat bran-containing diets for 4 or 8 weeks resulted in a significant ($p<0.05$) decrease in serum glucose concentration (Table III). This difference vanished after 12 weeks of experimental feeding.

Linear trend analysis of studied variables of rats fed sucrose-based diets with increasing wheat bran content for 4, 8, 12, and 16 weeks is given in table IV. In contrast to food efficiency ratio, food intake exhibited ascending linear trends ($p<0.05$) for all feeding periods, whereas body weight gain did not show such trends for the same periods. Descending linear trends ($p<0.05$) were obtained for total cholesterol (16 weeks), HDL- cholesterol (12 and 16 weeks), triglycerides (4 and 8 weeks), total lipids and phospholipids (4, 8, 12 and 16 weeks) and glucose (4 and 8 weeks). No linear trends were observed for the other lipid variables or lipid indices in all feeding periods.

Discussion

The present studies show that in rats, the addition of varying amounts of wheat bran to sucrose-based fiber-free diet induces changes in fasting serum glucose, total cholesterol, and HDL-C and food intake. These changes were shown to be time dependent. The wheat bran diets had only apparently random effects on these variables. These studies also show similar effects of wheat bran and fiber-free diets on body weight and serum LDL-C and triglycerides and their effects on ratios of HDL-C/LDL-C and total cholesterol/triglycerides were less noticeable. Unlike the other serum lipid fractions, total lipids and phospholipids decreased progressively in response to dietary wheat bran level irrespective to experimental duration.

Short-term feeding, 3-6 weeks of 5 to 20% wheat bran has not been shown to affect food intake and body weight in rats fed starch-based diets[23]. Similar results have been reported in animals fed sucrose-based diets[24], which also accord with the findings of the present study. Consistently, it has been demonstrated that in rats, the long-term regulation of food intake depends, at least in part, on internal cues related to energy balance; a pronounced increase in dietary fiber intake such as wheat bran led a compensatory increase in food intake so that body weight remained constant[25].

Many studies have investigated the effect of wheat bran on serum concentrations of glucose and lipids in humans[5,6,10] and animals[7-9], but findings are controversial. This might be due to the large discrepancy

Table IV
Orthogonal linear trend analysis of studied variables of rats fed sucrose-based diets with increasing wheat bran for 4, 8, 12 and 16 weeks

Variable[#]	*Feeding period (weeks)*[$]			
	4	*8*	*12*	*16*
Weight gain (g. day^{-1})	0.073	0.041	0.094	0.022
Food intake (g. day^{-1})	0.855$^{*(A)}$	0.416$^{*(A)}$	0.487$^{*(A)}$	0.415$^{*(A)}$
Food efficiency ratio$^{\infty}$	0.366$^{*(D)}$	0.241	0.297$^{*(D)}$	0.375$^{*(D)}$
TC (mg.dl^{-1})	0.077	0.102	0.192	0.287$^{*(D)}$
HDL-C (mg.dl^{-1})	0.173	0.110	0.268$^{*(D)}$	0.321$^{*(D)}$
LDL-C (mg.dl^{-1})	0.084	0.117	0.264	0.225
Triglycerides (mg.dl^{-1})	0.255$^{*(D)}$	0.334$^{*(D)}$	0.187	0.236
Phospholipids (mg.dl^{-1})	0.354$^{*(D)}$	0.300$^{*(D)}$	0.382$^{*(D)}$	0.303$^{*(D)}$
Total lipids (mg.dl^{-1})	0.298$^{*(D)}$	0.284$^{*(D)}$	0.367$^{*(D)}$	0.318$^{*(D)}$
HDL-C/LDL-C	0.214	0.205	0.191	0.232
TC/Triglycerides	0.154	0.172	0.209	0.110
Glucose (mg.dl^{-1})	0.455$^{*(D)}$	0.403$^{*(D)}$	0.238	0.117

[$]Values are coefficients of determination (r^2); $^{*}p < 0.05$; $^{(A)}$ascending; $^{(D)}$descending.
$^{\infty}$Body weight gain (g)/100g food intake.
[#]Abbreviations: TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.

between the various experimental protocols used. In fact, the type and complexity of the wheat bran source either purified or in natural products, the level in the diet, feeding duration, energy intake, basal diet composition and the experimental model used, are among many potential confounders that may contribute to this inconsistency. However, the aim of most of the previous studies was to evaluate the effect of wheat products including wheat bran fiber when added to cholesterol-supplemented or fat-modified diets in normal or various experimental models or pathological conditions, whereas studies involving sucrose-based diets are scarce. This certainly limits the comparison of the current results with those of the other studies.

The present study was specifically performed to test the effect of wheat bran when added to a sucrose-based fiber-free diet in varying amounts and administered to rats for different feeding periods. Under the present experimental conditions, a significant reduction in serum total cholesterol and HDL-C occurred in rats only after 12 weeks of feeding wheat bran, whereas a reduction in serum glucose occurred during 4 or 8 weeks and vanished after 12 weeks of experimental feeding. In this respect, very few studies have investigated wheat bran-sucrose interaction. Feeding normal and streptozotocin-induced diabetic rats with high sucrose (72%) or starch-wheat bran (20%) diets for 14 or 32 days has not been shown to influence serum glucose and triglycerides[26]. It has been reported that wheat bran attenuated, but did not completely prevent, the loss of insulin sensitivity associated with feeding sucrose (32%) for 3 weeks in rats[27]. In four groups of six healthy men who fed one of four carbohydrate-diets providing 0, 18, 36 or 52% of calories as sucrose in both low (<14 g) and high dietary fiber (>34 g) for 10 days each, it has been reported that dietary fiber including wheat fiber protects against sucrose-induced triglyceridemia but has no effect on total cholesterol and LDL-C during high sucrose diets[28]. More recently, reduced blood glucose and cholesterol concentrations, improved glucose and insulin tolerance, suppressed hepatic lipid accumulation and intestinal cholesterol absorption and prevented diet-induced increase in body weight have been documented in male C57BL/6J mice fed for 10 weeks on a high-fat (29%), high-sucrose (20%) diet containing (0.4%) wheat bran–derived alkylresorcinols[24]. Apparently, some of these reported results are consistent with our findings; however, a remarkable variation in the experimental protocols still exists.

