

# CORPET NEWS

Vol. 2

English Edition

*Coriolus versicolor*

*Distribution restricted to Veterinary Doctors and Nurses*

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## Immunonutrition with Mushrooms: Function of Glyconutrients

In both human and animal health, the main function of glyconutrients, when bound to proteins, is to facilitate communication between cells. Glico science is the study of carbohydrates and sugars and their respective biological functions. The (eight) 8 sugars or saccharides, which are indicated below, are needed for communication between cells and for the knowledge of their interaction, which is vital for the detection of cell degeneration and its subsequent impact on health.

- ♦ Glucose     ♦ Xylose
- ♦ Galactose   ♦ N-acetilgalatosamina
- ♦ Fucose     ♦ N-acetylglucosamine
- ♦ Mannose   ♦ N-acetylneuraminic acid

These glyconutrients, when properly bound to proteins (glycoproteins), allow effective intracellular communication and together with polysaccharides, they function as a precursor for the health of the immune system:

(<http://www.i-amperfectlyhealthy.com/Glyconutrients.html>)

### The Impact of Mushroom Nutrition in Intracellular Communication

Polysaccharides are important components of mushrooms. Monosaccharide's in glycoside bounds can produce molecular branches with a huge range of connections<sup>(1)</sup>. There are as many as 35.560 transformations for four (4) monosaccharide's, which provide variety and flexibility in the connections. The proteoglycan of mushrooms represent a system of transmission of information, which operate quickly<sup>(2)</sup>.

Since mushroom proteoglycans are responsible for the evolution of the "matrix" of the connective tissue in humans (animal), it may well be that the evolutionary development of unicellular organisms to multicellular require transmission of information, and as is often said, this transmission through the extracellular matrix of higher organisms can occur at the speed of sound<sup>(1). (3)</sup>.

### Which are the Enzymes Produced by Glyconutrients

As the nutrition with *Coriolus versicolor*, mushroom provides glyconutrients which in turn are responsible for essential enzymes. These enzymes develop three key functions which balance the immune system:

#### 1. Preventing Oxidative Stress

- ♦ Laccase Activity
- ♦ Superoxide Dismutase Activity (SOD)

#### 2. Avoiding Cell Growth

- ♦ Protease Activity
- ♦ Pyranose Oxidase Activity

#### 3. Promoting Detoxification

- ♦ Peroxidase Activity
- ♦ Cytochrome P-450 Activity



Combined with the enhancement of intracellular communication, these enzyme functions are key factors that balance or "rebalance" the immune system.

1. Pischinger A. Matrix and Matrix Regulation: Basis for a Holistic Theory in Medicine. Brussels, Belgium: Editions Haug International, 1991.

2. Alberts B, Bray D, Lewis J, et al. Molecular Biology of the Cell. 3<sup>rd</sup> ed. New York: Garland Publishing, 1994; p 17.

3. Smith JE, Rowan NK, Sullivan R, Medicinal Mushrooms: Their Therapeutic Properties and Current Medical Usage with Special Emphasis on Cancer Treatments. London: Cancer Research UK, 2000 p 220 [http://www.icnet.uk/labs/med\\_mush/med\\_mush.html](http://www.icnet.uk/labs/med_mush/med_mush.html)

# Tumors in Pets: prevention with the use of mushroom nutrition

LNIV  
Laboratório Nacional  
de Investigação Veterinária

XXIV<sup>o</sup> MEETING OF VETERINARIES FROM MACARONÉSIA  
Angra do Heroísmo, October 5th and 6th, 2006



X<sup>o</sup> INTERNATIONAL CONGRESS OF VETERINARY MEDICINE IN PORTUGUESE LANGUAGE  
Ponta Delgada, October 9th and 10th, 2006



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## INTRODUCTION

The holistic philosophy of veterinary doctors consists essentially of observing all aspects of the animal, showing openness to the application of all kinds of treatments. Normally, his attention is focused on nutrition and diet, environment, lifestyle of the animal, physical and psychological well being of the animal and in the prophylactic treatment. Communication between animal, owner and veterinary is essential.

The Holistic veterinaries use both conventional and alternative therapies, depending on each case. They consider that modern clinical techniques such as Ultrasound, CT, sophisticated laboratory tests and surgical interventions, are necessary for the diagnosis and treatment of animal diseases. They believe that alternative medicines (complementary, fitomedicine and acupuncture), play a significant role.

