ferences in carbachol activity in cornea or transcorneal receiver compartment for liposome-entrapped or free carbachol. However, 90 min after instillation the liposome vehicle was able to maintain significantly higher carbachol concentrations in the cornea and in the transcorneal receiver compartment. The authors propose that the liposome vehicle's ability to sustain drug levels at 90 min in the receiver compartment was due to the continuing presence of drug at the corneal surface.

Schaeffer and Krohn (39) studied in vitro liposome–corneal binding mediated by electrostatic adsorption. Stearylamine or dicetyl phosphate was used to modify the net charge of phosphatidylcholine–cholesterol liposomes. Rank ordering of liposome binding to excised rabbit corneas showed significantly greater affinity (about twofold) of positively charged liposomes compared with negatively charged liposomes. In turn, negatively charged liposomes bound twofold greater than neutral liposomes.

Recently, Guo and co-workers (40) have been able to demonstrate that the in vivo retention of radioiodinated liposomes in rabbit eyes is increased many-fold by using MLVs containing positively charged cholesteryl esters. They observed that liposome binding in the eye was saturable, and the half-life of liposome retention could be manipulated by varying the charged cholesteryl ester/phospholipid ratio, the length of the spacer arm separating amino function from the lipid head group, and lipid phase transition (fluidity).

Schaeffer and Krohn (39) investigated the in vitro transcorneal flux of the water-soluble drug penicillin G in MLV or LUV liposome vehicles of qualitatively different electrostatic charge. All liposome vehicles tested showed significantly improved drug delivery over an aqueous penicillin G solution. Penicillin G flux across rabbit corneas 1 hr after instillation exhibited the same charge-dependent rank ordering as lipid binding. Free drug added to preformed, empty liposomes did not show increased drug flux, suggesting that drug encapsulation and liposome binding was a prerequisite for improved delivery.

The transcorneal flux of the lipophilic drug indoxole incorporated in neutral phosatidylcholine liposomes or in a polysorbate 80 dispersion was evaluated in vivo with rats (39). At 1 hr after instillation, a 1.0 mg indoxole per milliliter liposome vehicle preparation provided the same drug concentrations in rat aqueous humor (about 20 μg/ml) as a 10.0 mg indoxole per milliliter polysorbate 80 vehicle. Furthermore, Schaeffer and Krohn discovered that the liposome vehicle caused none of the histological changes induced by polysorbate 80 ocular toxicity (unpublished results). Thus, in addition to improving the solubility of the anti-inflammatory agent indoxole, vehicle safety was improved.