La Micoterapia Funzionale come supporto e integrazione nel paziente oncologico. Le ricerche scientifiche

San Gregorio di Catania

10/11 Maggio 2019

Dr. Antonio Sacco

Cos'è la Micoterapia?




E' l'utilizzo dei funghi medicinali,
intesi come alimenti nutraceutici,
per modulare il sistema immunitario con un'azione di riequilibrio metabolico
e con azioni terapeutiche specifiche




MEDICINA FUNZIONALE

La **MEDICINA FUNZIONALE** utilizza un

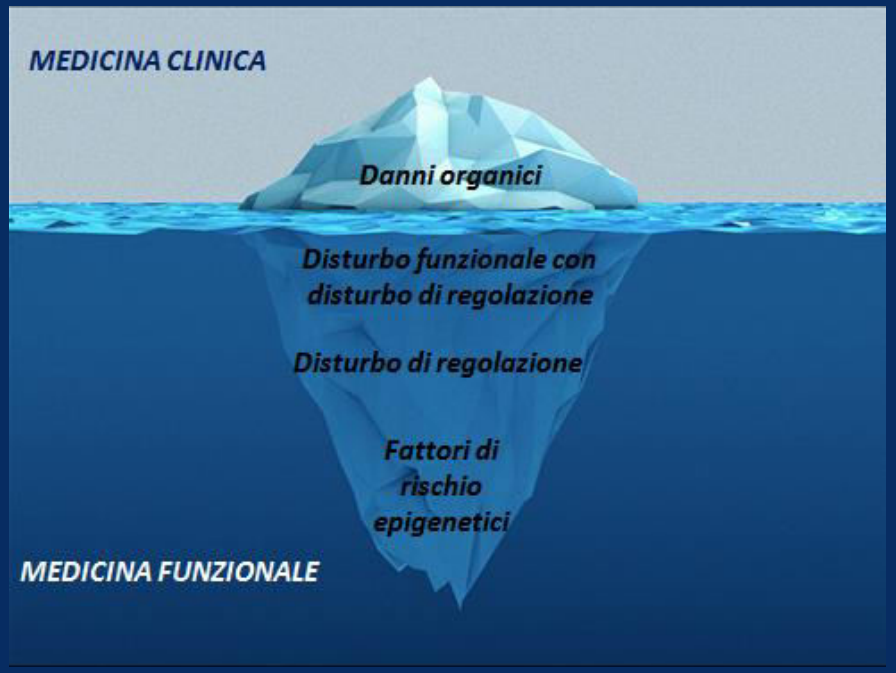
Approccio diagnostico-terapeutico

“paziente-mirato”

La **MEDICINA CONVENZIONALE**, invece, utilizza un

Approccio diagnostico-terapeutico

“malattia-mirato”



MEDICINA FUNZIONALE

- **La Medicina Funzionale offre un nuovo approccio al controllo e alla prevenzione di malattie croniche, inglobando l'arte e la scienza della pratica medica.**
- **Permette di comprendere disfunzioni di organi e apparati prima che si verifichino lesioni evidenziabili da esami di laboratorio o di imaging convenzionali.**
- **E' la cosiddetta *Medicina del Giorno Prima*.**
- **Integra metodiche diagnostiche tradizionali con sistemi di diagnosi funzionale più avanzati.**
- **Funzionale si riferisce allo studio dei processi fisiologici cellulari.**

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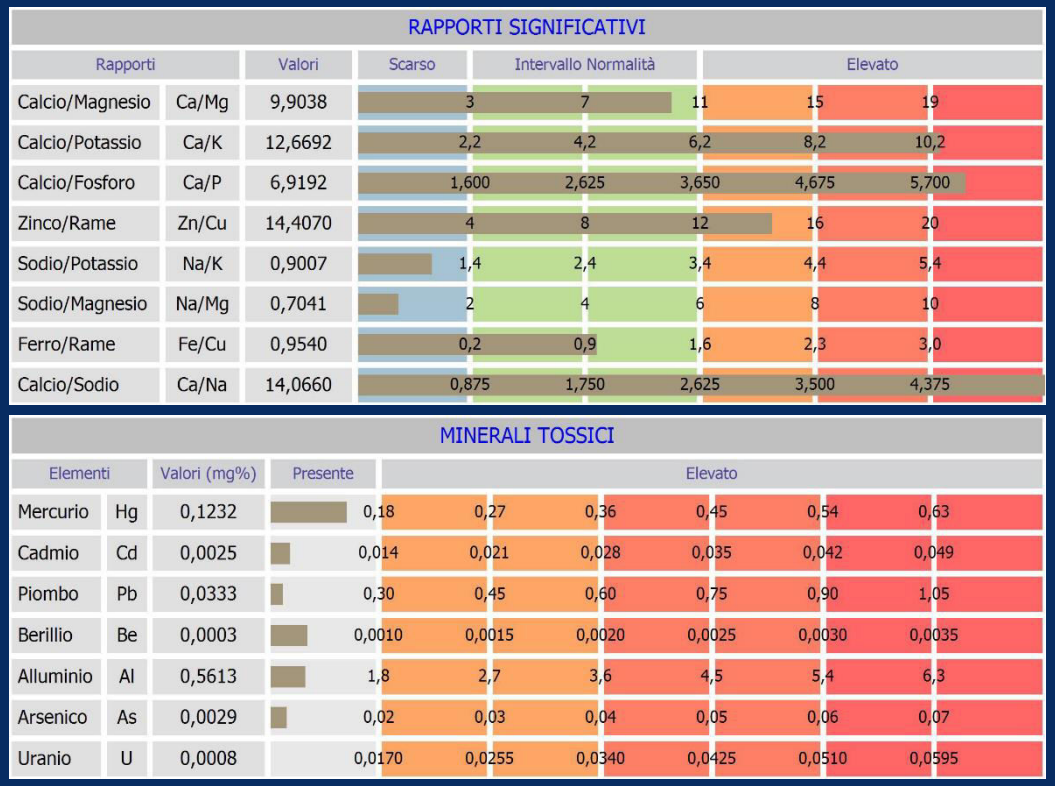
ANALISI MINERALE TISSUTALE DEL CAPELLO



RAPPORTI SIGNIFICATIVI

Rapporti		Valori	Scarso		Intervallo Normalità		Elevato	
Calcio/Magnesio	Ca/Mg	9,9038	3	7	11	15	19	
Calcio/Potassio	Ca/K	12,6692	2,2	4,2	6,2	8,2	10,2	
Calcio/Fosforo	Ca/P	6,9192	1,600	2,625	3,650	4,675	5,700	
Zinco/Rame	Zn/Cu	14,4070	4	8	12	16	20	
Sodio/Potassio	Na/K	0,9007	1,4	2,4	3,4	4,4	5,4	
Sodio/Magnesio	Na/Mg	0,7041	2	4	6	8	10	
Ferro/Rame	Fe/Cu	0,9540	0,2	0,9	1,6	2,3	3,0	
Calcio/Sodio	Ca/Na	14,0660	0,875	1,750	2,625	3,500	4,375	

MINERALI TOSSICI

Elementi		Valori (mg%)	Presente	Elevato				
Mercurio	Hg	0,1232	0,18	0,27	0,36	0,45	0,54	0,63
Cadmio	Cd	0,0025	0,014	0,021	0,028	0,035	0,042	0,049
Piombo	Pb	0,0333	0,30	0,45	0,60	0,75	0,90	1,05
Berillio	Be	0,0003	0,0010	0,0015	0,0020	0,0025	0,0030	0,0035
Alluminio	Al	0,5613	1,8	2,7	3,6	4,5	5,4	6,3
Arsenico	As	0,0029	0,02	0,03	0,04	0,05	0,06	0,07
Uranio	U	0,0008	0,0170	0,0255	0,0340	0,0425	0,0510	0,0595

MICOTERAPIA FUNZIONALE

- E' l‘uso dei funghi medicinali, sia in forma di alimenti che come integratori, per prevenire e correggere i fattori di rischio in soggetti sani e per trattare patologie cronico-degenerative, già in fase conclamata.

- Oltre al tropismo d’organo, si tiene conto della predominanza neurovegetativa al momento della prescrizione, rispettando l’individualità biochimica.

Macrofunghi e Microfunghi

- Macrofunghi sono quelli di cui comunemente vediamo i corpi fruttiferi
- Microfunghi: muffe, lieviti, fermenti, ruggini, spesso patogeni di piante o di animali; da questi si sono ricavati antibiotici e vari prodotti usati nella fermentazione industriale

MACROFUNGHI

- Basidiomiceti
  - Polipori

    Evolutivamente più antichi
  - Lamelliformi

    Più recenti, hanno sviluppato strategie di sopravvivenza
- Ascomiceti
  - Tra cui il Cordyceps spp

MICROFUNGHI

- Spesso patogeni per l'uomo

  Candida spp, Aspergillus fumigatus
- Ma anche utili

  - Penicillium notatum--> penicillina, tolypocladium inflatum--> ciclosporina
  - Saccharomyces cerevisiae--> produzione di birra e vino

Tradizione Orientale

Da molti secoli i funghi fanno parte del bagaglio terapeutico della medicina orientale

La prima notizia sull'uso dei funghi in MTC risale al trattato *Shen Nong Ben Cao,* scritto nel 250 AC:

Nella classe superiore**,** che comprende 120 erbe, le ***Erbe dell'imperatore*****,** sono inseriti 4 funghi :

- Ganoderma lucidum,
- Polyporus umbellatus
- Poria cocos
- Cordyceps sinensis

Almeno 300 specie di funghi sono usate da centinaia di anni nella pratica della Medicina Cinese, Coreana e Giapponese

Oriente e Occidente

- Evidenze scientifiche supportano l'importanza, per la salute, controllo e modulazione della dieta
- I funghi realizzano una **connessione tra dieta e medicina** soprattutto in Oriente e nell'Europa dell'Est.
- Medicina occidentale - **estratti** specifici di funghi, particolarmente studiati per la cura di malattie degenerative
- Fungo intero: complesso sinergico delle sostanze bioattive in esso contenute; azione di riequilibrio dell'omeostasi

