

OBSERVATIONAL NON-CONTROLLED STUDY
OF THE USE OF CORIOLUS VERSICOLOR SUPPLEMENTATION
IN 30 CANCER PATIENTS-Dr. Julian Kenyon (MD, MB ChB)*

INTRODUCTION

PSP, a polysaccharopeptide obtained from cultivated mycelia of the mushroom *Coriolus versicolor*, is a biological response modifier capable of showing diverse biological activities. It is a chemically homogenous substance possessing a molecular weight of approximately 100 kilodaltons. PSP is composed of 90% polysaccharides and 10% peptides. In addition to glucose, its polysaccharide constituents consist of five other sugars including arabinose, galactose, mannose, rhamnose and xylose. The polypeptide constituents contain more than twenty different amino acids, notably aspartic and glutamic acids. PSP exhibits immunomodulatory and anti-tumour activities with low cytotoxicity. It has been used in Asia, particularly in China, as an adjuvant in the clinical treatment of cancer to boost the immunological status of patients undergoing chemotherapy and/or radiotherapy. In addition, PSP exhibits analgesic, anti-viral and hepato-protective effects.

Cancer is the result of changes in key regulatory genes which control cell proliferation, differentiation and survival. Cancer development is a multi step complex process in which normal cells gradually progress to malignancy. Both the activation of the oncogenes and the inactivity of the tumour suppresser genes are critical steps in tumour initiation and progression. The failure of cancer cells to undergo programmed cell death, known as apoptosis, is a critical factor in the development of tumours. The immune response mounted by the body is of major importance in preventing this process happening, or if it has happened, moving it towards the direction of normal apoptosis. (Rudin C M & Thompson C B 1997).

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The activity of the immune system is firstly non-specific, mediated by natural killer cells, and secondly tumour antigen specific by mounting a cell mediated

immune response known as a thymic helper cell one (TH1) response. Most commonly cancer patients mount a marked thymic helper cell two (humoral immunity), a so-called TH2 response which involves production of large quantities of antibodies (Kenyon 2001 Gotos et al 1999).

TH1 cells produce one set of cytokines whilst another set of cells, the TH2 cells, produce another set of cytokines. The cytokines produced by the two cell groups both influence the anti-cancer defence mechanism in a different way. Amongst the cytokines produced by the TH1 cells there is Tumour Necrosis Factor Beta which is known for its ability to destroy cancer cells. However, if the TH1 response is suppressed, Tumour Necrosis Factor Beta can be produced by natural killer cells. An effective anti-tumour response is a cell mediated TH1 immune response. If the TH2 humoral response is excessively activated then a set of cytokines, amongst which is Interleukin 5, will be produced and these can negatively affect the anti-cancer defence mechanism either directly, or indirectly. A recent study has shown that medium and high cytotoxic activity of peripheral blood lymphocytes (mediated by TH1 lymphocytes and also natural killer cells in a non-specific way), is associated with reduced cancer risk. Whereas low activity is associated with increased cancer risk, suggesting a role for natural immunological host defence mechanisms against cancer (Kazue Imai et al 2000).

Telomerase is a ribonucleo protein polymerase and is an enzyme whose function is to maintain the essential genetic element of telomeres, the eukaryotic ends of chromosomes. Telomerase activity becomes suppressed in the ageing process, but activation of telomerase is regarded as essential to most cancers. This means that there is a specific association of human telomerase activity with cancer and usually it is high in cancer patients.

There is clinical evidence to show that patients' who have tumours that do not display telomerase activity are likely to eliminate the cancer, quite often spontaneously. It is considered that the repression of telomerase activity

could be one of the mechanisms for cancer regression (Shay J W & Wright W E 1998).

