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Antidiabetic Effect of Baker's Yeast in Alloxan Induced Diabetic Rats

Aisha Alfituri[*], Ahmed Behriz[**] and Abobaker Bashir[*]

[*] Pharmacology Faculty-University of Benghazi-Libya

[**] Faculty of Medicine- Cairo University-Cairo-Egypt

Abstract

Diabetes Mellitus is the most important public health problem in developed countries. It often leads to lethal complications if left untreated. Presently, no oral hypoglycemic agent or combination drug therapy exists to treat diabetes without toxicity or side effects. Insulin treatment also may lead to serious hypoglycemia and a reduction in its action by time. Therefore, the hypoglycemic effects of baker's yeast, which is considered a safe food were investigated. Diabetes was induced by intraperitoneal injection of Alloxan monohydrate at dose of 150mg/kg. After 14 days, rats with positive glucose urine dip stick were used for the study and oral yeast for another 14 days was started at a dose of 200mg/day and compared with oral Glibenclamide at dose of 0.5mg/kg. The blood glucose was increased significantly in the untreated Alloxan induced diabetic up to 229.8±22mg/dl, rats $p < 0.001$, as well as in the Glibenclamide treated diabetic rats up to190.6± 26 mg/dl, $p < 0.05$ as compared to the control normal group (74.8±5.7mg/dl). It was found that the administration of yeast significantly decreases the blood glucose up to 85.2± 5.9, $p \leq 0.001$. While no statistically significant decrease in the Glibenclamide treated group. The result showed that brewer's yeast has blood glucose lowering effect in diabetic model

Keywords: Baker's yeast, Diabetes Mellitus, Glucose signal transduction, insulin-mimetic phosphoinositolglycan peptide, Chromium.

الملخص:-.

يعد مرض السكري من أهم مشكلات الصحة العامة في الدول المتقدمة. وغالبا ما يؤدي إلى مضاعفات مميتة إذا ترك دون علاج. في الوقت الحاضر ، لا يوجد دواء لعلاج مرض السكري دون سمية أو آثار جانبية. علاج الانسولين قد يؤدي أيضا إلى نقص السكر في الدم وانخفاض في عمله بمرور الوقت. لذلك ، تم اختبار فاعليه خميره الخبز والتي تعتبر مصدر غذائي امن في مدي فعاليتها في تخفيض سكر الدم. تم إحداث داء السكري عن طريق حقن مادة ألوكسان مونوهيدرات بجرعة 150 ملغ / كغ. وبعد 14 يومًا ، تم استخدام الفئران التي يحتوي بولها علي جليكوز ، واعطيت خميره الخبز لمدة 14 يومًا اضافيه بجرعة مقدارها 200 ملغ / يوم ومقارنتها مع ماده الغليبنكلاميد بجرعة 0.5 مجم / كجم. النتيجة اظهرت ان نسبة الجلوكوز في الدم زادت بشكل ملحوظ في الفئران المحقونة بماده الالوكسان والفئران المحقونة بماده الالوكسان والتي تم علاجها بماده القليبكلاميد بالمقارنة مع الفئران السليمة, وأظهرت النتائج أن خميرة الخبزة لديها تأثير فعال في خفض مستوى الجلوكوز في الدم

الكلمات المفتاحية: خميره الخبز – مرض السكري – ماده الوكسان – نقل إشارة الجلوكوز – إنزيم الفوسفوانيزيتولجليكان المحاكى للانسلين – ماده الكروم

1. Introduction

Diabetes Mellitus (DM), especially the non-insulin dependent Diabetes Mellitus (NIDDM) has an enormous financial impact on the society. The total economic cost of DM comprised of medical care and lost productivity was estimated to be $ 92 billion (American Diabetes Association, 2003). The American Diabetic Association estimated as well the direct medical costs of diabetes at $ 54.2 billon, which include the cost of blood sugar tests and insulin, as well as the costs related to kidney failure, retinopathy and other diabetes related illnesses. The American Diabetes Association also said that the indirect costs of diabetes such as, lost productivity and premature death equal $ 46.6 billon. World estimates would place the total economic cost of NIDDM conservatively at over one trillion dollars (Tunceli et al, 2010). World estimates would place the total economic cost of NIDDM conservatively at over one trillion dollars (Tunceli et al, 2010). Presently, no oral hypoglycemic agent or combination

drug therapy exists to treat diabetes without toxicity or side effects. Insulin treatment also provides symptomatic relief rather than cure and may lead to serious hypoglycemia and reduction its action by time. The search for more effective and safer hypoglycemic agents therefore has continued to be an area of research of interest (Krishna et al., 2004; Pepato et al., 2003). The world health organization has recommended and encouraged the use of alternative therapy, especially in countries where access to conventional treatment of diabetes is not adequate (WHO 1980).

