

4

REFERENCES

REFERENCES

1. Berner, B. and Kydonieus, A., "Novel Drug Delivery Systems", in: Welling PG, Lasagna L and Banakar U.V., eds., *The Drug Development Process: Increasing Efficiency and Cost-effectiveness*. Marcel Dekker Series, Vol. 76, NY 1996, pp. 170-201.
2. Bhalla, H.L., "Status of Drug Delivery Systems in India" in the souvenir of the 3rd International Symposium on Innovation in Pharmaceutical Sciences and Technology, , 7-9th February, 1997, held at the B.V. Patel PERD Centre, India, PP. 67-71.
3. Valia, K.H. and Shah, N., **Oral controlled release drug delivery systems: A review of the patent literature.** Presented at the Presymposium Workshop on Oral Controlled Drug Delivery, February 5-6, 1997, at the B.V. Patel PERD Centre, India.
4. Senel, S., Capan, Y., Sargan, M.F., Ilinci, G., Solpan, D., Guven, O., Bodde H.E. and Hincal A.A., **Enhancement of transbuccal permeation of morphine sulphate by sodium glucodeoxycholate in-vitro.** *J. Control. Rel.*, 45(2), 153-162 (1997).
5. Bodde, H.E., De Vries, M.E. and Verhoef, J.L., **Developments in buccal drug delivery.** *Crit. Rev. Therap. Drug Carr. Syst.*, 8, 271-303 (1991) .
6. Ranga Rao, K.V., Ben-Amor, A. and Buri, P., **studies on buccoadhesive tablet formulation of codeine phosphate,** *STP Pharma.*, 5 (12), 899-903 (1989).
7. Nagai, T. and Konushi, R., **Buccal/gingival drug delivery systems.** *J. Control. Rel.*, 6, 353-360 (1987).
8. Smart, J.D., **Drug delivery using buccal-adhesive systems.** *Adv. Drug. Del. Rev.*, 11, 253-270 (1993).
9. Brook, I.M, Tucker, G.T, Tuckley, E.C. and Boyes R.N., **A lignocaine patch for dental analgesia, safety and early pharmacology.** *J. Control. Rel*, 10, 183-188 (1989).
10. Chien, Y.W, Nozaki, Y. and Ohta, M., **Transmucosal controlled systemic delivery of ISDN: *in-vivo/in-vitro* correlation.** *J. Control. Rel.:* 43(2&3), 105-114 (1997).
11. Guo, J.H. and Cooklock, K.M., **The effects of backing materials and multilayered systems on the characteristics of bioadhesive buccal patches.** *J. Pharm. Pharmacol.*, 48 (3), 255-257 (1996).
12. Pargal, A., "Oral Controlled Release Drug Delivery Systems- a Perspective", Chapter 7, in Vyas J.N. and Shah G eds. *Saket Pharma Handbook*, Saket Projects Ltd., 1997, pp. 427-435.
13. Deshpande, A.A, Rhodes, C.T, Shah, N.H. and Malick, A.W., **Controlled release drug delivery systems for prolonged gastric residence - An overview.** *Drug Dev. Ind. Pharm.*, 22(6), 531-539 (1996).

14. Hardy, J.G., Khosla, R., Davis, S.S. and Robertson, C.S., Gastrointestinal transit of small tablets in patients with ulcerative colitis. *Int. J. Pharm.*, 48, 79-82 (1988).
15. Mojaverian, P., Chan, K., Desai, A. and John, V., Gastrointestinal transit of a solid indigestible capsule as measured by radiotelemetry and dual gamma scintigraphy. *Pharm. Res.*, 6, 719-724 (1989).
16. Harris, D., Fell, J.T., Taylor, D.C., Lynch, J. and Sharma, H.L., Oral availability of a poorly absorbable drug hydrochlorthiazide, from a bioadhesive formulations in the rat, *Int. J. Pharm.*, 56, 97-102 (1989).
17. Ch'ng, H.S., Park, H., Kelly, P. and Robinson, J.R., Bioadhesive polymers as platform for oral controlled drug delivery II. synthesis and evaluation of some swelling, water insoluble polymer, *J. Pharm. Sci.*, 74, 399-405 (1985).
18. Bechgaard, H. and Baggesen, S., Propoxyphene and norpropoxyphene : influence of type of controlled release formulation on intra- and inter-subject variation, *J. Pharm. Sci.*, 69, 1327-1330 (1980).
19. Lilienfield, L.S. and Zapolski, E.J., Controlled release dextromethorphan using advanced ion-exchange technology. *Curr. Ther. Res.*, 33(4), 692-702 (1983).
20. Tozer, T.N., Friend, D.R. and McLecod, A.D., Kinetic perspectives on colonic delivery. *STP Pharma. Sci.*, 5 (1), 5-12 (1995).
21. Rubinstein, A., approaches and opportunities in colon-specific drug delivery. *Crit. Rev. Therap. Drug Carr. Sys.*, 12 (2&3), 101-149 (1995).
22. Kalala, W., Kinget, R., van der Mooter, G. and Samyn, C., Colonic drug-targeting: *In-vitro* release of ibuprofen from capsules coated with poly(ether-ester) azopolymers. *Int. J. Pharm.*, 139 (2), 187-195 (1996).
23. Haeberlin B., *In-vitro* evaluation of dexamethasone- β -D-glucuronide for colon specific drug delivery. *Pharm. Res.*, 10(11), 1553-1562 (1993).
24. Rubinstein, A., Tirosh, B., Baluom, M., Nassar, T., David, A., Radai, R., Gliko-Kabir, I. and Friedamn, M., The rationale for peptide drug delivery to the colon and the potential of polymeric carriers as effective tools. *J. Control. Rel.*, 46(1-2), 59-73 (1997).
25. Klotz, U., Clinical Pharmacokinetics of sulphasalazine, its metabolites and other prodrugs of 5-amino salicylic acid. *Clin. Pharmacokinet.*, 10 (4), 285-302 (1985).
26. Brown, J.P., McGarraugh G.V., Parkinson, T.M., Wingard, R.E. and Onderdonk, A.B., A polymeric drug for treatment of inflammatory bowel disease. *J. Med. Chem.*, 20, 1300-1307 (1983).

27. Thomas P., Richards, D., Richards A., Rogers L., Evans B.K., Dew M.J. and Rhodes, J. Absorption of delayed-release prednisolone in ulcerative colitis and Crohn's disease. *J.Pharm. Pharmacol.*, 37 (10), 757-758 (1985).
28. Ashford M., Fell J.T., Attwood D., Sharma H. and Woodhaad P.J., An *in vitro* investigation into the suitability of pH dependent polymers for colonic targeting. *Int. J. Pharm.*, 95, 193- 199 (1993).
29. Van Dan Moofer, G., Samyan, C. and Kinget, R., Azo polymers for colon-specific drug delivery. *Int. J. Pharm.*, 87, 37-43 (1992).
30. Van Dan Moofer, G., Samyan C. and Kinget, R. Azo polymers for colon-specific drug delivery II. Influence of the polymer on the degradation by the intestinal microflora. *Int. J. Pharm.* 97, 133-139 (1993).
31. Rubinstein, A., Nakar, D. and Sintov, A. Chondroitin sulfate: a potential biodegradable carrier for colon-specific drug delivery. *Int. J. Pharm.*, 84, 141-149 (1992).
32. Singh, S. and Singh, J., Transdermal drug delivery by passive diffusion and iontophoresis: a review. *Med. Res. Rev.*, 13(5), 569-621 (1993).
33. Piskin, E., Biodegradable polymers as biomaterials. *J. Biomater. sci. Polymer Edn.*, 6(9), 775-795 (1994).
34. Heller., Polymers for controlled parenteral delivery of peptide and proteins. *Adv. Drug. Del. Rev.*, 10, 163-204 (1993).
35. Gopferich, A., Bioerodible implants with programmable drug release. *J. Control. Rel.*, 44(2&3), 271-281 (1997).
36. Okada, H. and Toguchi, H., Biodegradable microspheres in drug delivery., *Crit. Rev. Ther. Drug. Carr. Syst.*, 12(1), 1-99 (1995).
37. Gurny, R., Tabatabay, C., Bernatchez, S.F., Merkli, A., Allenmann, E., Affabrouchad, C., Lescure, F. and Dolekar, E. Biodegradable polymers- Contemporary issues and new direction. *Eur. J. Hosp. Pharm.* 3(1), 15-20 (1993).
38. Weiner, N., Martin, F. and Riaz, M., Liposomes as a drug delivery system. *Drug. Dev. Ind. Pharm.*, 15(10), 1523-1554 (1989).
39. Margalit, R., Liposomes: Drug delivery and beyond. in Roseman TJ ed., *Controlled Release Newsletter* 13(2), June (1996) pp.12-14, *Controlled Release Society, Inc., USA.*
40. Crommelin, D.J.A., Daemen, T., Scherphof, G.F., Vingerhoeds, M.H., Heeremans J.L.M., Kluft C. and Storm G., Liposomes: vehicles for the targeted and controlled delivery of peptides and proteins. *J. Control. Rel.*, 46(1&2), 165-175 (1997).

