

Mechanism of Chinese medicinal herb

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ABSTRACT

Ganoderma lucidum called 'Lingzhi' (the mushroom of immortality) in China is a fungus widely used in the traditional Chinese medicine. Triterpenoids are found only in *G. lucidum*, and are the main pharmacological components of *G. lucidum*. 3-D structures of Ganoderic acid C1 and C2 are input into the INVDOCK programme. The identified proteins are considered potential targets of Ganoderic acid C1 and C2. The protein targets listed by INVDOCK have a strong association with cancer, breast cancer and colorectal cancer. There are also possible associations with AIDS.

INTRODUCTION

Ganoderma lucidum (Fr.) Karst. (Polyporaceae) is a species of basidiomycetes that belongs to Ganodermataceae of Aphyllophorales. The potential medicinal value and wide acceptability of *G. lucidum* have attracted intense interest in the search for pharmacological compounds from these edible mushrooms.

MATERIALS AND METHODS

G. lucidum has significantly higher amounts of Ganoderic acid C (see Table 1) at 89.5mg/kg of raw mushroom. Hence investigations will be centred on Ganoderic acid C. Ganoderic acid C is further divided into 2 subtypes C1 and C2 (Kikuchi et al., 1986).

The Chapman & Hall Combined Chemical Dictionary (CCD) was used to obtain the 2-dimensional structure of Ganoderic acid C1 and C2. Combined Chemical Dictionary (CCD) is a structured database holding information on chemical substances.

2D-molecular structures of Ganoderic acid C1 and C2 from Combined Chemical Dictionary (CCD) are automatically converted to three-dimensional models with the correct stereochemistry when pasted into the WebLab ViewerPro. WebLab ViewerPro is a tool for visualizing, building, and manipulating molecular and crystal structures and for sharing chemical information.

A computer method, and its application software INVDOCK, was used for computer-automated identification of potential protein targets of Ganoderic acid C1 and C2.

The 3-D structures of Ganoderic acid C1 and C2 (the small molecules being studied) are input into the INVDOCK programme; the software automatically searches a protein 3-D structure database (this database currently covers 9000 protein and nucleic acid entries) to

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identify the protein molecule that Ganoderic acid C1 and C2 can bind to. The identified proteins are considered potential targets of Ganoderic acid C1 and C2.

After obtaining the potential protein targets of Ganoderic acid C1 and C2 using INDOCK, the possible associated diseases were retrieved using Therapeutic Target Database (X. Chen et al., 2002).

RESULTS AND DISCUSSION

Table 1. Associated diseases of Ganoderic acid C1.

<i>Compound</i>	<i>Disease</i>	<i>Reference</i>
DNA POLYMERASE BETA	Viral infection	Perspectives in antiviral chemotherapy. <i>Fundam Clin Pharmacol.</i> 1990;4(4):357-72.
DIHYDROFOLATE REDUCTASE	Cancer	Novel inhibitors of Trypanosoma cruzi dihydrofolate reductase. <i>Eur J Med Chem.</i> 2001 May;36(5):395-405.
	Leprosy	In vivo activity of epiroprim, a dihydrofolate reductase inhibitor, singly and in combination with dapsone, against Mycobacterium leprae. <i>Int J Antimicrob Agents.</i> 2002 Jan;19(1):71-4.
PEROXISOME PROLIFERATOR ACTIVATE	Cancer	NIL
CYCLOPHILIN A	Cancer	The rapamycin-sensitive signal transduction pathway as a target for cancer therapy. <i>Oncogene.</i> 2000 Dec 27;19(56):6680-6.
PURINE NUCLEOSIDE PHOSPHORYLASE	Cancer	NIL
GUANYLYL CYCLASE	Colorectal cancer	Heterogeneity of guanylyl cyclase C expressed by human colorectal cancer cell lines in vitro. <i>Cancer Epidemiol Biomarkers Prev.</i> 1998 Jun;7(6):505-14.
FARNESYLTRANSFERASE	Breast cancer	Farnesyltransferase inhibitors in breast cancer therapy. <i>Cancer Invest.</i> 2002;20 Suppl 2:30-7.
	Cancer	Farnesyl transferase inhibitors as anticancer agents. <i>Eur J Cancer.</i> 2002 Sep;38(13):1685-700.
	Colorectal cancer	Therapeutics targeting signal transduction for patients with colorectal carcinoma. <i>Br Med Bull.</i> 2002;64:227-54.

HIV-1 PROTEASE	AIDS	Combination of protease inhibitors for the treatment of HIV-1-infected patients: a review of pharmacokinetics and clinical experience. Antivir Ther. 2001 Dec;6(4):201-29.
HIV PROTEASE	AIDS	Combination of protease inhibitors for the treatment of HIV-1-infected patients: a review of pharmacokinetics and clinical experience. Antivir Ther. 2001 Dec;6(4):201-29.

Table 2. Associated diseases of Ganoderic acid C2.

<i>Compound</i>	<i>Disease</i>	<i>Reference</i>
C-H-RAS P21 PROTEIN	Cancer	Ras family genes: an interesting link between cell cycle and cancer. J Cell Physiol. 2002 Aug;192(2):125-30
DIHYDROFOLATE REDUCTASE	Chagas' disease	Novel inhibitors of Trypanosoma cruzi dihydrofolate reductase. Eur J Med Chem. 2001 May;36(5):395-405.
	Leprosy	In vivo activity of epiroprim, a dihydrofolate reductase inhibitor, singly and in combination with dapsone, against Mycobacterium leprae. Int J Antimicrob Agents. 2002 Jan;19(1):71-4.
CYCLOPHILIN A	Cancer	The rapamycin-sensitive signal transduction pathway as a target for cancer therapy. Oncogene. 2000 Dec 27;19(56):6680-6.
PURINE NUCLEOSIDE PHOSPHORYLASE	Cancer	
GUANYLYL CYCLASE	Colorectal cancer	Heterogeneity of guanylyl cyclase C expressed by human colorectal cancer cell lines in vitro. Cancer Epidemiol Biomarkers Prev. 1998 Jun;7(6):505-14.
FARNESYLTRANSFERASE	Breast cancer	Farnesyltransferase inhibitors in breast cancer therapy. Cancer Invest. 2002;20 Suppl 2:30-7.
	Cancer	Farnesyl transferase inhibitors as anticancer agents. Eur J Cancer. 2002 Sep;38(13):1685-700.

	Colorectal cancer	Therapeutics targeting signal transduction for patients with colorectal carcinoma. <i>Br Med Bull.</i> 2002;64:227-54.
HIV-1 PROTEASE	AIDS	Combination of protease inhibitors for the treatment of HIV-1-infected patients: a review of pharmacokinetics and clinical experience. <i>Antivir Ther.</i> 2001 Dec;6(4):201-29.
HIV PROTEASE	AIDS	Combination of protease inhibitors for the treatment of HIV-1-infected patients: a review of pharmacokinetics and clinical experience. <i>Antivir Ther.</i> 2001 Dec;6(4):201-29.

Although there is no literature that states that Ganoderic acid C1 and C2 are directly responsible for the therapeutic effect of *G. lucidum*, there has been evidence to suggest that *G. lucidum* is likely to have anti-HIV and anti-tumour effects.

REFERENCES

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