Inonotus obliquus - Chaga

Ganoderma lucidum - Reishi

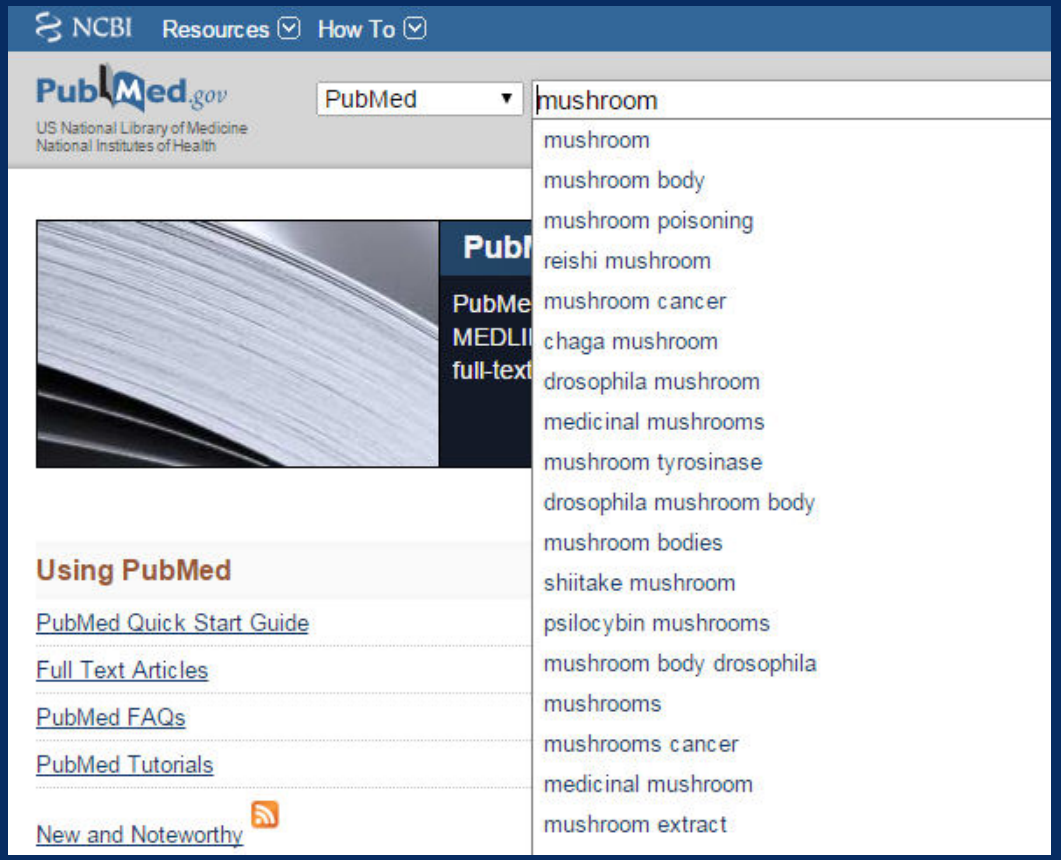
Ricerca scientifica

In PubMed:

Oltre 13200 studi scientifici sui funghi

Oltre 1180 lavori scientifici sui funghi in Oncologia

Oltre 800 lavori su funghi e beta-glucani



Dai funghi sono state estratte oltre 40 frazioni polisaccaridiche:

- Lentinan (*Shiitake*)
- PSK e PSP (*Coriolus versicolor*)
- D-fraction (*Maitake*)
- Betulin (*Chaga*)
- Schizophyllan (*Schyzophyllum commune)*

Farmaci di derivazione fungina

- Penicillina da Penicillium Notatum
- Cefalosporine da Acremonium Chrysogenum
- Acido fusidico da Acremonium Fusidioides
- Ciclosporina da Tolypocladium Inflatum
- Griseofulvina da Penicillium Griseofulvum
- Alcaloidi segale cornuta da Claviceps Purpurea
- Lovastatina contenuta naturalmente in Pleorotus Ostreatus
- Alcuni funghi contengono elevate quantità di vitamina D ed alcuni sono fonte naturale di Taxolo

Molecole bioattive

Le PROPRIETÀ dei funghi sono legate principalmente a 3 classi di composti:

Enzimi

- SOD (anti-ox)
- CATALASI (detossic.)
- LACCASI (detossic+anti-ox)
- GLUTATIONE-PEROSSIDASI
- GLUCOSO-2-OSSIDASI o
- PIRANOSO-OSSIDASI (antiprolif.neoplastica)
- PROTEASI (anti-prolif.neo)
- COMPLESSO Cyt P450(detossicazione)

Metaboliti secondari

Polisaccaridi

METABOLITI SECONDARI

-TRITERPENI

- LATTONI

- NGF (Hericium)

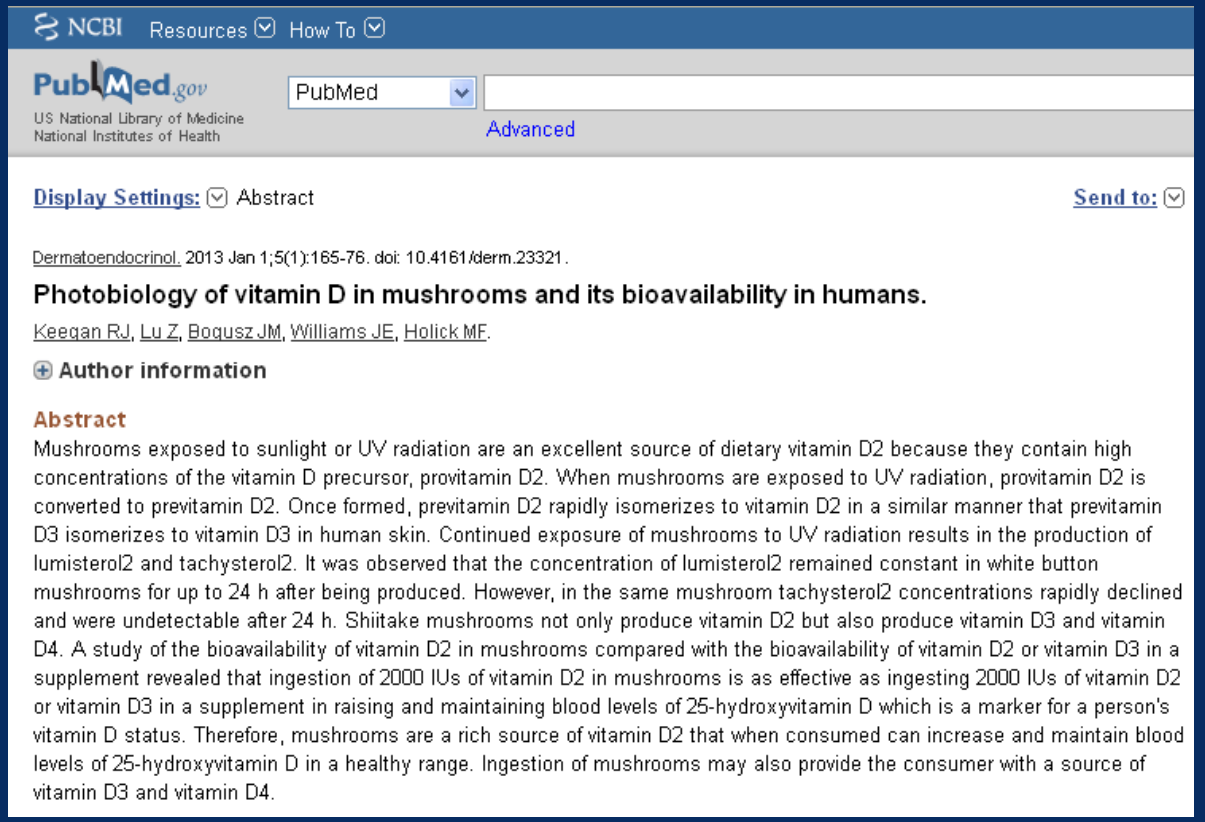
-LECTINE

- SOSTANZE CHELANTI

- ALCALOIDI

- STEROLI, ERGOSTEROLI

- STATINE (Lovastatina)



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Dermatoendocrinol. 2013 Jan 1;5(1):165-76. doi: 10.4161/derm.23321.

Photobiology of vitamin D in mushrooms and its bioavailability in humans.

Keegan RJ, Lu Z, Bogusz JM, Williams JE, Holick MF.

Author information

Abstract

Mushrooms exposed to sunlight or UV radiation are an excellent source of dietary vitamin D2 because they contain high concentrations of the vitamin D precursor, provitamin D2. When mushrooms are exposed to UV radiation, provitamin D2 is converted to previtamin D2. Once formed, previtamin D2 rapidly isomerizes to vitamin D2 in a similar manner that previtamin D3 isomerizes to vitamin D3 in human skin. Continued exposure of mushrooms to UV radiation results in the production of lumisterol2 and tachysterol2. It was observed that the concentration of lumisterol2 remained constant in white button mushrooms for up to 24 h after being produced. However, in the same mushroom tachysterol2 concentrations rapidly declined and were undetectable after 24 h. Shiitake mushrooms not only produce vitamin D2 but also produce vitamin D3 and vitamin D4. A study of the bioavailability of vitamin D2 in mushrooms compared with the bioavailability of vitamin D2 or vitamin D3 in a supplement revealed that ingestion of 2000 IUs of vitamin D2 in mushrooms is as effective as ingesting 2000 IUs of vitamin D2 or vitamin D3 in a supplement in raising and maintaining blood levels of 25-hydroxyvitamin D which is a marker for a person's vitamin D status. Therefore, mushrooms are a rich source of vitamin D2 that when consumed can increase and maintain blood levels of 25-hydroxyvitamin D in a healthy range. Ingestion of mushrooms may also provide the consumer with a source of vitamin D3 and vitamin D4.

METABOLITI SECONDARI

- ANTIBIOTICI
- REGOLATORI CICLO CELLULARE (fasi da G1/S a G2/M)
- INIBITORI della TRASDUZIONE segnale intracellulare AMPK-dipendente
- INIBITORI dell'NF-kB (nuclear factor kB), delle PROTEIN CHINASI alterate
- INIBITORI di AROMATASI, SULFATASI, di 5-αREDUTTASI (Tumori Ormono-dip)
- INIBITORI delle TOPOISOMERASI e DNA POLIMERASI tumorali
- INIBITORI METALLOPROTEINASI di MATRICE (inibizione NEOANGIOGENESI e METASTATIZZAZIONE)

POLISACCARIDI

Attività immunomodulante e antitumorale

- Chitina
- α glucani
- ***β-D- glucani***
- β mannani
- Ciclofurani
- glicoproteine

Beta-glucani

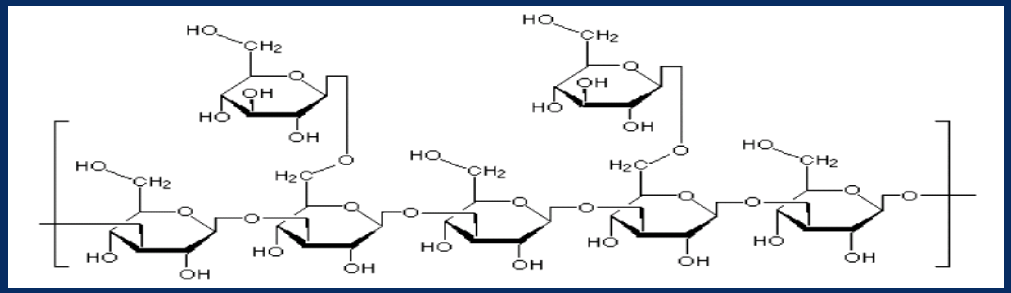
- Beta-glucani: polisaccaridi complessi caratterizzati da una struttura ripetitiva di molecole di D-glucosio, nella quale tali molecole sono unite da legami ß (1-3/1-6) ad altre molecole di glucosio.

