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Investigation into anti-epileptic effect and mechanisms of Ganoderma lucidum polysaccharides in *in vivo* and *in vitro* models

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There are about 60 million epileptic patients worldwide. Finding a more effective antiepileptic drug with fewer side effects is of continuing importance(1). Ganoderma lucidum, a mushroom having been used as Traditional Chinese Medicine, has showed the effect of antiepileptic effect with no side-effects(2). The aim of the present study was to assess the mechanisms of antiepileptic effects by Ganoderma lucidum polysaccharides (GLP).

In study 1, effect of GLP on calcium turnover, Ca^{2+}/calmodulin-dependent protein kinase type II α (CaMKII α) and ERK1/2 expression was investigated using primary hippocampal neurons from <1 day old rats. Neurons were cultured with normal medium (Control group), or Mg^{2+} free medium (Model I group) for 3 hours; neurons were incubated with Mg^{2+} free medium without GLP (Model II group), or with GLP (0·375 mg/ml) (GLP I group) for 3 hours and then cultured with the normal medium for an extra 3 hours; neurons were incubated with Mg^{2+} free medium for 3 hours and then cultured with a normal culture medium containing GLP for an extra 3 hours (GLP group II). In study 2, male Wistar rats ($n = 60$) were randomly divided into A) Control group; B) PBS group; and C) Epilepsy group: rats were given kainic acid (1·5 μg/μl was injected into hippocampus), then they were given GLP (i.p.) once a day for 7 days, GLP doses were D), 25 mg/kg; E), 50 mg/kg), and F, 100 mg/kg, respectively. Rat behavior and EEG were recorded. The number of immunohistochemical staining caveolin-1(Cav-1) and NF-κB positive cells was counted.

In study 1, GLP treatment increased CaMKIIα expression, and decreased calcium turnover. ERK1/2 had higher expression in cytoplasm and nucleus in Model groups compared with the normal Control groups ($P < 0·01$). In GLP group, the expression of ERK1/2 (Fig. 1) was inhibited. In study 2. Epileptic symptoms in rats of group C, D, E and F were observed in 7 minutes after kainic acid injection. In day 7, normal EEG, with lower wavelength of α and β wave, was recorded in group A and B; sharp and frequent wavelength was observed in group C, D, E or F (Fig. 2). Even more, compared to group C, more waves with lower wavelength existed in group D, E or F. The frequency of epilepsy discharge from initial 10–15/min reduced to 1/min after GLP treatment. Cav-1 positive cells (Fig. 2) and NF-κB positive cells in group C were significantly higher compared with group A and B. Compared with group C, GLP treatments further increased Cav-1 positive cells, but decreased NF-κB positive cells.

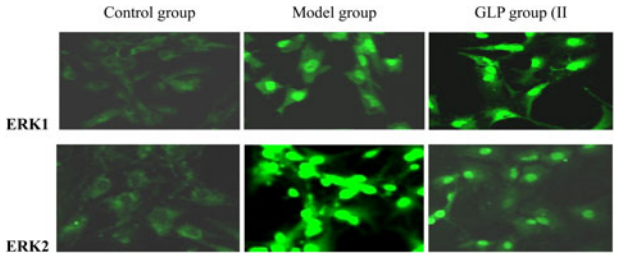

Fig. 1. Control group Model group GLP group (II)

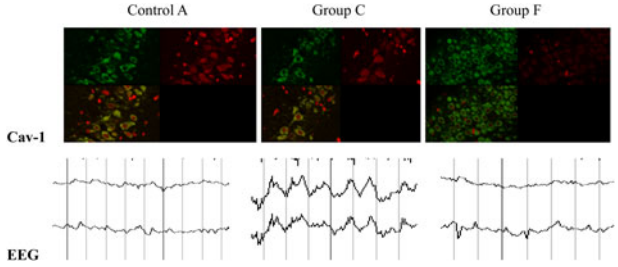

Fig. 2. Control A Group C Group F

In conclusion, GLP improved the epileptic behavior; inhibited calcium overloading and ERK1/2 and NF-KB expression; also stimulated CaMK II α and Cav-1 expression.

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