CHAPTER - 2

LITERATURE REVIEW
2.1 **SIMVASTATIN**

- Wang\textsuperscript{106} reported a derivative spectroscopic method for the determination of Simvastatin (SIM). Zero crossing point was selected at 243 nm.
- Tan\textsuperscript{107} reported RP-HPLC method for the analysis of SIM in human plasma. Lovastatin was ISTD and extracted with a mixture of cyclohexane & dichloromethane.
- Jamal\textsuperscript{108} reported a direct-injection LC-MS method for the quantification of SIM and its in-vivo generated prodrug SIM acid together.
- Barrett\textsuperscript{109} reported an isocratic LC method using mass spectroscopic detector for the analysis of SIM and its metabolite SIM hydroxy acid. Detection was performed in both positive and negative ionization mode.
- Senthamil selvan\textsuperscript{110} reported a LC method using mass spectroscopic detector for the accurate quantification of metaprolol succinate and SIM. Propranolol hydrochloride was ISTD.
- Nilesh Jain\textsuperscript{111} reported a spectrophotometric method for the analysis of EZM and SIM simultaneously. SIM estimation was carried out by dual wavelength method at 223 nm and 254.5 nm. EZM was estimated as a single component at 258.5 nm.
• Effat Souri\textsuperscript{112} reported a first derivative spectroscopic method for the determination of SIM and EZM simultaneously using zero crossing technique. At 219 and 265 nm measurements were carried out for SIM and EZM respectively.

2.2 EZETIMIBE

• Basha\textsuperscript{113} reported a gradient HPLC-UV method for simultaneous estimation of EZM and its phase-I and phase-II metabolites. Theophylline was ISTD.

• Sistla\textsuperscript{114} reported a reversed-phase HPLC method. Chromatographic conditions were Kromasil 100 C\textsubscript{18} column and detection wavelength 232 nm.

• Imran\textsuperscript{115} reported a stability indicating UV-spectroscopic methods for the estimation of EZM and carvedilol. Both the drugs are poorly soluble in water hence, 20\% v/v acetonitrile in triple distilled water was used as solvent for both the drugs.

• Olivera\textsuperscript{116} reported an analytical method based on LC-MS-MS for the analysis of EZM from human plasma. Etoricoxib was ISTD. Chromatographic conditions; C\textsubscript{18} analytical column, mobile phase of acetonitrile-water (85:15, v/v).

• Godse\textsuperscript{117} reported two spectrophotometric methods for the simultaneous analysis of EZM and atorvastatin. First method; simultaneous equations and second absorbance ratio. Absorbance
maximum of EZM 232.5 nm and absorbance maxima for atorvastatin 246.5 nm.

- Rajput\textsuperscript{118} reported a D\textsubscript{1} spectrophotometric method for the analysis of EZM and lovastatin by zero crossing method. Measurements were carried out at zero crossing points i.e.; 265.20 and 245.4 nm for EZM and lovastatin respectively.

- Vishnu\textsuperscript{119} reported a RP-LC-PDA method for atorvastatin, EZM and fenofibrate in their ternary mixture of pharmaceutical formulations. Chromatographic conditions were kromasil C\textsubscript{18} column, column temperature 40°C, and detector wavelength at 240 nm.

2.3 RABEPRAZOLE SODIUM

- Garcia\textsuperscript{120} reported a derivative method for RAB estimation. Water was used as diluent. First derivative spectra was obtained at N=5, $\Delta \lambda=4.0$ nm at a wavelength of 304 nm.

- Madhulikar\textsuperscript{121} reported RP-HPLC method for the estimation of RAB. Chromatographic conditions were YMC-C\textsubscript{18} ODS-AM stainless steel column, detection using a PDA detector.

- Lohe\textsuperscript{122} reported and validated spectrophotometric methods for estimation of RAB and diclofenac simultaneously. First method was based on simultaneous equation using two wavelengts
294 nm and 281.2 nm. Second method was graphical absorbance ratio using two wavelengths.

- Jain\textsuperscript{123} reported a spectroscopic method for the estimation of RAB sodium and amoxicillin trihydrate. The method was based on simultaneous equation using two wavelengths at 247 nm and 292 nm.