2. Literature Review

Baker yeast has been used for centuries in baking industry to expand or to raise dough. Also, it has been used to ferment the sugars of rice, wheat, barley and corn to produce alcoholic beverages. In addition, there are individuals who may ingest large quantities of Baker yeast daily, as those people who take the yeast as part of the healthy food regimen. Yeast is single-cell Eukaryotes under most environmental conditions (Campell and Duffus, 1988). It can be distinguished from plants, as it doesn't contain chlorophyll, and it is 2-10 times larger than bacteria (Rosini et al., 1982). Yeast cell wall is composed of chitin cellulose or hemicellulose depending on species. It is a saprophytic chemoorganotrophs (Claus, 1989). The most well-known and commercially significant yeast is the related species and strains of Saccharomyces cerevisiae. The aim of this study was to evaluate the role of dietary treatment by baker's yeast in the rats' diabetic model.

3. Methodology

The experiment involved 24 male Sprague Dawley rats, with a weight range of (194-373g). Diabetes was induced by intra peritoneal injection of Alloxan monohydrate at a dose of 150 mg /kg dissolved in sterile 0.9 % Normal saline. Since Alloxan is capable of producing fatal hypoglycemia as a result of the massive pancreatic insulin release, rats were treated with intra peritoneal injection of 20 % glucose solution 6 hours after Alloxan injection. Besides, the rats were kept for the next 24 hours on 5 % glucose solution bottle in their cages to prevent hypoglycemia (Dhandapani et al., 2002). After 14 days the urine was examined using the dip stick for glucose and those rats with positive result were selected and used for the study. Rats were then divided into four groups [n=6]. Group 1 comprised rats that fed a normal diet and Tap water for another 14 days and used as control normal group. Group 2 included rats that received Alloxan monohydrate only as described previously and used as control diabetic group. Group 3 contained within rats that received Alloxan monohydrate and treated with

Glibenclamide at a dose of 0.5 mg /kg /d for 14 days and used as an oral hypoglycemic treated group. Group 4 included rats that received Alloxan monohydrate and were given daily oral yeast at a dose of 200 mg/ rat dissolved in distal water introduced by oral tube for 14 days and used as yeast treated group. Fasted rats were sacrificed by decapitation in the next day morning and blood was taken for measuring blood glucose by the oxidase test method. The animals described as fasted were deprived of food for at least 12 hours before the end of the experiment, but allowed free access to water. Data were expressed by using descriptive analysis as the mean ± standard error of the mean [sem] , test of significance was carried out using one way analysis of variance [ONOVA] as appropriate Remington and Anthony (1985). The degree of significance was determined by using the Tukey. HSD, as well as Tamhane test for dependent samples. Probability values less than 0.05 were considered as significant.

4. Data and Results

General observation:

After induction of diabetes by Alloxan, It was noticed that there is a significant increase in the food and water intake in the untreated diabetic rats and also the Glibenclamide treated rats as compared to the control and the yeast group. There is also a significant increase in the urine out put both in the untreated diabetic group and the Glibenclamide treated group as compared to the control normal and the yeast group.

The effect on the body weight:

The changes in the body weight in the control, untreated and treated diabetic rats are shown in the Figure 1. It was noticed that there was mild weight loss during the four weeks period of the experiment in the untreated diabetic rats, as well as the treated diabetic rats with both Glibenclamide and yeast (14.6±1.4g) for the untreated diabetic rats , (5.5± 0.5g) for the Glibenclamide treated diabetic rats , and (9.4±0.9g) for the yeast treated diabetic rats. While the normal control showed mild weight gain (2.4 ± 0.2g). It also noted that the treatment with both Glibenclamide and yeast showed mild improvement in the weight loss as compared to the untreated diabetic rats.