41. Marjan, J.M.J. and Allen, T.M., Long circulating liposomes: past, present, and future. *biotechnology Advances* 14(2), 151-175 (1996).
42. Allen, T.M., Long circulating (sterically stabilized) liposomes for targeted drug delivery. *Trends Pharmacol. Sci.* 15(7), 215-220 (1994).
43. Damms, B. and Bains, W., The cost of delivering drugs without needles. in Roseman TJ ed., *Controlled Release Newsletter* 13(2), (1996) pp.8-11, *Controlled Release Society, Inc., USA*.
44. Illum, L., Farraj, N.F. and Davies, S.S., Chitosan as a novel nasal delivery system for peptide drugs. *Pharm. Res.*, 11, 1186-1189 (1994).
45. Smith P.L., Peptide delivery via the pulmanory route: A valid approach for local and systemic delivery. *J. Control. Rel.*, 46(1-2), 99-106 (1997).
46. Ascentiis, A.D., Bettini, R., Caponetti, G., Catellani, P.L., Peracchia, M.T., Santi, P. and colombo, P., Delivery of nasal powders of β -cyclodextrin by insufflation. *Pharm. res.*, 13(5), 734-738 (1996).
47. Raviola, G., The structural basis of blood-ocular barriers. *Exp. Eye. Res.*, 25 supp. 27-63 (1977).
48. Moroi, S.E. and Lichter, P.R., "Ocular Pharmacology", Chapter 65, in: Goodman and Gilman's *The pharmacological basis of therapeutics* 9th edition, McGraw Hill, 1995, pp. 1619-1645..
49. Pfister, R.R., The normal surface of conjunctiva epithelium: A scanning electron microscopic study, *Invest. Ophthalmol.*, 14, 267-272 (1975).
50. Allansmith, M.R. and O'Connor, G.R., Immunoglobulins: Structure, function and relation to the eye., *Surv. Ophthalmol.*, 14, 267-274 (1961).
51. Robinson, J.C., "Ocular anatomy and physiology relevant to ocular drug delivery", Chapter 2, in Mitra A.K ed., *Ophthalmic Drug Delivery Systems*. Drugs and Pharmaceutical sciences series, Vol. 58, Marcel Dekker, Inc., 1993, pp.29-57.
52. Mastman, G.L., Blades, E.J. and Henderson, J.W., The total osmotic pressure of tears in normal and various pathological conditions., *Arch. Ophthalmol.*, 65, 509-516 (1961).
53. Maurice, D.N., The use of flourescein in ophthalmological research., *Invest. Ophthalmol.* 6, 464-470 (1967).
54. Brieman, J.A. and Snell, C., The mechanisms of lacrimal flow., *Ophthalmologica.*, 159, 223-229 (1969).
55. Brown, S.I. and Dervichian, D.G., Hydrodynamics of blinking., *Arch. Ophthalmol.* 82, 541-549 (1969).

56. Grass, G.M. and Robinson, J.R., Mechanism of corneal drug penetration II: Ultrastructural analysis of potential pathways for drug movement. *J. Pharm. Sci.*, 77 (1), 15-73 (1985).
57. Grass, G.M. and Robinson, J.R., Mechanism of corneal drug penetration I: In-vivo and In-vitro kinetics., *J. Pharm. Sci.*, 77 (1), 3-14 (1985).
58. Harris, J.E. and Nordquist, L.T., The hydration of the cornea: I Transport of water from the cornea, *Am. J. Ophthalmol.*, 40, 100-112 (1955).
59. Bill, A., The aqueous humor drainage mechanism in the cynomolgus monkey (*Macaca*) with evidence for unconventional routes, *Invest. ophthalmol.*, 4, 911-919 (1965).
60. Sears, M.L., The aqueous, *Adler's Physiology of the Eye: Clinical Application*, 7th edition in: R.A. Moses, ed. Mosby, St. Louis, Chapter 7, 1981.
61. Schepens, C.L., Clinical aspects of pathological changes in the vitreous body, *Am. J. ophthalmol.*, 38, 8-18 (1954).
62. Mikkelsen, T.J., Chrai, S.S. and Robinson, J.R., Altered bioavailability of drugs in the eye due to drug-protein interaction, *J. Pharm. Sci.*, 62, 1648-1654 (1973).
63. Patton, T.F. and Robinson, J.R., Influence of topical anesthesia on tear dynamics and ocular bioavailability in albino rabbits, *J. Pharm. Sci.* 64, 267-272 (1975).
64. Chrai, S.S. and Robinson, J.R., Binding of sulfisoxazole to protein fraction of tears, *J. pharm. Sci.*, 65, 437-442 (1976).
65. Ahmed, I. and Patton, T.F. Importance of the noncorneal absorption route in topical ophthalmic drug delivery, *Invest. Ophthalmol. vis. sci.*, 26, 584-592 (1985).
66. Ahmed, I. and Patton, T.F., Disposition of timolol and inulin in the rabbit eye following corneal versus non-corneal absorption, *Int. J. Pharm.*, 38, 9-16, 1987.
67. Huang, A.J.W., Tseng, S.C.G. and Kenyon, K.R. Paracellular permeability of corneal of the tear film by electron microscopy, *Invest. Ophthalmol. vis. Sci.*, 24, 570-579 (1989).
68. Walsky, M.A., Jablonski., M.M. and Edelhauser, H.F. Comparison of conjunctival and corneal surface areas in rabbit and human, *Curr. Eye. Res.*, 7, 483-489 (1988).
69. Wang, W., Sasaki, H., Chien, D.S. and Lee, V.H.L. Lipophilicity influence on conjunctival drug penetration in the pigmented rabbits: A comparison with corneal penetration, *Curr. Eye. Res.*, 10, 571-578 (1991).

70. Lee, V.H.L. and Robinson J.R. Mechanistic and quantitative evaluation of precorneal pilocarpine disposition in albino rabbits, *J. Pharm. Sci.*, 68, 673-671 (1979).
71. Benson, H., Permeability of the cornea to topically drugs, *Arch. Ophthalmol.*, 91, 313-319 (1974).
72. Schoenwald, R.D. and Huang, H.S. Corneal penetration behaviour of β -blocking agents I: Physicochemical factors, *J. Pharm. Sci.*, 72, 1266-1272 (1983).
73. Chien, D.S., Sasaki, H., Bundgaard, H., Buur, A. and Lee, V.H.L. Role of enzymatic lability in the corneal and conjunctival penetration of timolol ester prodrugs in the pigmented rabbit, *Pharm. Res.*, 8, 728-736 (1991).
74. Francoeur, M.L., Sitek, S.J., Costello, B. and Patton, T.F. Kinetic disposition and distribution of timolol in the rabbit physiologically based ocular model, *Int. J. Pharm.*, 25, 275-284 (1985).
75. Misher, G.L. and Mikkelsen, T.J., Permeability of the n-alkyl p-aminobenzoate esters across the isolated corneal membranes of the rabbit, *Int. J. Pharm.*, 2, 239-246 (1979).
76. Schoenwald, R.D. and Ward, R.L., Relationship between steroid permeability across excised rabbit cornea and octanol-water partition coefficients, *J. Pharm. Sci.*, 67, 786-792 (1981).
77. BenErza, D. and Maftzir, G. Ocular penetration of cyclosporin A, *Invest. Ophthalmol. Vis. Sci.*, 31, 1362-1370 (1990).
78. Kupferman, A., Pratt, M.V., Suckewar, K. and Leibowitz, H.M. Topically applied steroids in corneal disease. III. The role of drug derivative in stromal absorption of dexamethasone, *Arch. Ophthalmol.*, 91, 373-379 (1974).
79. Mikkelsen, T.J., Chrai, S.S. and Robinson, J.R., Competitive inhibition of drug protein interaction in the eye fluids and tissues, *J. Pharm. Sci.*, 62, 1942-1949 (1973).
80. Smolen, V.F., Clevanger, J.M., Williams, E.J. and Bergdolt, H.W. Biophasic availability of ophthalmic carbachol. I: Mechanism of cationic polymers- and surfactant-promoted miotic activity, *J. Pharm. Sci.*, 62, 958-966 (1973).
81. Green, K. and Downs, S.J. Prednisolone phosphate penetration into and through the cornea, *Invest. Ophthalmol.*, 13, 316-321 (1974).
82. Patil, P.N. and Jacobowitz, D. Unequal accumulation of adrenergic drugs by pigmented and nonpigmented iris, *Am. J. Ophthalmol.*, 78, 470-479 (1974).
83. Shimuda, K., Baweja, R., Sokoloski, T. and patil P.N. Binding characteristics of drugs to synthetic levodopa melanin, *J. Pharm. Sci.*, 65, 1057-1064 (1975).
84. Atlasik, B., Stepien, K. and Wilczok, T. Interaction of drugs