- I ß-glucani hanno la capacità di legarsi a specifici recettori su neutrofili, monociti/macrofagi, NK, e linfociti B e T, stimolando così una risposta immunitaria.

Beta-glucani fungini

- IMMUNOSTIMOLANTI
- - 1,3/1,6 D-glucani
- - INSOLUBILI
- - ALTO e MEDIO p.m.

- NON IMMUNOSTIMOLANTI
- - Catene con legame radicalico 1,3/1,4 (es.cellulosa)
- - SOLUBILI
- - BASSO p.m (5.000-10.000 Dalton)



Non tutti i ß-D-glucani contenuti nei funghi hanno attività antitumorale. Questo tipo di attività sembra influenzata dalla solubilità in acqua, dalla dimensione delle molecole e dalle tipologie di legame (ß-(1-6)-bonding system in ß-(1-3) major chain).

Beta glucani BRM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Hum Exp Toxicol. 2013 Jun;32(6):647-54. doi: 10.1177/0960327112468173. Epub 2013 Feb 19.

Effects of β-glucan extracted from Agaricus blazei on the expression of ERCC5, CASP9, and CYP1A1 genes and metabolic profile in HepG2 cells.

da Silva AF[1], Sartori D, Macedo FC Jr, Ribeiro LR, Fungaro MH, Mantovani MS

- β-glucani sono considerati "biological response modifiers" (BRM) per la loro capacità di attivare il sistema immunitario

- Immunologi dell'Università di Louisville hanno scoperto che essi si legano al Recettore CR3 del complemento e il sistema immunitario li riconosce come non self

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J Biol Chem. 2012 Jan 27;287(5):3337-48. doi: 10.1074/jbc.M111.298307. Epub 2011 Dec 9.

Lectin site ligation of CR3 induces conformational changes and signaling.

O'Brien XM[1], Heflin KE, Lavigne LM, Yu K, Kim M, Salomon AR, Reichner JS.

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Curr Med Chem. 2012;19(25):4298-305.

Anti-tumor monoclonal antibodies in conjunction with β-glucans: a novel anti-cancer immunotherapy.

Xiang D[1], Sharma VR, Freter CE, Yan J.

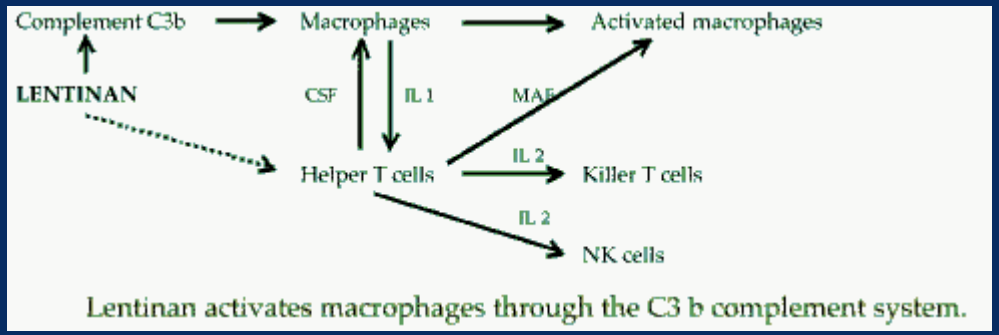
Author information

Abstract

Monoclonal antibodies (mAbs) have greatly advanced the field of anti-cancer immunotherapy and have made a major impact in clinical medicine. While more mAbs have been approved by the FDA and entered into the clinical therapeutic arena with indications to treat various solid tumors and hematologic malignancies, extensive efforts have also been made to make mAb therapy more effective. Combination therapy of anti-tumor mAbs with chemotherapeutic drugs has been widely used in the clinical patient care. In addition, many immune stimulating agents have been specifically studied for this very purpose. One compound in particular, β-glucan, has shown very promising and exciting results in pre-clinical animal models and early phase human clinical trials. β-Glucans are naturally occurring, abundant polysaccharides with different structures that can be extracted and purified from fungi, bacteria, oats and barley. The active components of yeast-derived β-glucan exert their unique immune stimulating functions by binding specifically to complement receptor 3 (CR3) via lectin-like domain (LLD) and activating CR3 to promote cellular cytotoxicity of iC3b-coated cancer cells. In addition, particulate yeast-derived β-glucan stimulates both innate and adaptive anti-tumor immune responses. This review covers the anti-cancer mechanisms of anti-tumor mAbs and β-glucans, the pre-clinical studies done with β-glucans in conjunction with anti-tumor mAbs in human carcinoma xenograft models, and the preliminary results of human clinical trials with different β-glucans, as well as those of phase I/II and III studies using the combination of yeast-derived soluble β-glucan and anti-tumor mAbs.

Shiitake: Lentinan

- Bassa biodisponibilità orale
- Attività antitumorale indiretta
- Potenzia l'azione di farmaci chemioterapici
- Rafforza il sistema immunitario
- Attività immunomodulante



Lentinan activates macrophages through the C3 b complement system.

Il β-glucano si lega con alta affinità ad uno dei due siti di legame del recettore **CR3** su neutrofili, NK, monociti-macrofagi. Il frammento C3b del complemento si lega all'altro sito di legame del recettore CR3.
Il **doppio legame** è essenziale per la capacità cancer-killer.

Shiitake: Lentinan

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Surg Oncol. 2014 Nov 20. pii: S0960-7404(14)00083-8. doi: 10.1016/j.suronc.2014.11.002. [Epub ahead of print]

Lentinan reduces tumor progression by enhancing gemcitabine chemotherapy in urothelial bladder cancer.

Sun M[1], Zhao W[2], Xie Q[1], Zhan Y[1], Wu B[3].

Author information

Abstract

It has been shown that chemotherapy has limited antitumor activity against advanced urothelial bladder cancer (UBC). Consequently, there is an urgent need to develop effective therapeutic methods for patients with advanced UBC. In the present study, the inhibitory effects of lentinan alone, gemcitabine alone, or lentinan combined with gemcitabine on the proliferation of the UBC cell line, T24, were investigated. The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide assay, annexin V fluorescein isothiocyanate/propidium iodide staining, and flow cytometry were used to determine the proliferation and apoptosis of T24 cells in each treatment group. Survival-related protein expression was analyzed by western blotting. Increased concentrations of lentinan, or lentinan combined with gemcitabine, positively correlated with decreased T24 cell proliferation. Lentinan combined with gemcitabine chemotherapy significantly inhibited UBC cell proliferation. Gemcitabine has the ability to induce T24 cell apoptosis, and this effect is enhanced when it is combined with lentinan.

KEYWORDS: Apoptosis; Gemcitabine; Lentinan; Proliferation; Urothelial bladder cancer

Schizophyllum comune: schyzophyllan

J Cancer Res Clin Oncol. 2012 Sep;138(9):1579-96. doi: 10.1007/s00432-012-1224-0. Epub 2012 May 3.

Schizophyllan inhibits the development of mammary and hepatic carcinomas induced by 7,12 dimethylbenz(α)anthracene and decreases cell proliferation: comparison with tamoxifen.

Mansour A[1], Daba A, Baddour N, El-Saadani M, Aleem E.

⊕ **Author information**

Abstract

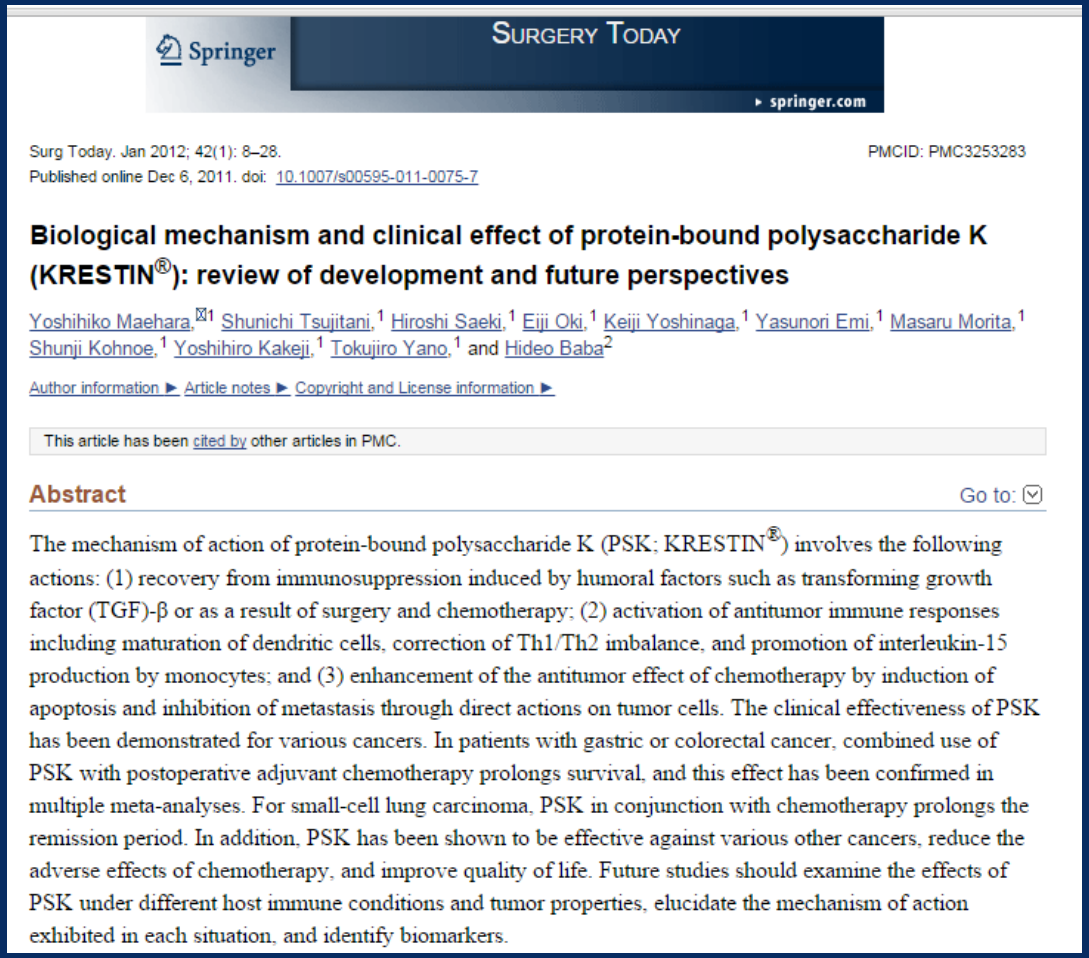
BACKGROUND: Breast cancer is one of the leading causes of cancer mortality among women. Some anticancer compounds have been isolated from mushrooms. The aim of the present work was to study the anticancer effects of schizophyllan (SCH), a β-D: -glucan extracted from the mushroom Schizophyllum commune alone or in combination with tamoxifen (TAM) on 7, 12 Dimethylbenz(α)anthracene (DMBA)-induced carcinomas in mice.