- Heralgi\textsuperscript{124} reported a spectroscopic method for the estimation of RAB and itopride hydrochloride. The method was based on simultaneous equation (Vierodts method). In phosphate buffer (pH) 7.4 RAB shows absorbance maxima at 283 nm and itopride hydrochloride at 258 nm.

- Singhvi\textsuperscript{125} reported two spectroscopic methods for the estimation of RAB and itopride hydrochloride. First method was based on simultaneous equation using two wavelengths at 265.2 nm and 290.8 nm. Second method was based on two wavelengths; wavelengths selected for itopride hydrochloride were 278 and 298.8 nm and for RAB sodium 253.6 and 275.2 nm. For RP-HPLC method Phenominix C\textsubscript{18} column was used.

- Suganthi\textsuperscript{126} reported a HPTLC method for the estimation of RAB and itopride hydrochloride. Chromatographic conditions were silica gel 60 F\textsubscript{254}, detection wavelength at 288 nm. The R\textsubscript{f} values for RAB and itopride hydrochloride were 0.23±0.02 and 0.75±0.02 respectively.
2.4 ONDANSETRON HYDROCHLORIDE

- Koufopantelis\textsuperscript{127} reported a liquid chromatography/positive ion electro spray mass spectrometric assay for the analysis of methotrexate, folic acid and Ondansetron (OND) in human serum. Alfuzosin was used as internal standard.

- Manisha Puranik\textsuperscript{128} reported HPTLC method for the analysis of OND with omiprazole and RAB respectively in solid dosage form. Chromatographic conditions were silica gel 60 F\textsubscript{254}, mobile phase of dichloromethane-methanol (9:1 v/v), detection wavelength at 309 nm and 294 nm for OND with omiprazole and RAB respectively.

- Shirish Patel\textsuperscript{129} reported a HPLC method for the determination of RAB sodium and OND in pharmaceutical dosage form. Chromatographic conditions were ODS Hypersil C\textsubscript{18} column, mobile phase of ammonium acetate buffer pH 5.5-water-methanol (25:15:60 v/v/v), flow rate 1ml/min, detection wavelength 275 nm.

- Michelle\textsuperscript{130} reported a HPLC method for separation and quantitation of OND in human plasma and ultraviolet detection at 305 nm. Liquid–liquid extraction of OND from plasma was done. Internal standard method was used for quantitation.

- Keliu\textsuperscript{131} reported an enantioselective method for the estimation of OND enantiomers using liquid chromatography-tandem mass spectroscopy in human plasma.
• Sradhanjali\textsuperscript{132} reported a simple, sensitive spectrophotometric method in UV region for the analysis of OND. $\lambda_{\text{max}}$ of OND in water was at 310 nm.

2.5 **DOMPERIDONE**

• Kalirajan\textsuperscript{133} reported a RP-HPLC method for simultaneous analysis of RAB and domperidone (DOM). Chromatographic conditions were C\textsubscript{18} column, detection wavelength 290 nm.

• Shwetha\textsuperscript{134} reported a spectrophotometric method for estimation of RAB sodium and DOM simultaneously. The method was based on ratio spectra derivative spectrophotometry. The D\textsubscript{1} amplitudes of first derivative spectra were at 230 nm and 250 nm to determine RAB sodium and DOM respectively.

• Patel\textsuperscript{135} reported a first order derivative spectrophotometry method for simultaneous estimation of DOM and RAB sodium. The absorbance values were at 253.2 nm and 266.6 nm for the estimation of DOM and RAB sodium.

• Patel\textsuperscript{136} reported a HPLC method for the estimation of pantoprazole, RAB, esomeprazole, DOM and itopride. Chromatographic conditions were Hypersil BDS C\textsubscript{18} column, detection wavelength 210 nm.

• Mohammed\textsuperscript{137} reported a HPLC method for the simultaneous analysis of methylparaben, propylparaben, and DOM in oral
suspension. Chromatographic conditions were Optimapak OP C₈, Column, and detection wavelength at 280 nm.

- Lakshmi¹³⁸ reported a simple RP-HPLC method for the determination of omiprazole and DOM. Chromatographic conditions were Hypersil ODS column, wavelength 280 nm.
- Prasanna reddy¹³⁹ reported and validated a RP-HPLC method for the estimation of pantaprazole and DOM. Chromatographic conditions were Hypersil BDS column, and detection wavelength 280nm.

