VETERINARY HEALTHCARE

CORPET Handbook
For Horses and Ponies

CORPET
750 grams Coriolus versicolor biomass powder

Complementary feedstuff to assist recovery from viral infections.

ANEID PRESS
CORPET Handbook

Coriolus versicolor

HORSES and PONIES

for Veterinary Medicine Practitioners
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NOTE:

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Recommended Price: 15€ (VAT included)/ £10.50/$20.00
I. MUSHROOM NUTRITION AS IMMUNONUTRITION FOR HORSES AND PONIES

It has been known for over a century that some enzymes can be used in the prevention and even treatment of several clinical conditions and enzyme utilization in the form of mushroom nutrition supplementation may be useful for supporting the immune system in patients with either toxic overload or with viral infection directly linked to oncological risk \(^{(1)}\) \(^{(2)}\) \(^{(3)}\) \(^{(4)}\).

In general, the oral administration of certain enzymes contributes to the efficacy of the following functions which can reduce chronic toxic overload in the organism \(^{(4)}\):

- Restores balance to the internal environment (such as neutral pH levels)
- Removes toxic substances
- Helps re-establish intestinal bacterial equilibrium
- Strengthens the immune system
- Improves cell metabolism

**Mushroom Nutrition and Chronic Fatigue Syndrome-Post Viral Syndrome**

An example of how mushroom nutrition can improve the immune system was demonstrated using *Coriolus versicolor* (biomass) supplementation in thirty (30) Chronic Fatigue Syndrome (CFS) patients \(^{(5)}\).

CFS patients with combinations of high antibody levels to Epstein Barr Virus (EBV) and/or Herpes Simplex Virus (HHV6) and Cytomegalovirus (CMV) were given 6 tablets (3 g) per day of *Coriolus versicolor* supplementation for two weeks, followed by 3 tablets (1.5 g) per day for six weeks \(^{(6)}\).

After supplementation, the following changes in immune parameters were noted \(^{(7)}\):

a) T cell activation (CD3 + CD26) in two-thirds of the patients.

b) Natural Killer Cells—before treatment the average NK cell level was 129.64/mm\(^3\). After treatment this had increased to 175.00/mm\(^3\), an increase of 35%.

In summary, *Coriolus versicolor* supplementation significantly improved the immune profile of the CFS patients over 8 weeks of supplementation \(^{(8)}\).


\(^{(6)}\) Ibid., page 107.

\(^{(7)}\) Ibid., page 108

\(^{(8)}\) Ibid., page 109
Mushroom Nutrition and Human Papillomavirus Infection (HPV)

More recent work with *Coriolus* supplementation for Human Papillomavirus Virus (HPV) patients has revealed that daily supplementation (3 g per day) of *Coriolus versicolor* (biomass) over one year had a significant impact on the risk factors for CIN-1 HPV Low Grade Squamous Intrapithelial Lesion (LSIL) patients. For example, in 13 CIN-1 (LSIL HPV) patients who took *Coriolus* supplementation\(^9\):

a) Only 2 patients had a positive cytology (LSIL) at the end of 1 year (remained at a CIN-1 status and did not return to CIN-0), a 85% success rate.

b) Of the 6 patients categorized as “high risk” (HPV+) at the beginning of the trial; at the end of the trial all 5 were categorized as “low risk” (HPV-).

A new evaluation will take place after two years with cervical cytology, colposcopy (eventual biopsy) and HPV tipification\(^10\).

While these clinical results are considered encouraging for CIN-1 (LSIL HPV) patients, the question is “How does *Coriolus versicolor* assist the body’s immune system?”. In the following sections the impacts of protein-bound polysaccharide complexes as well as the enzymatic action that characterizes *Coriolus versicolor* are reviewed.

The role of protein-bound polysaccharide complexes in *Coriolus versicolor*

Since the 1960’s, extracts of *Coriolus versicolor*, known as PSK (Polysaccharide-K /Krestin) and PSP(Polysaccharide-Peptide), have been used in China and Japan as adjunct nutrition to improve the immune system of patients undergoing chemotherapy and/or radiotherapy\(^11\)\(^12\).

In Japanese trials since 1970, PSK significantly extended survival at five years or beyond in cancers of the stomach, colon-rectum, oesophagus, nasopharynge and lung (non-small cell types), and in an HLA B40-positive breast cancer subset\(^13\). PSP was subjected to Phase II and Phase III trials in China and in double-blind trials significantly extended five-year survival in oesophageal cancer as well as significantly improving quality of life, providing substantial pain relief and enhancing immune status in 70-97 percent of patients with cancers of the stomach, oesophagus, lung, ovary and cervix\(^14\).

PSK and PSP boost immune cell production, ameliorate chemotherapy symptoms and enhance tumour infiltration by dendritic and cytotoxic cells. Their extremely high tolerability, proven benefits to survival and quality of life and compatibility with chemotherapy and radiotherepy makes them well suited for cancer management regimes in Japan and Hong Kong\(^15\).

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10 Ibid., page 3.


14 Ibid., page 1-4

The molecular mechanisms of biological response modification are not completely understood, although PSK and PSP are potent immunomodulators with specific activity for T-cells and for antigen-presenting cells such as monocytes and macrophages\(^\text{(16)}\).