- with ocular melanin *in vitro*, *Exp. Eye. Res.*, 30, 325-332 (1980).
85. Lee, V.H.L. and Robinson J.R., Disposition of topically applied pilocarpine in the pigmented rabbit eye, *Int. J. Pharm.*, 11, 155-162 (1982).
 86. Lee, V.H.L. and Li, V.H.K. Prodrugs for improved ocular drug delivery, *Adv. Drug. Deliv. Rev.*, 3, 1-27 (1989).
 87. Petersen, R.A., Lee, K.J., and Donn, A. Acetylcholinesterase in the rabbit cornea, *Arch. Ophthalmol.*, 73, 370-378 (1965).
 88. Lee, V.H.L., Esterase activities in adult rabbit eyes , *J. Pharm. Sci.*, 72, 239-246 (1983).
 89. Stratford, R.E. and Lee, V.H.L., Aminopeptidase activity in the albino rabbit extraocular tissues relative to the small intestine., *J. Pharm. Sci.*, 74, 731-739 (1985).
 90. Lee, V.H.L., Morimito, K.W., and Stratford, R.E. Esterase distribution in the rabbit cornea and its implications in ocular drug bioavailability *Biopharm. drug. Dispos.*, 3, 291-298 (1982).
 91. Hecht, G., Roehrs, R.E., Lang, J.C., Rodeheaver, D.P. and Chowhan, M.A., "Design and Evaluation of Ophthalmic Pharmaceuticals Products" Chapter 13, in Banker G.S and Rhodes C.T eds., *Modern Pharmaceutics, 3rd edition, Marcel Dekker Series Vol. 72, Drugs and Pharmaceutical Sciences Series, 1996, pp. 489-546.*
 92. Mackeen, D.L., Aqueous formulations and ointments. *Int. Ophthalmol. clin.*, 33(5), 93-101 (1993).
 93. Olejnik, O., "Conventional systems in Ophthalmic Drug Delivery", Chapter 9, in Mitra A.K ed., *Ophthalmic Drug Delivery Systems. Drugs and Pharmaceutical sciences series, Vol. 58, Marcel Dekker, Inc., 1993, pp.177-198.*
 94. Schoenwald, R.D. and Stewart, P., Effect of particle size on ophthalmic bioavailability of dexamethasone suspension in rabbits. *J. Pharm. Sci.* 69, 391-397 (1980).
 95. Kupferman, A., Pratt, M.V., Suckower, K. and Leibowitz, H.M. Topically applied steroids in corneal diseases III. The role of drug derivative in stromal absorbance of dexamethasone. *Arch. ophthalmol.* 91, 373-379 (1974).
 96. Green, K. and Downs, S.J., Prednisolone phosphate penetrates into and through the cornea. *Invest. Ophthalmol. Vis. Sci.*, 13, 316-322 (1974).
 97. Wilson, C.G., Olejnik, O. and Hardy, J.G., Precorneal drainage on polyvinyl alcohol solution in the rabbit assessed by τ -scintigraphy. *J. Pharma. Pharmacol.* 35(1), 451-454 (1983).
 98. Giannaccini, B. and Alderigi, Semisolid ophthalmic vehicles. *Boll. Chim. Farmaceutico.* 128, 257-266, 1989.

99. "Ophthalmic Products" in Lund W. Ed., *The Pharmaceutical Codex*, 12th edition: The principle and practice of Pharmaceutics., The Pharmaceutical Press, 1994, pp.160-169.
100. Chrai, S.S., Makoid, M.C., Eriksen, S.P. and Robinson, J.R., Drop size and initial dosing frequency problems of topically applied ophthalmic drugs. *J. Pharm. Sci.* 63, 333-343 (1974).
101. Chrai, S.S., Patton, T.F., Mehta, A. and Robinson, J.R., Lacrimal and instilled fluid dynamics in rabbit eyes., *J. Pharm. Sci.* 62, 1112-1121 (1973).
102. Mishima, S., *Clin. Pharmacokinet. Invest. Ophthalmol. Vis. sci.* 21 (4), 504-554, 1981.
103. Nagataki, S. and Mishima, S., Pharmacokinetics of instilled drugs in the human eye. *Int. Ophthalmol. Clin.*, 33(4), 33-49 (1993).
104. Gurny R, Ibrahim H, Aebi A, Buri P, Wilson CG, Washington N, Edman P and Camber O; Design and evaluation of controlled release systems for the eye. *J. Control. Rel.*, 6, 367-373 (1987).
105. Saettone, M.F., Giannaccini, B., Chetoni, P., Galli, G. and E.Chielline. Vehicle effects in ophthalmic bioavailability an evaluation of polymeric inserts containing pilocarpine, *J.Pharm. Pharmacol*, 36, 229-234 (1984).
106. Grass, G.M. and Robinson, J.R., Relationship of chemical structure to corneal penetration and influence of low-viscosity solution on ocular bioavailability, *J. Pharm. Sci.*, 73 (8), 1021-1027 (1984).
107. Romanelli, A., Valeri, P., Morrone, L.A., Pimpinella, G. Graziani, and Tita, G., Ocular absorption and distribution of benzdac after topical administration of rabbits with different vehicles, *Life. Sci.* 54 (13), 877-885 (1994).
108. Saettone, M.F., Monti, D., Torracca, M.T. and Chetoni, P., Mucoadhesive ophthalmic vehicles: Evaluation of polymeric low-viscosity formulations. *J. Ocular. Pharmacol.*, 10 (1), 83-92 (1994).
109. Saettone, M.F., Giannaccini, B., Teneggi, A., Savigni, P. and Tellini, N., Vehicle effects on ophthalmic bioavailability the influence of different polymers on the activity of pilocarpine in rabbits and man. *J. Pharm. Pharmacol* 34, 464-466 (1982).
110. Fitzgerald, Z.P., Hardy, J.G. and Wilson, C.G., A comparison of the effect of viscosity on the precorneal residence of solutions in rabbits and man. *J.Pharm. Pharmacol.* 38, 463-466 (1986).
111. Trueblood, J.H., Rossomondo, J., Carlton, W.H. and Wilson, L.A., Corneal contact times of ophthalmic vehicles: Evaluation by microscintigraphy., *Arch. Ophthalmol.* 93, 127-130 (1975).
112. Meseguer, G., Gurny, R., Buri, P., Rozier, A. and Plazonnel,

- B. Gamma scintigraphic study of precorneal drainage and assessment of miotic response in rabbits of various ophthalmic formulations containing pilocarpine, *Int. J. Pharm.* 95, 229-234 (1993).
113. Lee, V.H.L., Swarbrik, J., Redell, M.K. and Yang, D.C. Vehicle influence on ocular disposition of sodium cromoglycate in the albino rabbit. *Int. J. Pharm.* 16, 163-170 (1983).
 114. S.S. Chrai and J.R. Robinson., Ocular evaluation of methyl cellulose vehicle in albino rabbits. *J. Pharm. Sci.* 63, 1218-1223 (1974).
 115. Kim, S.W., Bae, Y.H. and Okano, T., Hydrogels: swelling, drug loading, and release, *Pharm. Res.* 9, 283-290 (1992).
 116. Gianaccini, B. and Alderigi, C., Semisolid ophthalmic vehicles. *Boll. Chim. Farm.* 128(9), 257-266 (1989).
 117. Robinson, J.R. and Mlynek G.M., Bioadhesive and phase-change polymers for ocular drug delivery., *Adv. Drug. Del. Rev.* 16, 45-50 (1995).
 118. Edsman, K., Carlfors, J. and Harju, K., Rheological evaluation and ocular contact time of some carbomer gels for ophthalmic use., *Int. J. Pharm.* 137, 233-241 (1996).
 119. Unlu, N., Ludwig, A., Van Ooteghem, M. and Hinacal, A.A., Formulation of carbopol 940 ophthalmic vehicles, and *in vitro* evaluation of stimulated lacrimal fluid on their physico-chemical properties, *Pharmazie*. 46, 78f4-788 (1991)
 120. Davies, N.M., Farr, S.J., Hadgraft, J. and Kellaway, I.W., Evaluation of mucoadhesive polymers in ocular drug delivery. I: viscous solutions., *Pharm. Res.* 8, 1039-1043 (1991).
 121. Bottari, F., Giannaccini, B., Peverini, D., Saettone, M.F. and Tellini, N. Semisolid ophthalmic vehicles II: evaluation in albino rabbits of aqueous gel type vehicles containing lidocaine and benzocaine. *Can. J. Pharma. Sci.* 14 (2), 39-43 (1979).
 122. Allen, R.C., Boys-Smith, J., Campbell, D., Rosenquist, R. and Van Buskirk, E.M., A one-year multicenter clinical trial of pilocarpine gel., *Am. J. Ophthalmol.* 97, 723-729 (1984).
 123. Schoenwald, R.D. and Boltralik, J.J. A bioavailability comparison in rabbits of two steroids formulated as high-viscosity gels and reference aqueous preparations., *Invest. Ophthalmol. Vis. sci.* 18 (1), 61-66, 1979.
 124. Kassem, M.A., Attia, M.A., Habib, F.S. and Mohamed, A.A., Activity of ophthalmic gels of betamethasone and phenylephrine hydrochloride in the rabbits's eye., *Int. J. Pharm.* 32, 47-54 (1986).
 125. Schoenwald, R.D., Ward, R.L., Desantis, L.M. and Roehrs, R.E. Influence of high-viscous vehicles on miotic effect of pilocarpine. *J. Pharm. Sci.* 62 (9), 1538-1542 (1973).

