Biopolymer based nanofiber topical patches for the management of diabetic fungal wounds

Thesis submitted in partial fulfilment

for the Award of Degree

DOCTOR OF PHILOSOPHY

By

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It is certified that the work contained in the thesis titled "**BIOPOLYMER BASED NANOFIBER TOPICAL PATCHES FOR THE MANAGEMENT OF DIABETIC FUNGAL WOUNDS**" by ***MANJIT*** has been carried out under my supervision and that this work has been not submitted elsewhere for a degree.

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Dedicated to the Almighty & My Family

Acknowledgement

First of all, I would like to pay the homage to the founder of Banaras Hindu University, Pandit Madan Mohan Malviya Ji, who made this glorious temple to realize spiritual, technical and scientific knowledge about this vast existing universe.

I would like to take this opportunity to express my invaluable gratitude to my supervisor Prof. Brahmeshwar Mishra for his immense support, guidance, expertise and encouragement throughout my tenure in the program. I am extremely grateful to him as he helped me in systemic completion of my research work. I feel very much honoured and it has been really a great privilege for me to work under his mentorship.

I am indeed obliged and sincerely thankful to Prof. (Mrs.) Siva Hemalatha, Head of Department of Pharmaceutical Engineering & Technology, Indian Institute of Technology (BHU) for her affection and kindly allowing me to use the facilities required to complete my research work.

I would like to express my gratitude to my RPEC committee members Dr. Ruchi Chawla and Dr. Abha Mishra for their significant contribution towards the fulfilment of doctorate program.

I would like to keep on record my profound respect & sincere thanks to my respected teachers Prof. Sanjay Singh, Prof. Sushil K. Singh, Prof. Sushant Shrivastava, Prof. Krishnamurthy Sairam, Prof. Senthil Raja, Prof. M. S. Muthu, Dr. Alakh N Sahu, Dr. Gyan Prakash Modi, Dr. Vinod Tiwari, Dr. Ashish Kumar Agrawal, Dr. Sunil Kumar Mishra, Dr. Prasanta Kumar Nayak, Dr. Shreyans Kumar Jain, Dr. Rajnish, Dr. Deepak Kumar, Dr. Dinesh Kumar, Dr. Jairam Meena, Dr. Ashok Kumar and Dr. Arun Khatri for their co-operation and valuable suggestions during my research work.

I express my gratitude to Dr. Biplob Koch Department of Zoology, Banaras Hindu University (BHU), for his guidance and kindly providing cell culture facilities.

I want to give special thanks to my collaborators; Prof. Ragini Tilak and Prof. Pradyot Prakash of Department of Microbiology, IMS (BHU) for helping me in Microbiological studies.

I pay sincere thanks to all the departmental non-teaching staff Mr. Virendra Kumar, Smt. Archana Singh, Mr. Arun Kumar, Mr. Mohd. Jameel, Mr. Akhila Nand Upadhyay, Mr. Atul

Kumar Gupta, Mr. Yashwant Singh, Mr. Anand Kumar, Mr. Surya Pratap Singh for their co-operation and help during my research work.

I gratefully acknowledge the Ministry of Education, New Delhi for providing me the necessary funding and fellowship to pursue research work.

I am thankful to my lab fellows especially to Kanchan Bharti, Manish Kumar, Abhishek Jha, for their help and support.

Words fail me to express my appreciation to Krishan Kumar, Himanshu Rai, Gaurav Singh, Ankit Namdev, Dr. Vikas, Ankit Malik, Bharat Sahu, Debdatta Mohpatra, Gori Shankar, Bhanuranjan Das, Anurag TK Baidya, Madhu Kiran, Sunil Kumar, Sanjay Dhakad, Dr.Virendra Kumar (Department of Zoology, BHU), Punit Tiwari (Department of Microbiology IMS BHU), Pawan Kumar Ojha (School of Material science, IIT BHU) for their support, generous care and the homely feeling in the campus. Their association has made my stay at IIT (BHU) a pleasurable and memorable experience. My bonding with them will be etched permanently in my memory.

It's my fortune to gratefully acknowledge the support of some special individuals my beloved friends Harsh Saini, Manoj Kumar, Sagar Suberwal, Priti Mondal and Nishi Agrawal they were always beside me during the happy and hard moments to push me and motivate me.

Finally, I am grateful to my beautiful family: My mother, Mrs. Santosh Saini, and father, Mr. Om Parkash Saini, brothers, Mr. Vikash Saini, Mr. Sandeep Saini, Mr. Sunny Saini and my sister-in-law Mrs. Jyoti Saini, Mrs. Alka Saini and Mrs. Mamta Saini have always been my source of inspiration and a pillar of strength in every aspect of my life. I want to dedicate my work to my parents as a token of love and affection towards them. All my work would have not been possible without the blessings and support of my parents. I am thankful to God for blessing me with such wonderful parents and family. As to my sweet little angles Mahi Saini, Manvi Saini and Drishti Saini, my love and longing for them are beyond words. They are the softest point of my heart. I am sorry for not being able to accompany or witness every step of them growing up till now. Last and definitely not least, I express my sincere thanks to my guardian angels who has been part of everything. Thank you, for everything you have done for me.