A recent publication presents evidence regarding the presence of specific receptors for protein-bound polysaccharides in antigen-presenting cells (APC), B-cells and Helper T-cells\(^\text{(9)}\). The binding of these complexes to these cells triggers a variety of immunological responses including modulation of immunoglobulin production, Helper T-cell differentiation and function and APC - TH interaction. At the same time several reports have been published regarding the induction of apoptosis in several human cancer cell lines due to binding of protein-bound polysaccharides from mushroom strains\(^\text{(17)}\)(\text{(18)})\(^\text{(19)}\).

Pharmacologically active polysaccharides and protein-bound polysaccharides can be isolated from mushroom fruit-bodies, culture mycelium or culture broth of several basidiomycetes strains such as \textit{Coriolus versicolor}. Besides protein-bound polysaccharides, \textit{Coriolus versicolor} contains several other biomolecules of clinical importance including enzymes and secondary metabolites (e.g. antibiotics and terpenes). The biomass form of \textit{Coriolus versicolor} contains protein-bound polysaccharides complexes and has demonstrated immune enhancement via increased NK cell activity.

**Enzyme and secondary metabolite content in Coriolus versicolor (biomass)**

Table I gives 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 \textit{Coriolus versicolor} (biomass). The impact of gastric acid was simulated (\textit{in vitro}) using the proteolytic enzymes pepsin and trypsin in order to determine the degree of degradation due to enzyme action in the human intestinal tract.

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**Table I**

Composition of 3 g of *Coriolus versicolor* Enzyme and Protein Analysis

<table>
<thead>
<tr>
<th></th>
<th>Absence of Proteolytic Enzymes</th>
<th>In presence of Pepsin</th>
<th>In presence of Trypsin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Protein (content)</td>
<td>103.8 mg</td>
<td>94.2 mg</td>
<td>99.6 mg</td>
</tr>
<tr>
<td>2 Reducing sugars</td>
<td>88.8 mg</td>
<td>87 mg</td>
<td>84.6 mg</td>
</tr>
<tr>
<td>3 Protein – bound polysaccharide</td>
<td>549 mg</td>
<td>483 mg</td>
<td>492.6 mg</td>
</tr>
<tr>
<td>4 Peroxidase activity</td>
<td>403.2 mU</td>
<td>362.4 mU</td>
<td>387 mU</td>
</tr>
<tr>
<td>5 Laccase activity</td>
<td>3129 mU</td>
<td>3069.6 mU</td>
<td>3210.6 mU</td>
</tr>
<tr>
<td>6 Glucoamylase/Beta – glucanase activity</td>
<td>41.4 U</td>
<td>30.0 U</td>
<td>37.2 U</td>
</tr>
<tr>
<td>7 Protease activity</td>
<td>35.4 U</td>
<td>30.0 U</td>
<td>31.2 U</td>
</tr>
<tr>
<td>8 Glucose 2 – Oxidase activity</td>
<td>297 mU</td>
<td>163.2 mU</td>
<td>270.0 mU</td>
</tr>
<tr>
<td>9 Cytochrome P - 450</td>
<td>3.06 nmoles</td>
<td>2.94 nmoles</td>
<td>3.12 nmoles</td>
</tr>
<tr>
<td>10 Cytochrome P - 450 reductase</td>
<td>71.4 mU</td>
<td>57.12 mU</td>
<td>66.6 mU</td>
</tr>
<tr>
<td>11 SOD activity</td>
<td>462.6 U</td>
<td>367.2 U</td>
<td>411 U</td>
</tr>
<tr>
<td>12 Secondary metabolites (Thrombin inhibitors)</td>
<td>59 %</td>
<td>54.2 %</td>
<td>52 %</td>
</tr>
</tbody>
</table>

1. Pepsin (500IU/g biomass) at pH 2 for 30 min at 37ºC in an incubator with orbital shaking
2. Trypsin (500IU/g biomass) at pH 7.6 for 30 min at 37ºC in an incubator with orbital shaking.

**Note:** One enzyme unit (U) is defined as the amount of enzyme required to convert one micromole of substrate to product per minute under certain experimental conditions. One milli-enzyme unit (mU) is defined as the amount of enzyme required to convert one nanomole of substrate to product per minute under certain experimental conditions.

Data presented in Table I demonstrates that in simulated digestive tract conditions (pepsin and trypsin) the level of enzyme and secondary metabolites decreased by a factor in the range of 15-20% (20).

**Enzyme effects in Coriolus versicolor supplementation: impact on the immune system**

As outlined in Table I, *Coriolus versicolor* biomass supplementation provides a natural route for enzyme administration. A summary of the mode of action of the aforementioned enzymes is given below:

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* Mushroom samples (in tablet form) were kindly provided by Mycology Research Laboratories Ltd. [www.mycologyresearch.com](http://www.mycologyresearch.com)
Enzymes Preventing Oxidative Stress

i. **Laccase (benzenediol: oxygen oxidoreductase; EC 1.10.3.2)** is present in its active form and catalyses the reduction of di-oxygen to water and the oxidation of a wide range of phenolic or related compounds. This enzyme also catalyses the oxidation of 3-hydroxyanthranilic acid (3-HAA) into cinnabarinic acid (CA) which is of great clinical interest since 3-HAA is produced in large quantities by interferon-γ primed mononuclear phagocytes (7). Furthermore, 3-HAA has been shown to act as a powerful scavenger of reactive oxygen species. On the other hand, cinnabarinic acid (CA) is one of the major products of oxidation of 3-HAA, suggesting that laccase may prevent oxidative damage in mammalian tissues. In a similar manner, a mammalian protein, ceruloplasmin, like laccase, is a member of the blue copper oxidase class of enzymes which also catalyse the conversion of 3-HAA into CA (21).