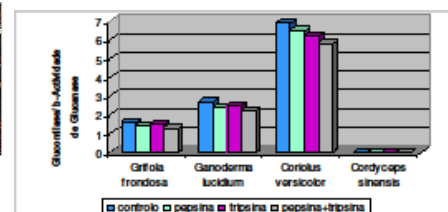
Medicinal Mushrooms are known for their properties in balancing the functioning of the immune system. They have been used for centuries to treat different diseases. It is evident that **each mushroom has specific anti-carcinogenic properties**. The anti-tumor activity has been demonstrated with *Grifola frondosa* (Maitake), *Coriolus versicolor*, *Ganoderma lucidum* (Reishi), *Letinula edodes* (Shiitake), *Agaricus blazei*, and *Cordyceps sinensis*. **Miraculous mushrooms do not exist.**

Not all of these mushrooms were subjected to rigorous scientific studies. The main anticancer constituent in these mushrooms is the  $\beta$ -glucan. This polysaccharide is basically a combined amino acid molecule that stimulates or modulates the immune system, by activating immune cells, such as macrophages and T-cell support, and increases levels of haemoglobin to produce a greater response to bacteria, viruses or tumor cells. It protects the liver and acts as a tonic in the central nervous system and heart, lowers cholesterol levels and inhibits allergic reactions. It enhances the production of interleukin-1 and 2, it is anti-inflammatory and inhibits the growth of malignant tumors. These polysaccharides do not act directly on the tumor cells, instead, they influence by activating the function of the immune system of the host. In addition to polysaccharides, mushrooms contain enzymes (peroxidase, laccase, protease, glucoamylase,  $\beta$ -glucanase, cytochrome P450, cytochrome P450 reductase, SOD), which strengthen the immune system. With advancing age, some viral infections and other causes are highly related to the development of cancer. The immune system of the animal can become so weak that the normal immune functions have no ability to fight tumor cells.

Enzyme Analysis, <i>Coriolus versicolor</i> (biomass) Protein and Sugar in the presence of Trypsin	<i>Coriolus versicolor</i> 500 mg
1 Protein Content	17.3 mg
2 Reducing Sugars	14.8 mg
3 Protein - bound polysaccharide	82.1 mg
4 Peroxidase Activity	64.5 mU
5 Laccase Activity	535.1 mU
6 Glucoamylase / $\beta$ -glucanase Activity	6.2 U
7 Superoxide Dismutase Activity (SOD)	68.5 U
8 Cytochrome P-450	0.52 nmoles
9 Cytochrome P-450 reductase	11.1 mU



Prophylactic Care	
Dog / Cat (weight)	<i>Coriolus versicolor</i> (grs/Day)
< 10 Kg	1.0
10 a 30 Kg	2.0
> 30 Kg	4.0



Ongoing research aims to study mushroom immunonutrient supplementation for small pets, as a clinical tool for strengthening the immune system of the animals. This study was carried out using a mushroom (*Coriolus versicolor*) biomass, which is commercially available for use in animals and humans. Clinical experience has shown that dogs and cats with six years of age or more, benefit with the application of *Coriolus versicolor* supplementation as a factor supporting the immune system as well as a detoxifying agent that can absorb free radicals accumulated with advancing age. Supplementation with the mushroom levels the normal function of the immune system in animals of a certain age, at risk of developing cancer.

After a period of application of this supplementation, positive changes were found in immune parameters (increased activity of T cells, increased natural killer (NK) cells). In a study, conducted at the IPO (Portuguese Institute of Oncology) in Coimbra, it was proved that in viral infections (HPV strains), daily supplementation with *Coriolus versicolor* within a year had a significant impact on risk factors for patients (women) with cervical cancer. This work is also supported by the application of *Coriolus versicolor* supplementation in patients with chronic fatigue syndrome (CFS), as after six weeks of supplementation, an increase of 35% in the activity of NK cells as well as in the activation of T cells (CD3 + CD26) was found in 66 % of the patients.

