

CONTENTS

LIST OF TABLES	ix
LIST OF FIGURES	xiii

CHAPTER 1: INTRODUCTION

1.1	AN OVERVIEW OF THE PROBLEM	1
1.2	CONVENTIONAL CONTROL MEASURES	1
1.3	THE USE OF CONTROLLED-RELEASE TECHNOLOGY	2
1.4	SCOPE OF THE PRESENT STUDY	2

CHAPTER 2: HISTORICAL BACKGROUND

2.1	INTRODUCTION	5
2.2	POLYMER SYSTEMS FOR CONTROLLED RELEASE	7
2.2.1	Brief Descriptions of Controlled-Release Technologies	7
2.2.1.1	Reservoir systems with a rate-controlling membrane	7
2.2.1.1.1	Micro- and macrocapsules	7
2.2.1.1.2	Membrane systems	9
2.2.1.2	Reservoir systems without a rate-controlling membrane	9
2.2.1.3	Monolithic systems	9
2.2.1.4	Laminated structures	10
2.2.1.5	Other physical methods	11
2.2.1.6	Retrograde chemical reaction systems	11
2.2.2	Basic Components of Controlled-Release Devices	12

2.3	RELEASE CHARACTERISTICS OF CONTROLLED-RELEASE SYSTEMS	12
2.3.1	Reservoir Systems with a Rate-Controlling Membrane	13
2.3.2	Reservoir Systems without a Rate-Controlling Membrane	13
2.3.3	Monolithic Systems	15
2.3.3.1	Physically dissolved, non-erodible plastic or elastomeric matrix	15
2.3.3.2	Physically dispersed, non-erodible plastic or elastomeric matrix	15
2.3.3.3	Monolithic erodible systems	15
2.3.4	Laminated Structures	16
2.3.5	Other Physical Methods - Osmotic Pumps	16
2.3.6	Retrograde Chemical Reaction Systems	16
2.4	MONOLITHIC PLASTIC AND ELASTOMERIC DEVICES	17
2.4.1	The Preparation of Monolithic Devices	17
2.4.1.1	Monolithic plastic devices	17
2.4.1.2	Compounding of monolithic elastomeric materials	17
2.4.2	Release Mechanisms	18
2.4.2.1	General considerations	18
2.4.2.2	Release from plastic matrices	19
2.4.2.3	Release from elastomeric matrices	20
2.4.3	Theoretical Principles of Controlled Release from Monolithic Devices	21
2.4.3.1	Homogeneous monolithic devices containing only dissolved solute	21
2.4.3.2	Mathematical model for diffusion from cylindrical monolithic devices	24
2.4.3.3	Homogeneous monolithic devices containing dispersed solute	27
2.4.3.4	Granular or porous monolithic devices	31
2.4.3.5	Monolithic devices and the effects of boundary layers	32

2.4.4	Factors which Influence the Kinetics of Solute Release from Monolithic Devices	34
2.4.4.1	Concentration of solute in polymer matrix	35
2.4.4.2	Diffusion coefficients	36
2.4.4.3	Partition coefficients	36
2.4.4.4	Solubility of the solute	37
2.4.4.5	Additional factors	38
2.4.5	Factors which Influence the Release Lifetime of Monolithic Elastomeric Devices	39
2.4.5.1	The choice of the base polymer	39
2.4.5.2	The effect of fillers	40
2.4.5.3	The effect of vulcanization conditions	41
2.4.5.4	The effect of device geometry	41
2.4.5.5	The effect of agent loading	41
2.5	MEMBRANE-CONTROLLED DEVICES	42
2.5.1	Fick's Law Applied to Membranes	42
2.5.2	Measurement of Diffusion Coefficients	45
2.5.3	Factors which Influence the Diffusivity	45
2.5.4	Factors which Influence Partition	46
2.5.5	Kinetics of Solute Release from Membrane Devices	47
2.5.5.1	Agent release from a constant-activity source	47
2.5.5.2	Agent release from a non-constant-activity source	49
2.5.6	Design Considerations for Membrane-Controlled Devices	50
2.5.6.1	Membrane variables	50
2.5.6.2	Reservoir variables	50
2.5.6.3	Issues related to the recipient environment	52
2.5.6.4	The time lag and the burst effect	52

