#### FORMULATION OF MULTIPAL LATE SYSTEM OF A BRONCHODILATOR AND ANTI INFLAMMATORY COMBINATION FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

A

dissertation

Submitted for the partial fulfillment of the requirement for

The Award of Degree of

#### MASTER OF PHARMACY

(PHARMACEUTICS)



2021-2022

Supervised by

Dr. ALPANA RAM M. Pharm., Ph.D. ASSOCIATE PROFESSOR (PHARMACEUTICS) Submitted by

VAGESH VERMA M. Pharm IV Semester (PHARMACEUTICS) Enroll No: GGV/20/06345 Roll No: 20704009

DEPARTMENT OF PHARMACY, GURU GHASIDAS

VISHWAVIDYALAYA, BILASPUR (C.G.)

#### FORMULATION OF MULTIPARTICULATE SYSTEM OF A BRONCHODILATOR AND ANTI INFLAMMATORY COMBINATION FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

А

dissertation

Submitted for the partial fulfillment of the requirement for

The Award of Degree of

#### MASTER OF PHARMACY

(PHARMACEUTICS)



2021-2022

Supervised by

**Dr. ALPANA RAM** 

M. Pharm., Ph.D. ASSOCIATE PROFESSOR

(PHARMACEUTICS)

#### Submitted by

VAGESH VERMA

M. Pharm IV Semester (PHARMACEUTICS) Enroll No: GGV/20/06345 Roll No: 20704009

#### **DEPARTMENT OF PHARMACY, GURU GHASIDAS**

VISHWAVIDYALAYA, BILASPUR (C.G.)



# गुरू धासीदास विश्वविद्यालय, बिलासपुर GURU GHASIDAS VISHWAVIDYALAYA, BILASPUR

(A Central University established by the Central University Act 2009 No. 25 of 2009)

#### DEPARTMENT OF PHARMACY

#### FORWARDING CERTIFICATE

This is to certify that Mr. Vagesh Verma S/O Shri. Santosh Kumar Verma, M. Pharm IV semester Pharmaceutics) of this institute has submitted his dissertation work entitled "FORMULATION OF IULTIPARTICULATE SYSTEM OF A BRONCHODILATOR AND ANTI INFLAMMATORY COMBINATION FOR COPD" for the partial fulfillment of the requirement for the award of degree of Master of Pharmacy (Pharmaceutics) with his truly and honestly observed inference during his research vork under the supervision of Dr. Alpana Ram. His work is original, satisfactory and is not submitted nywhere else for the award of any degree.

I hereby forward his dissertation for the award of **M. Pharm. degree in Pharmaceutics** during the cademic session 2021-2022.

**HEAD OF DEPARTMENT** 

Dr. Bharti Ahirwar

(Associate Professor) Head Department of Pharmaoy Guru Ghasidas Vishwavidyalaya

Bilaspur 45-99



(A Central University established by the Central University Act 2009 No. 25 of 2009)

1111

### **DEPARTMENT OF PHARMACY**

CERTIFICATE

This is to certify Mr. Vagesh Verma S/O Shri. Santosh Kumar Verma, M. Pharm IV Semester Pharmaceutics) of Department of Pharmacy has submitted his dissertation work entitled FORMULATION OF MULTIPARTICULATE SYSTEM OF A BRONCHODILATOR AND ANTI NFLAMMATORY COMBINATION FOR COPD" for the partial fulfillment of the requirement for the Award of Degree of Master of Pharmacy (Pharmaceutics) with his truly & honestly observed inference luring his research work. He has completed his project work under my guidance. His work is original, attisfactory and is not submitted anywhere else for any degree.

hereby forward his dissertation for the award of Master of Pharmacy (Pharmaceutics) during the cademic session 2021-2022.

Dr. Alpana Ram

Associate Professor (Pharmaceutics) (SUPERVISOR)



# गुरू घासीदास विश्वविद्यालय, बिलासपुर GURU GHASIDAS VISHWAVIDYALAYA, BILASPUR

(A Central University established by the Central University Act 2009 No. 25 of 2009)

#### **DEPARTMENT OF PHARMACY**



hereby declare that my M. Pharm dissertation work entitled "FORMULATION OF IULTIPARTICULATE SYSTEM OF A BRONCHODILATOR AND ANTI INFLAMMATORY COMBINATION FOR COPD" is my own work conducted under the supervision of Dr. Alpana Ram. The same is submitted to the Department of Pharmacy, Guru Ghasidas Vishwavidyalaya, Bilaspur (C.G.) or the partial fulfillment of the requirement for the Award of Degree of Master of Pharmacy in Pharmaceutics during the academic session 2021-2022.

