Hematologic and Metabolic Effects of Dietary Supplementation with *Agaricus sylvaticus* Fungi on Rats Bearing Solid Walker 256 Tumor

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Background: **Many mushrooms have been used since ancient times for their nutritional and therapeutic properties. Alterations of hematologic parameters are commonly observed in patients with cancer, mainly due to the presence of some inflammatory mediators that have hemolytic effects, and yet can stimulate white blood cell release. Abnormalities in biochemical parameters are also found due to alterations in carbohydrate, protein, and lipid metabolism.** ***Objective:*** **The aim of the present study was to evaluate the effects of *Agaricus sylvaticus* on hematologic and biochemical parameters of rats inoculated with Walker 256 tumor.** ***Methods:*** **The animals were divided into 4 groups, with 20 in each group. Group 1 was inoculated with Walker 256 tumor and treated with *A. sylvaticus*. Group 2 was inoculated with Walker 256 tumor and administered a placebo solution. Group 3 was not inoculated with the tumor and was treated with *A. sylvaticus,* and Group 4 was not inoculated with the tumor and was administered a placebo solution. The rats were sacrificed after 12 days of treatment, and blood was collected following heart sectioning.** ***Results:*** **Statistically significant differences between Groups 1 and 2 were observed in red blood cell count, hematocrit, hemoglobin, C-reactive protein, urea, and triglyceride levels. No significant differences between these two groups were noted in hematimetric indices, leukocyte counts, creatinine, and glucose levels. No significant differences in hematologic and biochemical parameters were noted between Groups 3 and 4.** ***Conclusion: A. sylvaticus*** **is able to reduce anemia and improve biochemical parameters in animals with cancer and has no adverse effects on the blood cells of healthy animals.** Exp Biol Med 233:1341–1347, 2008

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Introduction

Anemia is a complication commonly observed in patients with cancer that can be caused by bleeding, nutritional deficiencies, bone marrow damage, tumor infiltration in bone marrow, and the malignant process itself. The inflammatory cytokines associated with tumor genesis, such as tumor necrosis factor-α (TNF-α) and interleukin-1 (IL-1), can inhibit the proliferation of erythrocytic progenitors (1).

Radiotherapy and chemotherapy often result in hematopoietic and immune dysplasia because hematopoietic stem cells are damaged during the procedures and committed hematopoietic and immune cells are then depleted. Consequently, patients often experience anemia, lymphocytopenia, thrombocytopenia, and/or granulocytopenia, which can lead to infection and increasing morbidity and mortality (2, 3). Abnormalities of leukocyte counts are also found and are due to the presence of some inflammatory mediators (4).

Anemia has been found to not only reduce the quality of life, but also to reduce survival rates. Patients with normal values of hemoglobin present less fatigue, better physical well-being, and generally higher quality of life when compared to patients with low levels of hemoglobin (1). Anemic patients are treated with hematopoietic agents such as epoetin alfa, which is a well-established treatment option (5).

Alterations in protein, carbohydrate, and lipid metabolism have been reported in patients with cancer. Although it has been hypothesized that the tumor itself is responsible for these metabolic abnormalities, alterations in nutrient intake, nutritional status, and cancer treatment may be important contributing factors (6).

Metabolic alterations associated with malignant disease have been widely studied. Abnormal levels of urea, creatinine, triglycerides, and glucose due to the nutritional status of patients have been described (7). In cancer, levels of C-reactive protein (CRP) are also altered and are an indicator of a patient's prognosis (8). CRP is an acute-phase reactant produced in the liver in response to inflammatory cytokine IL-6. CRP is a serologic marker of inflammation that can be used to investigate the association between inflammation and risk of cancer (9). Plasma levels rise dramatically in response to tissue injury and fall rapidly after recovery or treatment (10). Elevated levels of CRP are a marker of poor prognosis in patients with prostate cancer and are high in men with bone metastasis (11, 12).

