

**POLYURETHANE / CLAY BASED
NANOCOMPOSITE FILMS AND NANOFIBRES
FOR TOPICAL DRUG DELIVERY APPLICATION**

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**DEPARTMENT OF TEXTILE TECHNOLOGY
INDIAN INSTITUTE OF TECHNOLOGY DELHI
FEBRUARY 2015**

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FOR TOPICAL DRUG DELIVERY APPLICATION**

by

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DEPARTMENT OF TEXTILE TECHNOLOGY

Submitted

In fulfillment of the requirements of the degree of
DOCTOR OF PHILOSOPHY

to the



INDIAN INSTITUTE OF TECHNOLOGY DELHI
FEBRUARY 2015

Dedicated
Only & Only
To
My Father

CERTIFICATE

This is to certify that the thesis entitled, “Polyurethane / Clay based Nanocomposite Films and Nanofibres for Topical Drug Delivery Application” submitted by Mrs. Kasturi Saha to the Indian Institute of Technology Delhi, for the fulfillment of award of the degree, Doctor of Philosophy, is a record of bonafied research work carried out by her under my supervision and guidance. The thesis has been prepared in conformity with the rules and regulations of Indian Institute of Technology Delhi, New Delhi.

The thesis, in my opinion, is worthy of consideration for award of the degree of Doctor of Philosophy in accordance with the regulations of the Institute. To the best of my knowledge, the results embodied in the thesis have not been submitted to any other University or Institute for the award of any other Degree or Diploma.

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Abstract

At present 95% of all new therapeutics have poor pharmacokinetics and biopharmaceutical properties. Therefore, there is a need to develop suitable drug delivery systems that distribute the therapeutically active drug molecule only to the site of action, without affecting healthy organs and tissues. Topical drug delivery is defined as the application of a drug containing formulation to the skin to treat various cutaneous disorders directly or any other wound and wound related infection. Advantages of topical drug delivery through hybrid nanoparticles include achievement of high efficacy with very little dose to a specific site, improving physiological and pharmacological response, patient compliance and the option of termination of the medication if and when required.

The thesis investigates the application of nanocomposite film and nanofibres based on thermoplastic polyurethane containing drug loaded clays for topical drug delivery applications. The emphasis is on comparing release kinetics by taking into consideration various aspects like, drug concentration, role of clay (acting as a drug carrier), effect of morphology (nanofibre vs. film) and nature of drug. One of the important aim of this research work is to study drug release mechanisms i.e. nature of release (burst, delayed, sustained or controlled) in the presence of clay where drug loaded clay tactoids are immobilized in a polymeric nanocomposite in the form of nanofibres and films, as compared to the case when a drug is directly loaded in polymer solution prior to film and nanofibre preparation. Although there is a lot of literature available on drug loaded films and nanofibres, there appear to be no reports

where drug loaded onto nanoclay has been incorporated into polymer and converted to film and nanofibres for topical drug delivery.

In the present study, montmorillonite nanoclay has been used as a drug carrier. The emphasis is on studying the effect of loading of two kinds of drug i.e. chlorhexidine acetate (antiseptic) and sulfanilamide (antibiotic) into clay mineral interlayer spacing via ion exchange reaction. These drug loaded clays exhibit strong activity against both gram - positive and gram - negative bacteria. The drug release profile of intercalated species into PBS media indicates sustained release activity in comparison with neat drug which initially shows burst release followed by slow release profile.

The drug loaded clays were further incorporated into the polymer matrix via solution intercalation. Nanofibrous webs via electrospinning and cast films via solution casting have been produced. The emphasis is on studying the release kinetics of these two drugs in both nanofibre and film forms and its effect on the mechanism of action in presence and absence of clay. The other important aspect of this research is to investigate the nature of drug and also the role of clay as a carrier of drug on in vitro release studies.