I further declare that to the best of my knowledge the thesis does not contain any part of vork, which has been submitted for the award of any degree either in the University or in any other Jniversity/ Deemed University without proper citation.

Date:

Place: Bilaspur (C.G.)

VERMA

M. Pharm IV Semester (Pharmaceutics) GGV/20/06345



11110

#### AKNOWLEDGEMENT

irst and foremost, praises and thanks to the God, the Almighty, for his showers of blessings throughout my esearch work to complete the research successfully.

would like to express my deep and sincere gratitude to my research supervisor, Dr. Alpana Ram, M. harm., Ph.D., Associate Professor, Department of Pharmacy, GGV Bilaspur C.G, for giving me the pportunity to do research and providing invaluable guidance throughout this research. Her dynamism, ision, sincerity and motivation have deeply inspired me. She has taught me the methodology to carry out he research and to present the research works as clearly as possible. It was a great privilege and honor to vork and study under her guidance. I am extremely grateful for what she has offered me. I would also like to hank her for her friendship, empathy, and great sense of humor. I am extending my heartfelt thanks for her cceptance and patience during the discussion i had with her on research work and thesis preparation.

take pride in acknowledging the insightful guidance of **Dr. Bharti Ahirwar Head of Department of harmacy GGV Bilaspur C.G,** for sparing his valuable time whenever I approached him and showing me he way ahead despite of his busy schedule.

would like to offer my special thanks to **Dr. Pooja Mongia Raj Assistant Professor, Delhi harmaceutical Sciences and Research University** Without his enthusiasm, encouragement, support and ontinuous optimism this thesis would hardly have been completed.

am immensely thankful to my teachers Dr. V D Rangari, Dr. K. Kesavan, Dr. Akhilesh Jain, Dr. avishankar Pandey, Dr. S.K. Lanjhiyana, Dr. Shivani Rai Paliwal, Dr. Manoj Kumar, Dr. Sunil ain, Dr. Kedar Meena, Dr. S.H. Bodakhe, Dr. Vivekanand Mandal and Non-Teaching staff especially Ir. Virendra Kumar Verma, Mr. Murlidhar Gupta, Mr. Nityanand Singh, Mr. Dhirendra Sahu, Irs. Veena Vaishnav, Mr. Miri, Mr. Vishnu for organizing required resources and for the assistance.

am extremely grateful to my parents for their love, prayers, caring and sacrifices for educating and reparing me for my future. I express my thanks to my Mother, Father, Brother and Sister for their upport and valuable prayers.

would like to say thanks to my seniors and batchmates; Rashmi Manikpuri, Rashmi Madhariya, irdesh Kumar, Shivani Behera, Sanand Kumar Pradhan. My Special thanks goes to my friends who elped me to complete this thesis successfully. I am grateful to for her contribution in preparing the Thesis.

inally, my thanks go to all the people who have supported me to complete the research work directly r indirectly.

VAGESH VERMA M. PHARMA IV SEM. (PHARMACEUTICS)

# **CHAPTERS**

CHAPTER NO.	CHAPTERS	Page No.
CHAPTER 1	INTRODUCTION	1-19
CHAPTER 2	DRUG AND POLYMER PROFILE	20-32
CHAPTER 3	LITERATURE SURVEY, PLAN OF WORK & RESEARCH ENVISAGED	33-44
CHAPTER 4	PREFORMULATION	45-49
CHAPTER 5	MATERIALS AND METHODS	50-60
CHAPTER 6	STABILITY STUDY	61-66
CHAPTER 7	RESULTS AND DISCUSSION	67-116
CHAPTER 8	SUMMARY AND CONCLUSION	117-120
CHAPTER 9	BIBLIOGRAPHY	121-131