ii. **Superoxide Dismutase (SOD).** Cellular damage is induced by reactive oxygen species (ROS) which can be either free radicals (e.g. reactive anions containing oxygen atoms) or molecules containing oxygen atoms that either produce free radicals or are activated chemically by them. Examples of ROS include hydroxyl radicals, superoxide and hydrogen peroxide. There are several sources of ROS under physiological conditions such as aerobic respiration, sunlight, UV radiations, chemical reactions and metabolic processes (e.g. peroxisomal β-oxidation of fatty acids, hepatic cytochrome P450 metabolism of xenobiotic compounds). However, under normal physiological conditions, ROS are degraded by the action of superoxide dismutase (SOD), catalase or glutathione (GSH) peroxidase. SOD catalyses the reduction of superoxide anions to hydrogen peroxide. SOD has been shown to play an important role in several clinical conditions, including Alzheimers, Parkinsons, cancer and aging (Fig.1) (22) (23) SOD is a key agent in combating chronic toxic overload.

As NK cells are susceptible to reactive oxygen species (ROS) and lose their activity due to the effects of ROS. Cancer bearing hosts usually suffer from oxidative stress (OS) or toxic overload, and this causes the NK activity to decrease to a significantly lower level than normal. Superoxide dismutase (SOD) mimicking substances found in *Coriolus versicolor* and iron–chelating chlorine e6-Na (FeCNa), can restore the NK cell activity of cancer bearing hosts, when collaborating with catalase (24).

The relationship between the presence of SOD and effective NK cell activity in *Coriolus versicolor* biomass may explain the effectiveness of *Coriolus versicolor* biomass supplementation in increasing NK cell activity in Chronic Fatigue Syndrome patients who initially have low NK cell activity.

**Enzymes that inhibit cell growth**

i. **Protease activity.** The white-rot basidiomycete *Coriolus versicolor* manifests a significant amount of proteolytic activity. This fungus synthesises intracellular and extracellular proteases which are involved in the regulation of laccase and peroxidase activity in cultures of *Coriolus versicolor*. One protease specifically cleaves protein substrates (i.e. fibrinogen and casein) by hydrolysing certain peptide bonds. This enzyme is important for two main reasons. Firstly, it has high fibrinolytic activity and hence has potential as a therapeutic agent in the treatment of thrombosis. Secondly, this enzyme could be of use in protein sequencing due to its unique specificity. Proteolytic enzymes have been shown to degrade cancer cells as well as toxins whereas cellulases and β-glucanases strengthen the immune system and provide more ATP for cell energy. (26)
ii. **Pyranose oxidase**, also known as **glucose-2-oxidase (pyranose: oxygen 2-oxidoreductase; EC 1.1.3.10)** catalyses the oxidation of several aldopyranoses producing hydrogen peroxide and 2-keto-D-glucose. Several species of basidiomycetes express this enzyme which also catalyses one-electron reduction of several different classes of xenobiotic compounds. This enzyme plays an important role in the clinical diagnosis of diabetes as well as in the production of fine chemicals and antibiotics (e.g. cortalcerone) \(^{(27)}\). The reaction product of glucose 2-oxidase catalysed reaction (i.e. \(\beta\) -glucosone) has been found to exhibit anti-tumour activity \((in \text{ vitro})\) against Ehrlich ascites tumour cells by inhibiting cell proliferation \(^{(28)}\).

**Enzymes involved in Detoxification**

i. **Peroxidases** \((EC\ 1.11.1.7)\). These are a family of isoenzymes produced during secondary metabolism in white-rot basidiomycetes. These enzymes catalyse hydrogen peroxide-dependent one-electron oxidation of a wide range of phenolic and related compounds which result in the formation of aryI cation radicals. These radicals are converted non-enzymatically into several end-products. Currently, there is great interest in these enzymes because they can be used in the detoxification of a broad range of environmental pollutants including PCBs and dioxins \(^{(29)}\).

ii. **Cytochrome P-450**. The human race is constantly exposed to external toxins (e.g. polluted environment, cigarette smoke, alcohol, medication) as well as endogenous toxins (e.g. by-products from nutrient degradation, digestive tract bacterial waste products) which must undergo a detoxification process in the cell \((Fig. 2)\). Cytochrome P-450 complex catalyses the oxidation and reduction reactions of several xenobiotic compounds i.e. chemotherapeutic agents. However, some reactions catalysed by cytochrome P-450 also generate free radicals which may cause secondary cellular damage. In order to prevent such cell injury, an adequate supply of key antioxidant substances as well as free radical quenchers are required, such as reduced glutathione, superoxide dismutase \((SOD)\), \(\beta\) -carotene and vitamin \(E\) \(^{(30)(31)}\). Cytochrome P-450 is a key agent against chronic toxic overload.