2.6 GATIFLOXACIN

- Sowmya¹⁴⁰ reported a HPTLC method for the estimation of GFN in human plasma. Paracetmol was used as internal standard. GFN in plasma was extracted with dichloromethane of pH 4.5. Chromatographic conditions were silica gel 60 F₂₅₄, detection wavelength at 291 nm.
- Saleh¹⁴¹ reported RP-HPLC method for the GFN stability in human plasma. CFN was used as internal standard. Chromatographic conditions were X Terra MS C₁₈ column, detection wavelength 293 nm.
- Hoang¹⁴² reported liquid chromatography with a column-switching technique for simultaneous quantification of GFN, Levofloxacin,
and MFN in human serum samples. Fluoroquinolones (FQs) separated on a Supelcosil analytical column.

- Brain\textsuperscript{143} reported and validated RP-HPLC method for GFN in human serum and urine. Serum proteins were removed by ultrafiltration.

- Venugopal\textsuperscript{144} reported a UV-spectroscopic method for the estimation of GFN. GFN was estimated in 100 mM phosphate buffer (pH 7.4) at 286 nm and in 100mM HCl (pH 1.2) at 292 nm.

- Karthik\textsuperscript{145} reported LC/ESI-MS/MS method for GFN in human plasma. Solid phase extraction was used to extract drug and internal standard CFN from plasma.

- Xiashi\textsuperscript{146} reported a spectrofluorometric method for GFN. It was based upon the strong fluorescence of GFN after addition of fluorescence probe yttrium in buffer solution (pH 7.0).

- Bhanubhai\textsuperscript{147} reported a HPTLC method for GFN and ornidazole. Chromatographic conditions were silica Gel 60 F\textsubscript{254} TLC plate, mobile phase of n-butanol-methanol-6M ammonia in the ratio of 8:1:1.5v/v, detection wavelength at 302 nm.

**2.7. MOXIFLOXACIN**

- Vandana\textsuperscript{148} reported a HPTLC method for the estimation of moxifloxacin (MFN) hydrochloride. Chromatographic conditions
were stationary phase silica gel 60 F<sub>254</sub>, mobile phase of methylene chloride- methanol- strong ammonia solution and acetonitrile (10:10:5:10).

- Prabhakar<sup>149</sup> described a spectroscopic method for the assay of MFN based on the formation of complexes with alkaloidal precipitants.

- Lalitha Devi<sup>150</sup> reported a specific, stability indicating method for the analysis of MFN and its related substances. Chromatographic conditions were C<sub>18</sub> column, mobile phase of sodium dihydrogen orthophosphate dihydrate containing triethylamine of pH 3.0 (with orthophosphoric acid), and methanol, detection wavelength at 240 nm.

- Karthik<sup>151</sup> reported and validated a LC-ESI-MS method for the analysis of MFN in human plasma. LFN was ISTD. Solid phase extraction (SPE) was employed using Oasis HLB to extract MFN and LFN from plasma.

- Aleksandra<sup>152</sup> proposed a RP-HPLC method for the analysis of MFN in plasma. Chromatographic conditions were Supelco LC-Hisep shielded hydrophobic phase column, Fluorescence detector was used with excitation and emission at 290 nm & 500 nm respectively.
• Kumudha valli\textsuperscript{153} reported a RP-HPLC-UV method for
determination of MFN HCl. Chromatographic conditions were pre-
packed Luna C\textsubscript{18} column, detection wavelength at 293 nm.

2.8. SPARFLOXACIN

• Sharma\textsuperscript{154} reported three simple spectroscopic methods for the
estimation of sparfloxacin (SFN). Absorbance maxima at 280 nm
for method A and a sharp peak at 267nm in first derivative
spectra; method B, wavelength range of 296-298 nm for
method C.

• Najma\textsuperscript{155} described a RP-HPLC method for SFN and some H\textsubscript{2}
receptor antagonists such as cimitidine, ranitidine and famotidine
estimation. Chromatographic conditions were purospher STAR C\textsubscript{18}
column, mobile phase of methanol-water-acetonitrile
(54:41:5 v/v/v, pH adjusted to 2.7 by phosphoric acid), flow rate
1ml/min, detection wavelength at 232 nm for cimitidine and
250 nm for famotidine and ranitidine.