126. Hvidberg, J., Fusidic acid in acute conjunctivitis., *Acta. Ophthalmol.* 65, 43-47 (1987).
127. Hansen, S., Intraocular penetration of fusidic acid with topical fucithalmic., *Eur. J. Drug. Metab. Pharm.* 10, 329-331 (1985).
128. Van Bijsterveld, O.P., Andriesse, H. and Nielsen, B.H., Fusidic acid in tear fluid: Pharmacokinetic study with fusidic acid viscous eye drops., *Eur. J. Drug. Metab. Pharm.* 12, 215-218 (1987).
129. Kumar, S. and Himmelstein, K.J. Modification of in-situ gelling behaviour of carbopol solution by hydroxypropyl methylcellulose. *J. Pharm. Sci.*, 84 (3), 344-348 (1995).
130. Zignani, M., Tabatabay, C. and Gurny, R. Topical semi-solid drug delivery: Kinetics and tolerance of ophthalmic hydrogels. *Adv. Drug Del. Rev.*, 16, 51-60 (1995).
131. Cohen, S., Lobel, E., Trevogda, A. and Peled, Y. A novel in-situ ophthalmic drug delivery system from alginates undergoing gelation in the eye. *J. Control. Rel.*, 44(2&3), 201-208 (1997).
132. Udupa, N., Ocular controlled release drug delivery systems. *East. Pharm.* 65-67, August 1993.
133. Dumortier, G., Zuber, M., Chast, F., Sandouk, P. and Chaumeil, J.C. Comparison between a thermoreversible gel and an insert in order to prolong the systemic absorption of morphine after ocular administration., *S.T.P. Pharm. Sci.* 2, 111-117 (1992).
134. Gurny, R., Ibrahim, H. and Buri, P., The development and use of in situ formed gels, triggered by pH. in: P. Edman (Ed.). *Biopharmaceutics of Ocular Drug Delivery*, CRC Press, Boca Raton, pp.81-90.
135. Kumar, S., Haglund, B.O. and Himmelstein, K.J., In-situ forming gels for ophthalmic drug delivery., *J. Ocular. Pharmacol.* 10, 47-56 (1994).
136. Guzman, M., Aberturas, M.R., Garcia, F, Molpeceres, J. Gelation gels and polyoxyethylene-polyoxypropylene gels: Comparative study of their properties. *Drug Dev. Ind. Pharm.* 20 (12), 2041-2048 (1994).
137. Chen-Chow, PC. and Frank, S.G., In-vitro release of lidocaine from pluronic F-127 gels., *Int. J. Pharm.* 8, 89-99 (1981).
138. Dumortier, G., Zuber, M., Banges, N., Chast, F., Dutertre, H., Chaumeil, J.C., Lacrimal and plasmatic kinetics of morphine after an ophthalmic delivery of three different formulations., *Drug. Dev. Ind. Pharm.* 20(7), 1147-1158 (1994).
139. Miller, S.C. and Donnan. Effect of poloxamer-407 gel on the miotic activity of pilocarpine nitrate in rabbit.

Int. J. Pharm. 12, 147-152 (1982).

140. Sanzgiri, Y.D., Mashi, S., Crescenzi, V., Callegaro, L., Topp, E.M. and Stella, V.J., Gellan-based systems for ophthalmic sustained delivery of methylprednisolone., *J. Control. Release.* 26, 195-201 (1993).
141. Greaves, J.L., Wilson, C.G., Rozier, A. and Plazonnet, B., Scintigraphic assessment of an ophthalmic gelling vehicle in man and rabbit., *Curr. Eye. Res.* 9, 415-420 (1990).
142. Gunning, F.P., Greve, E.L., Bron, A.M. Bosc, J.M., Royer, J.G., George, J.L., Lesure, P. and serbat, D., Two typical carbonic anhydrase inhibitors sezolamide and drozolamide in gelrite vehicle: a multiple-dose efficacy., *Graefe's Arch. Clin. Exp. Ophthalmol.* 231, 384-388 (1993).
143. Thermes, F., Molon-Nobolt, S. and Grove, J., Effects of acetylsteine on rabbit conjunctival and corneal surfaces., *Invest. Ophthalmol. Vis. Sci.* 32, 2958-2963 (1991).
144. Rozier, A, Mazuel, C., Grave, J. and Plazonnet. Gelrite^R: A novel, ion-activated, in-situ gelling polymer for ophthalmic vehicles. Effect on bioavailability of timolol. *Int. J. Pharm.* 57, 163-168 (1989).
145. Gurny, R., Ibrahim, H. and Buri, P., Lattices and thermoreversible gels as sustained delivery systems to the eye, in: M.F. Saettone, M.Bucci. and P.Speiser, (Eds), Ophthalmic drug delivery. Biopharmaceutical, Technological and Clinical Aspects, Liviana Press, Padua, pp. 27-36.
146. Kreuter, J "Particulates (Nanoparticles and Microparticles)" Chapter 13, in Mitra A.K ed., Ophthalmic Drug Delivery Systems. Drugs and Pharmaceutical sciences series, Vol. 58, Marcel Dekker, Inc., 1993, pp.275-288.
147. Calvo, P., Alonso, M.J., Vila-Jato, J.L. and Robinson, J.R. Improved ocular bioavailability of indomethacin by novel ocular drug carriers. *J. Pharm. Pharmacol.* 48, 1147-1152 (1996).
148. Harmi, T., Speiser, P and Kreuter, J. A solid colloidal drug delivery systems for the eye: Encapsulation of pilocarpine in nanoparticles, *J. Microencapsul*, 3, 3-12, 1986.
149. Harmi, T., Speiser, P. and Kreuter, J. Optimization of pilocarpine loading onto nanoparticles by sorption procedures, *Int. J. Pharm.* 33:45-54 (1986).
150. Harmia-Pulkkinen, T., Ihantola, A., Tuomi, A and Kristoffersson, E. Manufacture of polyalkylcyanoacrylate nanoparticulates with pilocarpine and timolol by micellile polymerization : Factors influencing particle formation, *J. Microencapsul.*, 6, 87-93 (1989).
151. Sieg, J.W. and Tripplet, J.W., Precorneal retention of topically instilled micronized particles., *J. Pharm. Sci.* 69, 863-864 (1980).