Several medicinal mushrooms are available for medical use at the present time. More than 50 mushroom species exhibit anti-cancer activity in-vitro, or in animal models, and of these, 6 have been investigated in human cancers. All are non-toxic and very well tolerated. Two proteoglycans from *Corioulus versicolor*-PSK (Polysachharide/K) and PSP (Polysachharide-peptide) – have demonstrated the most promise. Both have been subject to Phase II and Phase III trials in China, and PSP significantly extended 5 years survival in oesophageal cancer. PSP also significantly improved quality of life, provided substantial pain relief and enhanced immune status in 70-97% of patients with cancers of the stomach, oesophagus, lung, ovary and cervix. PSK and PSP boosted immune cell production, ameliorated chemotherapy symptoms, and enhanced tumour infiltration by dendritic and cytotoxic T-cells. They have extremely high tolerability, proven benefits to survival and quality of life, and their compatibility to chemotherapy and radiation therapy makes them well suited for cancer management regimens (Kidd, P.M. “The use of mushroom glucans and proteoglycans in cancer treatment”. P.M. Altern Med Red 2000: 5 (1): 4-27).

MATERIALS & METHODS

A biomass powder of *Coriolus versicolor* was chosen as it has significantly higher content of PSP's to other mushroom preparations, specifically the biomass equivalents of *Grifola frondosa* (Maitake), *Ganoderma lucidium* (Reishi) and *Cordyceps sinensis*. This biomass form of *Coriolus versicolor* also has significantly greater peroxidase activity to biomass equivalents of *Grifola frondosa* and *Ganoderma lucidium* specifically. Lastly, it has higher beta-glucanasase activity to *Griofola frondosa* (Maitake) and *Cordyceps sinensis* as well as increased glucose 2-oxidase activity (Karmali A, University of Lisbon 2002).

The biomass powder contained the mycelium and the primordia (young fruitbody) of *Coriolus versicolor*, grown on a sterile substrate. The biomass powder was then manufactured, into 500 mg tablets under to Pharmaceutical GMP standards in the United Kingdom.

Thirty (30) patients were observed from the author's clinical practice. They had a variety of solid tumours, mostly stage 3 or stage 4. The breakdown by tumour type is given in Table I:

Table I
Patients by Tumour Type and Secondary Tumors

Condition	Patient Numbers	Secondary Tumors	Number of Secondaries
Hodgkin's Lymphoma	1	None	0
Prostate Cancer	8	Bone	6
Bowel Carcinoma	10	Liver	9
Breast Cancer	8	Metastases	8
Died During Study	3	Not Applicable	0
Total	30		23

Of the group of 30 patients who were selected to enter this study, 3 patients have died. Therefore this leaves us at 27 study results.

Interleukin 5, interleukin 12 (both at gene expression level), tumour necrosis factor beta (also at gene expression level) and telomerase were recorded at day 0, day 60 and day 120. (See Appendices II, III, IV, and V).

The supplementation schedule for *Coriolus versicolor* supplementation was three tablets (500 mg each tablet) three times a day (9 tablets) for the first month (4.5 grams per day), six tablets three times a day (18 tablets) for the second month (9.0 grams per day) and nine tablets three times a day (27 tablets) for the third (13.5 grams per day) and fourth (13.5 grams per day) months. (See Appendix I for outline of *Coriolus versicolor* supplementation schedule). Supplementation intake was conducted 30 minutes prior to every meal.

Table II
Coriolus versicolor
Supplementation Schedule

	Grams per day
1 Month 1	4.5
2 Month 2	9.0
3 Month 3	13.5
4 Month 4	13.5

RESULTS

Based on the aforementioned four immunological parameters, over the 120 day supplementation period, the average change in Interleukin 5, interleukin 12 (both at gene expression level), tumour necrosis factor beta (also at gene expression level) and telomerase was encouraging.

The summary of results was based on the recorded four (4) immunological parameters of 27 patients and outlined in Table III.

Table III
Summary of Results

	Day 0	Day 60	Day 120	Average Change
1 Telomerase	1727	1034	417	-75.9%
2 Interleukin 5 *	22540	28516	4482	-80.1%
3 Interleukin 12 * Tumour Necrosis Factor	13931	20968	29489	111.7%
4 Beta*(1)	27777	26113	31713	14.2%

***Gene Expression Level
(1) only 26 data points**

For patient specific information, please review the attached in Appendices II, III, IV and V for the respective data points per measurement data.