• Keumhan Noh\textsuperscript{156} reported a LC/MS method for the quantification
of SFN in rat plasma. Protein were precipitated with acetonitrile,
the analytes were chromatographed on a C\textsubscript{18} column and detected
by LC-MS.

• Cao\textsuperscript{157} reported a HPLC method for quantitative determination of
SFN injection. Chromatographic conditions were Waters Symmetry
C\textsubscript{18} column, the flow-rate was 1.0 mL/min, and detection wavelength was UV-298.8 nm.

- Herida\textsuperscript{158} reported a visible spectroscopic method for SFN determination. The basis of reaction was complexation of bromothymol blue 0.5% with SFN to form a yellow colour compound with maximum absorption at 385 nm.

- Herida\textsuperscript{159} reported a volumetric titration in non aqueous medium.

### 2.9. CIPROFLOXACIN

- Rele\textsuperscript{160} reported a gradient RP-HPLC method for ciprofloxacin (CFN) and DSP simultaneously in pharmaceutical dosage form. Separation was carried out on nucleosil C\textsubscript{18} column, detection at 265 nm. The mobile phase A consisted of 50 milli molar citric acid and potassium phosphate buffer. The mobile phase B of 100 \% v/v acetonitrile.

- Manuela\textsuperscript{161} reported a liquid chromatographic method for the quantitative analysis of CFN in plasma. Proteins were precipitated from plasma by means of 6\% perchloric acid. Chromatographic conditions were LiChrospher 60 RP select B, mobile phase of acetic acid 5\%-methanol–acetonitrile (90:5:5, v/v/v), and detection wavelength at 280 nm, internal standard as LFN.
• Scholl\textsuperscript{162} reported a RP-HPLC method with fluorescence detection for the quantification of CFN and its known metabolites urine, serum/plasma, bile, feces and tissues.

• Isabel\textsuperscript{163} reported a method for the analysis of CFN using solid-phase spectrophotometry.

• Han\textsuperscript{164} reported an analytical method, called enhanced chemiluminescence with flow-injection sampling for the determination of CFN. The method was based on the chemiluminescence reaction of the potassium permanganate–sodium thiosulfate with CFN.

• Novakovic\textsuperscript{165} reported a HPTLC method for CFN in coated tablets. Chromatographic conditions were stationary phase of Silica gel 60F\textsubscript{254}, solvent system of acetonitrile, ammonia 25%, methanol and methylene chloride (1:2:4:4, v/v/v/v).

• Chen\textsuperscript{166} reported a RP-HPLC method for the analysis of CFN and dexamethasone acetate in compound CFN ear drops on a C\textsubscript{18} column. The mobile phase pH 2.6 phosphoric acid solution and methanol was in the range of 30:70 V/V. Detection wavelength was set at 240 nm.

\textbf{2.10. OFLOXACIN}

• Lu Wei\textsuperscript{167} reported a gradient HPLC method for ofloxacin (OFN) and Dexamethasone acetate from compound OFN ear drops.
Chromatographic conditions were XDB – C₈ column, mobile phase methanol – potassium dihydrogen phosphate (0.02 mol/L), column temperature 30°C and detection wavelength at 240 nm.

- Tan Ruiwei⁶⁸ reported an RP- HPLC method for OFN and DSP from compound OFN nasal drops. Chromatographic conditions were Shimpack CLC ODS column, mobile phase of methanol-citric acid solution- acetonitrile- ammonium acetate solution- phosphoric acid solution (100:75:22:1:2), flow rate 1.0 ml/min and detection wavelength at 242 nm.

- Tang⁶⁹ reported a HPLC method for determination of OFN, tinidazole and DSP from compound OFN ear drops. Conditions were ODS stationary phase, mobile phase of 0.2% triethylamine in water (pH to 2.7 with phosphoric acid - acetonitrile (68:32, v/v), detection wavelength of 240 nm and internal standard as CPL.

- Wu Yang⁷⁰ reported a HPLC method for determination of OFN. Chromatographic conditions were Techsphere C₁₈ column, mobile phase consists of citric acid- acetonitrile- tetraethylenediamine (70:28:2, v/v), flow rate 0.8 ml/min, detection wavelength 293 nm.