Alternative strategies and therapeutic adjuvants to improve the quality of life of patients with cancer have been tested in recent years. Edible mushrooms have been used as important nutritional and/or therapeutic sources throughout the world (13). There is a significant interest in the use of fungi as dietary supplements, based on theories that they enhance immune function and promote health (2).

People in many countries use hot water extracts of some mushrooms due to their recognized medicinal properties. In China and Japan, these fungi became important ingredients in traditional medicine (14). The mushroom is used by people in Brazil as a dietary supplement (15).

The Agaricales order is one of the major classes of fungi and contains a great number of important species that are used as nutritional supplements and therapeutic resources (15). In the Agaricales order, there are four species of great interest: *Lentinus edodes*, *Pleurotus ostreatus*, *Volvariella volvacea*, and *Agaricus bisporus* (16).

Some medicinal mushrooms are used in combination with conventional cancer treatment. *Ganoderma lucidum* polysaccharides have been effective in inhibiting tumor growth in animal experiments and are used as adjuvants of antitumor therapy in clinics. Combinations of *G. lucidum* extracts with antitumoral drugs such as mitomycin or etoposide could antagonize the inhibitory effects of these drugs in mixed lymphocyte culture (16).

The main substances responsible for the pharmacologic effects of mushrooms are the β-D-glucans, which are structural cell polymers of many fungi and possess immunomodulator properties (17). Arginine also has important immunomodulator activity (18). Some mushrooms' lectins have antiproliferative, antitumoral, and immunoenhancing activities (19).

Agaricus sylvaticus is a mushroom native of temperate regions. No data on its antitumoral and toxic properties have been published, although some Internet sites mention it as poisonous species capable of causing flu-like symptoms (20).

The aim of the present study was to evaluate the capacity of *A. sylvaticus* to improve the hematologic and biochemical parameters of rats inoculated with Walker 256 tumor and to evaluate possible adverse effects of this mushroom.

Methods

Study Design. The study was prospective, randomized, blinded, and placebo controlled. Young, male, isogenic rats ($N = 80$; 90 days of age) were kept under identical temperature and artificial light exposure for 12 hrs a day in alternate cycles, and an identical amount of food and water were available (Labina-Purina, Brazil) *ad libitum* during the study. They were divided into four groups.

Group 1. Tumor/Agaricus ($n = 20$). The animals were inoculated with Walker 256 tumor and treated with *A. sylvaticus* solution by gavage every 12 hrs. This group was evaluated according to the efficacy of *A. sylvaticus* in improving the anemic state and biochemical parameters of animals with cancer.

Group 2. Tumor/placebo ($n = 20$). Animals were inoculated with Walker 256 tumor and administered a placebo solution every 12 hrs. The hematologic and biochemical parameters of this group were used for comparison with the results obtained in Group 1.

Group 3. Control/Agaricus ($n = 20$). The rats were not inoculated with Walker 256 tumor and received *A. sylvaticus* solution every 12 hrs. This group was evaluated for possible adverse reactions associated with *A. sylvaticus*.

Group 4. Control/placebo ($n = 20$). The animals were not inoculated with Walker 256 tumor and received a placebo solution every 12 hrs. The hematologic and biochemical parameters of this group were designated as our reference values.

The experimental group received 50 mg/kg/day of *A. sylvaticus* (Piedade, São Paulo, Brazil) water extract by gavage, in two daily administrations, until their death. The placebo group received a solution with the same composition as the solution administered to the experimental group, but without *A. sylvaticus*. Both groups underwent the same procedure, which consisted of administration of a liquid solution every 12 hrs by esophagic gavage, initiated 12 hrs after inoculation and maintained until life was interrupted (Day 13).

The project was approved by the Ethics Committee in Animals Studies of the University of Brasilia, Brazil, and the protocol of the General United Kingdom Coordinating Committee on Cancer Research was followed.