**Table IV
Statistical Data**

Interleukin 5

0 - 60 days	0.589691
0 - 120 days	0.039371 Significant p< . 05
60 - 120 days	0.007972 Significant p< . 01

Telomerase

0 - 60 days	0.039307 Significant p< .05
0 - 120 days	1.78E-05 Significant p<. 00001
60 - 120 days	0.018498 Significant p< .05

Interleukin 12

0 - 60 days	0.478791
0 - 120 days	0.133005
60 - 120 days	0.439141

**0 = 60 days starting value<3001
0.003306**

Note: When the cut off of evaluation of interleukin 12 using any patients who has a starting value of less than 3,001, there was a significant increase in production of interleukin 12.

DISCUSSION

These results show a significant drop in telomerase activity (-75.9%) in the group except four cases (Patients 3, 8, 11 and 15-See Appendix II). The average decrease in Interleukin 5 was -80.1%, the majority showed an increase in Interleukin 12 (111.7%) and slight increase in tumour necrosis factor beta (14.2%). This therefore shows that there is a general move towards a TH1 immune response in the majority of cases studied here.

To provide for greater ease of use, the use of tablet presentations of *Coriolus versicolor* should be replaced with a powder presentation in months 3 and 4 (13.5 gram per day).

CONCLUSION

This observational study on the use of *Coriolus versicolor* shows that there appears to be a differentiating effect on cancer cells by lowering telomerase activity and an encouragement of an immune function move towards a cell mediated TH1 immune response, which is a more effective anti-tumour response. This is indeed remarkable, as the majority of these cases were stage 3 and 4 cancers, many of them chemotherapy and radiotherapy failures.

The use of *Coriolus versicolor* supplementation as adjuvant nutritional therapy to support the immune system in Stage 3 and 4 cancer patients should be further studied.

References:

Gotos et al 1999 "Analysis of TH1 and TH2 cytokine production by peripheral blood mononuclear cells as a parameter of immunological dysfunction in advanced cancer patients." *Cancer Immunol.Immunother.*48:435

Kazue Imai et al. "Natural cytotoxic activity of peripheral blood lymphocytes in cancer incidents: an 11 year follow up study of a general population." *The Lancet* Vol. 356 – November 25th 2000 1795-1799.

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Appendix I

Coriolus versicolor Supplementation Schedule(1)(2)

Time Period	Tablets per Day	Grams per day	Tablets per Week
Week 1	3 tablets x 3 times per day	4.5	54
Week 2	3 tablets x 3 times per day	4.5	54
Week 3	3 tablets x 3 times per day	4.5	54
Week 4	3 tablets x 3 times per day	4.5	54
Week 5	6 tablets x 3 times per day	9	126
Week 6	6 tablets x 3 times per day	9	126
Week 7	6 tablets x 3 times per day	9	126
Week 8	6 tablets x 3 times per day	9	126
Week 9	9 tablets x 3 times per day	13.5	189

Week	10	9 tablets x 3 times per day	13.5	189
Week	11	9 tablets x 3 times per day	13.5	189
Week	12	9 tablets x 3 times per day	13.5	189
Week	13	9 tablets x 3 times per day	13.5	189
Week	14	9 tablets x 3 times per day	13.5	189
Week	15	9 tablets x 3 times per day	13.5	189
Week	16	9 tablets x 3 times per day	13.5	189

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(1) The biomass powder contained the mycelium and the primordia (young fruitbody) of *Coriolus versicolor*, grown on a sterile substrate. The biomass powder was then manufactured, into 500 mg tablets under to pharmaceutical GMP standards in the United Kingdom

(2) *Coriolus versicolor* was supplied by Mycology Rsearch Laboratories Ltd., Brough, United Kingdom (<http://www.mycologyresearch.com> or <http://www.aneid.pt>)

Appendix II
Average Telomerase
Activity
Over the 120 Day
Coriolus
Supplementation
Period