- Kapil⁷¹ reported a RP- HPLC method for cefexime and OFN in combined tablet dosage form. HPLC conditions were Hiq-Sil C₈ Neosphere column and UV – VIS detector set at 290 nm, mobile phase as 0.025 mM potassium dihydrogen phosphate buffer (70:30, v/v).
Dhandapani\textsuperscript{172} reported a reverse phase LC method for simultaneous analysis of OFN and ornidazole. Separation conditions were Phenominix C\textsubscript{18} column, detector set at 293 nm. GFN was used as internal standard.

Vipul\textsuperscript{173} reported a simple HPLC method for nitazoxanide and OFN. Chromatographic conditions were YMC pack- AM C\textsubscript{18}, 25-cm analytical column, flow rate 1ml/min, mobile phase of 10mM/L dipotassium hydrogen phosphate- acetonitrile (65:35 v/v); pH adjusted to 7 using ortho phosphoric acid, column temperature at 30° C.

\textbf{2.11. LOMEFLOXACIN HYDROCHLORIDE}

Rajasekaran\textsuperscript{174} reported a visible spectroscopic method for the estimation of LFN. Orange yellow colored chromogens are formed by reaction with 1 w/v ferric nitrate solution in 1% v/v nitric acid due to formation of quinolone derivatives with polyvalent iron; exhibits maximum absorption at 445 nm.

Sevgi\textsuperscript{175} reported a spectrofluorometric method for LFN. The reaction between the drug and 4- choro-7- nitrobenzodioxazole in borate buffer of pH 8.5 yields a highly fluorescent derivative; measured at 533 nm after excitation at 433 nm.

Fenxi\textsuperscript{176} reported a HPLC method for the estimation of LFN. Chromatographic conditions were C\textsubscript{18} column, mobile phase of
0.02 mol/L phosphoric acid solution of pH 2.6 (pH adjusted with triethyl amine) in the ratio of 85:15, v/v, detection wavelength of 287nm.

- Joana souse\textsuperscript{177} reported a liquid chromatographic method coupled with fluorescence detection for the combined estimation of norfloxacin, CFN and LFN in human plasma. Chromatographic conditions were C\textsubscript{18} column, detector was set at excitation/emission wavelength at 278/450 nm. Levofloxacin was ISTD.

- Maria\textsuperscript{178} reported a HPLC method for the some third generation fluoroquinolones such as GFN, levofloxacin, LFN and pefloxacin. Chromatographic conditions were LiChrospher 100 RP-18 column, and detection at 279-295 nm.

- Chitlange\textsuperscript{179} reported a stability indicating HPTLC method for the estimation of LFN in bulk and pharmaceutical formulations. Chromatographic conditions were precoated silica gel 60 F\textsubscript{254} plates, mobile phase of Chloroform: Methanol: Ammonia (10: 7: 3 v/v/v), densitometric scanning at 288 nm. LFN was subjected to forced degradation by acid, alkali, oxidation and dry heat.

- Alaveraz\textsuperscript{180} reported a voltametric method for LFN estimation. The calibration curve method was used for the LFN estimation in the concentration range of 7.0 x 10\textsuperscript{-6} to 7.0 x 10\textsuperscript{-5} M. The
polarographic method showed good selectivity with respect to both excipients and degradation products. This method was also to the quantitation of LFN in urine, and the renal excretion profile.

2.12. DEXAMETHASONE SODIUM PHOSPHATE

- Chen\textsuperscript{181} reported a gradient HPLC method to determine the trace amounts of Dexamethasone Sodium Phosphate (DSP) related substances on drug eluting stents. Separation of DSP from its impurities and degradation products using Zorbax eclipse XBD C\textsubscript{8} column, at a $\lambda_{\text{max}}$ of 239 nm. The method was robust and resistant to small variations chromatographic variables such as pH, mobile phase composition and column temperature.

- Hyung woo kwak\textsuperscript{182} reported a RP-HPLC method for vitreous levels determination of DSP. Prior sample clean up procedure using Waters Sep–Pak C\textsubscript{18} cartridge. Protein was separated and eluted with water. DSP sodium phosphate and paraben were eluted with methanol.

- Hu xiang\textsuperscript{183} reported a colorimetric method for Dexamethasone acetate from Dexamethasone cream at 484.5 nm. Drug was extracted using ethyl alcohol and treated with triphenyl tetrazolium chloride.
• Kazou\textsuperscript{184} reported a GC-MS method for DSP in biological fluids. Quantitation was done by selected-ion monitoring on the molecular ions of the tetra/trimethylsilyl derivative of DSP and of DSP M+9.