**Secondary Metabolites**

In addition to protein bound polysaccharides and enzymes, mushrooms have been shown to possess a large number of secondary metabolites (i.e. lectins, terpenoids, antibiotics and metal chelating agents), which may play an important role in the immune function of the host and hence could be of importance in immunotherapy of several disease states \(^{(32)}\).

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Mushroom Nutrition in Aging and Viral Infection

In sum, there are conditions in which the immune profile of a person (or animal) is compromised; either due to age or viral infection, as a result these persons (or animals) are subject to chronic toxic overload. For this reason, the immunonutrition properties in *Coriolus versicolor* (biomass) supplementation should be considered as a clinical tool for middle age patients (or animals) since *Coriolus versicolor* supplementation provides the delivery of:

1) Protein-bound polysaccharide complexes (beta-glucans) responsible for immune enhancement.

2) Enzymes that:
   a) prevent oxidative stress
      i) laccase activity
      ii) superoxide dismutase (SOD) activity
   b) inhibit cell growth
      i) protease activity
      ii) pyronase activity
   c) are involved in detoxification process
      i) peroxidase activity
      ii) cytochrome P-450 activity

3) Secondary metabolites.

The combined impact of these various modes of action are responsible for improving the immune profile, thereby allowing their immune systems to “control” or to eliminate the viral risk. However, it should be noted that *Coriolus versicolor* supplementation is not a substitute for medical procedures or medical products.
II. IMPORTANCE OF IMMUNONUTRITION IN HORSES AND PONIES

The objective for the balanced feeding of horses is to provide them all the nutrients required to satisfy the organism’s needs and all the substances that help the horse to maintain a metabolic balance. In veterinary medicine there is an interest to study the impact of natural substances, mainly herbal and mushroom derivates, that improve biological function, increase body health, enhance horses’ welfare and increase performances (Valle and Bergero 2005) [33].

Sport horses are subject to different stresses which can deteriorate the immune response. Immune system activity depends on several factors, such as nutrition and physical activity [34]. Immune impairment in horses can be attributed to the following factors:

1. Immune Impairment by Overtraining

Strenuous or incorrect exercise has been recognized as a stressful condition, which can significantly alter the horse’s immune response and its susceptibility to disease [35]. Several studies define the relationship among exercise and the immune response activity. If moderate training generally has beneficial effects on host defence mechanisms, high intensity exercise and overtraining might impair it. Exercise diminishes the lymphocyte function, and a decline in the number and cytolytic activity of natural killer cells which furthermore has detrimental effects on the immune system, e.g. suppressive effects, such as a decline in the ratio of CD4+ to CD8+ cells (Hines et al. 1996) [36].

2. Immune Impairment due to Age or Travelling Stress

Aging and travelling stress are also known to affect immune function. Older horses (as in older humans) have reduced immune function, but were more resistant to exercise-induced immune suppression than younger horses (Horohov et al. 1999). For this reason producing supplement for horses to support immune system activity appears to have real importance [37].

3. Immune Impairment due to Viral Infections-Post Viral Infection / HPV

The corresponding name for Chronic Fatigue Syndrome in Horses is referred to as Post-Viral Syndrome in horses. The viral infection is a response to the decrease in immune function caused by either, travelling stress, overtraining or exposure to inclement weather overtime. The equine form of HPV is known as Bovine Papillomavirus (BVP 1 or BVP 2) and can be contracted from travelling to different locations or via sexual contact. In sports horses the contraction of BVP 1 or BVP 2 infection can disqualify the horse from breeding programs.

34 Ibid page 4
36 Ibid page 4
37 Ibid page 4
The prevention of both Post Viral Syndrome and BVP infection with immune support is a widely accepted proactive in human health and may have a place in veterinary health with select “immunonutrition”.

4. Immune Impairment due to Oxidative Stress

In accordance with Moffarts et al. (2005) exists a relationship between exercise and oxidative tissue damage occurring in humans and in animals. Cellular damage can be created by ROS action. These compounds are generated during exercise in mitochondria, in the activate phagocytes during inflammation and by several enzymes. Their action, if not balanced by antioxidant defence, can cause damage on lipids, proteins, carbohydrates and ribonucleic acids. It contributes to accelerate muscle fatigue and muscle fibre damage, leading to exercise intolerance and poor performance (38). They have also a pivotal role in the pathogenesis of chronic inflammatory airway disease. According to Moffarts et al. (2004), horses have experience of oxidative stress during short term exercise and during racing, which in turn induces significant modifications of antioxidant status and in particularly on glutathione system (39).

Adequate training and dietary adequate supplements can improve antioxidant defences. Nutritional antioxidant supplementation might reduce oxidative damage by enhancement of antioxidant defence, thereby modulating inflammatory defences (Kirschvink et al. 2002). An increased free radical scavenging capacity reduces the free radical increase following physical exercise (Avellini at al. 1999). Then the risk of cell damage and exercise-induced myopathies and haemolysis linked to this phenomenon can be reduced (40).

These four immune impairment risks have been considered by which Mycology Research Laboratories in their development of Corpet (Coriolus versicolor) supplementation the equine market.