	Day 0	Day 60	Day 120
Patient			
1	3000	3000	91
2	2000	3000	0
3	200	130	1000
4	3000	80	1200
5	3000	3000	1400
6	1000	390	0
7	1200	0	580
8	3000	40	3000
9	120	390	0

10	1200	50	50
11	0	3000	990
12	3000	1000	430
13	20	270	0
14	580	290	0
15	0	420	130
16	3000	0	800
17	2240	3000	0
18	3000	1000	720
19	140	1060	100
20	3000	1000	0
21	3000	850	600
22	3000	1000	0
23	3000	1000	170
24	390	845	0
25	590	3000	0
26	960	50	0
27	3000	50	0
Total	46640	27915	11261
Average	1727	1034	417
Day	0	60	120

**Appendix III
Average Interleukin 5
Activity
over the 120 Day Coriolus
Supplementation Period**

	Day 0	Day 60	Day 120
Patient			
1	790	100000	14000
2	100000	50000	0
3	1000	50	0
4	300	100000	0
5	0	50	50
6	140	0	0
7	0	100000	100000
8	0	0	100
9	0	4500	0
10	50	650	0
11	52800	0	290
12	0	38500	0

13	0	50	50
14	50	100000	0
15	0	50	190
16	220	4600	0
17	500	100000	0
18	50	12300	3030
19	100000	4740	0
20	100000	50	0
21	1260	20790	0
22	50000	30000	0
23	1360	1000	0
24	100000	200	200
25	100000	100000	2000
26	0	2280	1000
27	50	130	100
Total	608570	769940	121010
Average	22540	28516	4482
Day	0	60	120

**Appendix IV
Average Interleukin 12
Activity
over the 120 Day Coriolus
Supplementation Period**

	Day 0	Day 60	Day 120
Patient			
1	0	50	50
2	0	500	100000
3	100000	100000	50
4	100	50	37000
5	0	25000	50000
6	100000	50	50000
7	0	100000	100000
8	0	50	240
9	0	100000	1000
10	0	100	500
11	3000	0	100000

12	6500	100000	250
13	25	100000	100000
14	350	2550	3000
15	50	2850	50
16	0	50	100000
17	0	50	0
18	1070	50	5000
19	0	4070	5000
20	0	1000	3000
21	100000	140	100000
22	0	50	1000
23	0	50	50
24	0	0	3000
25	0	1000	5000
26	65000	28900	30000
27	50	50	2000
Total	376145	566610	796190
Average	13931	20986	29489
Day	0	60	120

Appendix V
Average Tumour Necrosis Factor
Beta
Activity over the 120 Day Coriolus
Supplementation Period

	Day 0	Day 60	Day 120	
Patient				
1	0	100000	100	
2	0	100000	300	
3	0	50	50	
4	100000	50	40000	
5				No Data Supplied
6	0	100000	100000	
7	100000	50	50	
8	7000	75000	75000	
9	160	410	1000	
10	100000	50000	100000	
11	100000	0	50	

12	15000	0	100
13	0	580	600
14	0	50	50
15	50	50	70
16	0	50	50
17	0	230	1300
18	0	50	1000
19	100000	390	100000
20	0	1820	1760
21	0	50	1000
22	0	50	100000
23	0	0	50
24	100000	100000	100000
25	0	100000	100000
26	100000	50000	100000
27	0	50	2000
Total	722210	678930	824530
Average	27777	26113	31713
Day	0	60	120

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The Dove Clinic for Integrated Medicine (www.doveclinic.com) is focused on the treatment of chronic illness, particularly cancer, chronic fatigue syndrome, multiple sclerosis and Parkinson's disease.

Dr. Kenyon graduated in Medicine from Liverpool University Medical School in 1970 and went on to gain his MB Ch B in 1971.

Dr. Kenyon's other achievements are outlined below:

1980

-Founder Chairman, British Med. Acupuncture Society

-Honorary Specialist in Pain Relief Foundation Clinic Walton Hospital, Liverpool 1980-1982

-Founder Partner and Co-Director of the Centre for the Study of Complementary Medicine. (Resigned prior to acquisition by Boots the Chemist to focus on treating serious illnesses).