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Investigation into the Intake of Edible Mushroom *Pleurotus ostreatus* (Aqueous Extract Oyster Mushroom) on Biochemical Indices of Female Wistar Rats

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Abstract

Pleurotus ostreatus, popularly known as oyster mushroom, has nutraceutical properties that include hypocholesterolemic, hypoglycemic, antioxidant, anti-inflammatory, antitumor, hepatoprotective and hypotensive activities. Aqueous Extract Oyster Mushroom (AEOM) containing lyophilized *P. ostreatus* reconstituted in 0.9% saline solution was evaluated for its effect on body weight, biochemical indices and pancreas morphometry. Twelve healthy Wistar female rats were assigned to Control and AEOM groups, consisting of rats that received 0.9% saline solution and AEOM (100 mg/kg/day), respectively, administered by oral gavage at 3 mL/kg of body weight for 15 days. The animals had free access to commercial feed and water *ad libitum*. Blood was obtained by cardiac puncture and serum was used to biochemical determinations. Pancreas was excised, weighed and fixed in 4% neutral buffered formalin for histopathological examination. Initial and final body weights, and absolute and relative weights of pancreas did not differ between the groups. Total cholesterol, HDL-c, albumin and uric acid were lower in the AEOM group compared to the control group. The serum concentration of total proteins, glucose, triglycerides, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, lactate dehydrogenase, creatinine and urea were similar in the groups. Pancreas of rats treated with AEOM exhibited an in-

crease in the size of pancreatic islet. Thus, the use of AEOM is relatively safe at the dose studied and produces hypertrophy of the pancreatic islets without altering glycemic homeostasis.

Keywords

Edible Mushroom, Nutraceuticals, *Pleurotus ostreatus*, Aqueous Extract Oyster Mushroom, Biochemical Analyzes

1. Introduction

Pleurotus ostreatus, popularly known as oyster mushroom, is a type of edible mush-room widely cultivated worldwide in different lignocellulosic residues [1]. Provide important nutrients (selenium, potassium, riboflavin, niacin, vitamin D, protein and fiber) and bioactive compounds (lectins, proteases, fibrinolytic enzymes, protease inhibitors, and phenolic compounds) [1]-[9]. Studies report that their bioactive compounds are responsible by effects anti-inflammatory [10], antinociceptive [11], antioxidant [12] [13] [14] [15], antitumour [16] [17] [18], enhancer of iron bioavailability [19], gastroprotective [20], hepatoprotective [21] [22] [23], hypocholesterolemic [12] [24] [25] [26], hipoglycemic [2] [25] [27]-[39], immunomodulador [4] and nephroprotective [40] [41] (**Figure 1**).

Almost 20 years ago, a study in Bratislava, Slovak Republic, investigated the ap-plication of a diet with 4% of *P. ostreatus* in diabetic rats, and showed a significantly lower basal and postprandial glycaemia in relation to the control group [38]. After this study, several other works were published, investigating the dose, the form of administration, the rodent strain, the drug for inducing