The role of protein-bound polysaccharide complexes in *Coriolus versicolor*, and levels of various enzymes and secondary metabolites (thrombin inhibitors), have been researched in an attempt to explain the mechanism of action of this mushroom as an inhibitor of cancer, oxidative stress, growth of certain cells and detoxification. The combined impact of these various forms of action, improves the immune profile of both humans and animals, balancing the normal functioning of the immune system.

## CONCLUSIONS

*Coriolus versicolor* (biomass) contains important enzymes, polysaccharides bound to proteins and secondary metabolites, which play an important role in carcinogenesis. *Coriolus versicolor* is a form of immunonutrition, and not a substitute for a medicinal product or a medical procedure.

# Dietary Supplementation with Mushrooms applied as Immunonutrition in Dogs

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## Three Dogs with Visceral Leishmaniasis

Visceral Leishmaniasis or Kala-azar is a disease caused by protozoa of the genus *Leishmania*.

In Portugal, Visceral Leishmaniasis is an important disease, affecting dogs, wolves, foxes and man, with an incubation period of several months to several years.

Leishmanias reach the macrophage-rich organs such as the spleen, liver and bone marrow. Internal lesions are primarily characterized by lymphadenopathy, splenomegaly, hepatomegaly and external injuries, cutaneous manifestations, as furfurácea scaling, ulcers and areas of darkened skin, among others.

The immune system can respond effectively producing a cytotoxic response (TH1) that destroys the macrophage carriers of *Leishmania*. In these cases, the infection is controlled and the light symptoms disappear developing only cutaneous manifestations. However, if the immune system develops a humoral or Th2 response, with production of antibodies, the leishmanias which are in macrophages will not be destroyed, because they are out of reach of antibodies. In these cases the infection progresses to severe visceral leishmaniasis.

The traditional treatment refers to the antimony compounds, pentamidine, amphotericin or miltefosine. However, the administration of these drugs normally originates side effects which often lead to the sacrifice of sick animals, to prevent possible human contamination.

The use of a preventive vaccine is at the moment not yet available. We have therefore thought to use *Coriolus versicolor* \* as an immunonutrient aiming to enhance the immune system with a TH1 response, in order to prevent severe visceral leishmaniasis.

### Case Study 1: December 5th, 2005

Yorkshire Terrier Dog breed, aged 2 years and a half, weight: 4.7 kg, resident in Amadora, Portugal  
Clinical diagnosis confirmed by IFI test results  
Supplementation with *Coriolus versicolor*\* - Schedule: 4 tablets of 500 mg/day for a period of 6 months

### Case Study 2: December 24th, 2005

S. Bernardo Dog breed, aged 3 years, weight: 58 kg, resident in Sintra, Portugal  
Clinical diagnosis confirmed by IFI test results  
Supplementation with *Coriolus versicolor*\* - Schedule: 6 tablets of 500 mg/day for a period of 6 months

### Case Study 3: January 27th, 2006

Dog of unknown breed, aged 11 years, weight: 37 kg, resident in Lisbon, Portugal  
Clinical diagnosis confirmed by IFI test results  
Supplementation with *Coriolus versicolor*\* - Schedule: 6 tablets of 500 mg/day for a period of 6 months

In all the above mentioned cases, there was a regression of the previously verified symptomatology, and new laboratory control exams will follow.

\**Coriolus versicolor* (CORPET) is supplied by Mycology Research Laboratories Ltd (MRL) - <http://www.mycologyresearch.com>

For more information, please visit our website: <http://mycologyresearch.com/research/animalhealth>

*Coriolus versicolor* (CORPET) is available at:

Country	Distributor	Phone	E-mail
United Kingdom	Mycology Research Laboratories, Ltd. <a href="http://www.mycologyresearch.com">www.mycologyresearch.com</a>	+44 158 248 5209	<a href="mailto:info@mycologyresearch.com">info@mycologyresearch.com</a>
United States of America	MRL USA - <a href="http://www.mrlusa.com">www.mrlusa.com</a>	+1 888 675 8721	<a href="mailto:luna@mrlusa.com">luna@mrlusa.com</a>

# Dietary Supplementation with Mushrooms applied as Immunonutrition in Cats

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## Case Study 4: Cat with Hypertrophic Cardiomyopathy

### 1st Observation: March 24th, 2006

Sansão is a Cat, a Chartreux breed aged 5 years, which was presented to a clinical examination, showing symptoms of sadness, lack of appetite and showing a heart murmur, upon cardiac auscultation.