39 Ibid page 6
40 Ibid page 6
III. CORIOLUS VERSICOLOR SUPPLEMENTATION - CORPET

Applications of Corpet (Coriolus versicolor) for Horses and Ponies

Horses and ponies suffering from Post Viral Syndrome and Papova Virus should be considered candidates for Corpet (Coriolus versicolor) supplementation:

1. **Post Viral Syndrome (PVS)** - Horses and ponies used in either competition or sports are very exposed to viral infections when travelling or when in competition. In many cases, the horses may overcome an initial infection however, in sustained competition horse contract Post Viral Syndrome which reduces their performance and immune response.

2. **Bovine papillomavirus** (BVP) is a group of DNA viruses of the family Papilomaviridae that are highly prevalent in cattle causing warts (papillomas and fibropapillomas) of the skin and alimentary tract and urinary bladder. They are also thought to cause the skin tumour equine sarcoïd in horses and donkeys. Commonly found on the limbs and head, sarcoïds may lie dormant for years then ulcerate. While they may be removed surgically or with heavy metal creams, they usually re-grow after removal. The reason for the re-growth is the continued presence of the BVP virus. Six types of BVP have been characterized with equine with BVP 1 and BVP 2 associated with equine sarcoïds[41]. The method of transmission is currently unclear; the involvement of face flies (Musca autumnalis) has been suggested and transmission via contaminated tack is likely[42][43]. The disease is the only known cross-species infection by a papillomavirus.

3. **Support Immune System in Older Horses** - Reactive Oxygen Species (ROS) can impair the immune system in older healthy horses. Supplementation with mushroom supplementation with bioavailable superoxide dismutase (SOD) content can offset the immune impact of ROS on the immune system.

Rational for use of Coriolus versicolor supplementation:

a) *Coriolus versicolor* supplementation in humans has demonstrated an ability to increase white cell count in horses; thereby reducing fatigue in horses with PVS.

b) Furthermore, *Coriolus versicolor* has been successful in reducing the size of sarcoïds that are active. However, *Coriolus versicolor* supplementation has limited success when the sarcoïds are dormant (see Section VI).

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41 Bovine Papillomavirus-Wikipedia, the free encyclopedia (http://en.wikipedia.org/wiki/Bovine_papillomavirus)
Corpet Supplementation Schedules-Horses and Ponies

Corpet supplementation schedules are determined by the weight of the horse (500 kilos) and pony (250 kilos). The supplementation requires two distinct stages:

a. **Loading stage** - is for the first 10 days. The loading stage allows for a cumulative absorption of the product. Corpet should be mixed with horse feed.

b. **Maintenance stage** - follows the loading stage and is typically a period of 70 days, commencing on day 11 and terminating on day 80. Depending upon the clinical situation, the maintenance supplementation schedule may be extended a further 120 to 365 days.

### Supplementation Schedules-Horses*

<table>
<thead>
<tr>
<th></th>
<th>Days 1-10</th>
<th>Days 11-80</th>
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</thead>
<tbody>
<tr>
<td>500 kg</td>
<td>Loading</td>
<td>Maintenance</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>25 grams per day mixed with meal</td>
<td>12.5 grams per day mixed with meal</td>
</tr>
<tr>
<td>Post Viral Syndrome</td>
<td>25 grams per day mixed with meal</td>
<td></td>
</tr>
<tr>
<td>Sarcoids</td>
<td>250 grams</td>
<td>875 grams</td>
</tr>
<tr>
<td>Number of Grams per Period</td>
<td>1 Tub of Corpet Coriolus with 10 gram spoon=750 grams</td>
<td></td>
</tr>
<tr>
<td>Total Tubs Required over 80 days</td>
<td>2 Tubs in Total</td>
<td></td>
</tr>
</tbody>
</table>

### Supplementation Schedules-Ponies*

<table>
<thead>
<tr>
<th></th>
<th>Days 1-10</th>
<th>Days 11-80</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 kg</td>
<td>Loading</td>
<td>Maintenance</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>12.5 grams per day mixed with meal</td>
<td>6.75 grams per day mixed with meal</td>
</tr>
<tr>
<td>Post Viral Syndrome</td>
<td>12.5 grams per day mixed with meal</td>
<td></td>
</tr>
<tr>
<td>Sarcoids</td>
<td>125 grams</td>
<td>472.5 grams</td>
</tr>
<tr>
<td>Number of Grams per Period</td>
<td>1 Tub of Corpet Coriolus with 10 gram spoon=750 grams</td>
<td></td>
</tr>
<tr>
<td>Total Tubs Required over 80 days</td>
<td>1 Tub in Total</td>
<td></td>
</tr>
</tbody>
</table>

*For horses or ponies with tumours, and undergoing chemotherapy, loading schedule should be maintained for duration of chemotherapy, and maintained for 60 days after termination of chemotherapy.
Composition of Corpet (Coriolus)

Corpet is comprised of Coriolus versicolor biomass powder with strain number CV-OH1. All raw materials for the manufacture of Corpet are supplied by Mycology Research Laboratories Ltd, a worldwide leader in the production of mushroom nutrition products.

The proprietary cultivation process for Corpet is conducted in California. The process involves the use of the "mother culture" of strain of Coriolus versicolor that has been developed and maintained in isolation and this is used to produce the spawn.

