

**EFFECT OF RICE BRAN AND ITS OIL ON LIPID  
PEROXIDATION AND INSULIN RESISTANCE INDUCED BY  
HIGH FRUCTOSE DIET IN RATS**

**Submitted By**

**Alshimaa Embaby Bayoumy Khalil**

B.Sc. of Science (Chemistry), Faculty of Science, Al Azhar University, 2006

Diploma in Analytical Biochemistry, Faculty of Science, Monofia University, 2007

A thesis submitted in Partial Fulfillment  
Of  
The Requirement for the Master Degree  
In  
Environmental Sciences

Department of Environmental Basic Sciences  
Institute of Environmental Studies and Research  
Ain Shams University

**2016**

**APPROVAL SHEET**  
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**This thesis Towards a Master Degree in Environmental  
Sciences Has been Approved by :**

**Name**

**Signature**

**1-Prof. Dr. Taha Abd El Azzem Mohamed Abd El Razek**

Prof. and Head of Department of Environmental Basic Sciences  
Institute of Environmental Studies and Research  
Ain Shams University

**2-Prof. Dr. Fatma Hassan Abd El Razek**

Prof. of Nutrition  
Faculty of Women  
Ain Shams University

**3-Prof. Dr. Hanan Mohamed Fathy Abd El Wahab**

Prof. of Biochemistry  
Faculty of Women  
Ain Shams University

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**Under The Supervision of:**

**1-Dr. Hanan Mohamed Fathy Abd El Wahab**

Assistant Prof. of Biochemistry

Faculty of Women

Ain Shams University

**2- Dr. Mona Abd El Galil Mohamed**

Assistant Prof. of Biochemistry

Faculty of Science

Al-Azhar University

**3-Dr. Hanaa Hussin El Sayed**

Assistant Prof. of Environmental Sciences

National Nutrition Institute

**2016**

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## **ABSTRACT**

The aim of this study was to evaluate the effects of rice bran (RB) or rice bran oil (RBO) on lipid metabolism and hepatic insulin receptor substrate-1 (IRS-1) as well as hepatic expression of 3-hydroxy 3-methyl glutaryl COA reductase gene expression (HMG-CoA) and oxidative stress. Forty healthy adult male albino rats "Sprague Dawley strain" weighing ( $130 \pm 10$ g) were divided into 4 groups (10 rats each). Group 1: animals received standard diet as control, while groups 2, 3 and 4 were fed on a HFD. Groups 3 and 4 animals fed HFD containing RB (5%) instead of cellulose and RBO (10%) instead of corn oil, respectively for 5 weeks. Rats fed high fructose diet (52.5 g/100 g diet) (HFD) were used as a model of insulin resistance in this context. Fructose feeding to rats caused significant elevations in levels of plasma glucose, serum insulin and lipid profile except HDL-C showed no significant difference, while serum total antioxidant capacity (TAC) was significantly reduced as compared to control. Hepatic concentration of IRS-1 was significantly decreased while levels of malondialdehyde (MDA) and HMG-CoA reductase mRNA were elevated compared to control group. Addition of RB or RBO to the HFD alleviated the hazardous effects of fructose. So supplementation of rice bran or its oil to fructose fed rats improves insulin resistance, reduced lipo- and glucotoxicity and attenuates oxidative stress to near normal levels of control group.

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### List of abbreviations

<b>4-AAP</b>	4-amino-antipyrine
<b>AKT</b>	a serine/threonine kinase
<b>AACC</b>	American Association of cereal chemists
<b>AOAC</b>	Association of Official Analytical chemists
<b>ATP</b>	Adenosine triphosphate
<b>Ca<sup>2+</sup> channels</b>	Calcium channels
<b>CAT</b>	Catalase
<b>CE</b>	Cholesterol esterase
<b>CHOD</b>	Cholesterol oxidase
<b>DNA</b>	Deoxyribonucleic acid
<b>FAS</b>	Fatty acid synthase
<b>FFA</b>	Free fatty acid
<b>G-6-Pase</b>	Glucose -6- phosphatase
<b>GOD</b>	Glucose oxidase
<b>GLUT</b>	Glucose transporter