To the best of our knowledge, this study is perhaps the first demonstration that links wheat bran intake with lipid parameters, particularly phospholipids and total lipids in sucrose-fed rats. It is generally accepted that this model has abnormal glucose and lipid metabolism, insulin resistance and all characteristic features of the metabolic syndrome[18,20]. The wheat bran was incorporated into isocaloric and isonitrogenous diets at four levels: 0, 5 10 or 20%, and fed *ad libitum* for 4, 8, 12 or 16 weeks. Male rats were used and changes in body weight and food intake were also considered. Interestingly, compared to control, wheat bran caused a marked decrease in serum concentrations of phospholipids and total lipids. This effect was also indicated by the descending linear trend response of these variables to wheat bran in all feeding periods. It is evident that most of the decrease in serum total lipids was due to the decrease in the phospholipids. It should be noted that food intake, weight gain and food efficiency ratio were normal during this study, eliminating the possibility of inadequate dietary intake and nutrient imbalance that might affect the results[29]. The reason responsible for these findings and their physiologic and clinical significance are not clear. However, the following discussion will focus on the available literature.

Much experimental and clinical research from the 1950s has shown relations between increased serum phospholipids and atherosclerosis, and thus cardiovascular disease[17,30,31]. The considerable presence of phospholipids in atheromatous plaques and their synthesis in the arterial wall have also been shown[32]. Furthermore, the relative efficacy of the various serum lipids including the phospholipids as predictors of atherosclerosis has been assessed[17]. Abnormally increased serum phospholipid concentrations in clinical or experimentally-induced diabetes including fructose or sucrose-induced diabetes have been repeatedly documented[15,16,19,33]. Undoubtedly, these data highlight the clear link between dietary sucrose and serum phospholipids and their possible role in the pathogenesis of insulin resistance, diabetes and cardiovascular disease. In this study, it is obvious that sucrose induced marked increase in serum phospholipids in all experimental periods, though initial values were not determined. The presently recorded serum phospholipid concentrations in rats fed high sucrose wheat bran-free diet were close to the reported values for rats given similar dietary regimens, and that after 16 weeks of wheat bran feeding, these concentrations remarkably decreased towards those reported for normal rats[33].

Nowadays, there is an increasing body of evidence suggesting a strong inverse association between increased consumption of whole grains including the wheat bran and its products and reduced diabetes and cardiovascular disease risk[3,4]. However, the exact mechanism explaining this relationship is not clear and attempts to translate it in terms of effect of wheat bran or other wheat foods on the classical atherogenic serum lipid fractions namely increased total cholesterol, LDL-C and triglycerides and reduced HDL-C have not been successful. This is perhaps due to the apparent disagreement about the effect of such products on these lipid fractions[5-12]. In this study, it is of particular interest to note the substantial phospholipid-lowering action of the wheat bran in high sucrose fed rats. To date, the literature on the influence of wheat bran on serum phos-

pholipid status in humans and animals is generally lacking. We found only few studies with consistent results that have investigated this aspect using cereals or their constituents, but not the wheat bran. Serum total lipids and phospholipids have been found to be significantly reduced with the high cereal diet, including wheat, and increased with the high sugar diet (44% of total calories) in 8 healthy individuals ingesting such diets for 4 weeks when the total calories and fats were held constant[34]. In 5 patients with hyperglyceridemia, a high sugar intake has been shown to raise serum phospholipids, whereas carbohydrate diet such as cereal starch lowered this variable[35]. The increase in serum phospholipids due to feeding sucrose (65%) to rats for 30 days has been shown to be generally depressed by such diet supplemented with 0.5% sodium phytate, a constituent of the wheat bran[33]. Despite the great differences in experimental approaches followed, these reported results are apparently consistent with our findings.

In the present study, it is important to note that the recorded effect for wheat bran on serum glucose and lipids was reinforced by significant linear trend responses. With the exception of total lipids and phospholipids, these responses were seen to be time dependent. Thus, it is conceivable that a sort of adaptation in the mechanisms of glycemic and lipidemic control may have occurred as a result of prolonged feeding of dietary wheat bran. These effects can also be associated with action of wheat bran on food intake and body weight. Such adaptation to grain fiber or wheat bran intake has been demonstrated in humans and animals[3,4].

Conclusions

Taken together, when incorporated into high-sucrose diets, varying amounts of wheat bran appear to exert a profound reducing effect on serum glucose and lipids particularly the phospholipids in rats. It would be of great importance to explore the mechanisms by which wheat bran and sucrose interact and modify phospholipid assimilation and metabolism under sucrose diet conditions. This could be useful to lessen the debate surrounding the claim that consumption of whole grains including wheat bran can reduce the risk of insulin resistance, diabetes and cardiovascular disease.

Conflict of interest statement

The authors report no conflict of interest.

Acknowledgment

The authors would like to thank the Deanship of Scientific Research at The University of Jordan for their financial support.

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