

Bioactive Components of *Ganoderma lucidum* (W.Curt.:Fr.) Lloyd Can Induce Apoptosis of Tumor Cells

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The antitumor activity of Ling Zhi or Reishi mushroom *Ganoderma lucidum* has been studied widely *in vivo* and *in vitro*, and many reports show that polysaccharides are the main antitumor active substances in *G. lucidum*, acting by improvement of the host immunity. In addition, it was also reported that an extract of *G. lucidum* killed the tumor cells *in vitro*. In our experiment, it was also found that crude extracts of *G. lucidum* (named LZ) and their fractions significantly inhibited the proliferation of different tumor cells, and the fractions induced SW620 cell apoptosis *in vitro*.

The antiproliferative capacity of LZ was tested using 11 tumor cell lines. LZ very strongly inhibited the growth of Jurkat, K562, SW620, LS180, and QGP-1 cell lines, and the IC₅₀ of LZ to them was measured as 180, 200, 180, 320, and 360 µg/mL, respectively. Moreover, LZ showed the capacity to inhibit the growth of S180 cell lines, the IC₅₀ is 420 µg/mL, and meanwhile it obviously inhibits the growth of MCF7 and Caco-2 only at 1000 µg/mL. However, LZ does not possess inhibitory capacity to BON, Panc-1, and HUH7 cell lines in the range of experimental concentrations.

In order to find out the bioactive components from crude extracts, LZ were divided into two parts by dialysis, and then they were further fractionated

using different chromatographic procedures. All fractions obtained were tested for their antiproliferative capacity to SW620 cells. LZ-2-2 and LZ-DW-2-a-3 were found to be active components of LZ. After incubation with LZ and LZ-2-2, SW620 cells were found to form apoptotic bodies *in situ* checked by light microscopy—their apoptosis activity was confirmed by staining with Annexin V-FITC conjugate. The apoptotic percentage of SW620 was quantified by flow cytometry. At the most effective concentration of 600 µg/mL, LZ induced 28% of cells to undergo apoptosis, 39.5% for LZ-2-2, and, at 1000 µg/mL, 51% for LZ-DW-2-a-3. The influence of LZ-2-2 and LZ-DW-2-a-3 on the cell cycle of SW620 cells during their apoptotic processes was analyzed by flow cytometry. Experimental results suggested that SW620 cells were arrested in the G₀ phase, and they could not transit from the G₂/M phase to the G₁ phase after treatment by LZ-2-2 or LZ-DW-2-a-3.

Until now, there has been no final answer as to how the extract of *G. lucidum* inhibited and killed the tumor cells. Our results revealed that some fractions from *G. lucidum* induced apoptosis of tumor cells, which means that *G. lucidum* exerts its antitumor function by the apoptosis pathway as well as by the immune pathway, which is accepted widely as a new pathway.