Rectal temperature 38.9°C.

He had laboratory exams had been made at the Veterinary Hospital of Restelo (Lisbon), on April 28th, 2006, and a cardiac ultrasound had been made at the Veterinary Institute of the Park, in Lisbon, by Dr. José Sales Luís, on May 8th, 2006, with the following results:

### 1. Biochemical Analysis and CVC

Biochemical Exams		CVC	
ALP	below 50 UI/L	White Blood Cells	8.89 m/mm <sup>3</sup>
GPT/ALT	26 UI/L	Lymphocytes	45.2 % (valor normal: 5-30)
Urea	27 mg/dl	Red Blood Cells	9.35 m/mm <sup>3</sup>
Creatinine	1.6 mg/dl	PLT	1542 m/mm <sup>3</sup>
Glucose	114 mg/dl	VMP	12,2 fl
Total Protein	6.3 g/dl		

### 2. Ultrasound

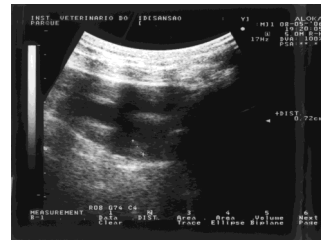


Fig. 1

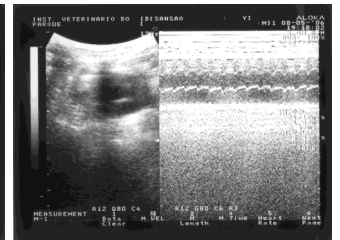


Fig. 2

### Ultrasound Report:

"Sansão has a moderate hypertrophic cardiomyopathy. He does have a murmur II / III upon auscultation which is justified by a mitral insufficiency. Furthermore, he has a small clot in the left atrium, 7mm. In relation to the clot there is a risk of thrombus."

**V.E.:** moderate concentric hypertrophy; **AE:** mild dilation; **RV:** not dilated; **AD:** not dilated; **Mitral:** insufficient

**Tricuspid:** functional; **Aorta:** functional; **Pulmonary:** not observed; **Other:** Good conductivity.

It was decided that Sansão should begin taking *Coriolus versicolor* supplementation from May 24th, 2006, with the following schedule:

**Days 1 to 30** - 1 tablet of 500mg, 2 times a day (crushed and mixed with food) .

**Days 31 to 120** - 1 tablet of 500mg per day (crushed and mixed with food) .

### 2nd Observation: July 24th, 2006

Rectal temperature 38.5 ° C.

The cat appeared to be in good health, with good energy and appetite.

A new ultrasound was required at the Veterinary Institute of the Park, in Lisbon, on August 2006, as well as laboratory exams at the Clinical Laboratory of Dr. Reymão Pinto, SA in Lisbon.

The results were as follows:

### 3. Ultrasound

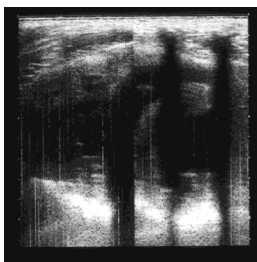


Fig. 3

### 4. Laboratory Analysis

Biochemical Exams	
GPT/ALT	48 UI/L
AST	19 U/L
Urea	68 mg/dl
Creatinine	1.29 mg/dl
Glucose	102 mg/dl

Endocrinology	
FT4 – Free Thyroxine	14.83 pmol/L

### Ultrasound Report:

"Sansão is stable regarding the evolution of the hypertrophic cardiomyopathy, does not have dilation of the left atrium and showed no signs of the clot".

### Ultrasound:

**VE:** concentric hypertrophy; **AE:** not dilated **RV:** not dilated; **AD:** not dilated; **Mitral:** functional; **Tricuspid:** functional

**Aorta:** functional; **Pulmonary:** not observed; **Other:** Good conductivity and good return.

### 3rd Observation: September 30th, 2006

Rectal temperature 38.5 ° C.

The cat appeared to be in good health, with good energy and appetite.