METHODS: We isolated SCH from S. commune. Female mice received DMBA, SCH, DMBA+SCH, DMBA+TAM or DMBA+TAM+SCH or vehicles. We studied mice survival, tumour incidence, histopathology, oestrogen receptor (ER) expression, cell proliferation by immunohistochemical detection of proliferating cell nuclear antigen (PCNA), apoptosis by TUNEL assay, as well as caspase-3 expression.

RESULTS: DMBA treatment resulted in mammary and hepatocellular carcinomas (HCC). Both SCH and TAM reduced the incidence of DMBA-induced mammary tumours by 85 and 75 %, respectively, and equally decreased the PCNA labelling index relative to DMBA. TAM treatment increased the incidence of- and PCNA index in HCCs relative to DMBA, while SCH suppressed these effects. TAM was more effective than SCH in the induction of apoptosis in both mammary and hepatic carcinomas. Caspase-3 levels correlated with the apoptotic index in most experimental groups.

CONCLUSIONS: Only one dose of SCH had similar therapeutic effects against DMBA-induced mammary carcinomas as 4 weeks of TAM treatment. This coupled with the ability of SCH to suppress hepatic lesions associated with TAM treatment provides the rationale for further investigating the combined therapeutic effects of TAM+SCH in preclinical models of ER-positive breast cancer, as well as in liver cancer.

Coriolus versicolor: PSK Krestin



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Surg Today. Jan 2012; 42(1): 8–28.
Published online Dec 6, 2011. doi: 10.1007/s00595-011-0075-7
PMCID: PMC3253283

Biological mechanism and clinical effect of protein-bound polysaccharide K (KRESTIN®): review of development and future perspectives

Yoshihiko Maehara,[✉1] Shunichi Tsujitani,[1] Hiroshi Saeki,[1] Eiji Oki,[1] Keiji Yoshinaga,[1] Yasunori Emi,[1] Masaru Morita,[1] Shunji Kohnoe,[1] Yoshihiro Kakeji,[1] Tokujiro Yano,[1] and Hideo Baba[2]

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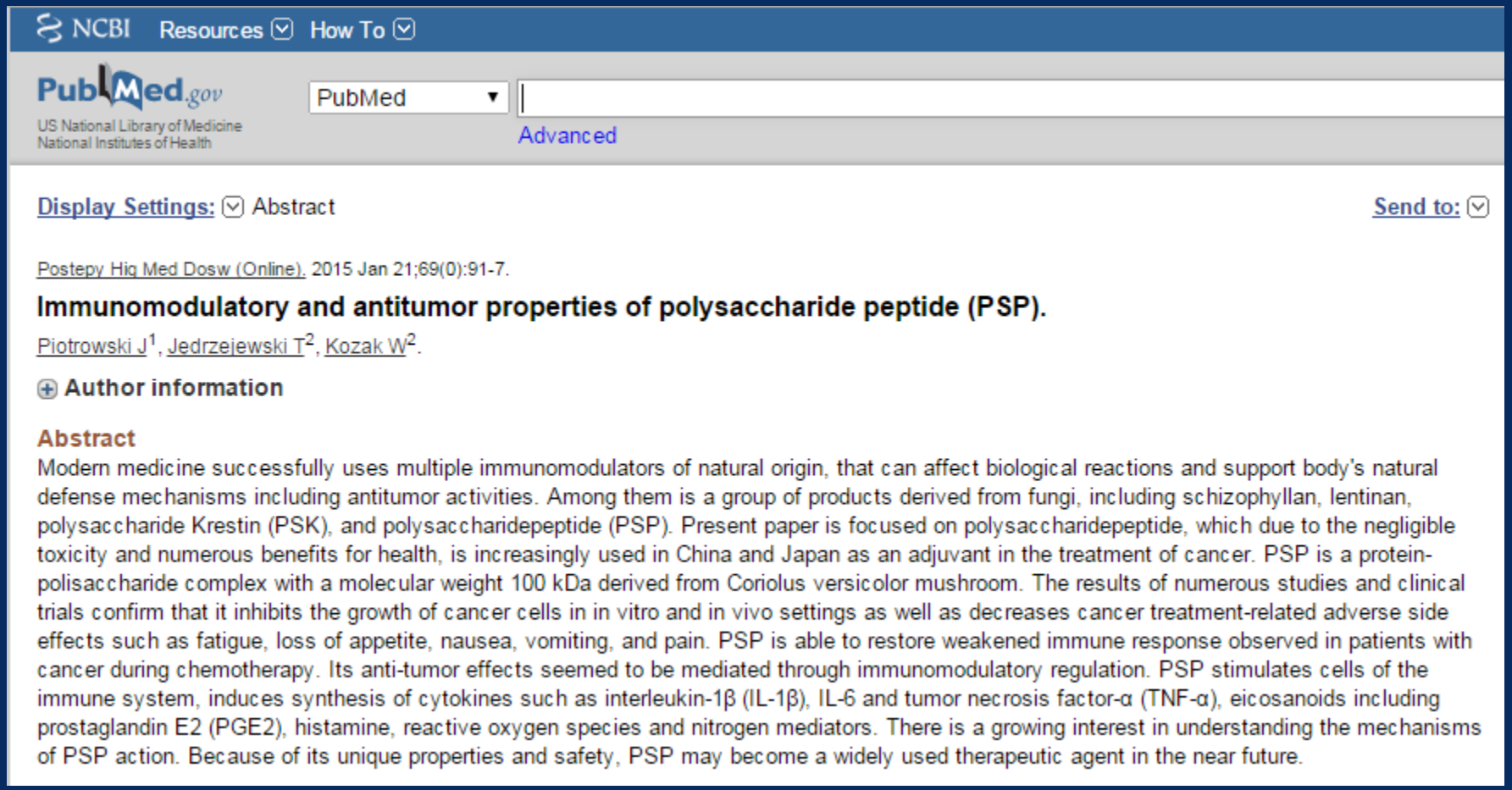
Abstract Go to:

The mechanism of action of protein-bound polysaccharide K (PSK; KRESTIN®) involves the following actions: (1) recovery from immunosuppression induced by humoral factors such as transforming growth factor (TGF)-β or as a result of surgery and chemotherapy; (2) activation of antitumor immune responses including maturation of dendritic cells, correction of Th1/Th2 imbalance, and promotion of interleukin-15 production by monocytes; and (3) enhancement of the antitumor effect of chemotherapy by induction of apoptosis and inhibition of metastasis through direct actions on tumor cells. The clinical effectiveness of PSK has been demonstrated for various cancers. In patients with gastric or colorectal cancer, combined use of PSK with postoperative adjuvant chemotherapy prolongs survival, and this effect has been confirmed in multiple meta-analyses. For small-cell lung carcinoma, PSK in conjunction with chemotherapy prolongs the remission period. In addition, PSK has been shown to be effective against various other cancers, reduce the adverse effects of chemotherapy, and improve quality of life. Future studies should examine the effects of PSK under different host immune conditions and tumor properties, elucidate the mechanism of action exhibited in each situation, and identify biomarkers.

- Diminuisce neoangiogenesi
- Induce apoptosi nelle cellule tumorali
- Inibisce la telomerasi nelle cellule tumorali
- Potenzia effetto farmaci carcinostatici
- Azione antimetastatica
- Azione immunomodulante (stimola NK, macrofagi e linfociti T)
- Potenzia effetto Tamoxifene
- Non ha interazioni negative con farmaci allopatici
- Antiaterogenico

Coriulus versicolor: PSP



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Postepy Hig Med Dosw (Online). 2015 Jan 21;69(0):91-7.

Immunomodulatory and antitumor properties of polysaccharide peptide (PSP).

Piotrowski J[1], Jedrzejewski T[2], Kozak W[2].

Author information

Abstract

Modern medicine successfully uses multiple immunomodulators of natural origin, that can affect biological reactions and support body's natural defense mechanisms including antitumor activities. Among them is a group of products derived from fungi, including schizophyllan, lentinan, polysaccharide Krestin (PSK), and polysaccharidepeptide (PSP). Present paper is focused on polysaccharidepeptide, which due to the negligible toxicity and numerous benefits for health, is increasingly used in China and Japan as an adjuvant in the treatment of cancer. PSP is a protein-polisaccharide complex with a molecular weight 100 kDa derived from Coriolus versicolor mushroom. The results of numerous studies and clinical trials confirm that it inhibits the growth of cancer cells in in vitro and in vivo settings as well as decreases cancer treatment-related adverse side effects such as fatigue, loss of appetite, nausea, vomiting, and pain. PSP is able to restore weakened immune response observed in patients with cancer during chemotherapy. Its anti-tumor effects seemed to be mediated through immunomodulatory regulation. PSP stimulates cells of the immune system, induces synthesis of cytokines such as interleukin-1β (IL-1β), IL-6 and tumor necrosis factor-α (TNF-α), eicosanoids including prostaglandin E2 (PGE2), histamine, reactive oxygen species and nitrogen mediators. There is a growing interest in understanding the mechanisms of PSP action. Because of its unique properties and safety, PSP may become a widely used therapeutic agent in the near future.

- Attiva le NK e ne aumenta l'attività citotossica
- Aumenta livelli di IL-2
- Aumenta rapporto CD4 helper/CD8 suppressors
- Stimola cellule Lymphokine-Activated Killer Cells

Coriolus versicolor

Phytomedicine. 2014 May 21. pii: S0944-7113(14)00204-9. doi: 10.1016/j.phymed.2014.04.020. [Epub ahead of print]

In vivo and in vitro anti-tumor and anti-metastasis effects of Coriolus versicolor aqueous extract on mouse mammary 4T1 carcinoma.