2.6	SOME APPLICATIONS OF CONTROLLED-RELEASE TECHNOLOGY	53
2.6.1	Monolithic Devices	53
2.6.1.1	Administration of pharmaceutical agents	53
2.6.1.2	Application of pest-control chemicals	55
2.6.1.2.1	Controlled release of pesticides from plasticized polyvinyl chloride matrices	55
2.6.1.2.2	Controlled release of pesticides from non-plasticized plastic matrices	55
2.6.1.2.3	Controlled release of trace nutrients from non-plasticized plastic matrices	56
2.6.1.2.4	Antifouling elastomers	57
2.6.1.2.5	Controlled release of molluscicides from elastomeric matrices	57
2.6.1.2.6	Elastomer-based schistolarvicides	58
2.6.1.2.7	Controlled release of herbicides from elastomeric materials	58
2.6.1.2.8	Control of acid mine drainage formation by inhibition of Thiobacillus ferrooxidans	59
2.6.2	Membrane-Controlled Devices	61
2.6.2.1	Silicone-rubber membranes	61
2.6.2.2	Ethylene vinyl acetate copolymer membranes	62
2.6.2.3	Polyurethane membranes	63
2.6.2.4	Other dense polymer membranes	63

CHAPTER 3: MATERIALS AND METHODS

3.1	INTRODUCTION	64
3.2	APPARATUS	64
3.3	MATERIALS	65
3.4	EXPERIMENTAL TECHNIQUES	66
3.4.1	Preparation of Rubber Masterbatch Formulations	66
3.4.2	Preparation of Rubber-SLS Formulations	67

3.4.3	Compression Moulding of Rubber-SLS Formulations to Effect Curing (Vulcanization)	67
3.4.4	Laboratory Determination of the Release Rates of SLS from Monolithic Rubber Pellets	69
3.4.5	Analysis of Eluates to Determine SLS Concentrations	73
3.4.6	Preparation of Controlled-Release Membranes	73
3.4.7	Determination of the Flux of SLS through Rubber Membranes	74
3.4.8	SLS Solutions Used in the Reservoir Compartment	78
3.4.9	Analysis of Solutions which were Collected from the Receiving Compartments	78
3.4.10	Determination of the Solubility Limits of SLS in Rubbers	79
3.4.10.1	Thermal analysis	79
3.4.10.2	Nuclear magnetic resonance (NMR) spectroscopy	79
3.4.11	Investigation of the Effect of SLS Loading on the Curing Kinetics of Rubber-SLS Formulations	79
3.4.11.1	Thermomechanical analysis (TMA)	79
3.4.11.2	Differential scanning calorimetry (DSC)	80
3.4.12	Light Microscopy	80
3.4.13	Scanning Electron Microscopy (SEM)	80

CHAPTER 4: RESULTS AND DISCUSSION

4.1	INTRODUCTION	82
4.2	THE SOLUBILITY LIMITS OF SLS IN NATURAL RUBBER (NR) AND SYNTHETIC POLYISOPRENE (IR)	82
4.2.1	^{13}C NMR Analysis of Rubber-SLS Formulations	82
4.2.2	Differential Scanning Calorimetry (DSC) Analysis of Rubber-SLS Formulations	83