152. Wood, R.W., Li, V.H.K., Kreuter, J., and Robinson, J.R. Ocular disposition of poly-hexyl-2-cyano[3-¹⁴C]acrylate nanoparticles in the albino rabbit, *Int. J. Pharm.*, 23, 175-183 (1985).
153. Marchal-Heussler, L., Maincent, P., Hoffman, M., Splitter, J., and Couvreur, P. Antiglaucomatous activity of betaxolol chlorhydrate sorbed onto different isobutylcyanoacrylate nanoparticle preparations., *Int. J. Pharm.*, 58, 115-122 (1990).
154. Smolin, G., Okumoto, M., Feiler, S., and Condon, D. Idoxuridine-liposome therapy for Herpes simplex keratitis, *Am. J. Ophthalmol.*, 91, 220-224 (1981).
155. Schaeffer, H.E., and Krohn, D.L. Liposomes in topical drug delivery, *Invest. Ophthalmol. Vis. Sci.*, 22, 220-226 (1982).
156. Singh, K., and Mezei, M., Liposomal ophthalmic drug delivery system I. Triamcinolone acetonide, *Int. J. Pharm.* 16, 339-344 (1983).
157. Meisner, D., Pringle, J., and Mezei, M. Liposomal ophthalmic drug delivery 3. Pharmacodynamic and biodisposition studies of atropine, *Int. J. Pharm.*, 55, 105-109 (1989).
158. Benita, S., Plenecassagne, J.D., Caves, G., Drouin, D., Le Hao Dong, P., and Sincholle, D. Pilocarpine hydrochloride liposomes: characterization *in vitro* and preliminary evaluation *in vivo* in rabbit eye, *J. Microencapsul.* 1:203-212 (1984).
159. Singh, K., and Mezei, M. Liposomal ophthalmic drug delivery system II. Dihydrostreptomycin sulfate, *Int. J. Pharm.*, 16, 339-343 (1984).
160. Schoenwald, R., "Chemical Delivery Systems with Enhanced Pharmacokinetic Properties" Chapter 15, in: Mitra A.K ed., *Ophthalmic Drug Delivery Systems*. Drugs and Pharmaceutical sciences series, Vol. 58, Marcel Dekker, Inc., 1993, pp.307-330.
161. Chien, D.S., Bundgaard, H., and Lee, V.H.L. Improving the ocular absorption of phenylephrine, *Biopharm. Drug. Dispos.*, 7, 453-459 (1986).
162. Bundgaard, H., Falch, E., Larsen, C., and Mikkelsen, T. Pilocarpine prodrugs I. Synthesis, physicochemical properties and kinetics of lactonization of pilocarpine acid esters, *J. Pharm. sci.*, 75: 36-42 (1996).
163. Karback, M.B., Podos, S.M., Harbin, T.S., Mandell, A. and Becker, B. The effects of dipivalyl epinephrine on the eye, *Am. J. Ophthalmol.*, 81, 768-773 (1976).
164. Brador, N., Designing safer ophthalmic drug by soft drug approaches., *J. Ocular. Pharmacol.* 10(1), 3-15 (1994).
165. Bawa, R., "Ocular inserts" Chapter 11, in Mitra A.K ed., *Ophthalmic Drug Delivery Systems*. Drugs and

Pharmaceutical sciences series, Vol. 58, Marcel Dekker, Inc., 1993, pp.223-261.

166. Matoba, A.Y. and McCulley, J.P., The effect of therapeutic soft contact lenses on antibiotic delivery to the cornea., *Ophthalmology*, 92, 1-13 (1985).
167. Leshner, G.A. and Gunderson, G.G., Continuous drug delivery through the use of disposable contact lenses., *Optometry: & Vis. Sci.* 70(12), 1012-1018 (1995).
168. Friederich, R.L., The pilocarpine Ocuser: A new drug delivery system., *Ann. Ophthalmol.*, 6, 12-24 (1974).
169. Urquhart, J., Development of the Ocuser pilocarpine ocular therapeutic systems-a case history in ophthalmic product development., in: Robinson J.R. Ed., "Ophthalmic Drug Delivery Systems", American Pharmaceutical Association, Washington, D.C., 1980, pp.105.
170. Gras, G.M., Cobby, J. and Makoid, M.C., Ocular delivery of pilocarpine from erodible matrices., *J. Pharm. Sci.*, 73(5), 618-624 (1984).
171. LaMotte, J., Grossman, E. and Hersch, J., The efficacy of cellulosic ophthalmic inserts for treatment of dry eye., *J. Am. Optom. Assoc.*, 56(4), 298-303 (1985).
172. Scrip #666, February 10, pp. 15 (1982).
173. New drug delivery system-more efficient treatment *Optican*, October 18, pp. 6 (1985).
174. Callagen, M.C., Engel, L.S., Clinch, T.E., Hill, J.M., Kaufman, H.E. and O'Callaghan, R.J. Efficacy of tobramycin drops applied to collagen shields for experimental staphylococcal keratitis., *Curr. Eye. Res.*, 13, 875-878 (1994).
175. Phinney, R.B., Schwartz., S.D., Lee., D.A. and Mondino, B.J., Collagen-shield delivery of gentamicin and vancomycin., *Arch. Ophthalmol*, 106, 1599-1606 (1988).
176. Sawusch, M.R., O'Brien, t.P. and Updegraff, B.S., Collagen corneal shields enhance penetration of topical prednisolone acetate., *J. Cataract Refract. surg.*, 15, 625 (1989).
177. Hwang, D.G., Stern, W.H., Hwang, P.H. and Macgowan-Smith, L.A., Collagen shield enhancement of topical dexamethasone penetration., *Arch. Ophthalmol.*, 107, 1375-1379 (1989).
178. Bawa, R., Dais, M., Nandu, M. and Robinson, J.R., "New extended release ocular drug delivery system- Design, Characterization & Performance Testing of Minidisc Inserts," Proceedings of the 15th International Symposium on controlled release of Bioactive Materials, Controlled release society, Inc., Lincolnshire, Illinois, 1988, pp. 106a-106b.
179. Richardson M.C. and Bently, P.H., "A New Ophthalmic Drug Delivery Systems" Chapter 17, in Mitra A.K ed., Ophthalmic

Drug Delivery Systems. Drugs and Pharmaceutical sciences series, Vol. 58, Marcel Dekker, Inc., 1993, pp.355-367.

180. Fitzerland, P., Wilson, C.G., Greaves, J.J., Frier, M., Hollingsbee, D., Gilbert, D. and Richardson, M. Scintigraphic assessment of the precorneal residence of a new ophthalmic delivery system (NODS) in man. *Int. J. Pharm.* 83, 177-185 (1992).
181. Kelly, J.A., Molyneux, P.D., Smith, S.A. and Smith, S.E., Relative bioavailability of pilocarpine from a Novel Ophthalmic Drug Delivery system and conventional eyedrop formulations., *Br. J. Ophthalmol.*, 73, 360-367 (1989).
182. Banga, A.K. and Chien, Y.W., Iontophoretic delivery of drugs: fundamentals, developments and biomedical applications, *J. Controlled rel.*, 7, 1-12 (1988).
183. O'Callaghan, R.J. and Hill, J.M. Iontophoresis of tobramycin for the treatment of experimental *Pseudomonas* keratitis in the rabbit. *Arch. Ophthalmol.* 106, 262-265 (1988).
184. Hobden, J.A., Reidy, J.J., O'Callaghan, R.J. and Hill, J.M., Ciprofloxacin iontophoresis for aminoglycoside-resistant pseudomonal keratitis., *Invest. Ophthalmol. vis. Sci.*, 31, 1940-1948 (1990).
185. ASHP Reports: Pharmacy-prepared ophthalmic products. ASHP technical assistance bulletin on pharmacy-prepared ophthalmic products. *Am. J. Hosp. Pharm.* 50, 1462-1463 (1993)
186. Agalloco., J A review of the U.S. FDA guideline on aseptic processing. *J. Parent. Sci. Technol.*, 46 (3), 78-84 (1992).
187. Mullins, J.D. and Hecht, G., "Ophthalmic Preparations" Chapter 86, in: Gennaro, A.R. Ed., Remington's Pharmaceutical Sciences 18th edn. MACK publ. Co., P.A. USA. pp. 1581-1595.
188. Richards, R.M.E. and McBride, R.J., The preservation of ophthalmic solutions with antibacterial combinations., *J. Pharm. Pharmacol.*, 24, 145-148 (1972).
189. Jurgens Jr, R.W., Preservatives for ophthalmic products., *Drug Cos. Ind.*, Feb. 56,58,60 (1970).
190. Conrad JM, Reay WA, Polcyn E and Robinson JR; Influence of tonicity and pH on lacrimation and ocular drug bioavailability. *J. Parent. Sci. Assoc.*, 32, (1978), 149-161.
191. Olejnik, O., "Conventional Systems in Ophthalmic Drug Delivery" Chapter 9, in Mitra A.K ed., Ophthalmic Drug Delivery Systems. Drugs and Pharmaceutical sciences series, Vol. 58, Marcel Dekker, Inc., 1993, pp.177-198.
192. Shirwaikar, A. and Gundu Rao, P. Ophthalmic irritation potential of propylene glycol. *Ind. J. Pharm. sci.* 57 (3), 109-112 (1995).