The effect on blood glucose:

Alterations in the blood glucose on the control normal, the untreated and the treated diabetic rats are given in the figure 2. The blood glucose was significantly increased in the untreated Alloxan induced diabetic rats up to 229.8±22mg/dl, p <0.001, as well as in the Glibenclamide treated diabetic rats up to190.6± 26 mg/dl, p <0.05 as compared to the control normal group (74.8±5.7mg/dl). It was found that the administration of yeast significantly decreased the blood glucose up to 85.2± 5.9, p≤ 0.001. While no statistically significant decrease in the Glibenclamide treated group.

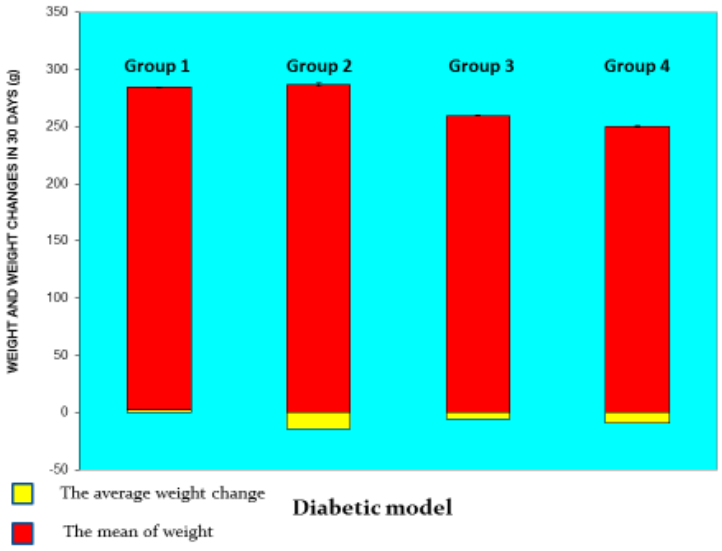

Figure 1: The effect of Glibeclamide and yeast on the body weight of the normal and diabetic rats.

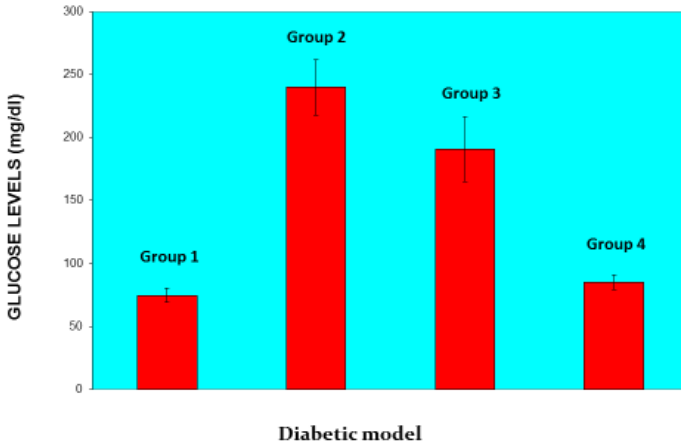

Figure 2: The effect of Glibenclamide and yeast on the blood Glucose level of normal and diabetic rats .