Luo KW[1], Yue GG[1], Ko CH[1], Lee JK[1], Gao S[1], Li LF[1], Li G[2], Fung KP[3], Leung PC[1], Lau CB[4].

Indicazioni:

Infezioni batteriche, virali (es.HSV, HIV, EBV…) e micotiche

Tumori ormonoresponsivi

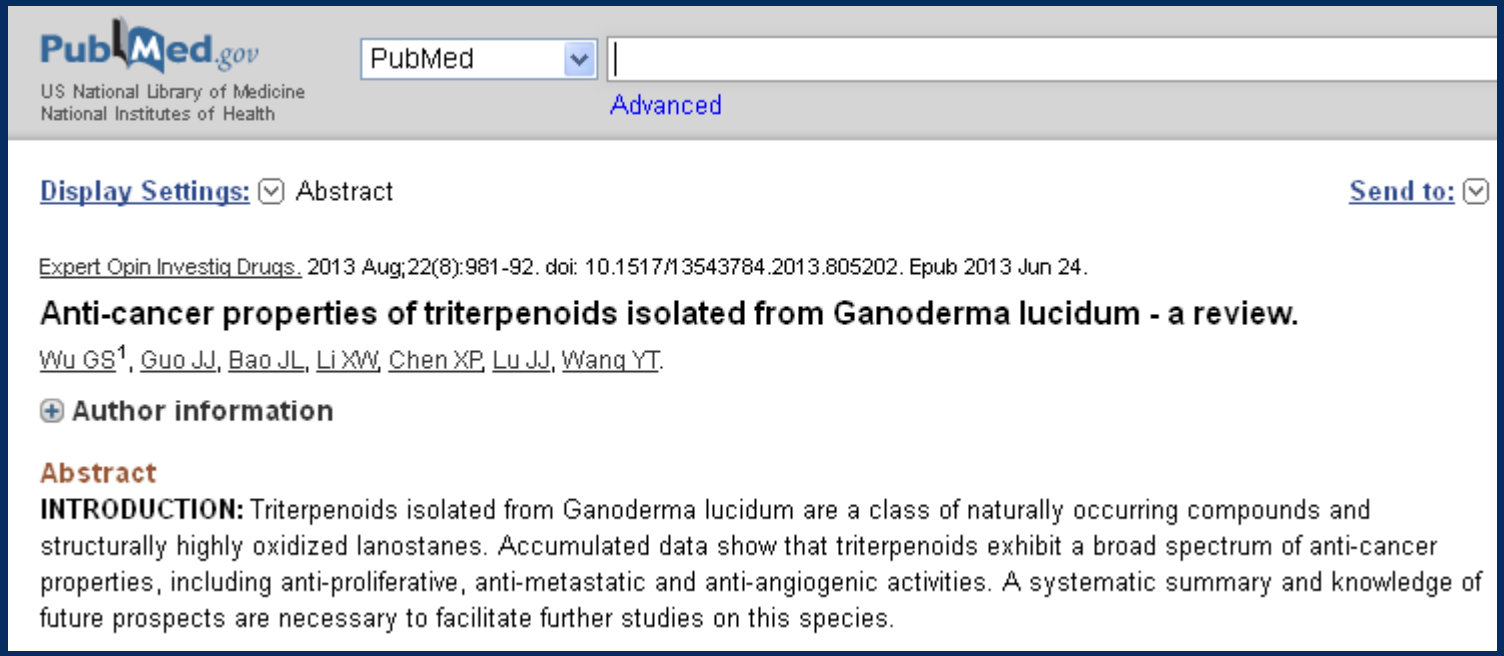
Effetti collaterali da CT e RT

Patologie autoimmuni TH2

Fibromialgia, Miastenia, A.R.

Leaky Gut Syndrome

Triterpeni



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Expert Opin Investig Drugs. 2013 Aug;22(8):981-92. doi: 10.1517/13543784.2013.805202. Epub 2013 Jun 24.

Anti-cancer properties of triterpenoids isolated from Ganoderma lucidum - a review.

Wu GS[1], Guo JJ, Bao JL, Li XW, Chen XP, Lu JJ, Wang YT.

Author information

Abstract

INTRODUCTION: Triterpenoids isolated from Ganoderma lucidum are a class of naturally occurring compounds and structurally highly oxidized lanostanes. Accumulated data show that triterpenoids exhibit a broad spectrum of anti-cancer properties, including anti-proliferative, anti-metastatic and anti-angiogenic activities. A systematic summary and knowledge of future prospects are necessary to facilitate further studies on this species.

- Triterpenoidi e derivati
  - attività citotossica e antitumorale
- Triterpeni
  - ac.ganoderici A e C di *Ganoderma lucidum* → Inibizione del rilascio di istamina
  - Epatoprotettivi (ac.ganoderico R,S)
  - Citotossici (ac.ganoderici T,V,W,X,Y,Z)

Triterpeni

Tumour Biol. 2014 Nov;35(11):11153-8. doi: 10.1007/s13277-014-2426-7. Epub 2014 Aug 8.

Betulin inhibits lung carcinoma proliferation through activation of AMPK signaling.

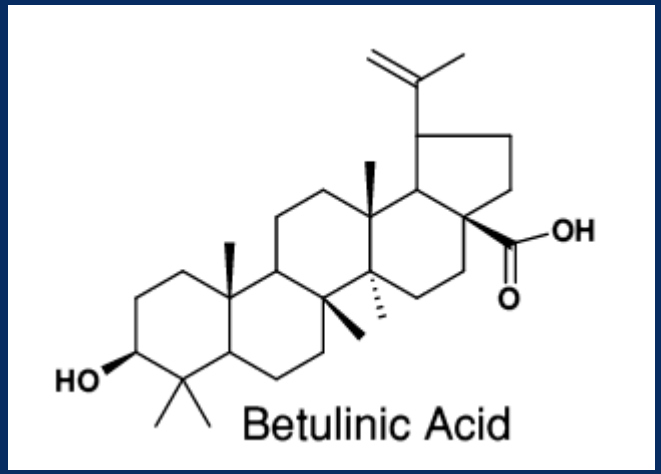
Li XD[1], Zhang YJ, Han JC.

⊕ **Author information**

Abstract

Betulin (lup-20(29)-ene-3β, 28-diol) is an abundant, naturally occurring triterpene. It is commonly isolated from the bark of birch trees and forms up to 30% of the dry weight of the extractive. In the present study, we revealed its antiproliferative effects and mechanisms using two lung carcinoma cells (A549 and NCI-292). By 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and bromodeoxyuridine (BrdU) incorporation assays, we found that betulin could efficiently inhibit cell growth and proliferation. Besides, several key genes of cell-cycle regulators were also affected by betulin treatment. At the molecular level, our results demonstrated that treatment with betulin was also associated with activation of AMP kinase and inhibition of mTOR/p70S6K/pS6 signaling in these cells. In agreement, inhibition of AMPK signaling largely reversed the antiproliferative roles of betulin. Taken together, these data provide evidence for a mechanism that may contribute to the antineoplastic effects of betulin and justify further work to explore its potential roles in lung cancer prevention and treatment.

- Attività antiproliferativa
- Antitumorale
- Controllo dei disordini metabolici, come obesità e sdr metabolica
- Antivirale (HCV, HSV..)
- Psoriasi



Betulinic Acid

Ricerca scientifica su nuovi funghi di interesse oncologico

Int J Med Mushrooms. 2014;16(1):17-28.

Telomerase inhibitory effects of medicinal mushrooms and lichens, and their anticancer activity.

Xu B[1], Li C[2], Sung C[3].

⊕ **Author information**

Abstract

Telomerase has been widely accepted as a cancer marker and a promising therapeutic target for novel anticancer drugs. The aim of this study was to investigate the in vitro telomerase inhibitory effects of mushrooms and their anticancer properties. The inhibitory effects of mushrooms and lichens against telomerase activity of HL-60 cells were systematically assessed using polymerase chain reaction based on assay of telomeric repeat amplification protocol. Telomerase inhibitory samples were further tested for antiproliferation effects against the gastric cell line SNU-1 using the MTT method. Ethyl acetate extract of Pleurotus ostreatus, ethyl acetate and water extracts of Lasiosphaera fenzlii, hexane extract of Strobilomyces floccopus, water extract of Sarcodon aspratus, and hexane, ethyl acetate, and water extracts from Umbilicaria esculenta showed strong positive telomerase inhibitory activity. Hexane extract of S. floccopus and water extracts from the edible lichen U. esculenta exhibited strong anticancer effects against SNU-1 cells through antiproliferation assay. The water extract of U. esculenta has a great potential to be developed into an anticancer agent that targets telomerase.

- Pleurotus ostreatus
- Lasiosphaera fenzlii
- Strobilomyces floccopus
- Sarcodon aspratus
- Umbilicaria esculenta

Preparati di funghi medicinali

- **Fungi *in toto*** essiccati freddo.
- **Estratti** standardizzati in beta-glucani e triterpeni concentrati.
- **Sinergici** (80% *in toto* e 20% estratti titolati in beta-glucani).
- **Bio-Superfood** 100% *in toto* (formule con più funghi).