Preparation of Animals and Inoculation of Tumors. The Walker 256 tumor was kindly provided by the Department of Physiology, IB/UNICAMP, Campinas, Brazil. The line originally came from the National Cancer Institute Bank, Cambridge, MA. The tumor was stored in the laboratory under liquid N_2 and was maintained through intraperitoneal passages in the rats. The rats received two inoculations of approximately 4×10^6 tumor cells in the dorsal-lumbar region.

Chemical Composition of *A. sylvaticus* Solution. The mushroom is grown in the soil, under direct sun, and so is called the sun mushroom. The mushroom is originally from Piedade and Tapiraí, São Paulo, Brazil. The

Table 1. Red Blood Cells and Hematimetric Indices of Rats Inoculated with Walker 256 Tumor and Treated with *A. sylvaticus* or Placebo[a]

Test[b]	*A. sylvaticus* (Group 1)	Placebo (Group 2)	Significance level
Erythrocytes	$4.48 \pm 1.01 \times 10^6$	$3.69 \pm 1.39 \times 10^6$	$P \leq 0.05$*
Hemoglobin (g/dl)	8.87 ± 2.21	7.56 ± 1.76	$P \leq 0.05$*
Hematocrit (%)	25.49 ± 5.94	22.32 ± 5.20	$P \leq 0.05$*
MCV (fl)	60.48 ± 7.22	57.81 ± 4.36	$P \geq 0.05$
MCH (pg)	20.67 ± 2.21	20.68 ± 1.62	$P \geq 0.05$
MCHC (%)	35.01 ± 1.08	34.11 ± 3.128	$P \geq 0.05$

[a] Univariate analyses (ANOVA). Tests: Bonferroni and Newman-Keuls. Results represent the mean ± SD ($n = 20$) in each group.
[b] MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration.
* Statistically significant.

composition of the final solution of extract *A. sylvaticus* was analyzed at the Japan Food Research Laboratories Center and revealed the presence of carbohydrates including β-glucans (18.51 g/100 g), lipids (0.04 g/100 g), ergosterol (624 mg/100 g), proteins (4.99 g/100 g), amino acids (arginine, 1.14%; lysine, 1.23%; histidine, 0.51%; phenylalanine, 0.92%; tyrosine, 0.67%; leucine, 1.43%; methionine, 0.32%; valine, 1.03%; alanine, 1.28%; glycine, 0.94%; proline, 0.95%; glutamic acid, 3.93%; serine, 0.96%; threonine, 0.96%; aspartic acid, 1.81%; tryptophan, 0.32%; cysteine, 0.25%) and micronutrients in trace quantities. The placebo group was managed with and aqueous solution containing the same nutritional value, but without *A. sylvaticus* extract.

Hematologic Analysis. On Day 13, all animals were sacrificed under anesthesia and blood samples were collected following heart sectioning. A hemogram was performed using an impedance method with an automated device (Cell-Dyn 3500 apparatus), where the variables erythrocytes, hemoglobin, hematocrit, mean corpuscular volume of erythrocytes, and mean corpuscular hemoglobin were included in the red blood cell analysis, and the various leukocytes, lymphocytes, and neutrophils were analyzed. The values were compared to the normal ranges of these parameters in healthy rats.

Biochemical Analyses. The blood collected from the animals was also used to perform biochemical analyses. The colorimetric enzymatic method was used to determine triglyceride, creatinine, urea, and glucose levels. For the amount of CRP, the turbimetric method was used.

Statistical Analyses. Data are presented as mean ± 1 SD or frequencies. Statistical analyses were performed using Variance Analyze–ANOVA (Prism 3.0). Categorical data were compared with use of the Bonferroni and Newman-Keuls tests. A P value <0.05 was considered significant.