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<b>GPx</b>	Glutathione peroxidase
<b>GK</b>	Glycerol kinase
<b>GK</b>	Glucokinase
<b>GPO</b>	Glycerol-3-phosphate oxidase
<b>HbA1c</b>	Glycated Hemoglobin
<b>HCD</b>	High cholesterol diet
<b>HDL-C</b>	High density lipoprotein cholesterol
<b>HFCS</b>	High fructose corn syrup
<b>HFD</b>	High fructose diet
<b>HOMA-IR</b>	Homeostasis model assesement insulin resistance index
<b>HRP</b>	Horse radish peroxidase
<b>H<sub>2</sub>O<sub>2</sub></b>	Hydrogen peroxide
<b>HMG-CoA</b>	Hydroxymethyl glutaryl Coenzyme A
<b>IDL</b>	Intermediate density lipoprotein
<b>IRS-1</b>	Insulin receptor substrate-1
<b>IR</b>	Insulin resistance

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<b>Kda</b>	Kilo Dalton
<b>LCAT</b>	Lecithin cholesterol acyl transferase
<b>LPL</b>	lipoprotein lipase
<b>LDL-C</b>	Low density lipoprotein cholesterol
<b>MDA</b>	Malondialdehyde
<b>MCF-7</b>	Michigan Cancer Foundation-7
<b>MABs</b>	Monoclonal antibodies
<b>MOR</b>	$\mu$ -opioid receptor
<b>P</b>	Phosphate
<b>PPAR</b>	Peroxisome proliferator activated receptors
<b>POD</b>	Peroxidase enzyme
<b>PI3-kinase</b>	Phosphinositid 3-kinase
<b>PEPCK</b>	Phosphoenolpyruvate carboxykinase
<b>PDVF</b>	Polyvinylidene fluoride
<b>ROS</b>	Reactiv oxygen species
<b>RB</b>	Rice bran

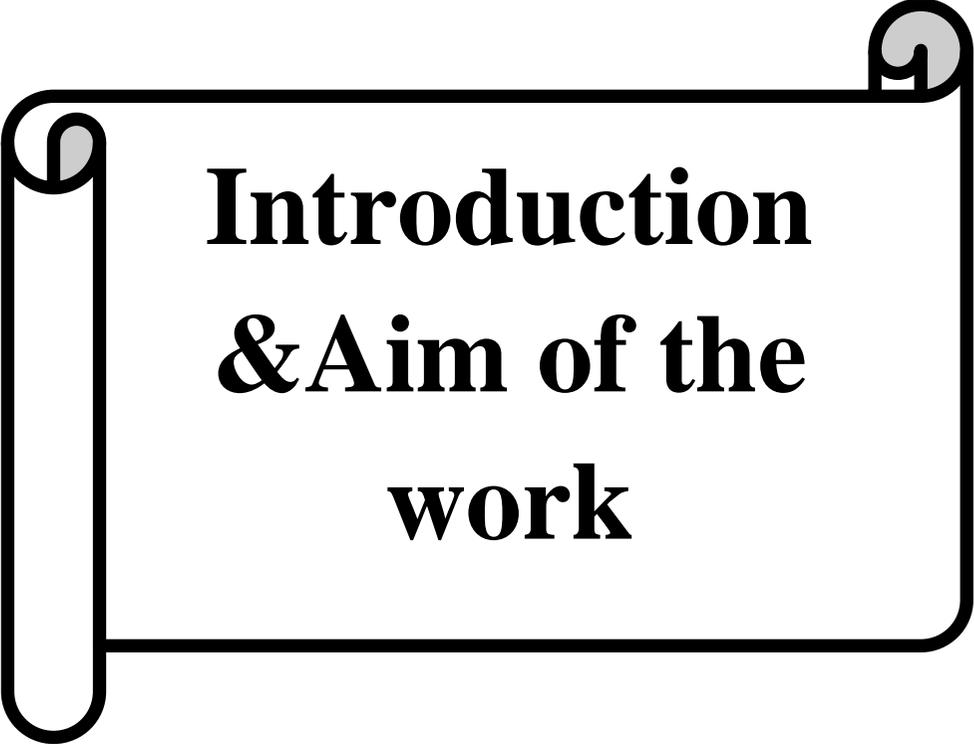
<b>RBO</b>	Rice bran oil
<b>Rpm</b>	Round per minute
<b>SDS</b>	Sodium dodecylsulfate
<b>SD</b>	Sprague Dawley
<b>SOD</b>	superoxide dismutases
<b>SRB</b>	Stabilized rice bran
<b>SPSS</b>	Statistical package for social science
<b>STZ</b>	Streptozotocin
<b>TBA</b>	Thiobarbituric acid
<b>TBARS</b>	Thiobarbituric acid Reactive Species
<b>TAC</b>	Total antioxidant capacity
<b>TC</b>	Total cholesterol
<b>TDF</b>	Total dietary fiber
<b>TAG</b>	Triacylglycerol
<b>VLDL-C</b>	Very low density lipoprotein cholesterol
<b>Zn</b>	Zinc