Reishi
Estrazione standardizzata in β-/α-glucani e triterpeni

65 Kg di fresco

15 kg di secco

1kg di estratto

Produzione biologica esclusivamente europea GMP

Ruolo terapeutico dei funghi

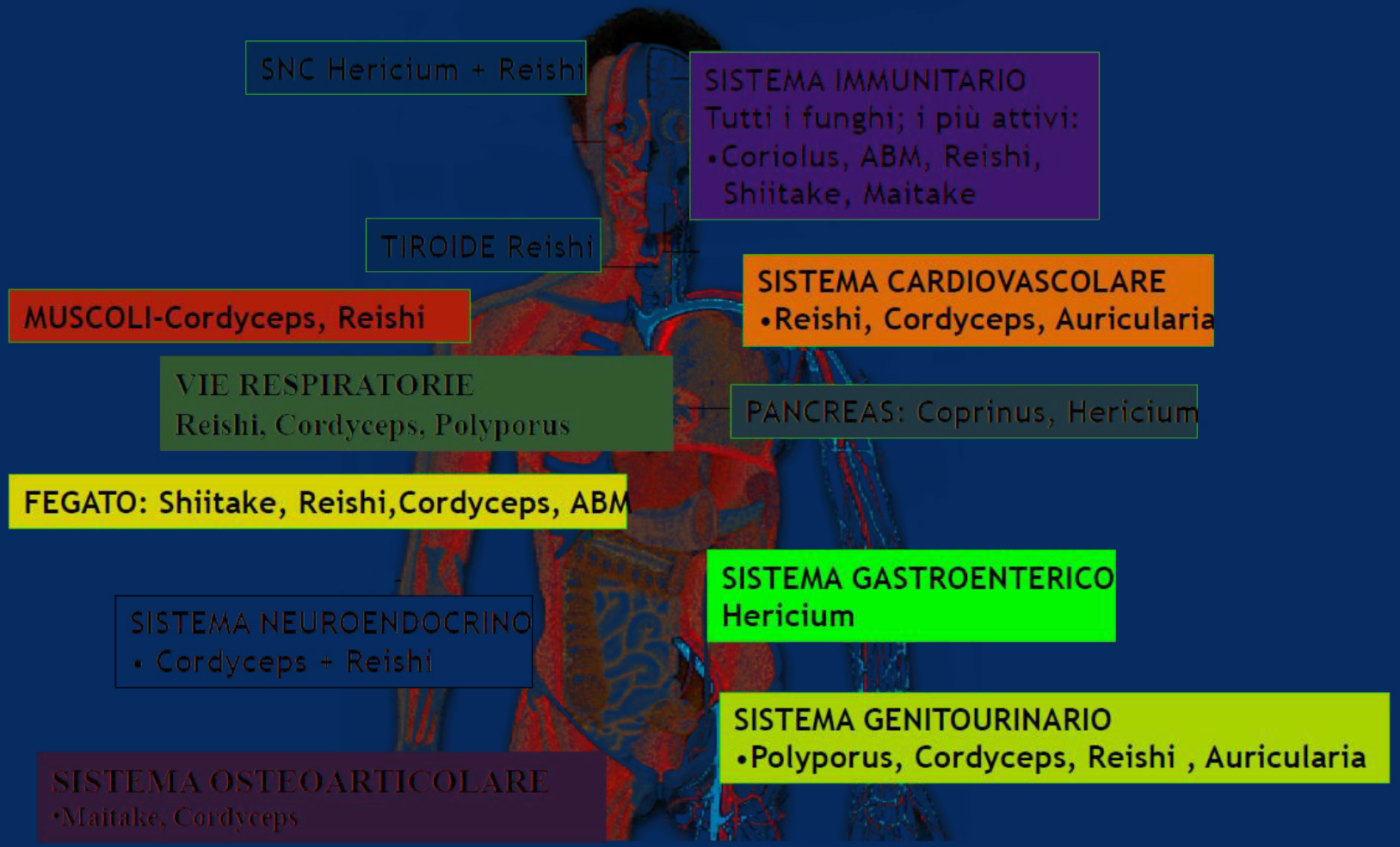
Tutti i funghi hanno in comune le tre seguenti funzioni:

- immunomodulazione
- azione antinfiammatoria
- detossificazione epatica

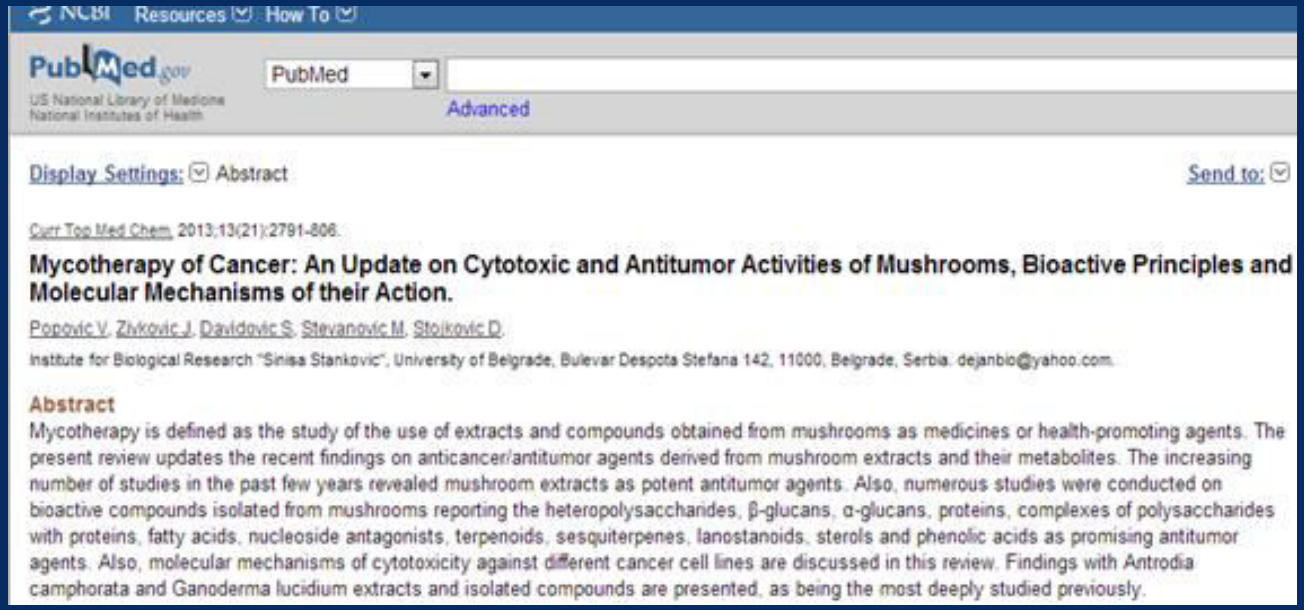
Mentre ogni fungo in base al suo tropismo d'organo ha effetti specifici sulle seguenti funzioni:

- fluidificazione del sangue
- chelazione dei metalli pesanti
- antagonizzazione delle spinte anomale di crescita cellulare
- sinergia con chemio-radioterapia
- regolazione livelli di glicemia colesterolo e trigliceridi nel sangue
- anti-diabetiche
- supporto performance sportive
- anti-tumorali
- riequilibrio batteri intestinali

Tropismo d'organo dei funghi



Proprietà antineoplastiche dei funghi medicinali



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Curr Top Med Chem. 2013;13(21):2791-806.

Mycotherapy of Cancer: An Update on Cytotoxic and Antitumor Activities of Mushrooms, Bioactive Principles and Molecular Mechanisms of their Action.

Popovic V, Zivkovic J, Davidovic S, Stevanovic M, Stoikovic D.

Institute for Biological Research "Sinisa Stankovic", University of Belgrade, Bulevar Despota Stefana 142, 11000, Belgrade, Serbia. dejanbio@yahoo.com.

Abstract

Mycotherapy is defined as the study of the use of extracts and compounds obtained from mushrooms as medicines or health-promoting agents. The present review updates the recent findings on anticancer/antitumor agents derived from mushroom extracts and their metabolites. The increasing number of studies in the past few years revealed mushroom extracts as potent antitumor agents. Also, numerous studies were conducted on bioactive compounds isolated from mushrooms reporting the heteropolysaccharides, β-glucans, α-glucans, proteins, complexes of polysaccharides with proteins, fatty acids, nucleoside antagonists, terpenoids, sesquiterpenes, lanostanoids, sterols and phenolic acids as promising antitumor agents. Also, molecular mechanisms of cytotoxicity against different cancer cell lines are discussed in this review. Findings with Antrodia camphorata and Ganoderma lucidium extracts and isolated compounds are presented, as being the most deeply studied previously.

Anti-angiogenica
Pro-apoptotica
Citotossica diretta (NK)
Anti-mutagena
Antiproliferativa
Antimetastatica
Citostatica

PNEI modulante
Anti-infiammatoria
Anti-ossidante
Rigenerazione tissutale
Radio e chemio-protezione

Ganoderma Lucidum (Reishi)

- È chiamato fungo dell'immortalità o dei 10.000 anni
- È annoverato tra le dieci sostanze naturali più efficaci
- È l'antiossidante ed antidegenerativo per eccellenza
- Calma la mente e tonifica il corpo
- È un adattogeno
- Riduce l'ipertensione da stress e l'infiammazione cronica sistemica
- Riduce il colesterolo plasmatico e regola l'infiammazione dell'endotelio
- Controlla l'ansia, favorisce il sonno e abbassa la percezione dello stress

Ganoderma Lucidum (Reishi)

Sostanze bioattive contenute:

- Circa 400 composti bioattivi tra cui
  - 140 triterpeni – terpenoidi
  - Oltre 200 tipi di polisaccaridi e glicoproteine
  - Nucleotidi
  - Cerebrosidi
  - Steroli precursori ormonali
  - Acidi grassi
  - Minerali (germanio in grande quantità, Fe, Cu, Zn, Mg, Mn, K, Ca)
  - Vitamine gruppo B e acido folico
  - 17 amminoacidi tra cui tutti gli essenziali
  - Proteine con specifiche attività
  - Enzimi antiossidanti (SOD, laccasi) ed enzimi detossificanti (citP450)
  - Adenosina
  - Sostanze ad attività antistaminica – acido ganodermico C e D

Phytother Res 1999 Sep; 13(6):529-31 Triterpene antioxidants from ganoderma lucidum.
Zhu M, Chang Q, Wong LK, Chong FS, Li RC, Department of Pharmacy, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China.
Lakshmi B, Ajith TA, Sheena N, Gunapalan N, Janardhanan KK., Teratog Carcinog Mutagen 2003;23 Suppl 1:85-97 Antiperoxidative, anti-inflammatory, and antimutagenic activities of ethanol extract of the mycelium of Ganoderma lucidum occurring in South India.
Acta Medica (Hradec Kralove) 1999; 42(4):123-5 Anti-inflammatory triterpenoids from mysterious mushroom Ganoderma lucidum and their potential possibility in modern medicine. Patocka J, Department of Toxicology, Purkyne Military Medical Academy, Hradec Kralove.