Neat drug loaded nanoweb illustrated a larger zone of inhibition as compared to the drug loaded clay due to higher diffusion rate of neat drug into the agar media as compared to drug immobilized onto the nanoclay. Film samples exhibited a smaller inhibition zone as compared to the nanofibrous webs due to very high surface area and high porosity of nanofibres. Additionally nanofibrous web containing chlorhexidine acetate exhibits wider zone of inhibition

compared to sulfanilamide for both neat drug as well as drug loaded clays. This is due to the higher solubility of CA drug and faster diffusion in the agar media as compared to SA drug.

The drug release profile of film as well as nanofibrous sample containing neat drug indicates first order kinetics, whereas intercalated species exhibited zero order release kinetics. Therefore, there is a change of release kinetics from first to zero order after drug has been immobilized into clay interlayer spacing. Moreover, nanofibrous morphology exhibits higher drug release concentration due to large surface area to volume ratio and high porosity of the light weight nanofibrous forms as compared to the film sample. Moreover, the drug release profile also indicates that nature of drug has a striking effect on drug release behavior. CA drug loaded nanofibrous web exhibits higher drug release rate as compared to SA drug loaded nanofibrous web.

Thus it can be concluded that, overall drug release rate depends upon the types and nature of drug, initial drug loading concentration and immobilization of drug onto the clay and also on the morphological form of the polymer (film vs. nanofibrous web) which is acting as a vehicle for drug delivery. A particular advantage of this nanofibrous delivery system is the possibility of delivering uniform, large and controlled doses of bioactive agents at the wound site via the high surface area to volume ratio and high porosity of the light weight nanofibrous system as compared to cast film. This novel work has potential for application in topical drug delivery.

Contents

	Page Number
Certificate	i
Acknowledgements	ii
Abstract	v
List of Figures	xv
List of Tables	xx
Chapter 1 Introduction and Objective of the Work	1 - 13
1.1 General	2
1.2 Motivation	9
1.3 Objective of the Work	10
1.4 Outline of the Thesis	11
Chapter 2 Literature Review	14 - 70
2.1 General	16
2.2 Drug Delivery	17
2.2.1 Therapeutic agent	18
2.2.1.1 Chlorhexidine acetate: Antiseptic drug	19
2.2.1.2 Sulfanilamide: Antibiotic drug	21
2.2.2 Classification of drug delivery systems	22
2.2.2.1 According to physical state	22

2.2.2.2	According to route of administration	22
2.2.2.3	According to mechanism of drug release	23
2.3	Polymeric drug delivery systems	25
2.3.1	Mechanism and factors influencing drug delivery	27
2.3.2	Classification of drug release mechanism	28
2.3.2.1	Diffusion controlled system	28
2.3.2.2	Chemically controlled system	29
2.3.2.3	Swelling controlled system	30
2.3.2.4	Magnetically controlled system	30
2.3.3	Thermoplastic polyurethane (TPU) in drug delivery	30
2.4	Nanoclays in drug delivery	32
2.4.1	General characteristics of clay mineral	33
2.4.2	Clay minerals and human health	34
2.4.2.1	Oral application	34
2.4.2.2	Use as excipient	35
2.4.2.3	Clay minerals in spa	35
2.4.2.4	In aesthetic medicine	36
2.4.2.5	Topical application	36
2.4.3	Clay as drug delivery system	36
2.5	Topical drug delivery	38
2.5.1	Topical drug delivery via microfibrinous structures	39
2.5.1.1	Sutures	39
2.5.1.2	Wound dressing	41

2.5.2	Topical drug delivery via nanofibrous structures	44
2.5.2.1	Advantages of nanofibres	44
2.5.2.2	Electrospinning: Producing nanofibres	47
2.5.2.3	Advances in nanofibrous systems for drug delivery	50
2.5.3	Topical drug delivery via other forms	63
2.5.3.1	Film	63
2.5.3.2	Cylindrical matrix	66
2.5.3.3	Sponge	67
2.5.3.4	Hydrogel	68
2.6	Summary	69
Chapter 3	Synthesis, Characterization and in Vitro Release Study of Drug loaded Nanoclay	71 - 116
3.1	General	73
3.2	Synthesis and characterization of drug loaded nanoclay	75
3.2.1	Introduction	75
3.2.2	Materials and Method	76
3.2.2.1	Materials	76
3.2.2.2	Ball Milling of sodium montmorillonite clay	77
3.2.2.3	Synthesis of drug loaded nanoclay	81
3.2.2.4	Characterization of drug loaded nanoclay	83
3.2.2.5	Adsorption study	84
3.2.3	Results and Discussion	85