The cultivation process allows for the harvesting of the mycelium and the young fruiting body (primordia). This cultivation technique produces a Coriolus versicolor that is sterile and contains no pesticides, heavy metals, is free from foreign matter and is totally reproducible. The material is shipped to a HACCP Food Grade facility for packing into 250 g and 750 g powder tub presentation.

<table>
<thead>
<tr>
<th>Composition of Corpet (Coriolus)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
</tbody>
</table>

Mechanism of Action

Corpet is a non-specific immunomodulator that gradually (over four to five days) assists the equine immune system by:

1. Increasing white blood count.
2. Increasing CD4 levels
3. Increasing interleukin 12 activity
4. Decreasing interleukin 5 activity
5. Decreasing telomerase activity

In a more general manner, over a two week period, Corpet supplementation rebalances the relationship between cytokine TH1 and TH2 immune systems when challenged by either a virus or tumor activity. For more information please review the clinical research section of the website http://www.mycologyresearch.com.

Contra-Indications

There are no contra-indications for Corpet. However, large spectrum antibiotics usually disrupt the digestive system in horses and ponies; thereby reducing the absorption of Corpet. For this reason, Corpet supplementation should be undertaken 14 days after the termination of antibiotic use.
IV. CLINICAL CASE STUDIES IN HORSES AND PONIES

CASE STUDY 1:
Subject: Horse with Viral Infection
Diagnosis:
In January of 2000, a Gelding eventer had never recovered from a viral infection. Vet prescribed antibiotics, but no effect. The owner and vet made a decision to try Corpet (Coriolus versicolor supplementation).

Coriolus versicolor Supplementation
Initiated in January 2000:
Days 1-10 - 50 grams per day and mix with meals
Days 11-80 - 25 grams per day and mix with meals

Observations 1
In late January of 2000, after 10 days with 50 grams per day, noted improvement in horse’s attitude and stamina

Observations 2
In March, while on maintenance stage of Corpet, the horse ran very well at an international horse show and obtained 8th place.

CASE STUDY 2:
Subject: Warmblood Gelding with sarcoid on chest and above eye.

Diagnosis:
A horse weighing 600 kilos with sarcoid established near the eye. On November 3rd, 1999 the owner and the vet made the decision to try Coriolus versicolor supplementation.

Coriolus versicolor Supplementation
Days 1-60 -50 grams per day and mix with meals in the morning.

Observations 1

<table>
<thead>
<tr>
<th>Date</th>
<th>03/11/99</th>
<th>07/12/99</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplementation</td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>50 grams /day</td>
<td>without Corpet</td>
<td>with Corpet</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>12.9 g/dl</td>
<td>15.6 g/dl</td>
</tr>
<tr>
<td>Levels</td>
<td>low end of normal</td>
<td>middle/high end of normal</td>
</tr>
<tr>
<td>White Blood Cell</td>
<td>6.9 x 10(9) /L</td>
<td>7.3 x 10(9)/L</td>
</tr>
<tr>
<td>Count</td>
<td>low end of normal</td>
<td>Middle/high end of normal</td>
</tr>
</tbody>
</table>

In December 7th there was a noted improvement in white blood count and after six months a regression in sarcoid size.
CASE STUDY 3  
Subject: Anglo Arab & Irish Drought Horse with sarcoids

Diagnosis: 
In November of 1999, a 12 year old Drought horse with approximate body weight of 500 kilos has chronic sarcoids situated around stifle area. New sarcoid growths were observed around the inside of back legs. The horse had previously received heavy metal cream for the established sarcoids around the stifle area. The owner and vet made a decision to try Corpet (Coriolus versicolor supplementation).

Coriolus versicolor Supplementation
Initiated in November 11th, 1999.  
Days 1-60 = 50 grams per day and mix with meals in the morning.

Observations 1 
After 30 days of Corpet (Coriolus versicolor supplementation) at 50 grams per day. The changes in hemoglobin and white blood counts were significantly improved as demonstrated below:

<table>
<thead>
<tr>
<th>Date</th>
<th>07/11/99</th>
<th>07/12/99</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplementation&lt;/td&gt;</td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>50 grams /day</td>
<td>without Corpet</td>
<td>with Corpet</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>11.7 g/dl</td>
<td>15.3 g/dl</td>
</tr>
<tr>
<td>Levels</td>
<td>low end of normal</td>
<td>Middle/high end of normal</td>
</tr>
<tr>
<td>White Blood Cell</td>
<td>6.8 x 10(9) /L</td>
<td>9.8 x 10(9) /L</td>
</tr>
<tr>
<td>Count</td>
<td>low end of normal</td>
<td>Middle/high end of normal</td>
</tr>
</tbody>
</table>

Observations 2 
In March of 2000, with Corpet supplementation, new sarcoid growths (inside back legs) were seen to regress and eventually totally disappear.

However, when Corpet supplementation discontinued, sarcoids appear on chest and mare was placed back on Corpet supplementation.
V. BIBLIOGRAPHY


10)Domenico Bergero and Emanuela Valle, A critical analysis on the use of herbs and herbal extracts in feeding sport horses. Pferdeheilkunde 22 (2006) 5 (September/Oktober) Department of Animal Production, Epidemiology and Ecology, University of Torino, Grugliasco (TO), Italy


VI. ANSWERS TO QUESTIONS OFTEN ASKED

(CORPET)

QUESTION/ANSWERS

1° - What is CORPET?

