List of Tables

Table II. 1 Drugs are proposed to be classified according to the following scheme 8
Table II. 2 Outputs and Minimal Inputs for the Predictive ADME Software Packages (Bohets et al., 2001) 12
Table II. 3 Models to determine intestinal permeability with advantages and limitations. 19
Table II. 4 Transit profile (Mean ± SD) of the tablet core for fasted and fed volunteers. 34
Table II. 5 Pharmacokinetic data of Alfuzosin hydrochloride....38
Table II. 6 Urinary Symptoms of Benign Prostatic Hyperplasia....41
Table II. 7 Medications that affect Gastric Emptying (American Gastroenterological Association, 2004) ...53
Table II. 8 Methods used to study gastric emptying (Petring and Blake, 1993)....54
Table II. 9 Physiological interactions due to ingested food and fluid which may influence drug absorption (Welling, 1989)....59
Table IV. 1 List of Alfuzosin Hydrochloride and excipients used for Compatibility study along with Manufacturers....145
Table IV. 2 Composition of Kreb's Ringer Bicarbonate Solution. (www.Sigmaaldrich.com)....146
Table IV. 3 Solubility study of Alfuzosin Hydrochloride at various pH at 37 ± 0.5 °C 152
Table IV. 4 Solubility of Alfuzosin Hydrochloride in various solvents at ambient temperature....152
Table IV. 5 Water by KF and Related impurities (RI) of Alfuzosin Hydrochloride kept in open at 40°C/75% RH....153
Table IV. 6 Bulk Density and Tap Density of Alfuzosin Hydrochloride API 153
Table IV. 7 Data of Carr's index of Alfuzosin Hydrochloride API 153
Table IV. 8 Particle Size Distribution and Shape of Alfuzosin Hydrochloride 154
Table IV. 9 Impurity profile of Alfuzosin Hydrochloride....154
Table IV. 10 Data of FT-IR of Alfuzosin Hydrochloride 155
Table IV. 11 Data if X-Ray powder diffraction of Alfuzosin Hydrochloride....157
Table IV. 12 Alfuzosin HCl -Excipients Chemical compatibility study (Autoclave)....159
Table IV. 13 Alfuzosin HCl -Excipients Chemical compatibility study (60° C-Open) 160
Table IV. 14 Alfuzosin HCl -Excipients Chemical compatibility study (40°C/75 % RH-Open)....161
Table IV. 15 Alfuzosin HCl -Excipients Chemical compatibility study (water content)....161
Table IV. 16 Alfuzosin hydrochloride - Excipients physical compatibility study at 40°C/75%RH and 60°C 162
Table IV. 17 Dissolution profile of Marketed formulation in different media....162
Table IV. 18 Comparative Dissolution profile of Marketed Formulation at various rpm....163
Table IV. 19 Net water Flux values of Alfuzosin Hydrochloride in rat small intestine....164
Table IV. 20 Results of Effective Permeability (Peff) of Alfuzosin Hydrochloride in rat small intestine....164
Table IV. 21 Comparative percentage of Alfuzosin Hydrochloride absorbed in duodenum and ileum of rat intestine....169
Table IV. 22 Comparative percentage of disappearance of Phenol Red in duodenum and ileum of rat intestine 169
Table IV. 23 Grading system based on various compound analyzed....174
Table IV. 24 Unidirectional mucosal to serosal fluxes of unlabelled Alfuzosin....175
Table IV. 25 Physico- chemical properties and permeability of drugs at various regions in rat intestine 176
Table IV. 26 Gastrointestinal Transit rate constant ((ki) for each segment 179
Table IV. 27 Expression of mammalian aquaporins in gastrointestinal tissues (Tonghui and Verkman; 1999) 184
Table V. 1 List of Materials along with specifications and Manufacturer details 199
Table V. 2 Batches with different ratios of RSPO: RLPO....201
Table V. 3 Composition of Sample A and Sample B 202
Table V. 4 Comparisons of effective radiation dose with background radiation exposure for several radiological procedures described within the RadiologyInfo.org Web site 209
Table V. 5 Batches with different ratios of polymers....212
Table V. 6 Composition of Batches (B. No 05, B. No. 08, B. No. 12) with different ratio of polymers....212
Table V. 7 Composition with and without magnesium stearate (B.No 15 vs B.No 17) 214
Table V. 8 Composition of Batch. No. 23 with colloidal silicon dioxide in coating composition 216
Table V. 9 Comparative endothermic peaks of the samples to study the compatibility of magnesium stearate and colloidal silicon dioxide with Eudragit RSPO and RLPO: 218
Table V. 10 Physico-chemical parameters of core tablet of Approach IA of B.No 23....224
Table V. 11 Physico-chemical parameters of polymer coated tablets of Approach IA of B.No 23 224
Table V. 12 Composition with Approach IB of B. No. 02 225