Finally, I am grateful to have had the privilege of attending the prestigious Indian Institute of Technology (Banaras Hindu University) and Department of Pharmaceutical Engineering &

Technology, IIT (BHU). This experience has afforded me the opportunity to work with some of the best and brightest, and the resources for me to achieve great success. Thank you for this opportunity.

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Abbreviations & Symbols

%	Percentage
℃	Degree Celsius
Aq.	Aqueous
AgNP	Silver nanoparticles
AFM	Atomic force microscopy
ANOVA	Analysis of variance
ATR	Attenuated total reflectance
AUC	Area under the curve
C6	Coumarin-6
CH	Chitosan
DMEM	Dulbecco's modified eagle's medium
DSC	Differential scanning calorimetry
EE	Entrapment efficiency
FBS	Fetal bovine serum
FDA	United states food and drug administration
FTIR	Fourier transform infrared spectroscopy
GL-PCL	Gelatin coated PCL nanofiber
GL-PCL-LTZ	Luliconazole loaded GL-PCL nanofiber
GL-PCL-NAR	Naringenin loaded GL-PCL nanofiber
GL-PCL-LTZ./NAR	Luliconazole and naringenin loaded GL-PCL nanofiber
GL	Gelatin
h/hr	Hour(s)
HaCaT	Human epidermal keratinocytes
HPLC	High-performance liquid chromatography
i.p.	Intraperitoneal
kDa	Kilo Dalton
LZ/LTZ	Luliconazole
LOD	Limit of detection
LOQ	Limit of Quantification

LZNP	PLGA Luliconazole nanoparticle
MDR	Multi drug resistance
kV	Kilo volt
NIR	Near infrared
NF	Nanofiber
mg	Milligram
min	Minute
ml	Millilitre
MTT	3-(4,5-dimethylthiazolyl-2-yl)-2, 5 diphenyl-tetrazolium-bromide
NaOH	Sodium hydroxide
nm	Nanometre
NP/NPs	Nanoparticles
PBS	Phosphate buffer saline
PCL	Poly (Ɛ-caprolactone)
PVA	Poly vinyl alcohol
PLGA	poly(lactide-co-glycolide)
PVA/CH NF	PVA/CH nanofiber
PVA/CH-AgNP NF	AgNP loaded PVA/CH nanofiber
PVA/CH-LZNP NF	LZNP loaded PVA/CH nanofiber
PVA/CH-AgNP-LZNP NF	LZNP and AgNP loaded PVA/CH nanofiber
rpm	Revolutions per minute
S.D.	Standard deviations
sec	Seconds
SPM	Scanning probe microscopy
TEM	Transmission electron microscopy
TPGS	D-α-tocopheryl polyethylene glycol 1000 succinate
μg	Microgram
μl	Microliter
μM	Micromole
XRD	X-ray diffraction spectroscopy

Preface

Diabetic wounds pose a significant challenge in healthcare due to their slow healing process and susceptibility to complications. Individuals afflicted with diabetes often encounter difficulties in wound management, leading to prolonged suffering and increased healthcare costs. The conventional treatment methods, such as the application of marketed creams, exhibit several limitations that hinder their efficacy in diabetic wound healing. These limitations include the need for repetitive application over the wound area, short drug release time, and vulnerability to removal during daily activities. The inadequacies of conventional treatments underscore the pressing need for innovative solutions to address the complexities associated with diabetic wound management.

In recent years, nanotechnology has emerged as a promising avenue for revolutionizing wound care. Nanofiber-based dressings have garnered significant attention due to their unique properties, including high surface area-to-volume ratio, tunable porosity, and ability to encapsulate therapeutic agents. These characteristics make nanofibers an ideal platform for controlled drug delivery and enhanced wound healing. Leveraging the advantages of nanofibers, researchers have explored novel formulations to overcome the limitations of conventional treatments and provide effective solutions for diabetic wound management.

In this dissertation, we present a comprehensive investigation into the preparation of nanofiber-based dressings for diabetic wound healing. Our research focuses on the development of two distinct nanofiber formulations, each tailored to address challenges associated with diabetic wounds. The first approach involves the fabrication of Polyvinyl alcohol (PVA) and chitosan-based composite nanofibers loaded with Poly(lactic-co-glycolic acid) luliconazole nanoparticles (NPs) and silver nanoparticles. This formulation harnesses the combine effects of luliconazole, a potent antifungal agent, and silver nanoparticles, renowned for their antimicrobial and antioxidant properties, to combat infections commonly observed in diabetic wounds.

In the second approach, we explore the utilization of gelatin-coated Polycaprolactone (PCL) nanofibers loaded with luliconazole and naringenin. Naringenin, a flavonoid with antioxidant properties, is incorporated to mitigate oxidative stress, a critical factor impeding wound healing in diabetic individuals. By combining luliconazole with naringenin within a gelatin-coated PCL nanofiber matrix, we aim to enhance the therapeutic efficacy of the dressing while promoting the regeneration of damaged tissues.

Throughout this dissertation, we delve into the intricate details of nanofiber preparation, characterization, and evaluation of their performance in diabetic wound healing. Our research endeavours to contribute to the growing body of knowledge in the field of nanotechnology-enabled wound care, with a focus on addressing the unmet needs of diabetic patients. By elucidating the potential of nanofiber-based dressings loaded with therapeutic agents, we aspire to pave the way for the development of advanced wound management strategies that offer improved outcomes and enhanced quality of life for individuals grappling with diabetic wounds.