4.3	THE EFFECT OF THE SLS LOADING ON THE VULCANIZATION (CURING) OF CONTROLLED-RELEASE ELASTOMERIC FORMULATIONS	89
4.3.1	Determination of the Cure Rates of Rubber Masterbatch Formulations	89
4.3.2	Thermomechanical Analysis (TMA) of Rubber-SLS Formulations	89
4.3.3	Analysis of Rubber-SLS Formulations by Differential Scanning Calorimetry (DSC)	90
4.4	THE KINETICS OF THE RELEASE OF SLS FROM MONOLITHIC ELASTOMERIC PELLETS	98
4.5	FACTORS WHICH INFLUENCED THE RATE OF RELEASE OF SLS FROM MONOLITHIC ELASTOMERIC PELLETS	105
4.5.1	The Effect of the Initial SLS Loading	105
4.5.2	The Effect of the Addition of Release Promoters	111
4.5.3	The Effect of the pH of the Eluent	115
4.5.4	The Effect of the Base Polymer	118
4.5.5	The Effect of the Surface Area : Volume Ratio of Controlled-Release Pellets	121
4.6	THE EFFECTIVE DIFFUSION COEFFICIENTS OF SLS IN NATURAL AND SYNTHETIC RUBBERS	125
4.6.1	Numerical Method Used for the Calculation of Diffusion Coefficients	125
4.6.2	Procedure Followed for Calculating the Values of D	127
4.6.3	The Power Series	130
4.6.4	Agreement Between Experimental and Theoretically- Predicted Data	131
4.6.5	Concentration-Dependent Diffusion Coefficients	136

4.7	NUMERICAL PREDICTION OF THE RATE OF RELEASE OF SLS FROM CYLINDRICAL RUBBER-SLS COMPOSITE PELLETS	139
4.7.1	General Background	139
4.7.1.1	Mathematical description of physical phenomena	139
4.7.1.2	Discretization of differential equations	141
4.7.2	Discretization of the Fundamental Diffusion Equation for the Axisymmetric Problem	142
4.7.3	Iterative Solution Procedure	154
4.7.4	The FORTRAN Code PELLET	154
4.7.5	The Relationship between the Diffusion Coefficient (D) and the Concentration of SLS in the Pellet (C)	157
4.7.6	Comparison of Experimental Data with Theoretical Data Predicted by the Discretization Model	160
4.8	PILOT-SCALE STUDIES	171
4.9	THE KINETICS AND THE MECHANISMS OF RELEASE OF SLS THROUGH ELASTOMERIC MEMBRANES	173
4.9.1	Vulcanized NR and IR Membranes which Contained no SLS	173
4.9.2	NR and IR Membranes which Contained 10% SLS	177
4.9.3	NR and IR Membranes which Contained 35% SLS	181
4.10	FACTORS WHICH INFLUENCED THE RATE OF RELEASE OF SLS THROUGH ELASTOMERIC MEMBRANES	189
4.10.1	The Effect of the SLS Loading in the Membrane on Mass Flux	189
4.10.2	The Effect of the Type of Rubber Used on the Mass Flux of SLS	189
4.10.3	The Effect of Membrane Thickness on the Mass Flux of SLS	190
4.10.4	Analysis of the Relationships between Mass Flux, Transference and Membrane Thickness	199

CHAPTER 5: CONCLUSIONS AND SUGGESTIONS FOR FUTURE WORK

5.1	CONCLUSIONS	204
5.2	SUGGESTIONS FOR FUTURE WORK	207
	REFERENCES	208
	APPENDIX 1A: COMPOSITIONS OF RUBBER-SLS FORMULATIONS SERIES B TO G	233
	APPENDIX 1B: COMPOSITIONS AND DIMENSIONS OF RUBBER-SLS PELLETS USED IN EXPERIMENTS 2 TO 17	237
	APPENDIX 2A: ^{13}C NMR SPECTRA	248
	APPENDIX 3A: THE CHEMISTRY OF ACCELERATED SULPHUR VULCANIZATION OF RUBBERS	251
	APPENDIX 3B: MONSANTO RHEOGRAPHS	255
	APPENDIX 3C: LINEAR EXPANSION COEFFICIENTS OF RUBBER-SLS FORMULATIONS	258
	APPENDIX 3D: DSC ANALYSIS OF RUBBER-SLS FORMULATIONS	259
	APPENDIX 4A: DATA OBTAINED FROM ELUTION EXPERIMENTS	262
	APPENDIX 4B: THE PASCAL SOURCE CODE POLI	271
	APPENDIX 4C: STANDARD DEVIATIONS AND CORRELATION COEFFICIENTS	277
	APPENDIX 5A: PLOTS OF THE FRACTION OF SLS RELEASED AS A FUNCTION OF TIME	279
	APPENDIX 6A: THE PASCAL SOURCE CODE DIFFCALC	281
	APPENDIX 6B: LOTUS 1-2-3 WORKSHEET FILE ALSLS.WK1	284
	APPENDIX 6C: LOTUS 1-2-3 WORKSHEET FILE DIFFSLS.WK1	291
	APPENDIX 7A: THE FORTRAN CODE PELLET	295
	APPENDIX 7B: PLOT PROGRAM UNIPLLOT	309
	APPENDIX 7C: FORTRAN DATA FILES	321
	APPENDIX 7D: CONCENTRATION DISTRIBUTION OF SLS IN AN SBR PELLET AT DIFFERENT INTERVALS DURING THE ELUTION PERIOD	324
	APPENDIX 8A: THE BEHAVIOUR OF SURFACTANTS IN SOLUTION	333