Results

The hematologic parameters of healthy animals treated with placebo solution were designated as our reference values and were used for comparison with the other groups. All animals inoculated developed tumors, and all presented with anemia and biochemical abnormalities when compared to healthy animals. Hematologic and biochemical parameters of the animals with cancer treated with *A. sylvaticus* were compared with the parameters in animals with cancer that were administered placebo solution. Significant differences were noted in the number of erythrocytes, as well as hemoglobin and hematocrit levels. The hematimetric indices presented normal levels, and no significant differences were noted between Group 1 (tumor/Agaricus) and Group 2 (tumor/placebo) (Table 1). No statistically significant differences were noted in the leukocyte counts when Group 1 (tumor/Agaricus) and Group 2 (tumor/placebo) were compared (Table 2).

The healthy animals treated with *A. sylvaticus* presented no significant alterations in erythrocyte counts, leukocyte counts, and hematimetric indices when compared to healthy animals administered placebo solution. This finding indicates that the mushroom is not hazardous to blood cells (Tables 3 and 4).

Significant differences between Group 1 (tumor/Agaricus) and Group 2 (tumor/placebo) were noted in levels of triglycerides, urea, and CRP (Table 5). The healthy animals treated with *A. sylvaticus* (Group 3) presented no significant differences in biochemical parameters when compared to healthy animals administered the placebo solution (Group 4) (Table 6).

Discussion

Anemia is present in many patients with cancer at the time of diagnosis or as a result of chemotherapy (1). This is usually termed "anemia of chronic diseases," and the three categories of diseases associated with it are infection, inflammation, and neoplasia. Changes in the pattern of iron distribution are characteristic of this kind of anemia (21, 22, 23).

Animals inoculated with experimental tumor models also present anemia, and there is no clear explanation for this phenomenon. It is suggested that increased levels of pro-inflammatory cytokines, such as IL-1, IL-6, TNF-α, and INF-δ, would induce iron retention by the reticuloendothelial system, gastrointestinal tract, and liver, thereby exerting an inhibitory effect on erythroid precursors (24).

Table 2. White Blood Cells of Rats Inoculated with Walker 256 Tumor and Treated with *A. sylvaticus* or Placebo[a]

Test	*A. sylvaticus* (Group 1)	Placebo (Group 2)	Significance level
Leukocytes (/mm^3)	$9.22 \pm 4.21 \times 10^3$	$8.52 \pm 5.64 \times 10^3$	$P \geq 0.05$
Lymphocytes (/mm^3)	$3.00 \pm 1.68 \times 10^3$	$2.66 \pm 2.11 \times 10^3$	$P \geq 0.05$
Bastonetes (/mm^3)	0	0	0
Neutrophils (/mm^3)	$4.31 \pm 2.76 \times 10^3$	$3.97 \pm 2.78 \times 10^3$	$P \geq 0.05$
Eosinophils (/mm^3)	$0.23 \pm 0.13 \times 10^3$	$0.19 \pm 0.12 \times 10^3$	$P \geq 0.05$
Basophils (/mm^3)	$0.28 \pm 0.15 \times 10^3$	$0.25 \pm 0.1 \times 10^3$	$P \geq 0.05$
Monocytes (/mm^3)	$1.07 \pm 0.8 \times 10^3$	$1.65 \pm 1.2 \times 10^3$	$P \geq 0.05$

[a] Univariate analyses (ANOVA). Tests: Bonferroni and Newman-Keuls. Results represent the mean ± SD ($n = 20$) in each group.

In the present work, we observed a reduction in the number of red blood cells, hematocrit, and hemoglobin in both Group 1 (tumor/Agaricus) and Group 2 (tumor/placebo) compared with healthy animals administered a placebo solution. This observation is indicative of anemia of hemolytic origin, which has been described in other types of tumors. The red blood cell flux is greater in tumors than in normal tissues, and tumor cells have the capacity to lyse erythrocytes through a hemolytic factor (4).