Ganoderma Lucidum (Reishi)

Molecules **2013**, *18*, 7609-7630; doi:10.3390/molecules18077609

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Review

Hepatoprotective Effects of Mushrooms

Andréia Assunção Soares [1], Anacharis Babeto de Sá-Nakanishi [1], Adelar Bracht [1], Sandra Maria Gomes da Costa [2], Eloá Angélica Koehnlein [2], Cristina Giatti Marques de Souza [1] and Rosane Marina Peralta [1,*]

- Attività epatoprotettiva
- Migliora l'attività tiroidea
- Migliora l'ossigenazione
- Ripara i danni ossidativi
- Riduce il colesterolo e l'accumulo lipidico
- Protegge fegato e reni

Effetti del Ganoderma Lucidum

Azioni farmacologiche

- Supporto oncologico
  - Riduce gli effetti collaterali della chemio e della radio
  - Riduce i rischi di metastatizzazione
  - Migliora la qualità di vita
  - Riduce il dolore neoplastico
  - Aumenta i livelli di cellule NK e linfociti T citotossici e quindi la sorveglianza immunitaria
  - Effetto cardioprotettivo e cardiotonico
- Antibatterico e antivirale
- Azione antiandrogenica nell'IPB e nel K della prostata
- Azione epatoprotettiva e antiepatite B grazie all'acido ganoderico R con effetto antifibrotico
- Supporto al metabolismo energetico attivando il ciclo di Krebs, enzimi e mitocondri
- Antinvecchiamento
- Prevenzione neurodegenerativa (Parkinson e Alzheimer, attenua la neurotossicità indotta dalla Beta Amiloide)

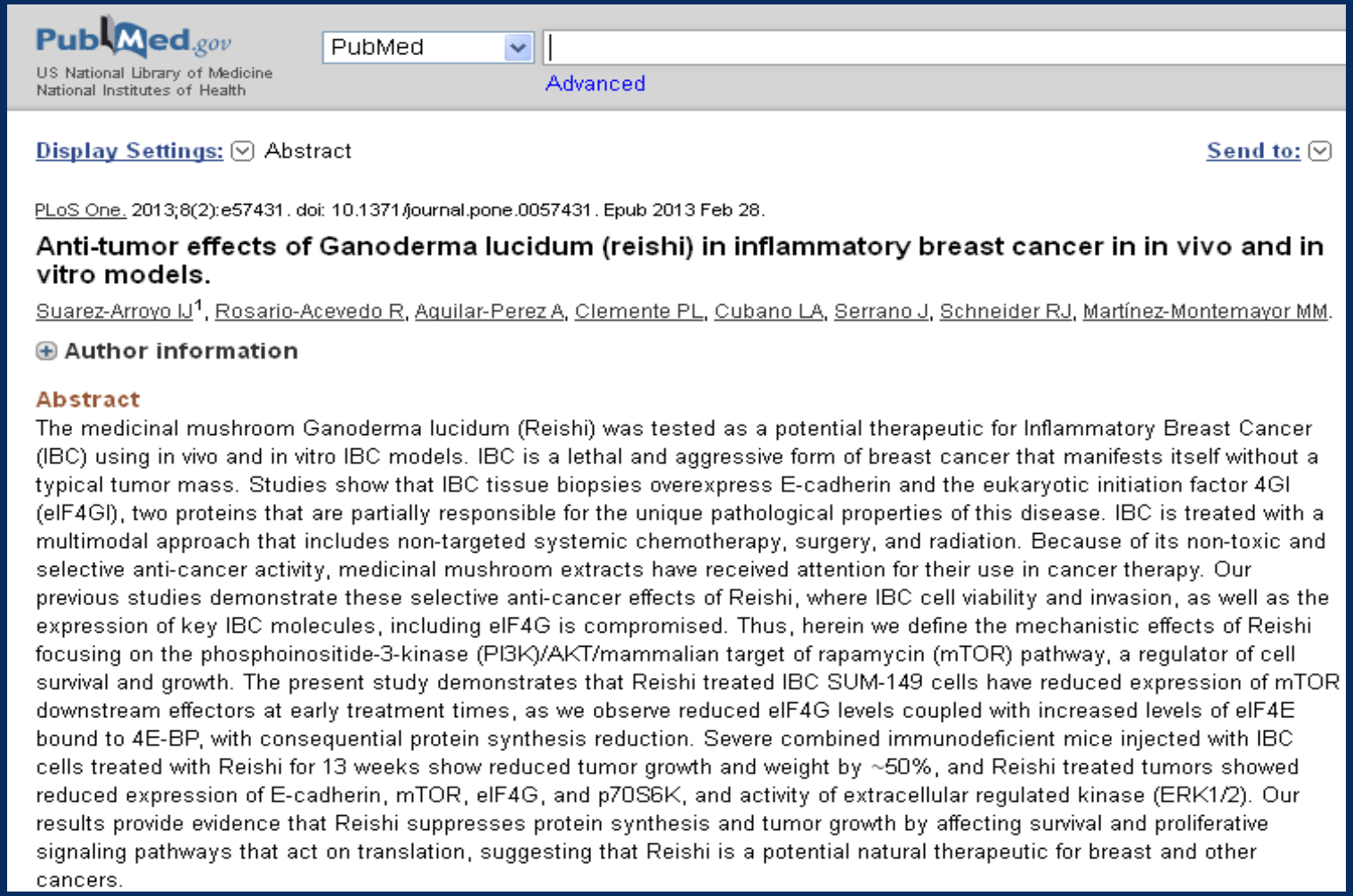
Ganoderma Lucidum (Reishi)

Azioni farmacologiche

- Effetti a livello cardiovascolare
  - Inibisce l'aggregazione piastrinica grazie ad acido ganodermico S ed adenosina con azione simile all'aspirina
  - Riduce l'ipertensione: 1) con meccanismo ACE Inibitore; 2) da inibizione sul SN Simpatico e azione vagotonica e ossigenazione, per cui riduce la pressione diastolica, rallenta il ritmo cardiaco, dilata i vasi periferici
  - Effetto ipocolesterolemizzante con due meccanismi: da inibizione della HMG-CoA Reduttasi, da inibizione dell'assorbimento enterico di colesterolo

- Effetto antinfiammatorio – 50mg di polvere di Reishi hanno un'azione simile a 5mg di idrocortisone
- Effetto antiallergico
- Effetto antiossidante
- Effetto immunomodulante
  - Ripristino dell'equilibrio TH1/TH2
  - Effetto di stimolazione su leucociti, macrofagi/monociti, NK e LAK
  - Aumento attività citotossica dei linfociti T e di IL-2

Ganoderma Lucidum (Reishi)



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PLoS One. 2013;8(2):e57431. doi: 10.1371/journal.pone.0057431. Epub 2013 Feb 28.

Anti-tumor effects of Ganoderma lucidum (reishi) in inflammatory breast cancer in in vivo and in vitro models.

Suarez-Arroyo IJ[1], Rosario-Acevedo R, Aguilar-Perez A, Clemente PL, Cubano LA, Serrano J, Schneider RJ, Martínez-Montemayor MM.

Author information

Abstract

The medicinal mushroom Ganoderma lucidum (Reishi) was tested as a potential therapeutic for Inflammatory Breast Cancer (IBC) using in vivo and in vitro IBC models. IBC is a lethal and aggressive form of breast cancer that manifests itself without a typical tumor mass. Studies show that IBC tissue biopsies overexpress E-cadherin and the eukaryotic initiation factor 4GI (eIF4GI), two proteins that are partially responsible for the unique pathological properties of this disease. IBC is treated with a multimodal approach that includes non-targeted systemic chemotherapy, surgery, and radiation. Because of its non-toxic and selective anti-cancer activity, medicinal mushroom extracts have received attention for their use in cancer therapy. Our previous studies demonstrate these selective anti-cancer effects of Reishi, where IBC cell viability and invasion, as well as the expression of key IBC molecules, including eIF4G is compromised. Thus, herein we define the mechanistic effects of Reishi focusing on the phosphoinositide-3-kinase (PI3K)/AKT/mammalian target of rapamycin (mTOR) pathway, a regulator of cell survival and growth. The present study demonstrates that Reishi treated IBC SUM-149 cells have reduced expression of mTOR downstream effectors at early treatment times, as we observe reduced eIF4G levels coupled with increased levels of eIF4E bound to 4E-BP, with consequential protein synthesis reduction. Severe combined immunodeficient mice injected with IBC cells treated with Reishi for 13 weeks show reduced tumor growth and weight by ~50%, and Reishi treated tumors showed reduced expression of E-cadherin, mTOR, eIF4G, and p70S6K, and activity of extracellular regulated kinase (ERK1/2). Our results provide evidence that Reishi suppresses protein synthesis and tumor growth by affecting survival and proliferative signaling pathways that act on translation, suggesting that Reishi is a potential natural therapeutic for breast and other cancers.

Proprietà anti-cancro:
anti-proliferativa, anti-metastatica, anti-angiogenetica

Agaricus Blazei Murrill

Contiene:

- Minerali
  - Na, Ca, Fe, K, P, Mg, Zn, Cu, Mn, Se
- Polisaccaridi
- Betaglucani
- Steroli, Ergosteroli
- Triperpeni
- Acido linoleico
- Vitamine gruppo B e D
- Enzimi
  - Tirosinasi, importante per la produzione di ubichinone, dopamina e melatonina
  - Polifenolo ossidasi
  - Glutatione Perossidasi
  - Sod Catalasi
- Fibre e chitina

Agaricus Blazei Murrill

Azioni farmacologiche:

- Marcata azione Antitumorale
- Modulatore dell'infiammazione cronica
- Ipoglicemizzante, ipolipemizzante
- Immunomodulante, antibatterico ed antivirale, antinfiammatorio
- Aumenta i livelli di adiponectina
- Epatoprotettore
- Antiallergico
- Antiaging


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Complement Ther Med. 2013 Oct;21(5):460-7. doi: 10.1016/j.ctim.2013.07.001. Epub 2013 Aug 12.

Quality of life improvements among cancer patients in remission following the consumption of Agaricus blazei Murill mushroom extract.

Ohno S[1], Sumiyoshi Y, Hashine K, Shirato A, Kyo S, Inoue M.

CONCLUSION: This preliminary longitudinal clinical study demonstrated that daily intake of ABM appears to improve both physical and mental components based on SF-8 qualimetric analysis.

ABM: Frazione A1 e A2

Cancer Sci. 2004 Sep;95(9):758-64.

Isolation of an anti-angiogenic substance from Agaricus blazei Murill: its antitumor and antimetastatic actions.

Kimura Y[1], Kido T, Takaku T, Sumiyoshi M, Baba K.