• Spangler\textsuperscript{185} reported a simple three stage gradient HPLC procedure for DSP, impurities, degradation products and product preservatives. Detection wavelength at 240 nm.

• Olga\textsuperscript{186} reported a method for DSP in urine. Proposed method was based on the enzymatic hydrolysis of urine samples. Eluates were derivatised. Detection, identification and quantification of residues were carried out by GC/MS in the negative chemical ionization mode.

• Mahesh\textsuperscript{187} reported a LC/MS/MS method for DSP and corticosterone in rat plasma. PA was the internal standard.

2.13. PREDNISOLONE ACETATE

• Abd EL- MAboud\textsuperscript{188} reported two methods for the assay of two binary mixtures of prednisolone acetate (PA) with tetracycline and with CPL.

• Patricia A Williams\textsuperscript{189} reported a RP-HPLC method for the separation of cortisone, hydrocortisone, PA and prednisone on a micro-particulate column. Cortisone acetate, hydrocortisone acetate and PA were separated using acetonitrile and water on the same column.
- Tamil selvan reported a UV spectroscopic method for the estimation of PA from tablet formulation. Spectroscopic parameters were absorption maxima at 244 nm, Beer’s law concentration range 2-12 µg/ml.

- Jayarama Reddy reported a voltametric method on PA, DSP and hydrocortisone using cyclic voltametry and differential pulse voltametry at bare carbon paste electrode and cyclodextrin modified carbon paste electrode in Britton-Robinson buffer solution (pH 3.0).

- Ali reported a HPLC method for OFN, tetrahydrazoline hydrochloride and PA in ophthalmic suspension. Chromatographic conditions were Waters Spherisorb ODS column, propylparaben as internal standard, detection wavelength set at 210 nm for OFN and tetrahydrazoline hydrochloride, 254 nm for PA and propylparaben and flow rates of 1.2 ml/min.

- Matin reported an analytical method for PA and prednisone in human plasma utilizing GLC and chemical-ionization mass spectrometry. Selective derivatization with Girard Reagent T to remove interference from endogenous hydrocortisone.

- Aburuz reported a solid phase extraction and HPLC method for specific determination of PA and hydrocortisone (cortisol) in both plasma and urine. Recoveries of PA and cortisol from plasma and urine were greater than 82%.
Valerie reported a LC-MS-MS method for quantitative estimation of prednisone, PA, DSP and cortisol in human serum.

2.14. CHLORAMPHENICOL

Yu Zi cheng reported a RP-HPLC method for chloramphenicol (CPL) and betamethasone in Xinfu cream. Chromatographic conditions were Bondapak column C18; detection wavelength of 240 nm, temperature was set at 45°C.

Shadoul reported a simple HPLC method for the combined analysis of DSP and CPL in eye drops formulation. Chromatographic conditions were C18 column, mobile phase acetonitrile- 5%v/v glacial acetic acid (36:64v/v).

Iqbal reported a HPLC method for dexamethasone, DSP and CPL. Chromatographic conditions were Shim-Pack CLC-ODS column, mobile phase of buffer pH 5.4- acetonitrile-methanol (1.73:1.16:1, v/v/v), column temperature 50°C, flow rate of 0.5ml/min, λmax at 254 nm with a total run time of less than 15 min.

Xio-Ben Chen reported a gradient UPLC analytical method for clenbuterol, CPL and diethylstilboestrol by isotope dilution ultra performance liquid chromatography tandem mass spectrometry.
• Cerkvenik\textsuperscript{200} reported an analytical method for determining CPL residues in muscle tissue by using gas chromatography-electron capture detection. Meta isomer of CPL was ISTD.

• Basilio\textsuperscript{201} reported a analytical method for CPL and its derivatives, CPL succinate sodium and d-(−)-threo-2-amino-1-[p-nitrophenyl]-1, 3-propanediol (CPL base). The basis of the method is the formation of the blue colour produced by the interaction of ammonium molybdate with the products of the alkaline hydrolysis of the drugs.

• Satinsky\textsuperscript{202} reported a separation method based on a reversed-phase sequential injection chromatography (SIC) technique for simultaneous determination of CPL and betamethasone in pharmaceutical eye drops.