The erythrocytes of animals with cancer exhibit an enhanced uptake of extracellular polyamines that can crosslink endogenous erythrocyte membrane proteins by forming weak bonds with adjacent negatively charged lipids or protein moieties. This process leads to rheologically abnormal red blood cells that could be trapped and destroyed by splenic macrophages because of their abnormal characteristics (4).

Biologically active substances with immunomodulator, anti-inflammatory, and antidiabetic effects, as well as substances that stimulate hematogenesis, are present in medicinal mushrooms (25).

Various metabolites of mushrooms, especially carbohydrates, have been reported to affect bone marrow cells and induce hematopoiesis (26). The β-D-glucans are responsible for the hematopoietic activity of a new cultivable mushroom, *Sparassis crispa*. The 6-branched 1,3-β-glucan of *S. crispa*, termed SCG, enhances the hematopoietic response of mice with cyclophosphamide-induced leukopenia from a qualitative as well as quantitative point of view (27).

A significant increase in the number of erythrocytes and the levels of hemoglobin and hematocrit was observed in animals of Group 1 (tumor/Agaricus) when compared to Group 2 (tumor/placebo), suggesting that compounds of the *A. sylvaticus* mushroom have beneficial effects on the anemia of animals with cancer.

The anti-inflammatory properties of many mushroom extracts have been reported, such as the metabolic extract of *Pleurotus pulmonarius*, which can reduce carrageenan-induced and formalin-induced paw edema in mice. The activity is comparable to that of the reference agent, diclofenac (28). The improvement of hematologic parameters due to the administration of *A. sylvaticus* solution may be related to the reduction of inflammatory mediators that can interfere with hematopoiesis.

In the present study, abnormalities in red blood cell counts were observed in animals with cancer, but the rates of mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration were normal in all animals with cancer. These parameters presented higher ranges in animals of Group 1 (tumor/Agaricus) compared with those of Group 2 (tumor/placebo), although no statistically significant differences were identified.

An increased number of leukocytes was found in animals with cancer, such as in other studies (4, 29). This condition is a consequence of autonomous production of colony-stimulating factors by tumors (30). These cytokines enhance the production of granulocytes and their release from bone marrow (31). No significant differences were determined in the number of leukocytes between Group 1 (tumor /Agaricus) and Group 2 (tumor/placebo), indicating

Table 3. Red Blood Cells and Hematimetric Indices of Healthy Rats Not Inoculated with Walker 256 Tumor and Treated with *A. sylvaticus* or Placebo[a]

Test	*A. sylvaticus* (Group 3)	Placebo (Group 4)	Significance level
Erythrocytes	$6.39 \pm 1.39 \times 10^6$	$6.15 \pm 1.53 \times 10^6$	$P \geq 0.05$
Hemoglobin (g/dl)	13.41 ± 1.25	13.41 ± 2.08	$P \geq 0.05$
Hematocrit (%)	39.39 ± 3.20	38.82 ± 4.03	$P \geq 0.05$
MCV (fl)	63.34 ± 11.98	61.65 ± 12.79	$P \geq 0.05$
MCH (pg)	22.91 ± 4.54	22.39 ± 4.57	$P \geq 0.05$
MCHC (%)	35.31 ± 1.53	35.22 ± 1.10	$P \geq 0.05$

[a] Univariate analyses (ANOVA). Tests: Bonferroni and Newman-Keuls. Results represent the mean ± SD ($n = 20$) in each group.