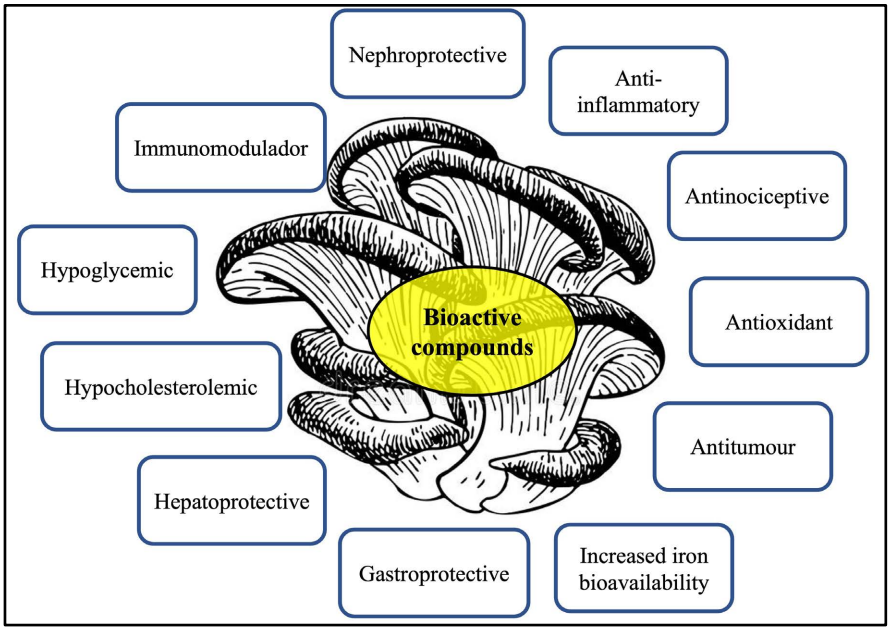

Figure 1. Effects of bioactive compounds from *P. ostreatus*.

diabetes (diabetic model), the period of the experiment and laboratory tests; everything to elucidate if the reduction of glucose happens after the animal receives the oyster mushroom [2] [27] [29] [30] [31] [32] [35] [42]. The hypoglycaemic effect of *P. ostreatus* has been attributed to increased insulin secretion and the action of this hormone in peripheral tissues [42], possibly mediated by AMP-activated protein kinase (AMPK) and c-AMP-response element binding protein (CREB) [31]. Although the acute and chronic oral hypoglycaemic and hyperinsulinaemic potential of *P. ostreatus* has been established, the cellular mechanism and its effects on pancreatic islet structure have been little explored [31].

To maintain glucose homeostasis, the pancreatic islets use a variety of adaptive mechanisms, including increased cell mass and number and increased insulin secretion capacity. When the secretion cannot meet the increased demand for insulin due to peripheral resistance to this hormone, hyperglycaemia may occur [43]. Studies that clarify these aspects may contribute to the expansion of knowledge about the pharmacological activity and the guidelines for the use of this mushroom species as a nutraceutical agent. Therefore, the objective of the present study was to evaluate the effects of the Aqueous Extract Oyster Mushroom (AEOM) on biochemical markers of nutritional status, and liver and kidney function, as well as on the structural adaptations of pancreatic islets of female rats.

2. Material and Methods

2.1. Experimental Animals

Twelve (12) healthy adult female Wistar rats weighing 150 to 180 g were used for this study. They were obtained from the Central Animal Facility of the Federal University of Mato Grosso, and were maintained under standard housing conditions in the animal section of Laboratory of Biological Evaluation of Food of the Department of Food and Nutrition, Federal University of Mato Grosso, Mato Grosso State, Brazil. The animals were adapted for two weeks preceding initiation of experimental regimen, received fed commercial (Labine chow) and clean tap water acessive ad libitum, exposed to clean tap water throughout the period of the study. The room temperature was maintained at approximately 25˚C, relative humidity at 55%, with a light cycle of 12 hours light and 12 hours dark. All animal experimental protocols were permitted by the Ethics Committee on Animal Research of the Federal University of Mato Grosso (Protocol No. 23108.039877/2021-21), and were carried out by its guidelines for animal use.

2.2. Experimental Design

The animals were allotted into two groups of six (6) rats and kept in groups of three (3) animals per standard plastic rat cage. The groups were named Control and AEOM, consisting of female rats that received 0.9% saline solution and AEOM (100 mg/kg/day), respectively, that were administered by oral gavage at 3

mL/kg body weight for 15 days.

2.3. Sample Collection

Twenty four (24) h after the last oral dose the AEOM, the animals were narcotized in a CO_2 and blood were obtained through heart punction into ordinary sample bottles. The blood samples were made to stand for 20 min for coagulation to occur, and afterwards centrifuged at 2000 rpm for 10 min and the supernatant (serum) collected and kept at 4˚C prior to biochemical assay. The pancreas was quickly excised, weighed, and immediately fixed in 4% neutral buffered formalin for histopathological examination.

2.4. AEOM

2.4.1. Obtaining

The oyster mushroom (*P. ostreatus*) was obtained from the Laboratory for Cultivation of Edible Fungi of the National Institute for Research in the Amazon (INPA), Culture Collection of Agrosilvicultural Microorganisms (strain code 1467).