3.2.3.1	XRD analysis	85
3.2.3.2	FT-IR spectra analysis	87
3.2.3.3	Thermogravimetric analysis	91
3.2.3.4	DSC analysis	94
3.2.3.5	EDX analysis	97
3.2.3.6	Adsorption study	100
3.2.4	Summary	101
3.3	Antimicrobial assessment and in vitro release studies of drug loaded clay	102
3.3.1	Introduction	102
3.3.2	Materials and Method	103
3.3.2.1	Materials	103
3.3.2.2	Antibacterial activity assay	104
3.3.2.2.1	Colony counting method	104
3.3.2.2.2	Disc diffusion test	105
3.3.2.3	Drug release study	106
3.3.2.3.1	Preparation of the PBS solution	106
3.3.2.3.2	In vitro release study	106
3.3.3	Results and Discussion	107
3.3.3.1	Antibacterial activity assay	107
3.3.3.1.1	Colony counting method	107
3.3.3.1.2	Disc diffusion test	109
3.3.3.2	Drug release study	112
3.3.4	Summary	116

Chapter 4	Optimization of Electrospinning process for Neat TPU, TPU - Drug and TPU - Drug loaded Clay based Nanocomposites	117 - 148
4.1	General	118
4.2.	Materials and Method	121
4.2.1	Materials	121
4.2.2	Preparation of neat TPU dope	122
4.2.3	Preparation of dope containing drug and drug loaded clay	123
4.2.4	Characterizations techniques	124
4.2.5	Preparation of electrospun nonwoven nanofibrous mat	125
4.2.6	Morphological analysis of nanofibre	125
4.3	Results and Discussion	125
4.3.1	Characterization of polymer dope	125
4.3.1.1	Particle size analysis	125
4.3.1.2	TEM analysis	127
4.3.1.3	Measurement of viscosity	128
4.3.1.4	Measurement of conductivity	129
4.3.1.5	Measurement of surface tension	131
4.3.2	Morphological analysis of neat TPU nanofibre	131
4.3.3	Morphological analysis of TPU nanofibre containing drug and drug loaded clay	143
4.4	Summary	147

Chapter 5	Preparation and Characterization of TPU - Clay based Nanocomposite	
	Nanofibrous Webs and Films	149 - 174
5.1	General	150
5.2	Materials and Method	152
5.2.1	Materials	152
5.2.2	Preparation of polymer dope	152
5.2.3	Preparation of nanofibrous web via electrospinning	153
5.2.4	Preparation of cast film via solution casting	154
5.2.5	Characterization techniques for nanofibrous web and cast film	155
5.3	Results and Discussion	157
5.3.1	Characterization of electrospun nanofibrous web	157
5.3.1.1	XRD analysis	157
5.3.1.2	Contact angle measurement	158
5.3.1.3	MVTR and porosity determination	159
5.3.1.4	Antibacterial activity: Disc diffusion test	161
5.3.2	Characterization of nanocomposite film	167
5.3.2.1	Morphology of films: SEM analysis	167
5.3.2.2	XRD analysis	168
5.3.2.3	Contact angle analysis	169
5.3.2.4	Antibacterial activity: Disc diffusion test	170
5.4	Summary	173

Chapter 6	In Vitro Drug Release Study of TPU - Drug loaded Clay based Nanocomposite Films and Nanofibrous Webs	175 - 194
6.1	General	176
6.2	Materials and Method	178
6.2.1	Materials	178
6.2.2	Methods: Drug release study	179
6.3	Results and Discussion	180
6.4	Summary	193
Chapter 7	Conclusion and Future Scope of Work	195 - 199
7.1	Conclusion	196
7.2	Future scope of work	199
References		200
Appendix		213
List of Publications		214
Author's Biography		217