193. Buchler, E.V. and Newmann, E.A. A comparison of eye irritation in monkeys and rabbits. *Toxicol. Appl. Pharmacol.* 6, 701-710 (1964).
194. McDonald, T.O. and Shadduck, J.A., Eye irritation, *Dermatology and Pharmacology* (H. Maibach and F.N. Marzulli, eds.), 1977, Wiley, New York, pp. 139-191.
195. Roehrs, R.E., "Regulatory Considerations" Chapter 23, in Mitra A.K ed., *Ophthalmic Drug Delivery Systems*. Drugs and Pharmaceutical sciences series, Vol. 58, Marcel Dekker, Inc., 1993, pp.471-490.
196. Schoenwald, R.D., Ocular Drug Delivery. Pharmacokinetic considerations., *Clin. Pharmacokinet.*, 18, 225 (1990).
197. Frangie, J.P. Clinical Pharmacokinetics of various topical ophthalmic drug delivery systems., *Clin. pharmacokinet.* 29(2), 130-138 (1995).
198. Makoid MC, Sieg JW and Robinson JR; Corneal drug absorption: An illustration of parallel first-order absorption and rapid loss of drug from absorption depot. *J. Pharm. Sci.*, 65 (1), 150-151 (1976).
199. Saettone, T.F. The validity of rabbits for investigation on ophthalmic vehicles: a comparison of four different vehicles containing tropicamide in humans and rabbits., *Pharm. Acta. Helv.* 57, 47-55 (1982).
200. Zweifach, B.W., Grant, L. and McCluskey, R.T., eds. The inflammatory process, New York 1965, Academic Press Inc.
201. Lee Stock, E. and Pendleton., Pharmacological treatment of ocular allergic diseases., *Int. Ophthalmol. Clin.* 21(2), 47-57 (1987).
202. Alio, J.L., Ayala, M.J., Mullet, M.E., Artola, A., Ruiz, J.M. and Bellot, J. Antioxidant therapy in the treatment of experimental acute corneal inflammation. *Ophthalmol. Res.* 27, 136-143 (1995).
203. Weiss S; Tissue destruction by neutrophils., *New Engl. J. Med.*, 320, (1989), 365-375.
204. Protzman, C.E., Spada, C.S. and Nieves, A.L. Studies on the ocular pharmacology of prostaglandin D₂. *Invest. Ophthalmol. Vis. Sci.* 31 (1), 138-146, 1990.
205. Ormerod, L.D., Abelson, M.B, and Kenyon, K.R. Standard models of corneal injury using alkali-induced filter paper discs. *Invest. Ophthalmol. Vis. Sci.* 30, 2148-2153 (1989).
206. Brown, S.L., Wassermann, H.E. and Dunn, M.W. Alkali burns of the cornea. *Arch. Ophthalmol.* 82, 91-112 (1969).
207. Chung, J.H, and Fagerholm, P. Corneal alkali wound healing in the monkey. *Acta. Ophthalmol.* 67, 685-693, 1989.

208. Leibowitz, H.M., Lass, J.H. and Kupferman, A. Quantitation of inflammation in the cornea. *Arch. Ophthalmol.*, 92, 427-430 (1974).
209. Kulkarni, P. and Srinivasan, B.D. Ocular inflammation: A pharmacological model. *Trends. Pharmacol. Sci.*, 8, 375-377 (1987).
210. Salminen, L. and Urtti, A., "Disease State Models" Chapter 7, in Mitra A.K ed., *Ophthalmic Drug Delivery Systems*. Drugs and Pharmaceutical sciences series, Vol. 58, Marcel Dekker, Inc., 1993, pp.137-160.
211. Flach, A.J., Cyclooxygenase inhibitors in ophthalmology., *Surv. Ophthalmol.*, 36, 259-284 (1992).
212. Editorial., Nonsteroidal Anti-inflammatory Drugs and Cataract Surgery., *Arch. Ophthalmol.*, 112, 891-894 (1994).
213. Muchowski, J.M., Unger, S.H., Ackrell, J., et. al. Synthesis and antiinflammatory and analgesic activity of 5-aryl-1,2-dihydro-3H-pyrrolo [1,2a] pyrrole-1-carboxylic acids and related compounds. *J. Med. Chem.*, 28, 1037-1049 (1985).
214. Physicians' Desk Reference, Sifton ed., 48th Edn., 1994, Publication, Medical Economics Data Product Co., N.J., pp.489-490.
215. Monograph on "Ketorolac Tromethamine," in The United States Pharmacopoeia-23rd revision First Supplement, The United States Pharmacopeial Convention Inc., 1995, pp. 2472-2474.
216. Kamath, B.V., Shivram, K. and Vangani, S. Spectrophotometric determination of ketorolac tromethamine by charge-transfer and ion-pair complexes. *Anal. Lett.*, 27(1), 103-122 (1994).
217. Kamath, B.V., Shivram, K. and Shah, A.C. Determination of diclofenac sodium, famotidine and ketorolac tromethamine by flow injection analysis using dichloronitrophenol. *J. Pharm. Biomed. Anal.*, 12 (3), 343-346 (1994).
218. Reddy, B.P., Suryanarayana, M.V., Venkatraman, S., Krupadanaam G.D. and Sastry, C.S.P. Purity evaluation of ketorolac tromethamine by high performance liquid chromatography. *Ind. Drugs.*, 30(4), 176-179 (1992).
219. Floy, B.J., Royko, C.G. and Fleitman, J.S. Compatibility of ketorolac tromethamine injection with common infusion fluids and administration sets. *Am. J. Hosp. Pharm.*, 47, 1097-1100 (1992).
220. Sane, R.T., Tirodkar, V.B., Desai, A.J., Patel, M.K. and Kulkarni, U.D., Application of different analytical methods for the determination of ketorolac tromethamine. *Ind. Drugs.*, 29(11), 489-493 (1992).
221. Jamali, F., Brocks, D.R. Clinical Pharmacokinetics of ketorolac tromethamine., *Clin. Pharmacokinet.*, 23 (6), 415-427 (1992).

222. Micaccla, M.J., Buckley, M. and Brogden, R.N. Ketorolac : A review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential. *Drugs*, 39(1), 81-109 (1990).
223. Leo, Gu., Hi Shi, C. and Johnson, D. Light degradation of ketorolac tromethamine. *Int. J. Pharm.* 41 (1-2) 105-113, (1988).
224. Hay Ball, P.J., Tamblyu, J.U., Holden, Y. and Wrobel, J., Stereoselective analysis of ketorolac in human plasma by high performance liquid chromatography. *Chirality*, 5(1), 31-35 (1993).
225. Jamali, F., Pasutto, F.M. and Lemko, C., HPLC of ketorolac enantiomers and application to pharmacokinetics in the rat. *J. Liq. Chromatography*, 12 (10), 1835-1850 (1989).
226. Flores-Murrieta, F.J., Granados-Soto, V., Gilberto, C.H, Herrera, J.E, and Hong, E. Comparative bioavailability of two oral formulation of ketorolac tromethamine Dolac^R and Exodol^R. *Biopharm. Drug. Dispos.* 15, 129-136 (1994).
227. Wu, A.T. and Massey, I.J., Simultaneous determination of ketorolac and its hydroxylated metabolite in plasma by HPLC. *J. Chromatography*. 534, 241-246 (1990).
228. Chowdary, R.S., Gangual, S.S., Jindal, K.C., and Khanna, S. Reverse phase HPLC of ketorolac and its application to bioequivalence studies in human serum. *J. Chromatogr. Biomed. Appl.* 614 (1), 180-184 (1993).
229. Hayball, P.J., Holwan, J.W., Nation, R.L., Massy Westropp, R.A, and Hamon, D.P.G. Marked enantioselective protein binding in humans of ketorolac. In-vitro-elucidation of enantiomer unbound fractions following facile synthesis and direct chiral HPLC resolution of tritium-labeled ketorolac. *Chirality*, 6(8), 642-648 (1994).
230. Jones, D.J. and Bjorksten, A.R. Detection of ketorolac enantiomers in human plasma using enantioselective liquid chromatography. *J. Chromatograph B. Biomed. Appl.* 4, 165-167, 661, (1997).
231. Mills, M.H., Mather, L.E, Gu, X.S. et. al. Determination of ketorolac enantiomers in plasma using enantioselective liquid chromatography on an α 1-acid glycoprotein chiral stationary phase and ultraviolet detection. *J. Chromatogr B. Biomed. Appl.* 5, 658, 177-182, (1994).
232. Vakily, M., Corrigan, B. and Jamali, F. The problem of racemization in the stereospecific assay and pharmacokinetic evaluation of ketorolac in humans and rats. *Pharm. Res.* 12, 1652-1657, (1995).
233. Leo, Gu., Hi Shi, C., and Johnson, D. Kinetics and mechanisms of the autoxidation of ketorolac tromethamine in aqueous solution. *Int. J. Pharm.* 41 (1-2) 95-104, (1988).