Table 4. White Blood Cells of Healthy Rats Not Inoculated with Walker 256 Tumor and Treated with *A. sylvaticus* or Placebo[a]

Test	*A. sylvaticus* (Group 3)	Placebo (Group 4)	Significance level
Leukocytes (/mm^3)	$6.08 \pm 2.64 \times 10^3$	$6.94 \pm 4.50 \times 10^3$	$P \geq 0.05$
Lymphocytes (/mm^3)	$4.06 \pm 1.94 \times 10^3$	$4.25 \pm 2.27 \times 10^3$	$P \geq 0.05$
Bastonetes (/mm^3)	0	0	0
Neutrophils (/mm^3)	$1.42 \pm 1.30 \times 10^3$	$1.25 \pm 0.93 \times 10^3$	$P \geq 0.05$
Eosinophils (/mm^3)	$0.19 \pm 0.12 \times 10^3$	$0.19 \pm 0.12 \times 10^3$	$P \geq 0.05$
Basophils (/mm^3)	$0.07 \pm 0.1 \times 10^3$	$0.11 \pm 0.09 \times 10^3$	$P \geq 0.05$
Monocytes (/mm^3)	$0.065 \pm 0.1 \times 10^3$	$0.024 \pm 0.04 \times 10^3$	$P \geq 0.05$

[a] Univariate analyses (ANOVA). Tests: Bonferroni and Newman-Keuls. Results represent the mean ± SD ($n = 20$) in each group.

that *A. sylvaticus* treatment was not able to return the number of leukocytes to normal levels.

Lymphocytopenia was also observed in animals with cancer, and this condition is not clearly understood (21). Impaired lymphocyte activation is a common feature in patients with cancer (32). Enhanced lymphocyte apoptosis was associated with an impairment of nuclear factor κB (NF-κB). The role of NF-κB as a survival factor has been extensively described, and this ubiquitous factor has been implicated in the transcriptional regulation of many inhibitors of apoptosis (33, 34). No significant differences were determined between cancer animals treated with *A. sylvaticus* and cancer animals treated with placebo.

The animals treated with *A. sylvaticus* that were not inoculated with Walker 256 tumor (Group 3) presented normal levels of red blood cells, hematimetric indices, and white blood cells compared to healthy animals treated with placebo solution (Group 4), suggesting that *A. sylvaticus* causes no damage to blood cells. Novaes *et al*. (15) studied the effects of this mushroom in an acute toxicity assay, and the results showed that *A. sylvaticus* has no toxic effects on blood cells.

A number of factors appear to mediate the increased production of CRP. In injury, the pro-inflammatory cytokines stimulate the production of CRP. In patients with cancer, CRP is stimulated by IL-6 and other factors (10, 35). Elevated levels of CRP are associated with poor patient outcome (12).

The properties of medicinal mushrooms also produce anti-inflammatory effects. Some metabolites can modulate the action of inflammatory cytokines. Immunosuppressive effects of mushrooms have also been observed (26). In the present study, cancer animals treated with *A. sylvaticus* presented lower levels of CRP, compared to cancer animals administered placebo. This finding indicates that *A. sylvaticus* may reduce pro-inflammatory cytokine levels and that the animals may have a better prognosis compared with animals treated with placebo.

Cancer-related anorexia/cachexia syndrome is a common finding and plays an important role in a patient's outcome. In addition to reduced food intake, numerous alterations in protein, carbohydrate, and lipid metabolism have been reported in patients with cancer. The breakdown of body proteins and oxidation of released amino acids generate ammonia, which is predominantly converted into urea by the liver. The rate of urea production is an indicator of net protein catabolism, which increases with the advancing tumor state. During periods of severe metabolic stress, protein catabolism and urea production may increase significantly (6, 36).

Rats inoculated with Walker 256 tumor presented higher levels of urea compared to healthy animals, but the cancer animals that received *A. sylvaticus* (Group 1) solution presented a significant decrease of blood urea levels compared to cancer animals treated with placebo (Group 2). The mushroom *A. sylvaticus* is rich in proteins and amino acids, and administration of amino acids and proteins as nutritional supplements reduce urea formation (37).