LIST OF TABLES

CHAPTER 2: HISTORICAL BACKGROUND

TABLES

2.1	Categorization of polymeric systems for controlled release	8
2.2	Typical compounding ingredients	18
2.3	Equations describing the release kinetics of a solute dissolved in a monolithic device	23
2.4	Equations describing the release kinetics of a solute dispersed in a monolithic device	30
2.5	Variables which influence the kinetics of solute release from monolithic devices	35
2.6	Drugs which have been released from monolithic matrices	54
2.7	Pesticides incorporated in plasticized PVC formulations	56
2.8	Commercially available non-plasticized pesticide emitters	56
2.9	Elastomer-soluble organotin agents for use in antifouling-rubber formulations	57
2.10	Commercial controlled-release molluscicides of the monolithic elastomeric type	58
2.11	Herbicides incorporated in elastomeric matrices	59
2.12	Sodium lauryl sulphate (SLS) - Rubber formulation used in field tests	61

CHAPTER 3: MATERIALS AND METHODS

3.1	Instruments used for the preparation and testing of controlled release formulations	65
3.2	Compositions of rubber masterbatch formulations	68
3.3	Compositions of natural rubber - SLS formulations: Series A	68
3.4	Dimensions of Mould I (10 mm - thick plate)	70
3.5	Dimensions of Mould II (5 mm - thick plate)	70
3.6	Compositions and dimensions of rubber-SLS pellets used in Experiment I	75
3.7	Compositions of controlled-release rubber-SLS formulations which were used for the production of membranes	75

3.8	The compositions and dimensions of membranes evaluated in diffusion experiments	76
3.9	Compositions of the rubber-SLS formulations which were analyzed by DSC	81

CHAPTER 4 : RESULTS AND DISCUSSION

4.1	The effective diffusion coefficients of SLS in cylindrical rubber-SLS composite pellets	137
4.2	Steady-state fluxes of SLS through NR and IR membranes	177
4.3	Steady-state fluxes of SLS through NR and IR membranes which contained 10% SLS	178
4.4	Steady-state fluxes of SLS through membranes which contained 35% SLS	182
4.5	Transference (T) of SLS through NR and IR membranes	199

APPENDIX 1A: COMPOSITIONS OF RUBBER-SLS FORMULATIONS: SERIES B TO G

A1	Compositions of styrene-butadiene rubber-SLS formulations: Series B	233
A2	Compositions of controlled-release formulations consisting of SLS and a 50 : 50 blend of natural-rubber and styrene-butadiene rubber: Series C	233
A3	Compositions of controlled-release formulations consisting of natural rubber, SLS and CaCO_3 : Series D	234
A4	Compositions of controlled-release formulations containing natural rubber, SLS and CaCO_3 : Series E	235
A5	Compositions of synthetic polyisoprene-SLS formulations: Series F	235
A6	Compositions of controlled-release formulations consisting of natural rubber, SLS and $(\text{NH}_4)_2\text{SO}_4$: Series G	236