# INDEX

S.NO.	TITLE	PAGE NO.
	CHAPTER – 1 [INTRODUCTION]	1-19
1.1	COPD	1
1.2	Phenotypes of COPD	2
1.3	Causes of COPD	3
1.4	Symptoms of COPD	4
1.5	Pathophysiology of COPD	5
1.6	Diagnosis of COPD	7
1.7	Treatment of COPD	9
1.8	Management of COPD by Ayurveda	11
1.9	Multiparticulate system of drug delivery	12
1.10	Biopotentiation of drugs using herbal options	14
1.11	Technical methods for preparation of beads	15
1.12	Multiparticulate system for oral drug delivery	16
1.13	Multiparticulate approach for high drug loading	16
1.14	QbD in formulation development	17
	CHAPTER – 2 [DRUG & POLYMER PROFILE]	20-32
2.1	Salbutamol	21
2.2	Curcumin	23
2.3	Piperine	25
2.4	Sodium alginate	27
2.5	Tamarind gum	29
2.6	Bentonite	32

¢

	CHAPTER – 3	33-44
3.1	Literature survey	34-41
3.2	Plan of work	42
3.3	Research envisaged	43
	CHAPTER – 4 [PREFORMULATION]	45-49
4.1	Introduction	46
4.2	Physical appearance	46
4.3	Determination of melting point	46
4.4	Determination of partition coefficient	47
4.5	Solubility studies	47
4.6	Percent drug purity	48
4.7	Preparation of standard curve of Salbutamol sulphate	48
4.8	Preparation of standard curve of Curcumin	48
4.9	FTIR studies	48
4.10	XRD studies	49
	CHAPTER – 5 [MATERIALS & METHODS]	50-60
5.1	MATERIALS	51
5.2	METHODS	51
5.2.1	Preparation method of beads	51
5.2.2	Formulation variable and optimization technique for beads preparation	52
5.3	CHARACTERIZATION	57
5.3.1	Particle size analysis by Compound microscope	57
5.3.2	Evaluation of swelling behaviour	57

5.3.3	Determination of Percentage Yield	57
5.3.4	Determination of Drug Entrapment Efficiency	57
5.3.5	Densities	58
5.3.6	Flow properties	58
5.3.7	DSC	58
5.3.8	SEM	58
5.3.9	In – Vitro drug release	58
5.3.10	Mathematical modeling	59
	CHAPTER – 6 [STABILITY STUDIES]	61-66
6.1	Introduction	62
6.2	Accelerated stability testing	62
6.3	Objective and purpose	63
6.4	Effect of storage on structural integrity of Salbutamol Sulphate beads	63
6.5	Percent residual drug content	64
6.6	Determination of Shelf life after 3 month	66
	CHAPTER – 7 [RESULTS & DISCUSSIONS]	67-116
7.1	PREFORMULATION STUDIES	68
7.1.1	Properties of Drugs	68
7.1.2	UV – Spectrophotometry	69-76
7.1.3	Fourier Infrared radiation measurement (FTIR)	77-84
7.1.4	X-Ray diffractometry (XRD)	85-88
7.1.5	Diffrential Scanning Calorimetry (DSC)	89-90
7.2	CHARACTERIZATION OF DEVELOPED SYSTEM	91-98
7.2.1	Scanning Electron Microscopy (SEM)	91

7.2.2	Micromeritic studies	93
7.2.3	Percentage Yield determination	96
7.2.4	Percent Entrapment Efficiency determination	97
7.2.5	Swelling Index determination	98
7.3	FORMULATION OPTIMIZATION (by Design Expert version 13)	99-106
7.3.1	Entrapment efficiency	100
7.3.2	Percentage yield	103
7.3.3	Particle size	105
7.4	IN-VITRO DRUG RELEASE STUDIES	107-115
7.4.1	In vitro drug release of Curcumin beads formulation	107
7.4.2	In vitro drug release of Salbutamol Sulphate marketed tablet	108
7.4.3	% Cumulative drug release of Salbutamol Sulphate various formulations (F1 to F-13)	109
7.4.4	In vitro drug release of Salbutamol Sulphate optimized beads formulation (F-4)	111
7.4.5	Comparison between formulated beads Vs Marketed Product	112
7.4.6	Mathematical modelling	113
7.5	STABILITY STUDIES	116
	CHAPTER – 8 [SUMMARY & CONCLUSION]	117-120
	CHAPTER – 9 [BIBLIOGRAPHY]	121-131