蜂王漿之抗老化生物活性相關研究

Studies on the anti-aging activity in royal jelly

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[摘要]

蜂王漿為一營養品，其可促使蜜蜂發育成蜂后。在民間療法中蜂王漿被認為具有抗老化，使人恢復活力、返老還童之功效。一些報告也指出，蜂王漿具有調節中樞神經系統、增加對疾病的抵抗性、以及免疫調節的功能等。本研究的目的，乃欲探討蜂王漿的抗老化作用並分離純化出其中之活性成分。祖原細胞為其有再生與分化等特性之幹細胞，在某些生長母子的調控下具有分化為神經細胞或神經膠細胞的功能，而有研究指出，隨著老鼠年紀的增加腦部祖原細胞伴隨著減少，因此，維持祖原細胞的數目式促進其分化皆有利於延緩老化的發生。因此本論文擬以上皮生長因子對應的祖原細胞，作為探討蜂王漿生物活性之研究模型，此外，本研究也建立以雷射誘導螢光偵測之毛細管電泳層析分析蜂王漿對神經細胞之神經傳遞物質產生之影響。另一方面，也使用果蠅培養模式評估蜂王漿是否能促進果蠅延命率。本研究，應用基因工程方法，成功的取得大量且具高活性上皮生長因子(Epidermal Growth Factor)，建立無血清之上皮因子對應的祖原細胞及神經細胞培養模式，發現蜂王漿可以促進祖原細胞分化與增生。經分子篩管柱層析、超臨界流體萃取、高效液相層析等分離純化步驟，在增生方面有 RJT4L4、RJT4L5、RJT4L6、RJT5L7、RJT5L8 等，在分化方面有 RJT6L2、RJT6L3、RJT6L4、RJT6L5、RJT9L3、RJT9L5 活性區分等。同時亦發現蜂王漿具有促進神經細胞增生與分化，增生方面有 RJT9、RJT10、RJT9H2、RJS2L3；分化方面有 RJSIL4、RJSIL5、RJS2L3、RJS2L4、RJS2L5、RJS4L2、RJS4L2 等區分，本研究發展以雷射 誘導螢光偵測之毛細管電泳層析分析神經細胞之神經傳遞物質含量，發現蜂王漿之 RJSIL4 、RJSIL5、RJS2L3、RJS2L4 可促進神經細胞之神經傳遞物質 Dopam、GABA、Glutamate 之生合成。另一方面，亦發現蜂王漿可延長果蠅壽命。這些蜂王漿含有的生物活性物質，目前已進行化學結構分析。本研究顯示蜂王漿含有能促 進祖原細胞增生與分化及對神經細胞與神經膠細胞之機能有顯著的調控作用的活性成分，並且可以延長果蠅的壽命。本研究首次對蜂王漿的抗老化作用提供了科學的佐證。

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Royal jelly is the nourishment food fed to bees to promote theirdevelopment into queen bees. Folklore had claimed that royal jelly has anti-aging and rejuvenating properties for human beings. In some reports , Royal Jellyhas profound effect on anti-aging by modulating CNS function, increasing resistance to disease, and promoting body immunity. The goal of thisresearch was to identify the active anti-aging activity and its in Royal Jelly. EGF-responsive brain progenitor cells are a population of stem cells inthe brain cortex. These progenitor cells can be induced into neurons or astrocytes in the presence of EGF. It has been reported that the cell population of brain progenitor cells decrease during the aging process.Thus, it provides a good strategy to delay the aging process by maintaining thecell population of the brain progenitor cells or differentiating these cells to functional cells. We used this EGF-responding brain progenitor cells asan anti-aging screening model to examine the biological activity of RoyalJelly. In addition, I developed the method for analyzing the neurotransmitter secretion of neuron cells by capillary electrophoresis with laser-induced fluorescence detection. The life span extension of Drosophila melanogstorwas used as an in vivo bioassay to evaluate the anti-aging effect of RoyalJelly. Using recombinant mEGF made by our laboratory in a serum free condition,this study had established a culture system for EGF-responding progenitor cells from rat embryonic brain cells. We found Royal Jelly could promote the proliferation and differentiation for brain progenitor cells. Afterisolation and purification step via molecular sieve column cliromatography、supercritical fluid extraction、HPLC chromatography. We found the purified fractionRJT4L4 、RJT4L5、RJT4L6、RJT5L7、RJT5L8 ofroyal jelly induce cell proliferation,and RJT6L2、RJT6L3、RJT6L4、RJT6L5、RJT9L3、RJT9L5 induce celldifferentiation. In the neural cell system, I found RJT9、RJT10、RJT9 H2、RJS2L3 inducedcell proliferation, and RJSIL4、RJSIL5、RJS2L3、RJS2L4、RJS2L5、RJS4L2、RJS4L2 induce cell differentiation. We also found that RJSIL4、RJSIL5、RJS2L3 、RJS2L4 promote secretion of neurotransmitters including dopamine, GABA,and glutamate by using capillary electrophoresis with laser-inducedfluorescence detection. In the in vivo test of Drosophila melanogastor, we found that Royal Jelly performed a significant role in the extension of its lifespan. The active anti-aging components of Royal Jelly were under chemicalstructure determination. This study showed Royal Jelly contains bio-active components for promotingthe proliferation and differentiation of brain progenitor cells anddifferentiated neural cells and also increase the life span of Drosophlla melanogastor.This study offers the first scientific evidence for the antiaging effect ofRoyal Jelly.