2.4.2. Dose Selection

The solution AEOM was prepared by reconstituting the dried and lyophilized mushroom (fruiting body of *P. ostreatus*) in 0.9% saline solution (100 mg/mL). Daily doses of 100 mg/mL of AEOM was chosen based in Grotto *et al.* [44] study, in which the mushroom did not promote hepatic damage in rats.

2.5. Biochemical Analysis

Commercial kits (Wiener Lab. Group, Brazil®) were used for the determination of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), creatinine, urea, uric acid, total proteins (TP), albumin (ALB), glucose (GLU) and lipid profile [total cholesterol (TC), triglycerides (TG) and HDL-c]. The LDL value was calculated according to the Friedewald equation: LDL-c = total cholesterol − (HDL + VLDL); VLDL-c = triglycerides/5. Analyzes were carried out in the State Department of Health of Mato Grosso, Blood Center, Cuiabá, State of Mato Grosso, Brazil. All chemicals/reagents used in this investigation were of purest analytical grade.

2.6. Changes in Body Weight

Rats in all groups were weighed on the first day and at the completion of the treatment protocols. The percentage change in body weight was calculated using:

$$\%\ \text{change in body weight} = \frac{\text{final body weight} - \text{initial body weight} \times 100}{\text{initial body weight}}$$

2.7. Relative Pancreas Weight

Pancreas weight was presented in absolute and relative values. Relative pancreas weight was calculated using the expression below:

$$\text{Pancreas}\left(\text{g}/100\text{g BW}\right)=\frac{\text{weight of pancreas}\left(\text{g}\right)\times 100}{\text{body weight}\left(\text{g}\right)}$$

2.8. Histopathological Scrutiny of the Pancreas

Four rats from each group were used for the histological studies. The pancreatic tissue was fixed in 4% paraformaldehyde solution for 24 hours at 4˚C, dehydrated in increasing concentrations of ethanol, clarified in xylene and embedded in paraffin using a histological processor (MTP 100, Slee, Mainz, Germany). The tissue was serially sectioned at 3 μm thickness using a microtome (RM2125, Leica Biosystems Nussloch, Germany) and then mounted on slides with an adhesive surface. Ten sequential sec-tions of the pancreas were deparaffinized in an oven at 60˚C for 2 h, followed by im-mersion in xylene and decreasing concentrations of ethanol. These slides were rehy-drated and stained with hematoxylin and eosin for determination of the pancreatic regions under a light microscope at 40× magnification (Axio Scope A1, Zeiss, Ober-kochen, Germany).

2.9. Statistical Analysis

The results were presented as mean ± standard deviation (S.D.) and analyzed using an unpaired Student's t-test. The significance level was set at $p < 0.05$. For the analysis of the results, the program "Statistic for Windows", (version 4.3, StatSoft, Inc., Tulsa, OK, USA).

3. Results and Discussion

3.1. The Effects of Administration of the AEOM on the Body and Pancreas Weights

The body and pancreas weights of the rats are presented in Table 1. Initial and final body weights and absolute and relative weights of pancreas did not differ between the groups.

3.2. The Effects of AEOM on Lipid Profile

The oral administration of AEOM for 15 days as shown in Table 2 caused a signifycant decrease ($p < 0.05$) in the levels of total cholesterol and HDL-c. AEOM did not alter TG and LDL-c levels.

Table 1. The effects of administration of the AEOM on the body and pancreas weights.

Treatment group	Somatic parameters				
	Initial body weight (g)	Final body weight (g)	Changes in body weight (%)	Weight of pancreas (g)	Weight of pancreas (g/100g BW)
Control	210 ± 8	217 ± 9	3.5 ± 1.8	0.48 ± 0.06	0.21 ± 0.04
AEOM	203 ± 13	217 ± 10	7.1 ± 4.0	0.47 ± 0.11	0.21 ± 0.04

Values expressed as mean ± SD (n = 6 per group).

Table 2. The effects of AEOM on lipid profile.