5. Discussion

Diabetic model was done by injecting Alloxan monohydrate, which induces diabetes by damaging the insulin secreting beta cells of the pancreas. This observation correlates with the previous researches finding that the blood glucose levels significantly increased in Alloxan untreated diabetic rats (Dhandapani et al., 2002). We used Glibenclamide, an oral hypoglycemic drug, to compare the effect of the yeast on reducing blood glucose. Glibenclamide acts at the pancreatic level and extra pancreatic level. At the pancreatic level, it increases secretion of formed insulin through binding with specific receptors on the beta cells' membrane linked to specific ATP sensitive K channels causing closure of the channels and depolarization. This effect will be followed by calcium influx and a subsequent release of insulin from its granules. While at the extra pancreatic level, Glibenclamide acts by increasing tissue sensitivity to insulin and also the number of insulin receptors (Panten et al., 1996). In the present study, the investigators compared the effects of Glbenclamide and yeast on the rat diabetic Alloxan treated model. It was found that the continuous treatment with the yeast for a period of two weeks caused a significant decrease in blood glucose levels of Alloxan induced diabetic rats more obvious than the Glibenclamide treated diabetic rats. The possible mechanisms by which the yeast brings about its hypoglycemic action may be explained on the basis of that the yeast may act by its glucose signal transduction property, which is an evolved mechanism by which most organisms sensing glucose in their environments and then making some appropriate response (Figure 3). Defect in these processes in the mammal results in a serious disease as diabetes. Baker's yeast, Saccharomyces cerevisiae, may have a role in the glucose signal transduction pathway, which is in agreement with the in-vitro study done by Pasula and Jouandol, (2007). In this study, they demonstrated that when S. cerevisiae sense glucose, it triggers a signal transduction pathway that induces the expression of the Hexose transporters (HXT) genes that encodes glucose transporters. In the absence of glucose, HXT genes are normally bound to the glucose transporter regulator 1 (Rgt1) transcription factor (repressor protein), which repress HXT gene expression in the conjunction with the two paralogous proteins (Mth1 and Std1). But, when the cells switched to the glucose rich medium, this sensed by two the surfaces glucose sensors (Snf3 and Rgt2). This leads to degradation of Mth1, which is required for the DNA binding to Rgt1. Subsequently, leading to the inhibition of the glucose induced hyperphosphorylation of Rgt1 which causes the hyperphosphorylation of Rgt1. Therefore, the binding to HXT gene is greatly reduced leading

to the expression of HXT gene encoding glucose transporters, which assists glucose transport to inside cells.

Another mechanism which may be involved in the baker's yeast hypoglycemic effect is by an insulin mimetic phosphoinositolglycan peptide. This peptide mimetic insulin action on glucose transport and metabolism. This is going with the in-vitro study done by Kessler et al. (1998). In that study, they extracted this peptide from S. cerevisiae and they used it in the rats' muscle and adipose tissue. The peptide showed same insulin action and additive response when mixed with insulin. On the other hand, chromium and glucose tolerance factor may have a role in hypoglycemic action of the baker's yeast. The best source of chromium is brewer's yeast. Two tablespoons of brewer's yeast yield about 120 micrograms of chromium an amount equal to the recommended daily allowance. Chromium is an essential trace mineral that helps the body to maintain normal blood sugar levels .In addition to its effect in diabetes (Riales and Albrink, 1981). Preliminary research has found that chromium supplementation also improves glucose in people with Turner's syndrome, a disease linked with glucose intolerance, a study done by Saner et al. (1983). Chromium is needed for the regulation of Glucose tolerance factor (GTF). A vital factor, which is essential for the production of a functionally effective insulin in combination with nicotinic acid and some proteins. The role of GTF is to moderate insulin activity first by potentiating and circulating insulin and then by reducing the amount required to be released. Brewer's yeast has at least 10 times more GTF activity than other natural food .GTF also contains amino acids such as glutamic acid ,glycine ,and cysteine . Both brewer's yeast 9g/d and trivial chromium 150-1000mcq/d have been shown significantly to improve blood sugar metabolism, when taken for several weeks to months (Riales and Albrink, 1981).

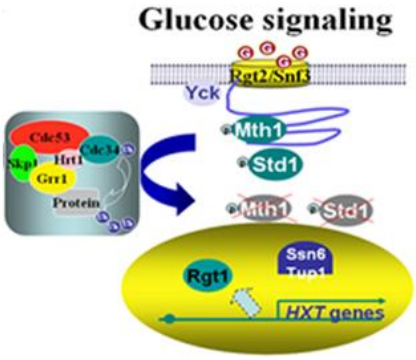

Figure 3: Glucose Signaling by Pasula and Jouandol, (2007).

6. Conclusion

It may be concluded that the baker yeast has blood glucose lowering effect on Alloxan induced diabetic rats' model. It could be indicated that the baker yeast may provide a new therapeutic way against diabetes and diabetes-related complications because of its availability, cheapness and effectiveness. A detailed study of the mechanism of action, side effects, and contraindication of this greatly nutritious vegan food product is highly recommended.

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