

以視網膜色素上皮細胞為眼底疾病模型 探討中藥霍山石斛之藥效

吳榮燦

國立陽明大學 生物藥學研究所暨新藥研究中心

高齡化社會的到臨，視力的保健也愈形重要，然而目前西方所發展的眼科用藥僅限於抗生素、類固醇等供暫時控制病情的藥物，對視網膜有關病變的治療藥物，則付之厥如。中藥及民間藥中有許多常用的眼科中藥，但其藥效則缺乏科學的佐證。因此，本研究以與眼睛機能息息相關的視網膜色素上皮細胞（RPE; Retinal epithelial cells）為對象，建立眼科藥物開發模型，期能以此模型來研發新藥及探討其作用機轉。

視網膜色素上皮細胞的最主要機能為吞噬錐狀細胞及桿狀細胞受光線刺激而脫落的外節，一氧化氮（NO; Nitric oxide）在眼內的各種機能上扮演重要的角色也在近幾化被廣為認知，然而，一氧化氮在視網膜色素上皮細胞的正常吞吃機能中扮演的角色仍然不明。有許多由視網膜色素上皮細胞病變所引起的視力障礙與疾病，如：增殖性視網膜病變，老年性黃斑部病變，糖尿病導致的視網膜病變等，其 bFGF，VEGF，IGF-1，TGF- α 等生長因子會呈現不同的表現。因此我們以視網膜色素上皮細胞的吞吃機能為指標，輔以一氧化氮產生的量及基因的調節來探討藥物的藥效與作用機轉。

霍山石斛是目前民間最名貴的眼科用藥，我們發現霍山石斛可能是經由促進視網膜色素上皮細胞產生微量的一氧化氮而增強其吞吃機能，証實了霍山石斛之藥效，為此傳統眼科中藥的藥效提供合理的理論基礎。我們進一步發現，霍山石斛可以選擇性調節在眼底疾病扮演重要角色的基因，如 bFGF、VEGF、TGF- α mRNA 的表現。目前霍山石斛的有效成份經超臨界流體萃取，分子篩層析，高速液態層析純化後，正待進行結構分析。

在本實驗中，我們建立以視網膜色素上皮細胞為眼底疾病試管內細胞及分子生物學研究的模型，提供藥物研發基礎。我們相信這些發現將來能有效地應用於眼科疾病的治療，對視力的維持能有重要的貢獻。

Studies in the Effect of *Dendrobii huoshanense* C.Z.Tang et S.J. Cheng on Biological Activity and Ocular Disease Related Gene Expression of Retinal Pigmented Epithelial Cells

Rong-Tsun Wu

Institute of Biopharmaceutical Science and Research Center for Drug
Discovery, National Yang-Ming University

To date, no drugs for ocular disease are shown to regulate the function of RPE (retinal pigment epithelial cells) which plays an important role in vision transduction. In present study, the RPE cells were used as an experimental model to develop drugs for the treatment of ocular disease and the mechanism of drugs.

The predominant function of RPE is the phagocytosis of rods and cones outer segments. Evidence is now emerging that NO (Nitric oxide) is a mediator of physiological and pathological processes in the retina. However, the role of NO in the normal phagocytic activity of RPE is unknown. In PVR (proliferative vitreoretinopathy), PDR (proliferative diabetic retinopathy) and AMD (aged-macular degeneration), the expression of bFGF (basic fibroblast growth factor), VEGF (vascular endothelial growth factor), IGF (insulin-like growth factor) and TGF- β (Transforming growth factor beta) are increased. Accordingly, we established the system of phagocytosis with FITC-ROS as an indicator in bovine RPE and evaluated its correlation to the production of NO and the expression of growth factors for PVR and PDR.

Dendrobii huoshanense C.Z. TANG et S.J. CHENG is a famous Chinese herbal medicine in maintenance of eyesight. We found that *Dendrobii* enhanced phagocytic activity and the production of NO in RPE. Besides, we also found that *Dendrobii* Caulis down-regulated the expression of bFGF, VEGF and TGF- β s selectively. The purification and identification of the active fractions from *Dendrobii* were under SFE, Sephadex-LH20 and HPLC. The structure of the active ingredients are under taken.

In this study, we established the in vitro bioassay models for developing the drug which might regulate the functions of RPE. We believed that these results might be useful in improving the therapy for ocular diseases.