Treatment group	Lipid profile			
	TC (mg/dL)	TG (mg/dL)	HDL-c (mg/dL)	LDL-c (mg/dL)
Control	89 ± 19	88 ± 24	54 ± 10	12 ± 6
AEOM	59 ± 11*	76 ± 16	34 ± 5*	14 ± 28

Values expressed as mean ± SD (n = 6 per group). *Indicates difference statistical (*t* Student test, $p < 0.05$).

3.3. The Effects of AEOM on the Concentrations of AST, ALT, ALP and LDH Activities Following Oral Administration of AEOM

The oral administration of AEOM for 15 days as presented in **Table 3** caused a non-significant change ($p \geq 0.05$) in the levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) activities in female rats.

3.4. The Effects of AEOM on the Concentrations of Creatinine, Urea and Uric Acid Concentrations

The oral administration of AEOM for 15 days as presented in **Table 4** caused a significant decrease ($p < 0.05$) in the level of uric acid. However not caused a significant change ($p \geq 0.05$) in the levels of creatinine and urea concentrationin the female rats.

3.5. The Effects of AEOM on the Concentrations of Total Proteins (TP) and Albumin (ALB), and Glucose (GLU)

The oral administration of AEOM for 15 days as presented in **Table 5** did not cause significant change ($p \geq 0.05$) in the levels of TP and GLUC, but reduced the serum albumin concentration in the female rats.

3.6. The Effects of AEOM on the Histopathological of the Pancreas

The histopathological examination of the control group showed physiological organization of the pancreas with no morphological alterations (**Figure 2(A)**). After 15 days of oral dosing of AEOM (**Figure 2(B)**) showed increasement in the pancretic islets size (H&E).

3.7. Discussion

AEOM is an extract based on *P. ostreatus*, an edible mushroom important source of bioactive compounds [1]. For this reason, edible mushroom extracts have been used as dietary supplements and recommended for the prevention and treatment of various diseases [45].

In the present study, we evaluated the use of AEOM by healthy adult rats and found similar body weight gain in both evaluated groups. However, we observed a significant reduction in serum albumin concentrations, a condition that can

Table 3. The effects of AEOM on the concentration of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) activities.

Treatment group	Hepatic function markers			
	AST (U/L)	ALT (U/L)	ALP (U/L)	LDH (U/L)
Control	157 ± 48	55 ± 7	378 ± 110	338 ± 60
AEOM	142 ± 23	60 ± 8	487 ± 154	316 ± 74

Values expressed as mean ± SD (n = 6 per group).

Table 4. The effects of AEOM on the concetrartion of creatinine, urea and uric acid.

Treatment group	Kidney function markers		
	Creatine (mg/dL)	Urea (mg/dL)	Uric acid (mg/dL)
Control	0.52 ± 0.04	45 ± 6	3.0 ± 0.6
AEOM	0.49 ± 0.03	42 ± 5	1.8 ± 0.2*

Values expressed as mean ± SD (n = 6 per group). *Indicates difference statistical (*t* Student test, $p < 0.05$).

Table 5. The effects of AEOM on the serum total protein, albumin and glucose concentrartions.

Treatment group	Total protein (g/dL)	Albumin (g/dL)	Glucose (mg/dL)
Control	7.3 ± 0.4	4.30 ± 0.08	87 ± 11
AEOM	7.1 ± 0.5	4.10 ± 0.09*	83 ± 9

Values expressed as mean ± SD (n = 6 per group). *Indicates difference statistical (*t* Student test, $p < 0.05$).