⊕ **Author information**

Abstract

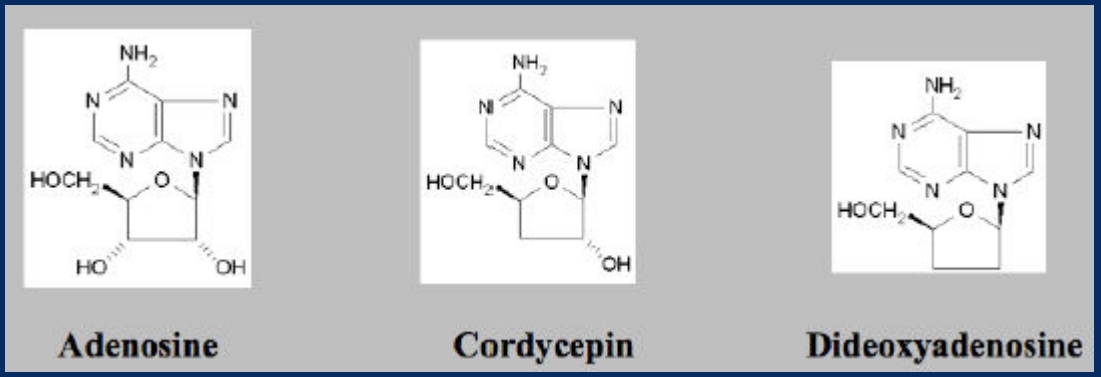
We previously found that ergosterol isolated from Agaricus blazei inhibited tumor growth through the inhibition of tumor-induced neovascularization. In the present study, we isolated further anti-angiogenic substances (A-1 and A-2) from this fungus using an assay system of angiogenesis induced by Matrigel supplemented with vascular endothelial growth factor, and A-1 was identified as sodium pyroglutamate. Next, we examined the antitumor and antimetastatic actions of A-1 using Lewis lung carcinoma (LLC)-bearing mice. A-1 (30, 100 and 300 mg/kg) inhibited tumor growth and metastasis to the lung. The reduction of the numbers of splenic lymphocytes, CD4+ and CD8+ T cells in LLC-bearing mice was inhibited by the oral administration of A-1 (30, 100 and 300 mg/kg). Further, A-1 increased the number of apoptotic cells of tumors and the numbers of CD8+ T and natural killer cells invading the tumors, and inhibited the increase of von Willebrand factor expression (a measure of angiogenesis) in the tumors. These results suggest that the antitumor and antimetastatic actions of A-1 (sodium pyroglutamate) may be associated with inhibition of the reduction of immune response caused by the tumor growth and tumor-induced neovascularization. This is the first report showing that sodium pyroglutamate isolated from A. blazei as an anti-angiogenic substance has potent antitumor and antimetastatic actions, as well as immune-modulatory activity, in tumor-bearing mice.

- Azione antiangiogenetica (A1 e A2)
- Attività antimetastatica (A1)
- Inibizione della crescita tumorale (A1)

Cordyceps sinensis

ATTIVITA' ANTIVIRALE e ANTITUMORALE

- Nucleosidi naturalmente alterati del Cordyceps mimano ARV sintetici: inibiscono la replicazione virale interrompendo la sintesi RNA->DNA a livello dei legami H tra le basi azotate
- Inibizione della trascrittasi inversa



Cordyceps sinensis

- Marcata azione di rigenerazione energetica dei reni
- Potenzia il sistema immunitario
- Anabolismo muscolare
- Azione antireplicativa virale e antitumorale
- Regolazione del metabolismo e controllo della glicemia
- Aumento della potenza sessuale
- Aumento metabolismo aerobico
- Azione di rigenerazione dei tessuti
- Azione antidepressiva
- Riduzione del rischio di rigetto da trapianti d'organo, in associazione a ciclosporina

Shiitake e TNF-α

Food Chem. 2014 Apr 1;148:92-6. doi: 10.1016/j.foodchem.2013.10.015. Epub 2013 Oct 14.

Anti-inflammatory effects of five commercially available mushroom species determined in lipopolysaccharide and interferon-γ activated murine macrophages.

Gunawardena D[1], Bennett L, Shanmugam K, King K, Williams R, Zabaras D, Head R, Ooi L, Gyengesi E, Münch G.

⊕ Author information

Abstract

Inflammation is a well-known contributing factor to many age-related chronic diseases. One of the possible strategies to suppress inflammation is the employment of functional foods with anti-inflammatory properties. Edible mushrooms are attracting more and more attention as functional foods since they are rich in bioactive compounds, but their anti-inflammatory properties and the effect of food processing steps on this activity has not been systematically investigated. In the present study, White Button and Honey Brown (both Agaricus bisporus), Shiitake (Lentinus edodes), Enoki (Flammulina velutipes) and Oyster mushroom (Pleurotus ostreatus) preparations were tested for their anti-inflammatory activity in lipopolysaccharide (LPS) and interferon-γ (IFN-γ) activated murine RAW 264.7 macrophages. Potent anti-inflammatory activity (IC_{50}<0.1 mg/ml), measured as inhibition of NO production, could be detected in all raw mushroom preparations, but only raw Oyster (IC_{50}=0.035 mg/ml), Shiitake (IC_{50}=0.047 mg/ml) and Enoki mushrooms (IC_{50}=0.099 mg/ml) showed also potent inhibition of TNF-α production. When the anti-inflammatory activity was followed through two food-processing steps, which involved ultrasonication and heating, a significant portion of the anti-inflammatory activity was lost suggesting that the anti-inflammatory compounds might be susceptible to heating or prone to evaporation.

- Antagonizza gli effetti a livello centrale e periferico del TNF-α, responsabile della cachessia neoplastica

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J Med Food. Jul 2013; 16(7): 602–617.
doi: 10.1089/jmf.2012.0222

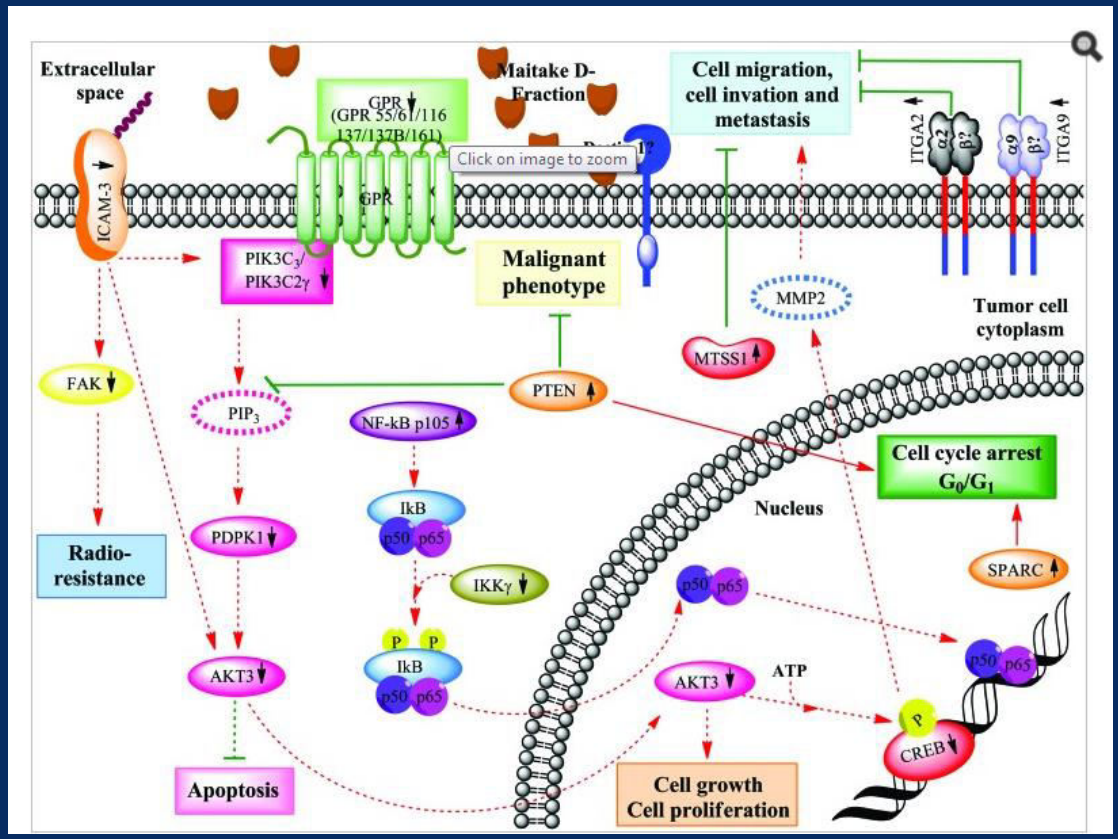
PMCID: PMC3719462

Genes Related to Suppression of Malignant Phenotype Induced by Maitake D-Fraction in Breast Cancer Cells

Eliana Noelia Alonso, Manuela Orozco, Alvaro Eloy Nieto, and Gabriela Andrea Balogh

Maitake D-Fraction

- Stimola apoptosi
  (in sinergia con la Vit C)
- Inibisce crescita e proliferazione cellulare
- Arresta ciclo cellulare
- Blocca la migrazione e le metastasi della cellula tumorale
- Riduce la farmaco-resistenza



Maitake e controllo glicemico

Diabetes Obes Metab. 2002 Jan;4(1):43-8.

Effects of a water-soluble extract of maitake mushroom on circulating glucose/insulin concentrations in KK mice.

Manohar V[1], Talpur NA, Echard BW, Lieberman S, Preuss HG.

Biotechnol Appl Biochem. 2013 Jul-Aug;60(4):446-52. doi: 10.1002/bab.1105.

Inhibitory potential of Grifola frondosa bioactive fractions on α-amylase and α-glucosidase for management of hyperglycemia.

Su CH[1], Lu TM, Lai MN, Ng LT.

La X-fraction abbassa il glucosio circolante con modalità dose-dipendente.

La combinazione della riduzione dei livelli di insulina e di glucosio ematico suggerisce un'azione di sensibilizzazione all'insulina. Non è stata evidenziata tossicità

Attività antidiabetica della Frazione X del Maitake:

- correlata al metabolismo del glucosio dopo il suo assorbimento
- aumento del numero dei recettori periferici all'insulina

Inibisce l'enzima alfa glucosidasi, responsabile dell'assorbimento degli zuccheri (effetto acarbosio-simile)

Vantaggi dell'utilizzo dei funghi in Oncologia

- Alta concentrazione di principi attivi, con effetto sinergico tra di loro e con i chemioterapici
- Riduzione effetti collaterali CT e RT
- Maggiore compliance alla terapia (riduzione del numero di integratori da assumere)
- Riduzione delle metastasi e
  delle recidive
- Tempi di recupero più rapidi
- Migliore qualità di vita

Conclusioni

- In Oncologia Integrata i Funghi Medicinali si rivelano un utile supporto terapeutico, comprovato da evidenze scientifiche, che permette di agire sulle cause e sui numerosi sintomi presenti contemporaneamente, potenziando l'effetto dei chemioterapici e diminuendo i loro effetti collaterali, riducendo l'uso di farmaci allopatici, migliorando la qualità e le aspettative di vita

Grazie per l'attenzione

San Gregorio di Catania
10/11 Maggio 2019

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