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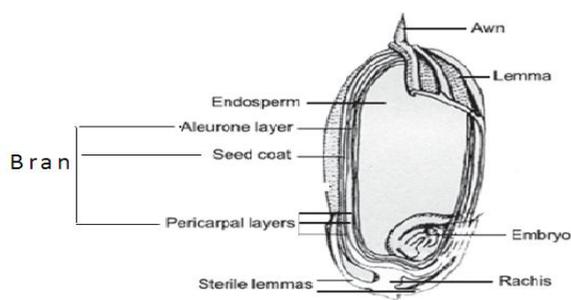


**Introduction  
& Aim of the  
work**

Agricultural wastes in Egypt range from 30-35 million tons per year of which only 7 million tons as animal feed and 4 million as organic manure are being utilized. The problem of agriculture wastes becomes very obvious and aggregated after the harvest of summer crops. Several factors have aggravated the problem including the absence of environmental awareness and the low level of knowledge and skills affecting the behavior of peasants in handling agricultural wastes. In addition, burning agricultural wastes in the rice cultivated fields generate many poisonous and harmful oxides and hydrocarbon (the black cloud) (**Abou Hussein and Sawan, 2010**).

Rice is one of the most important staple foods for a large part of human population. Global rice production is 645 million tons and this huge amount of production results in large amount of rice by-products (**Kubglomsong and Threerakulkait, 2014; Al-Okbi et al., 2014-a**). Rice bran is the major by-product generated during the milling process (**Kubglomsong and Threerakulkait, 2014**). Brown rice is results from dehusking of raw rice and brown rice is covered by bran layers which namely, pericarp, testa and aleurone layers. Bran is obtained by de-branning or polishing process and constitutes 5–10% of brown rice. It's mainly composed of protein, fiber, oil, vitamins, minerals and starch. Bran comes from endosperm during polishing (**Al-Okbi et al., 2014-a**). It is also a good source of antioxidants such as polyphenols, tocopherols, tocotrienols and  $\gamma$ -oryzanol which help in preventing the oxidative damage of body tissues and Deoxyribonucleic acid (DNA). Many studies reported that rice bran has cholesterol lowering properties, cardiovascular health benefits and anti tumor activity (**Tuncel et al., 2014**).

Rice bran contains 12–22% oil by weight (**Sharif *et al.*, 2014**). Crude rice bran oil is rich in unsaturated linoleic and oleic fatty acids and bioactive compounds such as  $\gamma$ -oryzanol, phytosterols, tocopherols, and tocotrienols (**Friedman, 2013**). In addition to nutritious components and health benefits of rice bran oil, some properties such as good stability, appealing flavour and long fry life, provide the rice bran oil in shortening (**Liang *et al.*, 2014**).



Rice grain structure (**Wopereis *et al.*, 2009**)

Over the past decades, the amount of dietary fructose consumption per capita has been dramatically increased mainly from high intake of sucrose and high fructose corn syrup, a common sweetener used in the food industry. A high flux of fructose to the liver, which is the main organ capable of metabolizing this simple carbohydrate, perturbs glucose metabolism and glucose uptake pathways. This leads to a significantly enhanced rate of de novo lipogenesis and triacylglycerol (TAG) synthesis, driven by the high flux of glycerol and acyl portions of TAG molecules from fructose catabolism. These metabolic disturbances appear to underlie the induction of insulin resistance commonly observed with high fructose feeding in both humans and animal models. Fructose induced insulin resistant states are commonly characterized by a profound metabolic dyslipidemia, which appears to result from hepatic and intestinal overproduction of atherogenic lipoprotein