Daily protein intake is essential for the preservation of muscle mass and body nitrogen reserves. The creatinine

Table 5. Biochemical Parameters of Rats Inoculated with Walker 256 Tumor and Treated with *A. sylvaticus* or Placebo[a]

Test	*A. sylvaticus* (Group 1)	Placebo (Group 2)	Significance level
CRP (mg/dl)	0.23 ± 0.20	0.46 ± 0.20	$P \leq 0.05$*
Creatinine (mg/dl)	0.635 ± 0.123	0.725 ± 0.725	$P \geq 0.05$
Urea (mg/dl)	74.05 ± 40.09	104.5 ± 65.81	$P \leq 0.05$*
Triglycerides (mg/dl)	276.35 ± 79.52	325.15 ± 76.64	$P \leq 0.05$*
Glucose (mg/dl)	126.05 ± 44.67	110.65 ± 58.54	$P \geq 0.05$

[a] Univariate analyses (ANOVA). Tests: Bonferroni and Newman-Keuls. Results represent the mean ± SD ($n = 20$) in each group.
* Statistically significant.

Table 6. Biochemical Parameters of Healthy Rats Not Inoculated with Walker 256 Tumor and Treated with *A. sylvaticus* or Placebo[a]

Test	*A. sylvaticus* (Group 3)	Placebo (Group 4)	Significance level
CRP (mg/dl)	0.23 ± 0.23	0.21 ± 0.19	$P \geq 0.05$
Creatinine (mg/dl)	0.56 ± 0.08	0.55 ± 0.07	$P \geq 0.05$
Urea (mg/dl)	59.10 ± 7.99	55.65 ± 8.49	$P \geq 0.05$
Triglycerides (mg/dl)	159.80 ± 50.56	145.10 ± 46.09	$P \geq 0.05$
Glucose (mg/dl)	215.20 ± 59.90	197.15 ± 26.63	$P \geq 0.05$

[a] Univariate analyses (ANOVA). Tests: Bonferroni and Newman-Keuls. Results represent the mean ± SD ($n = 20$) in each group.

level has been shown to be a useful marker of protein in evaluation of nutritional status (38). Altered levels of creatinine were observed in cancer animals compared to healthy animals. No significant difference was observed between levels of creatinine of the animals with cancer treated with *A. sylvaticus* and those given placebo.

Tumor cells are known to have a high rate of glucose consumption and to show increased rates of aerobic glycolysis (39). In experimental animal models, hypoglycemia is a characteristic finding. *In vivo* studies of human tumors have demonstrated significant glucose use and lactate production (40).

In the present study, animals with cancer presented lower levels of glucose compared to healthy animals. Rats treated with *A. sylvaticus* (Group 1) presented glucose values nearer the normal range, when compared to those treated with placebo (Group 2), although this difference was not statistically significant.

Tumor-bearing animals have decreased activity of the enzyme lipoprotein lipase (LPL), which is responsible for triglyceride clearance. One possible mechanism of the decreased LPL level is hypoglycemia, which is induced by the presence of the tumor. Glucose stimulates LPL translation and post-translational processing in cultured rat adiposities (40).

The triglyceride levels of the animals with cancer were abnormal, but those treated with *A. sylvaticus* (Group 1) presented a significant reduction compared to cancer animals treated with placebo (Group 2). This finding may be related to the improvement of glucose levels.

Food and diet play a major role in determining the quality of life of patients with cancer. Some therapies are focused on altered nutrient intake (41); the aim of nutritional support is the prevention of nutritional decline and, if the patient's status does decline, the slowing of progression to cachexia (42).

The improvement of biochemical parameters noted in this study indicates that animals experience fewer metabolic abnormalities as a result of the nutritional properties of *A. sylvaticus*. The antitumoral effects of this mushroom can improve an animal's general state of health, consequently improving hematologic and biochemical parameters.

In the present study, *A. sylvaticus* treatment was able to reduce anemia in animals with cancer. Biochemical parameters were nearer the normal levels in animals treated with this mushroom. These results suggest that administration of *A. sylvaticus* extract has beneficial effects in rats with Walker 256 tumor, especially in the hematopoietic system.

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