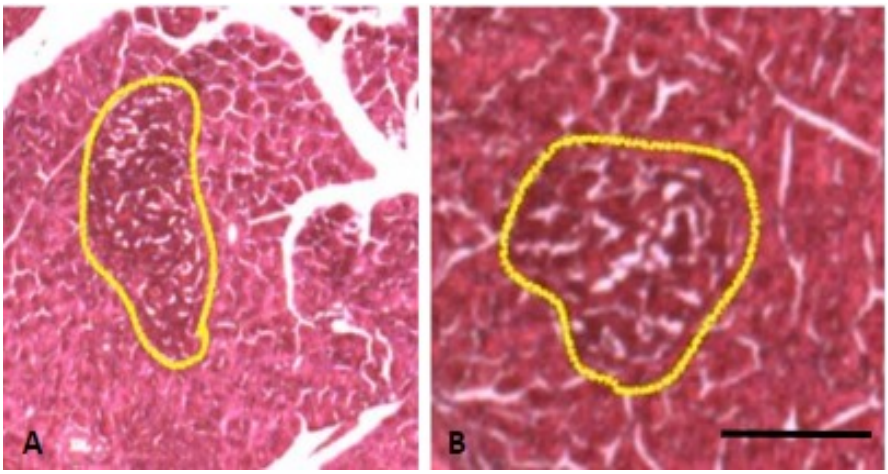

Figure 2. Photomicrographs of the pancreatic islets section of the group control (A) and group treated with AEOM (B) at 15 days. The pancreatic islets were outlined in yellow. H&E ×40. Bar = 10 μm.

result from reduced hepatic synthesis, increased catabolism and vascular permeability, and intestinal and renal loss [46]. Malnutrition, inflammation, liver disease are some situations that can contribute to the reduction of albumin synthesis [46]. Considering preserved body weight and unaltered total serum protein concentration, it is reasonable to assume that treatment with AEOM did not contribute to the deterioration of the nutritional status of the animals. Body weight fluctuations serve as a sensitive indicator of the general health status of animals [47] and normal serum total proteins are indicators of preserved nutritional status [48]. Additionally, unaltered values of AST, ALT, ALP and LDH are indicative that the AEOM did not cause liver damage [21] [22] [23] [44]. Renal loss of albumin is also an unlikely hypothesis, in view of the preserved renal function, judging by the similar serum concentrations of urea and creatinine in the evaluated groups. The reduction in serum uric acid seen in rats treated with AEOM and also observed in other studies with rodents treated with *P. ostreatus*, *Agrocybe aegerita* and *Ganoderma applanatum* [36] [37] [38] [39] has been associated with increased urinary acid excretion uric acid [36] [37], which is negatively related to albuminuria [49].

In the present study, treatment with AEOM reduced total cholesterol, as in murine models of hypercholesterolemia and diabetes [50] [51] [52]. The hypocholesterolemic effect of *P. ostreatus* has been attributed to the presence of polyunsaturated fatty acids, mainly eicosapentaenoic and docosahexaenoic acids [53] and polysaccharides that positively modulate the serum lipid profile [24], as well as the stimulating effects of intestinal cholesterol excretion [50] [51]. Interestingly, in the present study, a reduction in HDL-c was observed, as opposed to reports of the positive modulatory effect of *P. ostreatus* or some of its components, such as polysaccharide residues, on HDL-c in models of diet-induced hypercholesterolemia [26] [54], in mice with alloxana-induced diabetes [28] and in HIV-infected humans on antiretroviral therapy [55]. Epidemiological studies show a strong inverse correlation between HDL-c and cardiovascular disease risk [56] [57], suggesting that in this study *P. ostreatus* had a detrimental effect on cardiovascular health. However, the reduction in HDL-c observed here may not be a cause for concern, considering the antioxidant properties of *P. ostreatus* [12] [13] [14] [15].

The histomorphological evaluation of the pancreas showed larger pancreatic islets in the AEOM group compared to the control group. Despite the hypertrophy of the islets, the glycemia of the animals treated with *P. ostreatus* did not differ from that of the control animals. This result was not surprising, since the size of the islets does not seem to be related to the increase in their functional capacity or with the hormonal content. It has been shown that insulin secretion from small islets is greater compared to large islets, with a correlation with greater insulin content/area, greater density of insulin-secreting granules and greater insulin content/volume. Central β cells of large islets appear to contain less insulin/cell with a lower insulin granule density than peripheral β cells [58] [59] [60].

4. Conclusion

The result of this present investigation showed that AEOM is safe at the dose studied, had a positive effect on lipid profile and produced hypertrophy of the pancreatic islets without altering glycemic homeostasis.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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