*\*Coriolus versicolor* (**CORPET**) is supplied by Mycology Research Laboratories Ltd (MRL) - <http://www.mycologyresearch.com>



# Dietary Supplementation with Mushrooms applied as Immunonutrition in Dogs

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## Case Study 5: “Boss”, Irish Setter Breed (9 years of age) with a Prostate Tumor

(see page 5 – CORPET NEWS, Vol. 1 – March/2006)

**Observation:** Boss continued being observed regularly, maintaining the recommended supplementation (3 tablets of 500mg of *Coriolus versicolor*). Below, are the results of the last abdominal ultrasound, which took place on September 2006, at the Veterinary Hospital of Restelo (Lisboa):

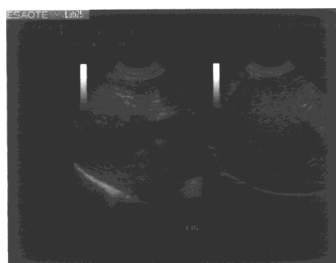


Fig. 1

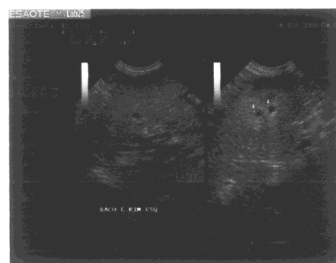


Fig. 2

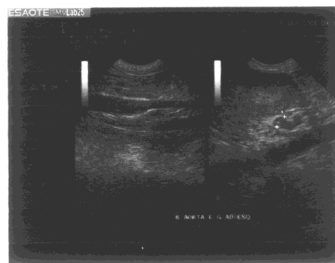


Fig. 3

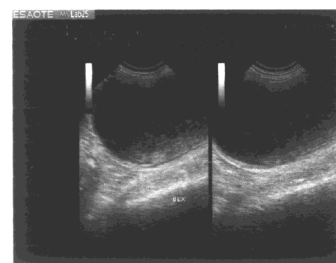


Fig. 4

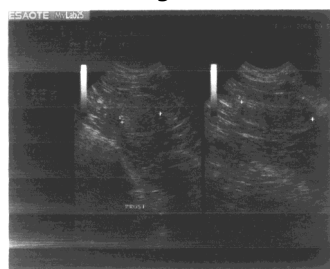


Fig. 5

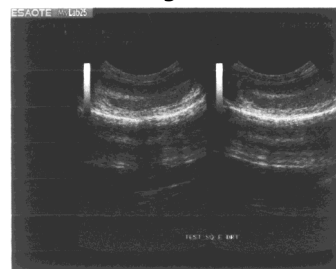


Fig. 6

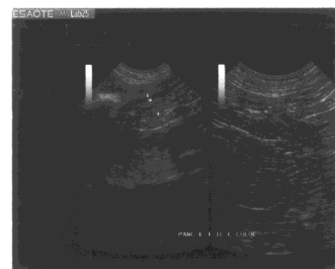


Fig. 7

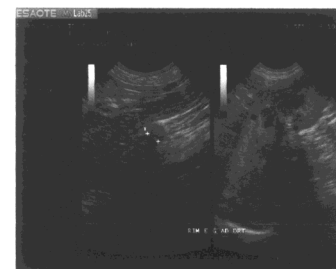


Fig. 8

## Comments

- ♦ Liver with normal dimensions and regular contours, with maintained echogenicity, homogeneous parenchyma, focal hepatic lesions not observed, with ultrasound expression. Observed segments of the great vessels, normal portal and suprahepatic veins. No ectasia of the intrahepatic billiards was observed.
- ♦ Without evidence of pure free fluid at the intra-peritoneal level of peri-hepatic, peri-splenic and inter-loops.
- ♦ Distended gallbladder, thin wall and echogenic fluid content.
- ♦ Normodimensional spleen, with regular contours, with maintained echogenicity, with homogeneous ecostructure, without evidence of focal splenic lesions with ultrasound expression.
- ♦ Kidneys with normal dimensions, regular contours, with increased and normal cortico-medullary differentiation. Absence of ectasia-caliceal system pile bilaterally as well as no signs of stones or masses. In the cortical region of both kidneys, small hypo echoic nodules are observed, thin anecogenic Wall and posterior acoustic enhancement.
- ♦ Noemodimensioned left adrenal gland, with normal ecostructure, without evidence of focal lesions with ultrasound expression. Right adrenal gland with a slightly increased size (8 mm).
- ♦ Partially distended bladder, with regular contours, inside echoes with very small movement can be observed. Apparently it has no thickening of the wall and no evidence of gallstones or parietal lesions with end luminal projection.
- ♦ The observed portions of the gastro-intestinal tract are shown to be normal by ultrasound.
- ♦ Pancreatic segments visualized normal and with homogeneous ecostructure.
- ♦ Apparently, testicle dimensions are normal, with regular contours and conserved ecostructure. No epididymal changes are observed. No evidence of peri-testicular or scrotal fluid ectasia.