List of Tables

Table V. 13 Physical parameters of core tablet of Approach IB of B.No 02....226
Table V. 14 Chemical parameters of Drug coated tablets of Approach IB of B.No 02....227
Table V. 15 Physico-chemical parameters of polymer coated tablets of Approach IB of B.No 02....227
Table V. 16 Gastric Retention time of Dummy tablets of B.No 23 of Approach IA in Healthy volunteers under Fasted condition....230
Table V. 17 Gastric Retention time of Dummy tablets of B.No 23 in Healthy volunteers under Fed condition....232
Table V. 18 Mean plasma concentration (ng/mL) of B.No 23 and Marketed formulation under fasting and Fed state (N=8 volunteers)....236
Table V. 19 Summary of Pharmacokinetic Results of marketed Formulation under Fasting and Fed condition (N=8 volunteers)....236
Table VI. 1 List of Materials along with specifications and Manufacturer details....253
Table VI. 2 Comparative formulation of B.No. 01, B.No 02 and B.No 03 for development of core tablet...257
Table VI. 3 Characterization and Behavior of core tablets of B. No. 01, B.No 02 and B. No 03....257
Table VI. 4 Barrier properties of different % of coating of Ethyl cellulose (10 cps) at different time intervals....258
Table VI. 5 Final composition of B.No. 06....258
Table VI. 6 Optimized parameters for Core tablet....260
Table VI. 7 Optimized parameters for Barrier coating....260
Table VI. 8 Optimized parameters for Drug Coating....260
Table VI. 9 Optimized parameters for Polymer Coating....261
Table VI. 10 Gastric Retention time of Dummy tablets of B.No 06 in Healthy volunteers under Fasted condition....262
Table VI. 11 Gastric Retention time of Dummy tablets of B.No 06 in Healthy volunteers under Fed condition....264
Table VII. 1 SENTRY POLYOX water-soluble Resins NF for Pharmaceutical Applications....275
Table VII. 2 Properties of selected METHOCEL products for use in pharmaceuticals....278
Table VII. 3 Characteristic data of the soluble Kollidon grades....279
Table VII. 4 General Properties of the soluble Kollidon grades in pharmaceuticals....280
Table VII. 5 List of Materials along with specifications and Manufacturer details....281
Table VII. 6 Formulation composition with 20% (B.No 01) and 40% (B.No 02) Polyethylene Oxide....285
Table VII. 7 Formulation composition with HPMC K100 MCR (39.71%) and Polyethylene oxide (12.86%) (B. No 16) vs. HPMC K100 MCR (57.14%) and Polyethylene oxide (20.0%) (B. No 47)....286
Table VII. 8 Physico-Chemical parameters of B. No 16 and B. No. 47....287
Table VII. 9 Gastric Residence time of Dummy formulation of B.No 47 in Fasted State....289
Table VII. 10 Gastric Residence time of Dummy formulation of B.No 47 in Fed State....292
Table VII. 11 BE limit of B. No 16 vs Marketed Formulation in Fed state....296
Table VII. 12 Pharmacokinetic Parameters of B. No 16 vs Marketed Formulation in Fed State....296
Table VII. 13 Test/Reference ratio of Pharmacokinetic parameters in individual volunteers (B. No 16 vs Marketed Formulation)....297
Table VII. 14 Pharmacokinetic Parameters of Test formulation (B.No 16) in fed state....297
Table VII. 15 Pharmacokinetic Parameters of Reference (Marketed Formulation) in fed state....297
Table VII. 16 Analysis of Variance Tables for Ln (C max), Ln (AUC0-t), Ln (AUCinf)....298
Table VII. 17 BE limit of B.No 47 vs Marketed Formulation in Fasted State....300
Table VII. 18 Pharmacokinetic Parameters of B.No 47 vs Marketed Formulation in Fasted State....300
Table VII. 19 Test/Reference ratio of Pharmacokinetic parameters in individual volunteers (B. No 47 vs Marketed Formulation)....300
Table VII. 20 Pharmacokinetic Parameters of Test formulation (B.No 47) in fasted state....301
Table VII. 21 Pharmacokinetic Parameters of Reference (Marketed Formulation) in fasted state....301
Table VII. 22 Analysis of Variance Tables for Ln (C max), Ln (AUC o-t), Ln (AUCinf)....301
Table VII. 23 BE limit of B.No 47 vs Marketed Formulation in Fed state....303
Table VII. 24 Pharmacokinetic Parameters of B.No 16 vs Marketed Formulation in Fed State....303
Table VII. 25 Test/Reference ratio of Pharmacokinetic parameters in individual volunteers (B. No 47 vs Marketed Formulation)....304
Table VII. 26 Pharmacokinetic Parameters of Test formulation (B.No 47) in fed state....304
Table VII. 27 Pharmacokinetic Parameters of Reference (Marketed Formulation) in fed state....304

