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Cover Story

Targeting to retina by submicron-sized liposomes

Delivery of a drug to the eye using eyedrops has been one of the most commonly used methods in topical drug delivery. While simple, the efficiency of drug delivery has been very low, losing most of the drug in seconds by drainage before absorption. Advances in ophthalmic drug delivery have been usually based on increasing the bioavailability through design of controlled release systems that can release a drug for days and weeks in the conjunctival sac. Most of the ophthalmic formulations, however, are only for delivery of drugs to cornea and conjunctiva. Delivery of drugs into the posterior segment of the eye has been difficult without using invasive methods.

There are many diseases that cannot be treated with conventional eyedrops. For example, diseases, such as age-related macular degeneration, diabetic macular edema and endophthalmitis, are posterior segment-related diseases which require intravitreal injection. Those are the leading causes of vision impairment and blindness that have to be treated efficiently. Repeated intravitreal injections are associated with potential risks of complications, such as cataracts, vitreous hemorrhages and retinal detachment. Moreover, patients may not comply with such regimens. Thus, there is a pressing need for noninvasive delivery systems targeting the posterior segment of the eye. Drug delivery to the posterior segment of the eye by topical administration with eyedrops is highly desirable for increased convenience and compliance, as well as to minimize risks and side effects. However, there has been no report in which a drug carrier system can target the retina in a noninvasive way, until now.

The article by Professor Takeuchi and his group published in this issue [1] is the first report that describes possibility of drug delivery to the retina in the eye with eyedrops containing liposomal drug particles. Fluorescence emission of coumarin-6 formulated into submicron-sized liposomes (ssLip) was clearly obtained in the retina

in mice after administration using an eyedrop formulation. Such fluorescence was not observed after administration of multilamellar vesicles. Clearly the nanosize is an important factor. The ssLip based on L- α -distearoyl phosphatidylcholine showed higher fluorescence emission in the retina than that based on egg phosphatidylcholine. The former is more rigid than the latter, indicating more rigid nanovehicles are more efficient. The study by Professor Takeuchi has clearly shown that the rigid, nanosized liposomes are highly useful in noninvasive delivery of drugs to the retina. Images of the entire eye showed that delivery of liposomes to the posterior segment of the eye may occur mainly via non-corneal pathway after administration. This observation represents a major breakthrough in ophthalmic drug delivery using a simple eyedrop formulation. There is no doubt further advances in nanoformulations can successfully lead to development of clinically useful products.

Reference

- [1] K. Hironaka, Y. Inokuchi, Y. Tozuka, M. Shimazawa, H. Hara, H. Takeuchi, Design and evaluation of a liposomal delivery system targeting the posterior segment of the eye, *J. Control. Release* 136 (2009) 247–253.

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