## Conclusion

The echogenicity of the renal cortex may correspond to processes related to aging and if there is a clinical suspicion of kidney failure, it is recommended to evaluate kidney function, if it has in fact suffered changes. We must consider that there is a nonspecific nephropathy (DD: nephritis glomerular, interstitial nephritis and acute tubular necrosis). Both kidneys have small cysts that do not show to have pathological significance.

Taking into account the absence of clinical signs of hyperadrenocorticism, the increase in size, of the right adrenal gland, should involve a situation of benign adenoma hyperplasia or non-functional, often found in older animals. However, it is recommended to monitor any clinical or laboratory signs of Cushing (DD: pituitary Cushing, malignant neoplasm of left adrenal gland) .

The bladder internal echoes should correspond to sediment, which may also be cellular and must be correlated to its importance and aetiology with the clinical picture and any laboratory tests, including urine tests.

The prostate is slightly stunted, not showing any nodular or cystic lesions. Initially it is supposed to be a benign prostatic hyperplasia which responded well to therapy.

# 10<sup>th</sup> Congress of the European Society of Veterinary and Comparative Nutrition

## Cancer Prevention with Supplementation of Diets with Botanicals



ESCVN/ ECVCN – 5 – 7<sup>th</sup> October 2006  
Nantes - France



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### INTRODUCTION

This work was conducted with a mushroom (*Coriolus versicolor*) which is in the market for human and animal use. Mushroom polysaccharides, particularly  $\beta$ -glucans, have anti-tumour and immunomodulating properties. These polysaccharides do not directly attack cancer cells, but instead exert their effects by activating immune responses in the host.

The use of  $\beta$ -glucans as adjuvants for monoclonal antibody treatment has also been explored, because  $\beta$ -glucans bind to the complement receptor and enhance leukocyte killing of tumour cells through naturally occurring anti-tumour antibodies.  $\beta$ -glucans also appear to recruit tumouricidal granulocytes, dramatically enhancing tumour killing when combined with monoclonal antibody therapy. Mushroom  $\beta$ -glucans affect immune function by infiltrating, through specific receptors, tumours and activating dendritic cells, suppressing certain enzymes, or by influencing mitotic activity. Recent work in HPV cervical cancer in women have shown positive role of mushrooms.

The vicious circle of chronic toxic overload is described in which there is a series of detoxification steps leading to oxidative stress, causing free radical production which results in health conditions generally solved with non-steroid anti-inflammatory and antibiotics. These drugs induce increased permeability of the intestinal wall which is responsible for an overloaded liver causing detoxification problems.