CORPET is the commercial name given to the CORIOLUS versicolor presentations which are used in Veterinary Medicine.

2° - In which cases would you advise Veterinaries to use the application of CORPET, as a dietary supplement, in horses and ponies?

In Fatigue due to aging
In viral problems ie Bovine papillomavirus / Post viral syndrome
In Pre-Post surgery
Before and/or undergoing Chemotherapy sessions
In palliative cancer care
In reinforcing the immune system

3° - Why is CORPET considered an immunonutrition?

Because, although it is used as a specific food supplement, it has the capacity of modulating and levelling the immune system.

4° - Must the supplementation with CORPET be administrated simultaneously with antibiotics which the animal might be taking?

Generally, the antibiotics can provoke malfunctions in the digestive system of small animals and horses, reducing the absorption of CORPET. For that reason, the supplementation must only be taken 14 days after the use of antibiotics.

5° - Why is the CORPET supplementation advised for Adult animals?

Because in horses and ponies over ten (10) years, it is crucial to reinforce their immune system.

6° - Why is the CORPET supplementation advised for animals with viral problems?

Certain virus (Papova virus and Bovine Papillomavirus (BVP1 and BVP 2) ) are directly related with Post Viral Syndrome in horses and in the development of sarcoids in horses.

When these virus are detected, the use of CORPET supplementation is advisable to level the normal function of the immune system, to eliminate and/or reduce the fatigue induced by those virus.
7° - Why is the CORPET supplementation advised for animals in Pre-Post Surgery?
Four weeks before a surgery, the immune system of an animal must be levelled so that it can support the process of healing. During the four weeks post surgery, the immune system must be balanced to accelerate the process of healing. For that reason the use of CORPET supplementation is recommended, to support the immune system of animals undergoing surgery.

8° Why is the CORPET supplementation advised for animals subjected to intense physical effort?
Because the animals that participate in sportive events are subject to physical effort and stress, and that weakens the immune system.

9° - The supplementation schedule for CORPET, consists in two phases in horses and ponies. Please describe the supplementation schedule?
   a) Phase one – in which the product is administrated in large quantities, during
      - Ten (10) days – horses and ponies
      The loading stage allows the absorption and accumulation of the product
   b) Maintenance Phase – during a period of
      - 70 days – horses and ponies
      The supplementation schedule for maintenance depends on the clinical case, and might prevail from six (6) months to one (1) year.

10° - What is the role of the existing enzymes in CORPET?
The role of mushroom enzymes in CORPET (Coriolus versicolor) is the triple activity through the enzymes action.

   - prevents the oxidative stress through the action of Lacase and the Dismutase Superoxid (SOD)\(^{13}\)(\(^{14}\))
   - inhibits the cellular proliferation through the Protease and Oxidase Piranase\(^{13}\)(\(^{14}\)) action
   - induces the detoxification through the action of the Peroxidase and Citocromo P-450\(^{13}\)(\(^{14}\)) activity

11° - Which are the contra-indications for the use of CORPET?
There are no contra-indications known for CORPET application.

12° - How to use the CORPET supplementation?
Mixed with the food

13° - Which are the presentations of CORPET?
   - Bottles of 60 tablets x 500mg.
   - Bottles of 750 gr. powder with a 10 gr spoon (horses)
**XXIVº ENCONTRO DOS MÉDICOS VETERINÁRIOS DE MACARÓNIA**

**Tumores em Animais de Companhia: prevenção utilizando cogumelos**

**XXIVº ENCONTRO DOS MÉDICOS VETERINÁRIOS DE MACARÓNIA**  
**Angra do Heroísmo, 5 e 6 de Outubro 2006**  
**Xº CONGRESSO INTERNACIONAL DE MEDICINA VETERINÁRIA EM LINGUA PORTUGUESA**  
**Ponta Delgada, 9 e 10 de Outubro 2006**

Kasmali, A. 1; Graça Basuto, J.2 e Fernandes, T. H.3  
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3 CNIG, ISEL, alvarim@isel.isel.pt

**INTRODUÇÃO**

A necófitia holotéca dos médicos veterinários consiste essencialmente em observar todas as facetas do animal, mostrando abertura a todo o tipo de tratamento a adotar. Informar, concentrar-se na nutrição e dieta, meio ambiente, estate do voto do animal, bem estar físico e psicológico do paciente, na profilaxia e na terapêutica. A comunicação entre animal, dono, o medico-veterinário e o economista.

Os médicos-veterinários holotécnicos usam as terapias convencionais e alternativas, conforme o caso. Consideram que as modernas técnicas clínicas (ultrassonógrafo, TRC, testes laboratoriais subsidiados e intervenção cirúrgica), são necessárias para o diagnóstico e tratamento dos doentes dos animais. Consideram que as modalidades da medicina alternativa (complementar) (aplicação da fitomedicina, acupuntura), desempenham papel significativo.