234. Brandl, M., Magill, R, Verma, R, and More, G.S., Approaches for improving the stability of ketorolac in powder blends. *J. Pharm. Sci.*, 84 (10), 1151-1153, (1995).
235. Brandl, M., Couley, D., Dave, J, and Darcy, J., Racemization of ketorolac in aqueous solution. *J. Pharm. Sci.*, 84 (9), 1045-1048, (1995).
236. Chowan, Z.k, and Chi, L.H. Drug-excipient interactions resulting from powder mixing I: Possible mechanism of interaction with starch and its effect on drug dissolution. *Pharm. Tech.* 9, 84-97, (1985a).
237. Chowan, Z.k, and Chi, L.H. Drug-excipient interactions resulting from powder mixing II: Possible mechanism of interaction with crospovidone and its effect on in-vitro drug dissolution. *Pharm. Tech.* 9, 28-41, (1985b).
238. Chowan, Z.k, and Chi, L.H. Drug-excipient interactions resulting from powder mixing III: Solid state properties and their effect on drug dissolution. *J. Pharm. Sci.* 75, 534-541, (1986a).
239. Chowan, Z.k, and Chi, L.H. Drug-excipient interactions resulting from powder mixing IV: Role of lubricants and their effect on in-vitro dissolution. *J. Pharm. Sci.* 75, 542-545, (1986b).
240. Chowan, Z.k, and Chi, L.H. Drug-excipient interactions resulting from powder mixing V: Role of sodium lauryl sulphate. *Int. J. Pharm.* 60, 61-78, (1990).
241. Ong, J.T.H., Chowan, Z.k, and Samuels, G.J., Drug-excipient interactions resulting from powder mixing VI: Role of various surfactants. *Int. J. Pharm.*, 96, 231-242, (1993).
242. Rooks II, W.H., Maloney, P.J., Shott, L.D., Schuler, M.E., Sevelius, H., Stresberg, A.M. et. al. The analgesic and anti-inflammatory profile of ketorolac and its tromethamine salt. *Drug. Exp. Clin. Res.* 11 (8), 479-492, (1985).
243. Rooks, W.H., Pharmacological activity of ketorolac tromethamine., *Pharmacotherapy*, 10, 308-311 (1990).
244. Rooks II, W.H., Tomolonis, A.J., Maloney, P.J., Wallach, M.B., Schuler, M.E. The analgesic and anti-inflammatory profile of (±)- 5-benzoyl- 1,2-dihydro- 3H- pyrrolo(1,2a) pyrrole-1- carboxylic acid (RS-37619). *Agents and Actions*, 2 (5), 684-690, (1982).
245. Mahoney, J.M. and Waterbury, L.D. (±)- 5-benzoyl- 1,2-dihydro-3H- pyrrolo(1,2a) pyrrole-1-carboxylic acid (RS-37619): A non-irritating ophthalmic anti-inflammatory agent. *Invest. Ophthamol. Vis. Sci.*, 24, 151, (1983).
246. Mahoney, J.M. and Waterbury, L.D. Drug effects on the neovascularization response to silver nitrate cauterization of the rat cornea. *Curr. Eye. Res.* 4, 531-535, (1985).

247. Fraser-smith, E.B. and Matthews, T.R., Effects of ketorolac on *candida albicans* ocular infection in rabbits. *Arch. Ophthalmol*, 105; 264-267, (1987).
248. Fraser-smith, E.B. and Matthews, T.R., Effects of ketorolac on herpes simplex virus type 1 ocular infection in rabbits. *Arch. Ophthalmol*. 105 (2), 264-267, (1987).
249. Fraser-smith EB and Matthews TR, Effects of ketorolac on *pseudomonas aeruginosa* ocular infection in rabbits. *J. Ocular. Pharmacol*. 4; 101-109, (1988).
250. Mroszozak, E.J., Lee, F.W., Combs, D., Sarnquist, F.H., Huang, B.L., Wu, A.T., Tokes., Maddox, and Cho, D.K. Ketorolac tromethamine absorption, distribution, metabolism, excretion and pharmacokinetics in animals and humans. *Drug. Metabol. Dispos*. 15, 618-626, (1987).
251. Olkkola, K.T. and Maunuksela, E.L. The pharmacokinetics of post-operative intravenous ketorolac tromethamine in children. *Br. J. Clin. Pharmacol*. 31, 182-184, (1991).
252. Jung, D., Mroszezak, E.J. and Bynum, L. Pharmacokinetics of ketorolac tromethamine in humans after i.v, i.m and oral administration. *Eur. J. Clin*. 35, 423-425, (1986).
253. Gillis, J.C. and Brogden, Ketorolac - A reappraisal of its pharmacodynamic and pharmacokinetic properties and therapeutic use in pain management. *Drugs* 53 (1), 139-188, (1997).
254. Jallad, N.S., Garg, D.C., Martinez, J.J., et. al. Pharmacokinetics of single-dose oral and intramuscular ketorolac tromethamine in the young and elderly. *J. Clin. Pharmacol*. 30, 76-81, (1990).
255. Pages, L.J., Martinez., J.J., Garg, D.C., et. al. Pharmacokinetics of ketorolac tromethamine in hepatically impaired vs young healthy subjects. (abstract No. 78), *J. Clin. Pharmacol*. 27, 724, (1987).
256. Brown, C.R., Moodie, J.E., Phillips, E., et.al. Pharmacokinetic and pharmacodynamic (PK/PD) of ketoroalc tromethamine i.m, i.v, following major orthodpedic surgery (abstract)., *Clin. Pharmacol. Ther.*, 53, 222 (1993).
257. Garg, D.C., Mroszak, E., Combs, D., et.al., Ketorolac pharmacokinetics (PK) following continuous infusion and repeated bolus injection (abstract)., *Clin. Pharmacol. Ther.*, 53, 222 (1993).
258. Fu. R.C. and Lidgate, D.M., In-vitro rabbit corneal permeability study of ketorolac tromethamine. A non-steroidal anti-inflammatory agent. *Drug. Dev. Ind. Pharm*. 12 (14), 2403-2430, (1986).
259. Lidgate, D.M., Fu, R.C. and Fleitman, J.S. Corneal permeability of ketorolac tromethamine when formulated with

- tobramycin. *Drug. Dev. Ind. Pharm.* 15 (11), 1779-1795, (1989).
260. Ling, T.L. and Combs, D.L. Ocular bioavailability and tissue distribution of [¹⁴C] ketorolac tromethamine in rabbits. *J. Pharm. Sci.* 76 (4), 289-294, (1987).
 261. Rabiha, P.K., Fiscella, R.G. and Tessler, H.H. Intraocular penetration of periocular ketorolac and efficacy in experimental uveitis. *Invest. Ophthalmol. Vis. Sci.* 37 (4), 613-618, (1996).
 262. Flach, A.J., Dolan, B.J. and Irwine, A.R. Effectiveness of ketorolac tromethamine 0.5 % ophthalmic solution for chronic aphakic and psuedoaphakic cystoid macular edema. *Am. J. Ophthalmol.* 103 (4), 479-486, (1987).
 263. Flach, A.J., Jaffe, N.S., Akers, W.A., et. al. The effect of ketorolac 0.5 % solution in reducing post-operative inflammation: Double mask parallel comparison with dexamethasone 0.1% solution. *Ann. Ophthalmol.* 21, 407-411, (1989).
 264. Flach, A.J., Kraff, M.C., Sanders, D.R. and Tanenbaum, L. The quantitative effect of 0.5 % ketorolac tromethamine solution and 0.1% dexamethasone sodium phosphate solution on post-surgical blood aqueous barrier. *Arch. Ophthalmol.* 106, 480-483, (1988).
 265. Flach, A.J., Graham, J., Kruger, L.P., Stegman, R.C. and Tanenbaum, L. Quantitative assessment of post-surgical breakdown of the blood aqueous barrier following administration of 0.5 % ketorolac tromethamine solution. A double masked paired comparison with vehicle- placebo study. *Arch. Ophthalmol.* 106, 344-347, (1988).
 266. Ballas, Z., Blumenthal, M., Tinkelman, D.G., Kriz, R. and Rupp, G., Clinical evaluation of ketorolac tromethamine 0.5% ophthalmic solution for the treatment of seasonal allergic conjunctivitis., *Surv. Ophthalmol.*, 38, 141-148 (1993).
 267. Tinkelman, D.G., Upp, G., Kaufman, H., Pugely, J., Schultz, N., Double-masked, paired-comparison clinical study of ketorolac tromethamine 0.5% ophthalmic solution compared with placebo eyedrops in the treatment of seasonal allergic conjunctivitis., *Surv. Ophthalmol.*, 38, 133-140 (1993).
 268. Iyer, V, ketorolac (Toradol (RM) induced lithium toxicity. *Headache.* 80, 442-444, (1994).
 269. Santoni, G., Tonsini, A., Graftein, P., Mura, P., Furlanetto, S. and Pinzanti, S., Determination of atropine sulphate and benzalkonium chloride in eye drops by HPLC., *Int. J. Pharm.*, 93, 239-243 (1993).
 270. Riegelman, S. and Sorby, D.L., "EENT Preparation", Chapter 16, in Martin, E.W ed., *Husa's Pharmaceutical Dispensing*, 6th edition, Mack Publishing Co., 1996, pp. 311-341.
 271. Plamondon, J.E. and Nairu, J.G., The effects of surfactants on the rate of decarboxylation of P-aminosalicylic acid in acidic aqueous solution., *J. Pharm. Sci.*, 86(2), 205-208