List of Tables

Table VII. 28 Analysis of Variance for Ln (C max), Ln (AUC o-t), Ln (AUCinf) 305
Table VII. 29 Description of media and duration in USP Apparatus III 311
Table VII. 30 Description of media and duration in USP Apparatus III 312
Table VII. 31 Description of media and duration in USP Apparatus III 313
Table VII. 32 Bio-equivalence Limits of B.No 16 Vs B.No 47 under Fed condition 317
Table VII. 33 Bio-equivalence Limits of B.No 47 (Fasted vs Fed State) 317
Table VII. 34 Comparative Cmax, AUC and AUC inf values of B.No 16 and B.No 47 under Fasted and Fed condition 317
Table VII. 35 Comparative Mean Residence Time (MRT) of B.No 16 and 47 318
Table VII. 36 Formulation composition with 50% (B.No 158) vs 60% (B.No 159) vs 69% (B.No. 147) of HPMC K100MCR keeping 11% PVP K90 constant 324
Table VII. 37 Comparative physico-chemical parameters of B.No 147 and B.No. 158 324
Table VII. 38 Dissolution profile of Formulations B.No 147 vs B.No 158 vs B.No 159 compared with the marketed formulation 325
Table VII. 39 Pharmacokinetic Parameters of B.No 147 vs Marketed Formulation in Fasted State 327
Table VII. 40 BE limit of B.No 147 vs Marketed Formulation in Fasted state 327
Table VII. 41 Test/Reference ratio of Pharmacokinetic parameters in individual volunteers (B. No 147 vs Marketed Formulation) 328
Table VII. 42 Pharmacokinetic Parameters of Test formulation (B.No 147) in Fasted State 328
Table VII. 43 Pharmacokinetic Parameters of Reference (Marketed Formulation) in Fasted State 329
Table VII. 44 Analysis of Variance Tables for Ln (Cmax), Ln (AUC o-t), Ln (AUC o-∞) 329
Table VII. 45 BE limit of B.No 147 vs Marketed Formulation in Fed state 331
Table VII. 46 Pharmacokinetic Parameters of B.No 147 vs Marketed Formulation in Fed State 331
Table VII. 47 Test/Reference ratio of Pharmacokinetic parameters in individual volunteers (B. No 147 vs Marketed Formulation) 331
Table VII. 48 Pharmacokinetic parameters of Alfuzosin ER following Single dose (10mg) administration of Test drug (B.No 147) under Fed condition 332
Table VII. 49 Pharmacokinetic parameters of Alfuzosin ER following Single dose (10mg) administration of Reference drug (Marketed Formulation) under Fed condition 332
Table VII. 50 Analysis of Variance Tables for Ln (Cmax), Ln (AUC o-t), Ln (AUC o-∞) 332
Table VII. 51 Pharmacokinetic Parameters of B.No 158 vs Marketed Formulation in Fasted State 334
Table VII. 52 BE Limits of B.No 158 vs Marketed Formulation in Fasted state 334
Table VII. 53 Test/Reference ratio of Pharmacokinetic parameters in individual volunteers(B. No 158 vs Marketed Formulation) 335
Table VII. 54 Pharmacokinetic Parameters of Test formulation (B.No 158) in fasted state 335
Table VII. 55 Pharmacokinetic Parameters of Reference (Marketed Formulation) in fasted state 336
Table VII. 56 Pharmacokinetic Parameters of B.No 158 vs Marketed Formulation in Fed State 337
Table VII. 57 BE limit of B.No 158 vs Marketed Formulation in Fed state 337
Table VII. 58 Test/Reference ratio of Pharmacokinetic parameters in individual volunteers(B. No 158 vs Marketed Formulation) in fed state 338
Table VII. 59 Pharmacokinetic Parameters of Test formulation (B.No 158) in fed state 338
Table VII. 60 Pharmacokinetic Parameters of Reference (Marketed Formulation) in fed state 339
Table VII. 61 MRT (mean residence time) vs MDT (mean dissolution time) of B.No 147 and B.No 158 in fasted and Fed state 340
Table VII. 62 Dry mix blend uniformity analysis at different mixing time points 341
Table VII. 63 IPA content at different temperature in granules 342
Table VII. 64 IPA content at different time interval in granules 342
Table VII. 65 Effect of different hardness on dissolution profile of Alfuzosin HCl ER Tablets 343
Table VII. 66 Content uniformity of Alfuzosin hydrochloride ER tablets 10 mg 343
Table VII. 67 Stability Data of Alfuzosin Hydrochloride Extended Release Tablets 10 mg (B.No.147) 343
Table VII. 68 Comparative dissolution profile at various stability conditions and in different packaging (B.No. 147) 344
Table VII. 69 Bio-equivalence study of B. No 147 Vs B. No 158 under Fed condition 345
Table VII. 70 Bio-equivalence study of B. No 147 Vs B. No 158 under Fasted condition 345
Table VII. 71 Comparative Cmax, AUC and AUC inf values 346
Table VII. 72 Comparative Cmax, AUC and AUC inf values 346

List of Tables

Table VII. 73 Comparative Pharmacokinetic parameters of Marketed formulation of extended release (ER) and immediate release (IR) formulation 347
Table VII. 74 Comparative swelling properties of B.No 16 vs B.No 47 vs B.No 147 vs B.No 158 347
Table VII. 75 MRT vs MDT of B.No 147, B.No 159 and B.No 158 in Fasted and Fed state 351