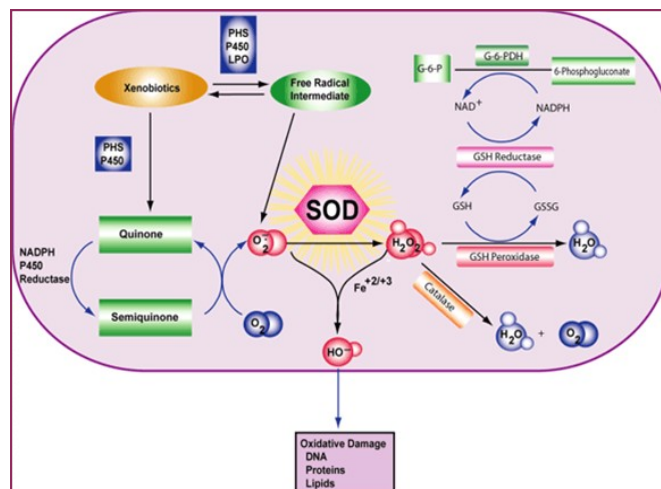
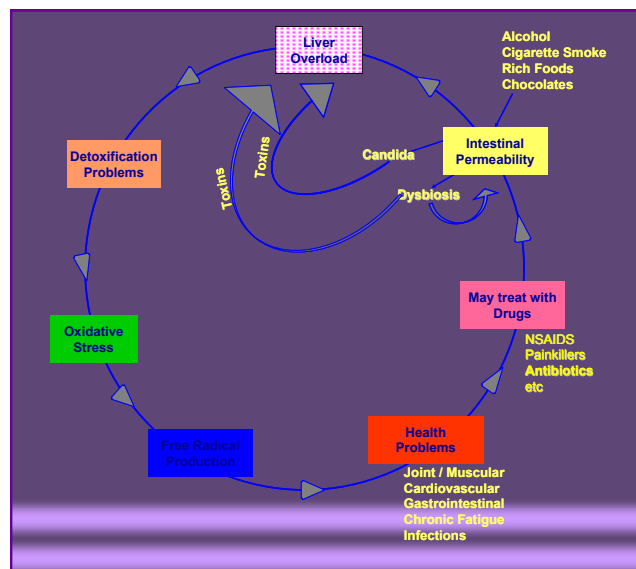
### RESULTS

Table I provides levels of SOD, cytochrome P-450, cytochrome P-450 reductase (NADPH dependent), laccase, peroxidase, protease,  $\beta$ -glucanase, protein-bound polysaccharides and secondary metabolites in 6 tablets (3 g) of *Coriolus versicolor* (biomass).

In Table I the impact of gastric acid was simulated when comparing the enzyme content in the absence of proteolytic enzymes, in pepsin and in trypsin. The purpose of this comparison was to determine the degradation of enzyme action in the intestinal tract of the human body.

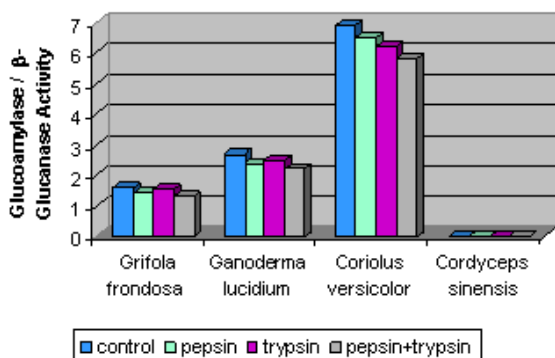
<i>Coriolus versicolor</i> *	Absence of Proteolytic Enzymes	In presence of Pepsin	In presence of Trypsin
1 Protein (content)	103.8 mg	94.2 mg	99.6 mg
2 Reducing sugars	88.8 mg	87 mg	84.6 mg
3 Protein - bound polysaccharide	549 mg	483 mg	492.6 mg
4 Peroxidase activity	403.2 mU	362.4 mU	387 mU
5 Laccase activity	3129 mU	3069.6 mU	3210.6 mU
6 Glucoamylase/beta-glucanase activity	41.4 U	30.0 U	37.2 U
7 Protease activity	35.4 U	30.0 U	31.2 U
8 Glucose 2 - Oxidase activity	297 mU	163.2 mU	270.0 mU
9 Cytochrome P-450	3.06 nmoles	2.94 nmoles	3.12 nmoles
10 Cytochrome P-450 reductase	71.4 mU	57.12 mU	66.6 mU
11 SOD activity	462.6 U	367.2 U	411 U
12 Secondary metabolites (Thrombin inhibitors)	59 %	54,2 %	52 %

### The Vicious Circle of Chronic Toxic Overload



### Prevention in Dogs/Cats

Weight	<i>Coriolus versicolor</i> (g/ Dia)
< 10 Kg	1.0
10 a 30 Kg	2.0
> 30 Kg	4.0



### CONCLUSIONS

Mushrooms contain several important enzymes, protein-bound polysaccharides, and secondary metabolites which play an important role in carcinogenesis, through specific receptors, such as:

Increase in the activity of T and NK Cells, in enzyme profiles, proteases, cytochrome P450 reductase, laccase,  $\beta$ -glucanase, peroxidase and SOD.

Further research is required to study the effect of mushroom immunonutrition on the levels of other key proteins, enzymes and metabolites *in vivo* which are involved in cancer of virus origin.