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

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by

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Submitted
In fulfillment of the requirements of the degree of
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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.

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