Os cogumelos medicinais são bem conhecidos pelos seus proprietários no equilíbrio do funcionamento do sistema imunitário. Têm sido utilizados ao longo de séculos para o tratamento de variadas doenças. É evidente que cada cogumelo tem propriedades específicas anti-cancerígenas. A atividade anti-mutagénica foi demonstrada com o Cordyceps sinensis (Mantide), Cordyceps versicolor, Gomphus luxurians (Relínia), Lentinus edodes (Shiitake), Agaricus bisporus e Cordyceps sinensis. Não existe “mestura” cogumelos medicinais. Nem todos estes cogumelos foram submetidos a estudos científicos e acuratos. O principal constituinte anti-cancerígeno dos cogumelos medicinais é β-glucano. Este polissacarídeo, basicamente uma molécula combinada com aminoácidos, estimula ou modula o sistema imunitário, activando células imunitárias tais como os monócitos e as células-T de apoio, e aumenta os níveis de melatojina e a imunidade das células-T de apoio, e aumenta a produção de interleuquinas-1 e -2, induz inmunidade e imun opressor, bem como o crescimento de tumores malignos. Estes polissacarídeos não actuam diretamente nos cânceres cancerígenos, mas devem o seu efeito ativando o funcionamento do sistema imunitário do hospedeiro. Para além dos polissacarídeos, os cogumelos contêm aminoácidos (prolina, lisina, tirosina, glutamic acid, ß-glucano, citrato, P-450, atorvastatina, SOD, que reforçam o sistema imunitário. O aumento da idade, algumas infecções virais, as outras causas ativas têm relacionadas com o desenvolvimento do tumor. A sobrevida do sistema imunitário do animal chega a tal ponto, que as funções imunitárias normais não tem especificidade para combater as células tumorais.

### Análise de Estrutura, Proteínas e Apoio à Célula

<table>
<thead>
<tr>
<th>Carac.</th>
<th>Cordyceps versicolor</th>
<th>500 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Células</td>
<td>17,3 mg</td>
<td></td>
</tr>
<tr>
<td>2. Células</td>
<td>14,8 mg</td>
<td></td>
</tr>
<tr>
<td>3. Células</td>
<td>68,1 mg</td>
<td></td>
</tr>
<tr>
<td>4. Células</td>
<td>64,5 mg</td>
<td></td>
</tr>
<tr>
<td>5. Células</td>
<td>55,0 mg</td>
<td></td>
</tr>
<tr>
<td>6. Células</td>
<td>82,0 U</td>
<td></td>
</tr>
<tr>
<td>7. Células</td>
<td>66,6 U</td>
<td></td>
</tr>
<tr>
<td>8. Células</td>
<td>6,62 mg</td>
<td></td>
</tr>
<tr>
<td>9. Células</td>
<td>11,1 mg</td>
<td></td>
</tr>
</tbody>
</table>

### CONCLUSÕES

O **Cordyceps versicolor** (biomassa) contém importantes enzimas, polisacarídeos ligados às proteínas, e metabolitos secundários que desempenham um papel importante na carcinogênese. O **Cordyceps versicolor** é um produto de imunonutrição, e não um substituto de um medicamento ou de um procedimento clínico.
Cancer Prevention with Supplementation of Diets with Botanicals

ESCVD/ ECVN – 5 - 7th October 2006
Nantes

Karmali, A. and Fernandes, T.H.
ISEL, Rue Erasme Nantes, Labo - a.karmali@dei.iesl.fr.pt
 inbox@iesl.fr.pt

INTRODUCTION

This work was conducted with a mushroom (Cordyceps sinensis) which is in the market for human and animal use. Mushrooms polysaccharides, particularly β-glucans, have anti-tumor and immunostimulating properties. These polysaccharides do not directly attack cancer cells, but instead affect their effects by activating immune responses in the host. Use of β-glucans as adjuvants for monoclonal antibody treatment has also been explored, because β-glucans bind to the complement receptor and enhance leucocyte killing of tumor cells through naturally occurring anti-tumor antibodies. Sugars also appear to reveal tumoral granulocytes, dramatically enhancing tumour killing when combined with monoclonal antibody therapy. Mushroom β-glucans affect immune function by stimulating, through specific receptors, tumour and activating dendritic cells, supporting certain enzymes, or by influencing mitotic activity. Recent work in HPV cervical cancer in humans has shown a positive role of mushrooms.

The vicious circle of chronic toxicity defined is described in which there is a series of self-amplification steps leading to maladaptive stress, causing tissue and compound production which results in health conditions generally solved with non-steroidal anti-inflammatory and antioxidant. These drugs induce increased permeability of the intestinal wall which is responsible for an overload of their increasing detoxification problems.

Table 1 provides levels of SOD, cytochrome P-450, cytochrome P-450 reductase (NADPH dependent), lactase, para-chloroacetate, proteinase, p-glucanase, protein-bound polysaccharides and secondary metabolites in 1 tablet (8 g) of Cordyceps sinensis (Bionap).

In Table 2 the impact of exogenous SOD was studied when comparing the enzyme content in the absence of proteolytic enzymes, in piglet and in pig, the purpose of this comparison was to determine the degradation of exogenous action in the intestinal tract of the human body.

Glycosylation: β-glucanase Activity

CONCLUSIONS

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

- Increase in the activity of Т and NK Cells.
- In enzyme profiles, proteases, cytochrome P450 reductase, lactase, β-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.