- (1997).
272. Smith, G.G., Kennedy, D.R. and Nairu, J.G., Hydrolysis kinetics of benzocaine and homologues in the presence of a nonionic surfactants., *J. Pharm. Sci.*, 63, 712-716 (1974).
 273. Suleiman, M.S. and Najib, N.M., Kinetics of alkaline hydrolysis of indomethacin in the presence of surfactants and cosolvents., *Drug Dev. Ind. Pharm.* 16, 695-706 (1990).
 274. Oliveira De, A.G. and Chaimovich, H.J., Effects of detergents and other amphiphiles on the stability of pharmaceutical dosage forms., *J. Pharm. Pharmacol.*, 45, 850-861 (1993).
 275. Biological implications of surfactant presence in formulations. pg. 444, Chapter-7, in *Surfactant systems, their chemistry, pharmacy and biology*. Edited by. Attwood, D. and Florence, A.T. Chapman and Hall, N.Y. 1983.
 276. Reer, L., Bock, T.K. and Muller, B.W. In vitro corneal permeability of diclofenac sodium in formulation containing cyclodextrins compared to the commercial product Voltaren Ophtha. *J. Pharm. Sci.* 83 (9), 1345-1349, (1994).
 277. Loftsson, T. and Stefansson, E., Effect of cyclodextrins on topical drug delivery to the eye., *Drug Dev. Ind. Pharm.*, 23 (5), 473-481 (1997).
 278. Jansen T, Xhonneux B, Mesens J and Borgers M; Beta-cyclodextrins as vehicles in eye-drop formulations: An evaluation of their effects on rabbit corneal epithelium. *Lens and Eye Toxicity Research*: 7(3&4), 459-468, (1990).
 279. Jarho, P., Urtti, A., Pate, D.W., Suhonen, P. and Jarvinen, T., Increase in aqueous solubility, stability and in-vitro corneal permeability of anandamide by hydroxypropyl- β -cyclodextrin., *Int. J. Pharm.*, 137, 209-216 (1997).
 280. Jarvinen, K., Jarvinen, T., Thomson, D.O, and Stella, V.J. The effect of a modified β -CD, SBE4- β -CD, on the aqueous stability and ocular absorption of pilocarpine. *Curr. Eye. Res.* 13, 897-905, (1994).
 281. Freednan, K.A., Klein, J.W. and Crossan, C.E. Beta-cyclodextrins enhance bioavailability of pilocarpine. *Curr. Eye. Res.* 12 (7), 641-647, (1993).
 282. Loftsson, T., Fridriksdottir, H., Thorisdottir, S. and Stefansson, E. The effect of hydroxypropyl methylcellulose on the release of dexamethasone from aqueous 2-hydroxypropyl- β -cyclodextrin formulations. *Int. J. Pharm.* 104, 181-184, (1994).
 283. Kristinsson, J.K., Fridriksdottir, H., Thorisdottir, S., Sigurdardottir, A.M., Stefansson, and Loftsson, T. Dexamethasone-cyclodextrin polymer co-complexes in aqueous drops - Aqueous humor pharmacokinetics in humans. *Invest. Ophthalmol. Vis. Sci.* 37, 1199-1203, (1996).

284. Unlu, N., Ludwig, A., Van Ooteghem, M. and Hunca1, A.A. A comparative rheological study on carbopol viscous solutions and, the evaluation of their suitability as the ophthalmic vehicles and artificial tears. *Pharm. Acta. Helv.* 67, 5-10, (1992).
285. Newton, D.W., Beckker, C.H. and Torosion G., Physical and chemical characteristics of water soluble semisolids, anhydrous bases for ophthalmic use., *J. Pharm. Sci.*, 62(9), 1539-1543 (1973).
286. Allen, R.C., Boys-smith, J., Campbell, D., Rosenquist, R. and Van Buskirk, E.M., A one-year multicenter clinical trial of pilocarpine gel., *Am. J. Ophthalmol.*, 97, 723-729 (1984).
287. Croce, C.P., Fischer, A. and Thomas, R.H., "Packaging material science", Chapter 24, in Lachman, L. and Lieberman, H.A. and Kanig, J.L eds., *The theory and practice of Industrial Pharmacy.*, 3rd edition, Lea & Febiger Publications, Philadelphia, pp. 711-732.
288. Gilbert, J.C., Richardson, J.L., Davies, M.C., Parin, K.J. and Hadgraft, J. The effect of solutes and polymers on the gelation properties of pluronic F-127 solution for controlled drug delivery. *Int. J. Pharm.* 113-118, (1987).
289. Lindell, K. and Engstrain, S. In-vitro release of timolol from in-situ gelling polymer system. *Int. J. Pharm.* 95, 219-228, (1993).
290. Safwat, S.M., Sayed, H.A. and Ibrahim, S.A. In-vitro and In-vivo evaluation of certain non steroidal anti-inflammatory drugs in ophthalmic hydrogel forms. *Drug Dev. Ind. Pharm.* 14 (15-17), 2605-2624, (1988).
291. Remogen, H.B., International Harmonization: ICH 3 and further activities., *Drugs Made In Germany* 39 (2), 37-44 (1996).
292. Dietz, R., Feilner, K., Gernst, F. and grimm, W., Drug stability testing, classification according to climate zone., *Drugs Made in Germany* 36 (3), 99-103 (1993).
293. "Sterility Testing," in: *The United States Pharmacopoeia-22nd revision*, The United States Pharmacopeial Convention Inc., 1990, pp. 1478-1483.
294. "Preservative Effectiveness Testing," in *The United States Pharmacopoeia-22nd revision*, The United States Pharmacopeial Convention Inc., 1990, pp. 1478-1483.
295. Draize, J.H., Woodard, G, and Calvery, H.O. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. *J. Pharmacol. Exp. Ther.* 82, 377-390, (1944).

296. Weinreb, R.N., Caldwell, D.R., Goode, S.M., Horwitz, B.L., Leibowitz, R., Shrader, E.C., Stewart, R.H. and Williams, T., A double masked three month comparison between 0.25% betaxolol suspension and 0.5% betaxolol ophthalmic solution., *Am. J. Ophthalmol.*, 110, 189-192 (1992).
297. Schwartzkopff, T., Kewitz, H. and Pahlitzsch, T., Topical indomethacin: inhibition of corneal wound healing in guinea pigs after severe alkali burn., *Cornea.*, 4, 19-24 (1985).
298. Srinivasan, B.D. and Kulkarni, P.S., The role of arachidonic acid metabolites in the mediation of the polymorphonuclear leukocytes response following corneal injury., *Invest. Ophthalmol. Vis. Sci.*, 19, 1087-1093 (1980).
299. Patterson, C.A., Williams, R.N. and Parker, A., Characteristics of polymorphonuclear leukocytes infiltration into the alkali burned eye and the influence of sodium citrate., *Exp. Eye. Res.*, 39, 701-708 (1984).
300. Oliver, H., Lowry, M., Rosenbrough, J., Farr, A.L. and Randall, R.J. Protein measurement with the folin phenol reagent. *J. Biol. Chem.* 193, 265-275 (1951).
301. Kenyon, K.R., Berman, M., Rose, J. and Gage, J. Prevention of stromal ulceration in the alkali-induced rabbit cornea by glued-on contact lens. Evidence of the role of polymorphonuclear leukocytes in collagen degradation. *Invest. Ophthalmol. Vis. Sci.* 18 (6), 570-587 (1979).
302. Singh, G. and Foster, C.S., Epidermal growth factor in alkali-burned corneal epithelial wound healing., *Am. J. Ophthalmol.*, 103, 802-807 (1987).
303. Dua, H.S, and Forester, J.V. Clinical patterns of corneal epithelial wound healing. *Am. J. Ophthalmol.* 104, 481-489, (1987).
304. Nedelman JR, Gibiansky E and Law DTW; Applying Bailer's method for AUC confidence intervals to sparse sampling. *Pharm. Res.*: 12(1), 124-128 (1995).
305. Yuan J; Estimation of variance for AUC in animal studies. *J. Pharm. Sci.*: 82(7), 761-763 (1993).
306. Bailer A.J.; Testing for the equality of AUC when using destructive measurement techniques. *J. Pharmacokinet. Biopharm.*: 16(3), 303-309 (1988).
307. Sieg, J.W. and Robinson, J.R. Vehicle effects on ocular drug bioavailability I: evaluation of fluoromethalone. *J. Pharm. Sci.* 64 (6), 931-936 (1975).
308. Lehr, C.M., Lee., Y.H. and Lee, V.H.L. Improved ocular penetration of gentamicin by mucoadhesive polymer polycarbophil in the pigmented rabbit. *Invest. Ophthalmol. Vis. Sci.* 35 (6), 2809-2814 (1994).